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Editorial

Cough is a Significant Public Health Concern

Prof. Dr. Azhar Masud Bhatti
Editor-in-Chief

Introduction

Cough is forceful push of air that body uses to clear irritants, mucus and germs out of airways. Cough is the single most common reason for seeking medical attention and lack of suitable antitussive makes this a major unmet clinical need. Cough is one of the most common symptom encountered in medical practice and leading cause of outpatient and emergency department visits worldwide and also represents a significant public health concern.

Cough is among the most frequent complaints among patients visiting respiratory clinics. Symptom duration classifies cough into acute (<3 weeks), subacute (3–8 weeks), and chronic (>8 weeks). This classification has crucial diagnostic implications, making thorough history-taking essential in the table below.[1] Chronic cough (CC) is prevalent in adults in developed countries (10–20%), with global rates varying from 3.9% to 30% depending on geography, demographics, and environmental exposures (e.g., air pollution, occupational hazards).[2] For patients, CC can be distressing due to symptom severity, its complications, and lifestyle modifications required to avoid triggers. The impact extends beyond physical symptoms (e.g., stress incontinence, sleep disturbance, chest pain) to psychological (e.g., disappointment, depressive states) and social domains (e.g., social anxiety/isolation, decreased quality of life).[3]

Classifications and etiologies of cough

Acute	Subacute	Chronic
• Upper respiratory tract infections	• Post-infectious	• Upper airway cough syndrome
• Lower respiratory tract infections	• Cough	• Gastroesophageal reflux
• Hay fever, allergic rhinitis	• Pertussis	• Asthma
• Inhalational exposure	• Angiotensin converting enzyme inhibitors	• Angiotensin-converting enzyme inhibitors • Chronic bronchitis • Tracheobronchomalacia • Bronchiectasis • Lung cancer

Etiology

The etiology of CC is complex and multifactorial, often involving cough variant asthma (CVA), gastroesophageal reflux cough (GERC), and upper airway cough syndrome (UACS). Some patients may progress to refractory chronic cough (RCC) or unexplained chronic cough (UCC), both significantly impair quality of life. CC also imposes a substantial societal burden through healthcare costs and productivity losses. Therefore, developing strategies to manage symptoms, mitigate underlying causes, and enhance timely and accurate diagnosis and treatment is critical for CC research.[4]

Upper and lower respiratory tract infections most commonly cause an acute cough. However, clinicians must remain alert to potentially life-threatening conditions that can also present acutely, including asthma or chronic obstructive pulmonary disorder (COPD) exacerbations, pulmonary embolism, and acute heart failure. Common causes of acute cough include viral respiratory infections (e.g., influenza), acute bronchitis, pneumonia, pertussis, and tuberculosis in endemic areas, as well as upper airway inflammatory conditions such as acute rhinosinusitis and allergic rhinitis. Additional etiologies include aspiration syndromes, inhalation of environmental irritants, trauma, pleural irritation, and, less commonly, medication effects or malignancy.[5,6,7]

Subacute cough most often develops following a respiratory infection and is typically driven by persistent irritation of cough receptors due to ongoing or resolving airway or paranasal sinus inflammation. Many causes of subacute cough overlap with both acute and chronic etiologies, reflecting a transitional phase in the disease process. Chronic cough has a broader and more complex differential diagnosis. Asthma is a significant cause in adults and the leading cause in children, along with other eosinophilic airway disorders such as cough-variant asthma and nonasthmatic eosinophilic bronchitis.

Upper airway conditions, including upper airway cough syndrome and chronic rhinosinusitis, and lower airway diseases such as chronic bronchitis, COPD, bronchiectasis, and tracheo-bronchomalacia are also common contributors. Clinicians should also consider gastroesophageal and laryngopharyngeal reflux, chronic infections (e.g., tuberculosis, nontuberculous mycobacteria, fungal or parasitic infections), prolonged post-pertussis cough, structural airway abnormalities, and medication-related causes. Less common but

important causes include obstructive sleep apnea, interstitial lung disease, malignancy, and somatic cough disorder, underscoring the need for a systematic and comprehensive evaluation.[8,9]

Types of Cough

1. Dry Cough: no mucus, tickling throat, irritating cough, viral infection, allergy and asthma.
2. Wet / Productive Cough: Produces sputum, chest congestion, bronchitis, pneumonia and respiratory infection.
3. Whooping Cough: Severe coughing fits, "whoop" sound after coughing, pertussis infection
4. Barking Cough: Harsh barking sound, croup
5. Night Cough: Worse at night, asthma, postnasal drip, Gastroesophageal Reflux Disease (GERD)
6. Chronic Cough: Lasts >8 weeks, smoking, Chronic Obstructive Pulmonary Disease (COPD), Chronic Lung Disease.

Epidemiology / Prevalence

Cough is among the most common complaints in primary care, with chronic cough affecting approximately 8% to 10% of the global population; however, reported prevalence ranges from 2% to 18% across regions.[10] Rates are higher in North America, Europe, and Oceania than in Asia and Africa, likely reflecting environmental and lifestyle differences.

In the United States (US), more than 12 million individuals are affected annually.

In Pakistan, the prevalence of chronic cough varies significantly by age and urban exposure, with regional studies showing an estimated 12% among adults aged 40 and older in urban areas like Karachi. In contrast, the rate drops to around 3% to 5% among younger, broader demographics.

The high variation and concentration of chronic cough cases in Pakistan stem from several specific environmental and demographic factors:

Age & Demographics: Chronic cough prevalence is notably higher in older adults and females, largely driven by a lifetime of cumulative environmental exposures.

Urban Air Quality: Rapid urbanization in metropolitan cities like Karachi and Lahore has exposed populations to poor air quality and high levels of particulate matter.

Evaluation

History and Physical Examination plays a crucial role in the evaluation. Cough is a symptom rather than a diagnosis, and a thorough history and physical examination are fundamental steps in the evaluation. The clinical presentation varies based on the underlying etiology. The following discusses the presentations of some of the most common causes of cough, but is not all-inclusive.

Acute Cough

- **Acute bronchitis**: Dry or productive cough lasting less than 3 weeks, often following an upper respiratory infection; associated with wheezing and rhonchi that typically clear with coughing.
- **Acute decompensated heart failure**: Dyspnea, orthopnea, paroxysmal nocturnal dyspnea, bibasilar crackles, peripheral edema, S3 gallop, and possible hypotension or tachyarrhythmias.
- **Acute Rhinosinusitis**: Nasal congestion or discharge, facial pain or pressure, decreased smell, and postnasal drip.[11]
- **Allergic rhinitis**: Rhinorrhea, nasal itching, sneezing, cough, allergic conjunctivitis, and fatigue; exam findings include pale, edematous nasal mucosa, clear rhinorrhea, pharyngeal cobblestoning, and infraorbital darkening or edema.[12]
- **Asthma**: Episodic cough, wheezing, or dyspnea triggered by cold air, exercise, infections, or environmental exposures; cough may be the predominant or sole symptom in cough-variant asthma.[13] Intermittent expiratory wheezing is typical, whereas fixed or unilateral wheezing suggests an alternative pathology.
- **Bronchiolitis**: Primarily affects children younger than 2; begins with upper respiratory symptoms followed by wheezing, crackles, tachypnea, retractions, and sometimes fever.
- **COPD Exacerbation**: Worsening cough, wheezing, tachypnea, tachycardia, accessory muscle use, difficulty speaking, altered mental status, or signs of hypercapnia such as asterixis.[14]
- **Foreign body aspiration**: Acute cough, stridor, focal wheezing, tachypnea, or decreased air entry; severe cases present with respiratory distress, cyanosis, or altered mental status.
- **Pertussis**: Progressive cough that worsens after an initial catarrhal phase, followed by paroxysmal coughing fits with inspiratory "whoop," posttussive vomiting, and possible cyanosis; gradual resolution during the convalescent phase.
- **Pulmonary embolism**: Acute cough with dyspnea, pleuritic chest pain, tachypnea, hemoptysis, wheezing, or signs of deep vein thrombosis.

Chronic Cough

- **Bronchiectasis**: Chronic productive cough with daily mucopurulent sputum, recurrent infections, dyspnea, fatigue, wheezing, and occasional hemoptysis.
- **Chronic aspiration**: Cough associated with eating or drinking, especially thin liquids; may include focal wheezing, hemoptysis, or foul-smelling sputum.
- **Chronic Rhinosinusitis**: Nasal congestion or drainage, facial pressure, reduced or absent smell; cough is particularly prominent in children.
- **Cystic fibrosis**: Persistent productive cough with multisystem involvement, including failure to

thrive, pancreatic insufficiency, sinus disease, hepatobiliary disease, rectal prolapse, and nephrolithiasis.

- **Gastroesophageal reflux disease**: Cough associated with dysphonia, heartburn, regurgitation, or sour taste.
- **Interstitial lung disease**: Chronic cough and progressive dyspnea with fine inspiratory crackles, often in dependent lung zones.
- **Medication-induced cough**: Typically dry; angiotensin-converting enzyme inhibitor–associated cough develops within 1 week to 6 months of initiation, resolves within weeks of discontinuation, and recurs on rechallenge.
- **Nonasthmatic eosinophilic bronchitis**: Chronic nonproductive cough in patients with atopic tendencies, elevated sputum eosinophils, airway inflammation, and no airway hyperresponsiveness.
- **Obstructive sleep apnea**: Chronic cough accompanied by loud snoring, excessive daytime sleepiness, and morning headaches.
- **Protracted bacterial bronchitis**: Chronic wet cough lasting 4 weeks or longer, normal spirometry and chest radiography (aside from possible peribronchial cuffing), and resolution with a 2-week course of appropriate antibiotics.
- **Upper airway cough syndrome**: Frequent throat clearing, postnasal drip sensation, nasal discharge; exam findings include pharyngeal cobblestoning and visible secretions.

Treatment / Management

Acute Cough

Acute upper respiratory tract infection

Management of acute cough due to an upper respiratory tract infection is primarily supportive. Short-term use of acetaminophen or nonsteroidal anti-inflammatory drugs effectively relieves fever, headache, myalgias, arthralgias, ear pain, and malaise, with similar efficacy and good tolerability.[15] In adults and children older than 12, combination antihistamine–decongestant products may provide greater symptom relief than either agent alone. Antibiotics, antihistamines used alone, and antiviral therapies do not improve outcomes and may cause harm.

Acute Rhinosinusitis

Only 0.5% to 2% of cases of acute rhinosinusitis (ARS) are bacterial.[16] Some experts recommend saline nasal irrigation with buffered, physiologic, or hypertonic saline using sterile or bottled water. The actual benefit of saline irrigation is unclear.[17] However, irrigation has minimal adverse effects, and anecdotal reports indicate that it may improve nasal symptoms in some patients. Likewise, clinicians can also offer topical nasal steroids for patients with both ARS and acute bacterial rhinosinusitis (ABRS).[18]

If symptoms fail to improve or worsen, amoxicillin or amoxicillin–clavulanate is first-line therapy for 5 to 7 days.

Influenza

Influenza is typically self-limited. However, infection is associated with increased morbidity and mortality in select populations. The treatments of these patients with antivirals:

Oseltamivir is the antiviral medication of choice for influenza. Additional alternatives are baloxavir, zanamivir, and peramivir.

Pertussis

The following patients should receive antimicrobial treatment for pertussis:

- All individuals older than 1 year with a clinical or lab-confirmed diagnosis who present within 3 weeks of the onset of cough
- All individuals younger than 1 year, pregnant individuals, patients with asthma, COPD, or an immunocompromising condition, and those aged 65 and older who present within 6 weeks of cough onset.

Preferred treatment is azithromycin or clarithromycin; trimethoprim-sulfamethoxazole is an alternative, except in infants younger than 2 months due to the risk of kernicterus. Early treatment (within 7 days) may shorten symptom duration. Patients are most contagious during the first 3 weeks of illness or the first 5 days of treatment.

Acute lower respiratory tract infections

Like most upper respiratory tract infections, acute bronchitis is most commonly viral in etiology, and management is supportive. Antivirals and antibiotics have not shown benefit in the treatment of acute bronchitis.[19]

Bronchiolitis

Management of mild bronchiolitis consists of nasal suctioning and adequate hydration. Medications are unnecessary unless caregivers elect to treat fever when present. Moderate to severe symptoms will likely need evaluation in an emergency department. Treatment consists of supplemental oxygen when necessary and nasal suctioning. Clinicians do not routinely use bronchodilators to manage bronchiolitis; however, they may trial nebulized epinephrine or albuterol in infants and children who present with wheezing and respiratory distress.

Pneumonia

The choice of antibiotic therapy for community-acquired pneumonia depends on the expected pathogen, patient age, risk factors, comorbidities, and local resistance patterns.[20] According to the 2019 American Thoracic Society/Infectious Diseases Society of America guidelines, the preferred empiric antibiotic regimen for community-acquired pneumonia in healthy outpatients 64 and younger is high-dose amoxicillin. Monotherapy with doxycycline or a macrolide, such as azithromycin or clarithromycin (if the local S

pneumoniae macrolide resistance rate is below 25%), is an acceptable alternative. Macrolide resistance rates among S pneumoniae are often greater than 30% in the United States and exceed 25% in nearly the rest of the world.

Patients 65 and older or with chronic lung, liver, or kidney disease, asplenia, a history of cancer, alcohol use disorder, patients who smoke, or those treated with antibiotics within the last 3 months, should receive amoxicillin-clavulanic acid and a macrolide or doxycycline. Patients who are unable to tolerate amoxicillin-clavulanate should receive a third-generation cephalosporin such as cefpodoxime in combination with a macrolide or doxycycline. Clinicians prescribe a respiratory fluoroquinolone for patients who cannot tolerate a third-generation cephalosporin.

Hospitalized individuals with pneumonia are treated with a respiratory fluoroquinolone or β-lactam antibiotics, along with doxycycline or a macrolide.[21]

Asthma exacerbation

Clinicians manage an acute asthma exacerbation with short-acting inhaled bronchodilators and steroids. Patients with severe symptoms (respiratory rate greater than 30 breaths per minute, pulse greater than 120 beats per minute, use of accessory muscles, drowsiness, diminished breath sounds, and hypoxia should receive treatment in the emergency department.

Heart failure

Supplemental oxygen, noninvasive ventilation when indicated, loop diuretics, and sodium restriction for volume overload are the cornerstones of the treatment of acute decompensated heart failure. Vasodilators such as nitroprusside lower systemic vascular resistance and left ventricular afterload in patients with severe hypertension, acute mitral regurgitation, or acute aortic regurgitation. Nitroglycerine lowers venous tone to relieve respiratory distress when the diuretic response is inadequate.

Intravenous inotropes such as dobutamine or milrinone may be necessary in patients with severe systolic dysfunction and end-organ hypoperfusion; however, the use of inotropes in the setting of acute decompensated heart failure with preserved ejection fraction is not appropriate.

Pulmonary embolism

Hemodynamic status and bleeding risk guide treatment of a pulmonary embolism. High-risk patients with low bleeding risk receive systemic thrombolysis followed by anticoagulation. High-risk individuals with a high bleeding risk undergo catheter-directed therapy or surgical embolectomy.

Subacute and Chronic Cough

Management of subacute and chronic cough targets the underlying cause. In children, watchful waiting for 2 to 4 weeks is appropriate, as most cases are postviral and self-limited. Inhaled steroids, bronchodilators, and oral medications do not benefit postinfectious cough. A short trial of bronchodilators or inhaled corticosteroids may be considered for suspected cough-variant asthma, while a 4-week trial of acid suppression is appropriate when GERD features such as recurrent regurgitation, dystonic neck posturing in infants, or heartburn in older children or adults are present.

Tuberculosis requires standard multidrug therapy. Clinicians should discontinue ACEIs and other cough-inducing medications when possible and strongly encourage smoking cessation. Asthma and COPD therapy should be optimized if present.

Intranasal glucocorticoids are the mainstay of therapy for upper airway cough syndrome with antihistamines, ipratropium, or azelastine as adjuncts. Lack of improvement after 2 to 3 weeks makes this diagnosis unlikely.

Differential Diagnosis

Acute

The following are common differential diagnoses for patients presenting with an acute cough:

Acute bronchitis, Acute exacerbations of COPD or asthma, ARS, Acute viral upper respiratory infection, Allergic rhinitis, Aspiration syndromes, Bronchiolitis, Cerebrospinal fluid leak, Chemical or inhalation injury, Congestive heart failure, Croup, Pertussis, Pneumothorax, Pneumonia and Pulmonary embolism

Subacute

The following are common differential diagnoses for patients presenting with a subacute cough:

Bronchiectasis, Chlamydophila pneumonia, Mycoplasma pneumonia, Pertussis, Post-infectious cough and Tuberculosis

Chronic

The following are common differential diagnoses for patients presenting with a chronic cough:

Asthma, Chronic aspiration, Chronic bronchitis, Chronic rhinosinusitis, COPD, GERD, Interstitial lung diseases, Malignancy, Medication effects, Neurogenic cough, Nonasthmatic eosinophilic bronchitis, Obstructive sleep apnea, Somatic cough syndrome and Upper airway cough syndrome

The following are additional but less common potential causes of cough:

Amyloidosis, Cerumen impaction, causes stimulation of the auricular branch of the vagus nerve or Arnold nerve, Esophageal achalasia, Tracheoesophageal fistula, Esophageal-tracheobronchial reflex, Holmes-Adie syndrome (anisocoria, abnormal deep tendon reflexes, and patchy areas of hyperhidrosis or anhidrosis, along with chronic cough), Inflammatory bowel disease, Ortner syndrome or compression of the left recurrent laryngeal nerve caused by enlarged vascular structures, such as an enlarged left atrium due to mitral stenosis, Paradoxical vocal fold motion, Pediatric autoimmune neuropsychiatric disorder associated with group A streptococci,

causing motor tics, Peritoneal dialysis due to GERD, pulmonary edema, or pleuroperitoneal communication, Pneumonitis, Premature ventricular contractions, Relapsing polychondritis, Sarcoidosis, Syngamus laryngeus infection, Tracheobronchial collapse, Sensory neuropathy due to B12 deficiency and Zenker or distal esophageal diverticulum

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Original Article

Endoscopic Subtotal Inferior Turbinectomy is a Safe Procedure

Saddam Sahib Atshan[1], Firas Baqir Al-Hameed[1], Aymen Ahmed Mohsin[2], Mustafa Haseeb Alali[3], Firas T. Obeid[2] and Ahmed Al Abbasi[4]

ABSTRACT

Objective: To evaluate the effectiveness of endoscopic subtotal inferior turbinectomy (ESIT) on nasal obstruction and the consequences of this approach.
Study Design: Prospective interventional cohort study.
Place and Duration of Study: This study was conducted within Basra between October 2023 to October 2025.
Methods: The total number of patients who were undertaken endoscopic subtotal inferior turbinectomy and followed up for one year was 425 patients. Post-operative evaluation was conducted using clinical assessment, including endoscopic examination and a structured questionnaire completed by patients during follow-up visits.
Results: All patients reported improvement in nasal obstruction postoperatively. Headache and nasal discharge were improved in approximately 83% and 76% respectively. Thirty-three patients (out of 425) developed haemorrhage after removal of the packs and only five patients required surgical interference to stop bleeding. No statistically significant difference was observed in the onset of haemorrhage postoperatively between day 1(after removal of nasal pack) and day 3-10 (p=1.000). Crusting was demonstrated in 40% of patients during the first three months and it disappeared in the following period. Mucosal adhesion was noticed in patients who were required septoplasty as well as inferior turbinectomy. Re-enlargement of turbinates were been noticed in 2.1% of patients postoperatively during follow up period.
Conclusion: Endoscopic subtotal inferior turbinectomy is safe procedure and effective in treating nasal obstruction.
Key Words: Endoscopic subtotal inferior turbinectomy, nasal obstruction, inferior turbinate hypertrophy

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INTRODUCTION

Inferior turbinate enlargement is a common cause of nasal obstruction, presented in more than 70% of patients who were evaluated for nasal airway obstruction.[1] The enlargement is either due to soft tissue swelling or due to increase bone thickness. There are different factors can be involved in inferior turbinate hypertrophy, such as allergic and non-allergic (vasomotor) rhinitis, septal deviation with compensatory changes, hormonal effect, rhinitis medicamentosa and inferior turbinate pneumatization.[2-5] When conservative and medical treatment of turbinate enlargement fails, surgical intervention is often required.[6] One of these procedures is inferior turbinectomy which improves nasal airflow and nasal obstruction. However, this procedure remains debated because of post operative complications and physiological consequences, for example post-operative haemorrhage and crusting are reported complications for this procedure. Excessive resection of inferior turbinate may alter normal nasal airflow and heat/ water exchange function and consequently empty nose syndrome may develop. This condition is characterized by paradoxical nasal obstruction, dryness, and abnormal perception of air flow despite a patent nasal cavity.[7] On the other hand, a computational fluid dynamics study showed a minimal impairment under certain environmental conditions (temperature = 12–40 ◦C; relative humidity = 13–80%).[8] The aim of this study is to evaluate the safety of endoscopic subtotal inferior turbinectomy in southern Iraq where the climate is hot and humid in Summer and mild in Winter.

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METHODS

This was a prospective interventional cohort study with a follow up for one year duration. It was undertaken in

Basra, southern Iraq, at Basra Teaching Hospital between October 2023 to October 2025. During this period, 577 patients underwent endoscopic subtotal inferior turbinectomy with or without septoplasty. The total number of patients who were followed up for one year duration was 425 patients. Exclusion criteria included patients who had nasal polyposis, nasal masses, tumour, unilateral turbinate enlargement or chronic rhinosinusitis.

Preoperatively, all patients were assessed using endoscopic examination and CT scan of the nose and sinuses to exclude other co-existing nasal conditions.

The procedure was undertaken by the same team for all patients. Septoplasty was performed first, if required, turbinectomy scissor were used to excise the turbinates endoscopically and any bleeding point was electrocauterized. For patients who underwent septoplasty, bilateral nasal splints were applied. After that, merocele nasal packs were inserted bilaterally. On day one, the packs were removed and patients were discharged home on nasal saline irrigation for three months. One week later, splints were removed and nasal cleansing were performed. At weekly intervals, patients were seen three times. To evaluate the success of the operation and to determine types of complications that could occur, patients were followed up after three months, six months and after a year. During the last two visit, patients were given a questionnaire that asked about the following aspects: whether they have developed improvement or worsening in nasal breathing, headache, nasal discharge, olfactory dysfunction or noted nasal dryness. Endoscopic examination was performed to assess if there was any crusting, mucosal adhesion or re-enlargement of turbinates.

Statistical analysis was performed using SPSS version 25. Categorical variables were compared using McNemar test or Fisher's exact test when appropriate. A p-value < 0.05 was considered statistically significant.

RESULTS

The total number of patients who had subtotal turbinectomy during the period of our study was 577. However, only 425 patients were followed up for one year and included in this cohort. Sixty four percent of patients were males and the median age of all patients was 35 years (IQR:12; range:15-68 years. Age distribution is shown in the table 1.

All patients who had bilateral nasal obstruction stated that this complaint relieved significantly after the operation. Headache and nasal discharge improved in 82% and 76% of patients postoperatively, respectively (McNemar test, P< 0.01).

There were no patient complaints of worsening in any symptom; however, a subset of patients noticed no improvement or progression of symptoms; particularly smell dysfunction, see table 2.

Table No. 1: Age distribution in the present study

Age	Number (n)	Percentage (%)
Under 20 years	10	2.4
20-29	90	21.2
30-39	196	46.1
40-49	97	22.8
50-59	26	6.1
60 and above	6	1.4
Total	425	100%

Table No. 2: Postoperative improvement of symptoms

Symptoms	Preoperative	Postoperative improvement	
		Yes	No
Nasal obstruction	425 (100%)	425 (100%)	0
Headache	180 (42.35%)	149 (82.77%)	31
Nasal discharge	74 (17.4%)	56 (75.67%)	18
Olfactory dysfunction	40 (9.4%)	18 (45%)	22

McNemar test, P< 0.01:

On the other hand, ESIT was associated with variable complications. Nasal crusting for example was observed in 170 patients (40%) during the first three months after the surgery. However, after this period this feature disappeared completely. Nasal bleeding occurred in 7.8% of patients (33 patients), of which just above half of cases (18 patients) started after day 3 postoperatively. Two patients required nasal packing to stop bleeding. However, immediate post-operative bleeding on day one was seen in 15 patients only. Two patients underwent nasal packing to control bleeding and only one patient required re-admission to the theatre to manage bleeding through endoscopic electrocauterization of bleeding points at the posterior end of inferior turbinate, see figure 1 and table 3.

Small percent of patients who had septoplasty at the same time of ESIT developed nasal mucosal adhesion at 6.8% (n=29). Nevertheless, no adhesion was seen among patients who had sole subtotal turbinectomy.

Re enlargement of inferior turbinate developed in a few numbers of cases at only 2% (n=9). This enlargement was mild and not obstructing nasal cavity as it was assessed endoscopically. Nasal dryness was an uncommon feature, found only in 0.9% of patients.

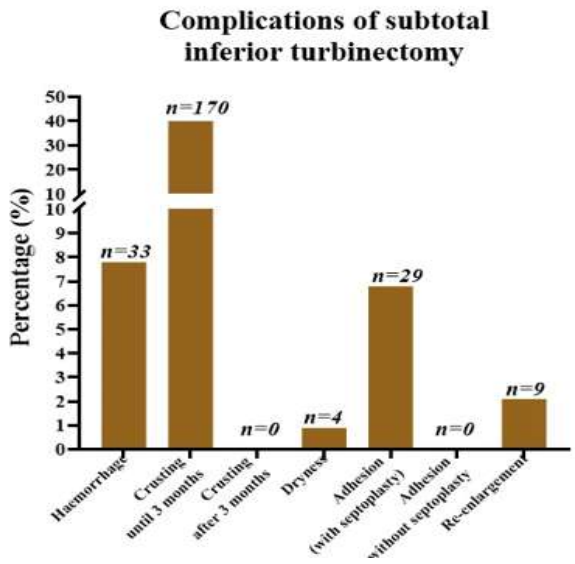

Figure No. 1: Complications of subtotal inferior turbinectomy

Table No. 3: Post turbinectomy haemorrhage

Haemorrhage time	(n)	(%)	Required intervention
Day 1(immediately after pack removal)	15	45.5%	3
Day 3-10	18	54.5%	2
Total	33	100%	5

P-value = 1.000

DISCUSSION

This cohort study showed that nasal obstruction improved in all patients who underwent ESIT. This significant improvement confirming that this procedure is highly effective in managing nasal obstruction due to inferior turbinate hypertrophy. Non-obstructive symptoms improved variably, more than three-quarters of patients with headache and nasal discharged experienced improvement. Olfactory symptoms showed improvement in 45% of individuals. This relatively modest response is understandable because olfactory impairment is not always directly related to inferior turbinate enlargement and it could be influenced by additional factors such as mucosal inflammation, airflow distribution to the olfactory cleft and other underlying sinonasal pathologies.

Khan et al found that 94.81 % of patients who had were undertaken total inferior turbinectomy demonstrated improvement in nasal obstruction. Similarly, nasal discharge and headache improved significantly.[9] A Systematic Review and Meta-analysis of long-term effect of turbinate surgery on allergic rhinitis was performed by Park et al and they found significant improvement in nasal obstruction and rhinorrhoea, (WMD, 4.60, 95% CI, 3.43-5.76), (WMD, 3.12; 95% CI, 1.97-4.28) respectively.[10]

Regarding the complications associated with turbinectomy, this study showed that 40% of patients suffered from nasal crusting in the first few weeks. However, this reduced over the next period and crust formation stopped in all patients after three months. Early crusting is attributed to the bone exposure after turbinate resection and it persists until re-epithelization of mucosa occurred and bone covered.[11,12] Mucociliary clearance, in addition, can be disrupted in the early weeks after the surgery and this may increase crust formation during this period. We observed that persistent nasal dryness was reported by 0.9% of patients. Features of empty nose syndrome or atrophic rhinitis were not seen in our patients. This could be because of neutral climate where the study is undertaken. This opinion is supported by a study performed by Siu et al. who conducted virtual surgery and computational fluid dynamics analyses. They concluded that air-mucosal heat exchange and moisture carrying capacity reduced in cold temperature in individuals with inferior turbinate surgery, whereas the effect under hot and humid conditions was minimal.

In this study, post ESIT bleeding occurred in 7.8% of patients. The number of patients who developed bleeding immediately after packs removal was 15. One patient experienced severe bleeding that did not stop with re insertion of bilateral nasal meroceles and required endoscopic electrical cauterization in the operating room. Two other patients required re-packing for another 24 hours, whereas the bleeding from the other 10 patients ceased without intervention. Just over half of bleeding attacks were within day-3 to day-10 postoperatively. Only two patients required nasal packing to control bleeding while the remaining patients did not require any surgical intervention and the bleeding stopped spontaneously. Delayed post-turbinectomy bleeding could be linked to normal mucosal healing process, including eschar separation, reactive vasodilatation and increased mucosal vascularity.[13] It is obvious that most of post-operative bleeding was manageable and treated conservatively.

Similar to our finding, Levey et al concluded that bleeding occurred in 8.4% of patients underwent partial inferior turbinectomy.[14] Rao et al, in contrast, showed a relatively lower bleeding rate after total inferior turbinectomy, at 5%.[15]

Synechia developed in 6.8% of patients (n=29); all of these patients underwent septoplasty as well as ESIT. Adhesion did not develop among patients whom underwent only ESIT. The risk of adhesion increased with the combined approach because of opposing of large mucosal surface, therefore meticulous mucosal preservation and postoperative care is essential to reduce this complication. Similarly, Khan et al reported that adhesion was observed in 5.9% of 135 patients underwent total inferior turbinectomy.[9]

Re-enlargement of inferior turbinates after subtotal resection was seen in nine patients (2%). The increase in turbinate size was noticed six months after the operation. This secondary hypertrophy could be due to continuous allergic or inflammatory rhinitis and for this

reason a long-term intranasal steroid could be recommended..

CONCLUSION

Endoscopic subtotal inferior turbinectomy was not associated with serious post-operative haemorrhage or long-term complications. Bleeding occurred in 7.8% of patients and only five patients were managed surgically to stop bleeding. Regarding preoperative symptoms, all patients experienced improvement in nasal obstruction and a substantial proportion of patients reported relief of headache and nasal discharge postoperatively. Olfactory dysfunction also improved in 45% of patients. These findings suggest that endoscopic subtotal inferior turbinectomy is relatively safe and effective in managing obstructive and non-obstructive symptoms associated with inferior turbinate enlargement.

Author's Contribution:

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Original Article

Diagnostic Significance of Combining Anti-Gliadin IgA and Anti-Tissue Transglutaminase IgA in Suspected Celiac Disease: A Cross-Sectional Study

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ABSTRACT

Objective: To explore the correlation between anti-gliadin IgA and anti-tTG IgA in 384 subjects suspected of celiac disease.

Study Design: Cross-sectional descriptive study.

Place and Duration of Study: This study was conducted at the Laboratories of the Biology Department, College of Education, University of Al-Qadisiyah, Iraq; February to December 2025.

Methods: ELISA testing of sera using commercial kits, with results interpreted against manufacturer-defined cut-off values.

Results: Positivity for anti-gliadin IgA occurred in 13.3% of cases, whereas 15.1% were positive for anti-tTG IgA. Co-positivity for both antibodies was seen in 8.1%, whereas 5.2% and 7.0% were positive only for anti-gliadin IgA and anti-tTG IgA, respectively. Paired analysis disclosed a highly significant correlation (χ^2=91.64, $p<0.001$, φ=0.49). More females were positive for both antibodies, consistent with established sex differences in autoimmune conditions.

Conclusion: Results underscore the combined utility of anti-gliadin IgA and anti-tTG IgA, particularly in discordant cases, supporting multiple-test strategies for improved celiac detection with reduced false negatives.

Key Words: Celiac Disease; Autoimmune Diseases; Transglutaminases; Gliadin; Immunoglobulin A; Gluten Sensitivity.

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INTRODUCTION

Wheat and gluten-containing grains constitute up to half of energy intake in many developing and developed nations. With their increasing dietary inclusion, celiac disease cases have risen dramatically worldwide.1 Celiac disease is now a global concern, no longer limited to those of European descent. Its seroprevalence is 1.4%, with a biopsy prevalence of 0.7%, predominantly among females, with rates increasing over recent decades.[2]

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Celiac disease is an autoimmune enteropathy, in which the body reacts excessively to the consumption of gluten, a protein found in wheat, barley, and rye. Gluten peptides are not completely digested but are deamidated by transglutaminase. Risk factors include early life infection, breast feeding, and changes in gut bacteria.[3] This causes villous atrophy, nutrient malabsorption, and gastrointestinal and extraintestinal manifestations, including diarrhea, bloating, abdominal pain, constipation, anemia, fatigue, and osteoporosis.[4]

Though the diagnosis of celiac disease relies on small bowel biopsy, serologic screening is based on highly sensitive serologic markers, especially IgA anti-tissue transglutaminase antibodies.[5]

The discovery of tTG as an autoantigen clarified that celiac disease was an autoimmune disorder.[6] Celiac disease results from both genetic and environmental factors. The first one is associated with the HLA-DQ2 and HLA-DQ8 alleles in chromosome6, present in 30-40% of patients.[7] The environmental factors include infection with viruses as well as dysbiosis of the gut microbiota. Celiac disease may be manifested in patients of any age and can present itself in various ways, namely, gastroenterologic, extra-intestinal, latent, potential, refractory, and seronegative. Even though the diagnosis is still based on small-bowel biopsy,

serology, such as the measurement of anti-tTG, endomysial, and deamidated gliadin peptide antibodies, are increasingly used in suspected cases.[6]

Recent data have revealed that high titers of IgA antibodies against tissue transglutaminase more than tenfold higher than the upper limit of normal could diagnose celiac disease effectively without a biopsy.[8]

This research was conducted with the purpose of analyzing the diagnostic efficacy of anti-gliadin and anti-tTG IgA antibodies and their relationship in celiac disease suspects.

METHODS

This cross-sectional descriptive study included 384 serum samples from males and females aged 18-55 years suspected of having celiac disease, attending a medical facility in Iraq.

Ethical Considerations: This study was approved by the institution's ethical review board (Approval no. 12284; date: 11-02-2025) and was carried out in accordance with the Declaration of Helsinki (2013). The samples were collected and analyzed in an academic setting under the guidance of qualified academics.

Patient Consent Statement: No direct patient consent was required, as all data were anonymized and collected as part of routine clinical care.

Inclusion criteria: Patients suspected to have celiac disease referred for serological testing based on clinical symptoms (such as weight loss, stunted growth, abdominal pain, lack of appetite, anemia, poor development, or diarrhea).

Exclusion Criteria: Participants previously placed on a gluten free diet, incomplete documentation, and samples unsuitable for testing (hemolyzed or inadequate volume).

Specimen Collection & Handling: 5 mL of venous blood sample was obtained from each participant, after which serum was extracted and stored at -20 degrees Celsius for future analyses.

Serology Assay: Thawed sera were allowed to reach room temperature and were further diluted according to the manufacturers' protocol. Gliadin IgA and tTG IgA antibodies were quantified by sandwich enzyme-linked immunosorbent assay (ELISA) test kit from EASKU (Germany) with cut off values (positive >18 U/mL, equivocal 12-18 U/mL, negative <12 U/mL).

Statistical Analysis: All 384 consecutive eligible patients were included. Statistical analyses were performed using SPSS version 26.0, employing descriptive statistics, chi-square (χ^2) test, and Phi correlation coefficient, with significance set at $p<0.05$.

RESULTS

Out of 384 patients, 13.3% had positive anti-gliadin IgA, while 15.1% had positive anti-tTG IgA. The number of patients who showed both antigens was 8.1%. The complete results are given in Table 1.

Table No. 1: Cross-tabulation between anti-gliadin IgA and anti-tTG IgA among suspected celiac disease cases

	anti-tTG IgA (+)	**anti-tTG IgA (−)**	**Total**
anti-gliadin IgA (+)	31 (8.1%)	20 (5.2%)	51 (13.3%)
anti-gliadin IgA (−)	27 (7.0%)	306 (79.7%)	333 (86.7%)
Total	58 (15.1%)	326 (84.9%)	384 (100%)

A Chi-square test revealed a statistically significant association between anti-gliadin IgA and anti-tTG IgA ($\chi^2 = 91.64$, df = 1, $p < 0.001$). The Phi coefficient ($\varphi = 0.49$) indicated a moderately strong positive correlation between the two antibodies, suggesting that individuals positive for one marker are more likely to be positive for the other.

Gender-Based Distribution: To further explore potential biological differences, gender-based analysis was conducted. Gender-based distribution is detailed in Table 2

Table No. 2: Gender-based distribution of anti-gliadin IgA and anti-tTG IgA results

Category	**Males**	**Females**	**Total**
Both anti-gliadin IgA and anti-tTG IgA (+)	9 (6.7%)	22 (8.8%)	31 (8.1%)
anti-gliadin IgA (+) only	7 (5.2%)	13 (5.2%)	20 (5.2%)
anti-tTG IgA (+) only	5 (3.7%)	22 (8.8%)	27 (7.0%)
Both anti-gliadin IgA and anti-tTG IgA (−)	113 (84.3%)	193 (77.2%)	306 (79.7%)
Total cases	134	250	384
% anti-gliadin IgA (+)	11.9%	14.0%	—
% anti-tTG IgA (+)	10.4%	17.6%	—

Females showed slightly higher positivity rates for both antibodies compared to males, with anti-tTG IgA positivity of 17.6% versus 10.4% respectively.

DISCUSSION

In this research, examining 384 samples produced a moderate correlation between anti-gliadin IgA and anti-tTG IgA ($\varphi=0.49$), which means that if a sample was positive for one, it would also test positive for other, but not necessarily to the same extent. This result has been

proved in other studies as well, in which anti-tTG and anti-endomysium antibodies were described as having a greatest potential as a serological marker for celiac disease, whereas anti-gliadin antibodies have a lower efficiency, though being a sort of early immune alert.[9]

In addition, as shown in previous literature, a combination of TTG testing with gliadin-associated antibodies has been proven to increase sensitivity in the diagnostic tests and make it easier to identify patients who would otherwise test negative for TTG, [10] adding value to our findings as shown in our study where some patients would test positive for anti-gliadin IgA alone, whereas others would test positive for anti-tTG IgA alone.

In addition, it has been shown that dual testing reaches a point of increasing sensitivity without sacrificing a comprehensive evaluation of cases, whereas anti-gliadin antibodies gave rise to occasional false positives that needed confirmation by biopsy of the intestines.[11] Therefore, it becomes important that our results underscore, in a complementary perspective, the role of both antibodies in identifying celiac disease.

Interpretation and Implications: All of these findings reinforce the complementary role of both antibodies in celiac screening. Furthermore, their co-positivity rate of 8.1% indicates that their combined use enhances diagnostic certainty, while their discordant rates of 5.2% for anti-gliadin-only and 7.0% for anti-tTG-only status reveal how differences in disease course, immune mechanism, and antigens exist.

Although anti-tTG IgA has been known for many years for its high sensitivity as well as specificity, anti-gliadin IgA can also be seen as a preliminary immunological marker, particularly in cases with partial villous infiltration and/or with a lack of classical symptoms. These findings also confirm the utility of a two-marker strategy in order to increase the rate of early detection with a low rate of false negatives.

The correlation factor $\varphi = 0.49$ and $p < 0.001$ between anti-gliadin IgA and anti-tTG IgA further strengthens their usage together for celiac screening. When analyzed on the basis of gender, it was found that females showed a higher overall positivity rate, which aligns with known autoimmune patterns. Simultaneous analysis of both provides a broader immunological screening, which further aids in improving the diagnostic acuity and early identification of CD.

A subgroup tested positive for anti-gliadin IgA but negative for anti-tTG IgA. Consistent with Hessinger and Vohra (2021), in which it was found that patients with a positive result for anti-gliadin but negative for anti-tTG were extremely unlikely to be diagnosed with celiac disease when histopathological analysis was done. These cases were commonly linked to other conditions of the gastrointestinal tract, including eosinophilic esophagitis. This indicated that in most cases of isolated anti-gliadin positivity, it can be a false positive result rather than a true manifestation of celiac autoimmune conditions.[12]

Anti-gliadin IgA and anti-tTG IgA positivity was higher in females, consistent with Ludvigsson's large-scale study showing greater celiac prevalence in females.[13] Rossi (2025) reported more extraintestinal manifestations and duodenal lesions in females despite similar dietary compliance between sexes.[14] A Mediterranean cohort similarly showed females presenting more frequently with severe symptoms including anemia, dyspepsia, and genital disorders, while weight loss and low BMI were more common in males.[15] Collectively, these findings support sex-related differences in celiac prevalence and presentation, explaining the higher female seropositivity in our cohort.

The tendency for higher seropositivity in females in our series also corresponds with findings of a genetic predisposition for females as reported in a study by Megiorni et al. in 2009, where celiac disease incidence was found to be almost twice as common in females as in males (F:M = 1.8) This study showed that a high-risk genotype of HLA-DQ2/DQ8 was present in 94% of females compared with 85% in males, which suggests that there may be a higher genetic susceptibility in females for developing this disease. In this study, it also became evident that there was a paternal transmission bias, as 61% of female patients received their HLA-DQ2 from their fathers, which suggests that genetic epigenetics differ between males and females in developing this condition. Thus, it appears that there are different patterns between males and females in developing this condition. Notably, in this study, it was also reported that in DQ2/DQ8-negative celiac cases, most were males with a proportion of F:M=0.7, suggesting that alternate immune mechanisms or non-HLA pathways may be responsible for illness development in some individuals.[16]

This parallels our discordant and dual-negative patterns, possibly reflecting atypical immune reactivity or non-classical HLA pathogenesis. Ciacci (2009) further noted that disease progression may differ by sex due to higher metabolic demands in women from menstruation, pregnancy, and breastfeeding.[15]

The U.S. Preventive Services Task Force systematic review reported sensitivity and specificity above 90% for IgA anti-tTG, with IgA endomysial antibodies also being highly specific. However, sensitivity drops to 57-71% in asymptomatic cases, highlighting the risk of missed diagnoses with single-test screening.[17]

Serological tests continue to play a prominent role in making a clinical diagnosis of celiac disease. According to Volta et al. (2023), anti-tTG IgA has a high sensitivity of 93.4%, with a higher value for endomysial antibodies of 99% for specificity.[18] A biopsy in pediatric patients is unnecessary when, in accordance with the 2020 ESPGHAN management instructions,

there is a concentration of TGA-IgA above ten times over normal values and, in a confirmatory blood test, reactivity with IgA anti-endomysial antibodies (EMA-IgA) is guaranteed. On these bases, with consent from parents, a biopsy can be safely avoided.[19] Although the current investigation focused on anti-tTG IgA and anti-gliadin IgA, other studies, such as that by Anbardar et al. (2022), have shown that adding more sensitive serologic markers, for instance, Immunoglobulin G anti–deamidated gliadin peptide antibodies (IgG anti-DGP), increases diagnostic sensitivity in specific clinical scenarios. This reflects the ever-improving clinical utility of serology and the importance of choosing appropriately adequate antibody panels for accurate, early diagnosis of celiac disease.[20]

This study from a single center involving 384 subjects suspected to have celiac disease using anti-gliadin IgA and anti-tTG IgA offers an interesting contribution to the understanding of antibodies among subjects suspected to be having the condition, albeit without a biopsy diagnosis. though future multi-center studies are warranted for further validation.

CONCLUSION

The current study determined the diagnostic accuracy and association of anti-gliadin IgA and anti-tTG IgA in 384 patients with suspected celiac disease. The former test exhibited greater positivity and moderate to strong correlation with anti-gliadin IgA test, implying that it can be used effectively for screening purposes. Concurrent positivity increased confidence in diagnosis whereas discrepancies were attributed either to early cases or individual immunological reactions. The predominance of females is consistent with previous observations regarding autoimmune diseases.

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Original Article

Correlation Between Body Mass Index and Intraocular Pressure in Adults: A Cross-Sectional Study

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ABSTRACT

Objective: To evaluate the correlation between BMI and IOP in adults at a tertiary care Hospital in Peshawar.
Study Design: A cross-sectional study.
Place and Duration of Study: This study was conducted at the Ophthalmology Unit Hayatabad Medical Complex Peshawar, from 1st February 2024 to 31st January 2025.
Methods: This was a cross-sectional study, performed over 12 months, involving 79 adult patients attending the Ophthalmology Outpatient Department. Subjects with ocular disease, systemic conditions that may affect IOP, and those taking medications that might affect BMI or IOP were excluded. BMI was classified based on WHO norms and IOP was assessed using Goldmann applanation tonometry. Pearson correlation and linear regression were performed to analyze the relationship between BMI and IOP.
Results: Mean height of the participants was 1.64 ± 0.08 m, mean weight was 65.18 ± 11.5 kg, mean BMI was 26.1 kg/m², and the mean IOP was 15.8 mmHg. There was a statistically significant positive correlation between BMI and IOP ($r = 0.58$, $p < 0.001$). The overweight (43%) and obese (48.1%) participants had higher IOP values than the participants with normal BMI (8.9%).
Conclusion: This study shows a strong correlation between BMI and IOP, indicating that there is a higher risk of having higher IOP in individuals with higher BMI. With the association of obesity and glaucoma, obesity should be incorporated into ophthalmological care. Ocular hypertension and glaucoma may be detected and prevented at an early age in overweight and obese people through regular IOP screening.

Key Words: Body Mass Index, Intraocular Pressure, Obesity, Glaucoma Risk, Ophthalmic Health, Epidemiology, Goldmann Applanation Tonometry, Ocular Hypertension

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INTRODUCTION

Intraocular pressure (IOP) is a physiological parameter of major importance to maintain the integrity of the eye. It is primarily regulated by the aqueous humor production/drainage ratio via the uveoscleral outflow pathways and trabecular meshwork. Increased intraocular pressure (IOP) has been linked to glaucoma, the primary cause of permanent blindness[1]. Variation in IOP can lead to changes in eye health, and may need to be monitored in persons without glaucoma. Underweight, normal weight, overweight and obesity are typically described in terms of body mass index (BMI), which is a measure based on an individual's weight and height. Since 1975, the prevalence of obesity around the world has more than tripled, making it a significant public health concern[2]. The systemic effects of obesity have come into the spotlight, including cardiovascular disease, metabolic syndrome, and now eye health.

There are a number of studies reporting different results regarding the relationship between BMI and IOP. There is some evidence of a positive relationship, higher BMI associated with higher IOP. This correlation can be explained by several mechanisms, including increased episcleral venous pressure, systemic inflammation, and hormonal changes such as increased cortisol (2015). Other studies, however, have failed to find any association, suggesting that this relationship is complex and needs to be explored more extensively (2018).

Given the increasing load of obesity and aging population in Pakistan, the correlation between BMI and IOP is of special clinical relevance. The presence of modifiable risk factors for higher levels of IOP can help in early intervention strategies and help prevent the development of glaucoma. This topic is of growing

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interest but little local information is available to review this correlation within the Pakistani population.[3-5]

In Pakistan, there are limited studies that have investigated the association between BMI and IOP in adults, particularly in Peshawar. Genetic, environmental and lifestyle factors vary significantly and so there is a need for region-specific data. This study aims to address this gap and investigate the association between BMI and IOP in the adult population of Hayatabad Medical Complex, Peshawar. The outcome will contribute to the existing knowledge base and contribute to clinical practice in the region.

METHODS

This cross-sectional study was conducted at Ophthalmology Unit Hayatabad Medical Complex Peshawar, from 1st February 2024 to 31st January 2025. The study included 79 adult patients (18 years and above) attending the Out Patient Department (OPD) for routine eye examination or for any eye complaint other than IOP or BMI. Patients with any known ocular disease (including glaucoma or uveitis), systemic disease (including diabetes or hypertension) or on any medication that might affect the IOP or weight were excluded to ensure validity of findings.

Sample size of 79 participants was determined by convenience sampling based on the feasibility of data collection within the study period and availability of eligible patients. The inclusion criteria were: adults (18 years or older), and the ability to provide informed consent, with no previous history of eye surgery, trauma, or systemic disease that might affect IOP or BMI. Patients with a history of refractive surgery or eye trauma, pregnant or lactating women, and patients on drugs known to affect IOP or weight were excluded.

Data were collected using a structured proforma, which included anthropometric data such as height and weight, and demographics such as age and gender of participants. The height was taken in cm using a stadiometer, and weight in kg by a calibrated weighing scale. BMI was calculated by dividing height (measured in square meters) by weight (measured in kilograms). The World Health Organization (WHO) database defines underweight as BMI < 18.5 kg/m2, normal weight as BMI 18.5–24.9 kg/m2, overweight as BMI 25–29.9 kg/m2, and obese as BMI > 30 kg/m2. IOP was determined by trained ophthalmologist using Goldmann applanation tonometer. Both eyes were recorded and the average IOP was analyzed for both eyes. To minimize the diurnal variation, IOPs were obtained in the early morning (9:00 AM) and late morning (12:00 PM).

The study was approved by the Institutional Review Board (IRB). All participants were provided their consent in written before study initiation. Confidentiality was always maintained when working with patient information. Data analysis was done using the SPSS 25.0. Demographic and clinical characteristics were summarized using descriptive statistics (Means ± SD), frequencies, and percentages. Correlation between BMI and IOP was analyzed by Pearson correlation test. P values were considered statistically significant if they were ≤ 0.05. After controlling for other relevant variables (age and sex), the association between BMI and IOP was assessed using linear regression analysis.

RESULTS

Mean age was 41.6 ± 12.3 years (ranged 18–65 years). There were 42(53.2%) males and 37 (46.8%) females. According to BMI classification 9 (11.4%) were underweight, 26 (32.9%) normal, 24 (30.4%) overweight, and 20 (25.3%) were obese. The average BMI of the subjects was 26.1 ± 4.8 kg/m². Table-1

Table No. 1: Demographic and Clinical Characteristics

Variable	Mean ± SD / n(%)
Age (years)	41.6 ± 12.3
Male	42 (53.2%)
Female	37 (46.8%)
BMI (kg/m²)	26.1 ± 4.8
<18.5 kg/m²	9 (11.4%)
18.5–24.9 kg/m²	26 (32.9%)
25–29.9 kg/m²	24 (30.4%)
≥30 kg/m²	20 (25.3%)

The mean IOP across all participants was 15.8 ± 2.6 mmHg (range: 11–22 mmHg). The mean IOP in the underweight group was 13.9 ± 2.1 mmHg, in the normal weight group was 14.8 ± 2.3 mmHg, in the overweight group was 16.2 ± 2.5 mmHg, and in the obese group was 17.6 ± 2.4 mmHg. Table-2

Table No. 2: Mean IOP Across BMI Categories

BMI Category	Mean IOP (± SD)
Underweight	13.9 ± 2.1 mmHg
Normal weight	14.8 ± 2.3 mmHg
Overweight	16.2 ± 2.5 mmHg
Obese	17.6 ± 2.4 mmHg
Overall Mean IOP	15.8 ± 2.6 mmHg

Statistically significant positive correlation between BMI and IOP were recorded ($r = 0.58$, $p < 0.001$), indicating that higher BMI was associated with increased IOP levels. Table-3

Table No. 3: Correlation Between BMI and IOP

Variable	Mean ± SD	Pearson's Coefficient (r)	P-value
BMI (kg/m²)	26.1 ± 4.8	0.58	<0.001
Intraocular Pressure (mmHg)	15.8 ± 2.6		

The regression model demonstrated that BMI was an independent predictor of IOP ($\beta = 0.47$, $p < 0.001$), while age ($\beta = 0.12$, $p = 0.29$) and gender ($\beta = -0.08$, $p = 0.41$) were not significantly associated with IOP. Table-4

Table No. 4: Multivariate Linear Regression Analysis Predicting IOP

Predictor Variable	Beta Coefficient (β)	p-value
BMI	0.47	<0.001
Age	0.12	0.29
Gender (Male)	-0.08	0.41

DISCUSSION

The present study revealed that there was a positive significant correlation between the I.O.P and B.M.I among the adult population who visited Ophthalmology Department of Hayatabad Medical Complex Peshawar. The mean IOP values of the participants gradually increased with their categories of BMI, with the highest mean IOP among the obese participants compared to underweight and normal weight participants. As well, Pearson correlation and regression indicated that BMI was an independent predictor of IOP when adjusted for age and gender.[6-10]

Our results corroborate those of several recent reports showing a positive association between obesity and increased IOP. Our results were comparable to those of Tham et al and Chan et al who reported increased IOP in overweight/obese adults in Korea and China, respectively[11,12]. These findings further support the link between higher BMI and elevated IOP in different populations. This consistency further supports the link between raised IOP and overweight or obesity in other population studies.

This association can be understood in a number of ways. The association of excess orbital and abdominal fat with increased episcleral venous pressure, sympathetic overactivity, elevated cortisol level, insulin resistance, and systemic inflammation with reduced aqueous humor outflow by the trabecular meshwork may account for the higher IOP in overweight and obese individuals we studied.[13-15]

In the present study, no significant relationship was observed between age and gender with IOP after adjustment in regression model. Other studies have shown higher IOPs with age while BMI had a greater effect in some recent studies, perhaps because they included different populations, different numbers of subjects, different ethnic groups and/or excluded subjects based on different criteria[16,17]. The exclusion of patients with diabetes and/or hypertension, glaucoma, and medication effect on IOP may have minimized confounding and allowed for the effect of BMI to become more apparent.

Our study showed a moderate positive correlation ($r = 0.58$), which was slightly higher than some previous studies[18]. This could be due to local lifestyle, dietary patterns, low levels of physical activity or increase in obesity prevalence over our population. In addition, the steady increase in mean IOP by BMI category bolsters the notion of a dose-response relationship between BMI and ocular hypertension. This has also been found in Indian and Japanese studies.[19,20]

The results of this study have clinical implications. Other occupational risk factors for glaucoma include high intraocular pressure and obesity can potentially play a role in the development of glaucoma indirectly through this risk factor. The routine eye examination in overweight and obese patients might assist in early detection and prevention of glaucoma-related visual loss. Weight loss and dietary changes might also have a beneficial effect on eye health.

Although these important findings were identified, the study has a number of limitations. The sample size was relatively small, and the sampling method was convenience sampling which made it difficult to generalize the findings. The cross-sectional design also does not allow for causality to be drawn. Furthermore, variables like central corneal thickness, lipid profile and exercise were not evaluated. Further studies are recommended to be conducted in the future with multi-centre, longitudinal follow-up design with larger sample size to assess the relationship between BMI and IOP.

CONCLUSION

BMI and IOP showed a strong positive correlation, suggesting that the two variables had a strong positive association. Because there is a well-documented association between high IOP and an increased risk of glaucoma, treatment of obesity should be a focus in ophthalmologic and primary care. Regular screening for IOP in overweight and obese individuals may aid in early detection and prevention of ocular hypertension and glaucoma. Further studies with larger numbers and longer follow-up is warranted to further clarify this relationship and its clinical implications.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Romaisa Kiran Baloch, Jawad Hamayon
Drafting or Revising Critically:	Rafiq Muhammad, Naz Ullah, Adnan Khan
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Comparative Efficacy of Glycolic Acid VS Salicylic Acid Peel in Acne Vulgaris

Yamna Hassan, Somaiya Rehman, Kashmala Asghar Khan and Nuzhat Naheed

ABSTRACT

Objective: To compare the efficacy and safety of glycolic acid versus salicylic acid chemical peels in patients with mild to moderate acne vulgaris.

Study Design: A prospective randomized comparative study.

Place and Duration of Study: This study was conducted at the Department of Dermatology, Lady Reading Hospital, Peshawar, from June 2023 to May 2024.

Methods: A total of 120 patients with mild to moderate acne vulgaris were enrolled and randomly divided into two equal groups. Group A received glycolic acid peel, while Group B received salicylic acid peel. Six peeling sessions were performed at two-week intervals. Total lesion count and Global Acne Grading System score were recorded at baseline and follow-up visits. Treatment response and adverse effects were also assessed.

Results: Both groups showed significant reduction in total lesion count and acne severity scores by week 12. Mean lesion count decreased from 29.4 ± 6.5 to 8.5 ± 3.9 in the glycolic acid group and from 30.1 ± 6.2 to 6.7 ± 3.5 in the salicylic acid group. Mean percentage reduction was higher with salicylic acid than glycolic acid. Excellent response was observed in 60.0% patients in the salicylic acid group and 46.7% in the glycolic acid group. Adverse effects were mild and transient.

Conclusion: Both peels were effective and safe, but salicylic acid showed faster and slightly superior clinical improvement in mild to moderate acne vulgaris.

Key Words: Acne vulgaris; Glycolic acid; Salicylic acid; Chemical peel; Acne severity; Dermatology

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INTRODUCTION

Acne vulgaris is a persistent inflammatory disease of the pilosebaceous unit that presents with comedones, papules, pustules, nodules, and potential scarring, and is mostly common to adolescents and young adults. It occurs in up to 80-90 percent of people at some point in life and has major psychosocial as well as cosmetic consequences[1]. The mechanism of pathogenesis is a complex of interconnected causes, such as follicular hyperkeratinization, sebum hyperproduction, colonization with Cutibacterium acnes, and inflammation[2]. Although several topical and systemic treatment options are available, prompt and lasting improvement is a challenge to therapy. Chemical peeling has come in as a useful adjunctive modality in the treatment of acne.

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It is characterized by the use of chemical agents provoking controlled epidermal exfoliation and the following regeneration that enhance the skin texture and decrease the number of lesions[3,4]. Superficial chemical peels, especially the alpha-hydroxy acids (AHAs) like glycolic acid and the beta-hydroxy acids (BHAs) like salicylic acid are very popular because of their effectiveness and good safety profile.

Glycolic acid is a widely used AHA that is made out of sugarcane and has the effect of reducing cohesion of corneocytes, epidermolysis and dermal remodeling[5]. It helps in desquamation and enhances post-inflammatory hyperpigmentation and is especially effective in acne and acne sequelae. Salicylic acid, conversely, is a lipophilic BHA that enters into the sebaceous follicles and has comedolytic anti-inflammatory, and antimicrobial effects, thus being particularly useful in oily and acne-prone skin[6].

There is recent evidence that chemical peels can have an important effect in acne lesions and skin quality in combination with traditional therapy[7]. A recent meta-analysis has also shown that superficial chemical peels, such as salicylic acid-based preparations, are one of the effective alternatives to manage mild-to-moderate acne[8]. Moreover, comparative and combination studies have also revealed that both glycolic acid and salicylic acid peels can provide clinical improvement, but there are differences in their mechanisms, depth of penetration, and tolerability profiles[9].

While chemical peels are widely used, there is considerable variability in clinical results and little agreement on the superiority of one peeling agent over another. Thus, it is necessary to compare the glycolic acid and salicylic acid peels to determine their efficacy, safety and acceptability.

This research will evaluate the effectiveness of glycolic versus salicylic acid chemical peels in the management of acne vulgaris, and therefore guide the development of evidence-based therapy for acne.

METHODS

This prospective, comparative clinical study was conducted in the Department of Dermatology, Lady Reading Hospital, Peshawar, from June 2023 to May 2024. A total of 120 patients with mild to moderate acne vulgaris presenting to the outpatient department were evaluated. Patients of both sexes, between 15 and 35 years of age, with at least three months of facial acne vulgaris, were included. Patients with nodulocystic acne, active facial infection, known allergy to peeling agents, history of keloid formation, pregnancy or breastfeeding, systemic retinoids used in the last six months, the use of topical anti-acne medication or chemical peels in the last four weeks, and those who refused to comply with follow-up were excluded from the study.

The sample size calculation was based on reported clinical efficacy of glycolic acid and salicylic acid peels in treating mild to moderate acne vulgaris with a 95% level of significance, 80% power and an estimated 20% difference in the response to treatment between the two groups. A sample size of 54 patients in each group was calculated; to allow for potential drop-outs, 60 patients were selected in each group, totalling 120 patients.

Following informed written consent, subjects were equally divided into two groups by computer-generated random number sequence. Group "A" (n=60) was treated with glycolic acid peel, and group "B" (n=60) with salicylic acid peel. Demographic data, duration of acne, skin type, acne severity and total lesion count were assessed on a proforma before starting the procedure. The Global Acne Grading System was used to score acne severity and the number of facial lesions were counted as comedones, papules, pustules and nodules.

The face was cleaned and degreased prior to each peel. In Group A, glycolic acid peel was applied in a fixed concentration depending on tolerance (starting with 35% and increasing gradually if needed). In Group B, salicylic acid peel was applied in a concentration of 20% to 30% according to tolerance and effectiveness. The peel was applied evenly to the affected areas on the face, except the periorbital and mucosal area. The peel was left on for a brief period of time during the first treatment and then prolonged in subsequent treatments based on erythema, burning, frosting, and tolerance. Glycolic acid peel was neutralized with sodium bicarbonate solution but salicylic acid peel was left to self-neutralize and was then washed off. Bland moisturizer and sunscreen were applied after the peel.

The patients were treated with six peeling sessions, two weeks apart. Patients were instructed to avoid prolonged sun exposure, scrubbing, waxing, bleaching products and unsupervised topical acne treatment during the period of study. Non-comedogenic moisturizer and sunscreen were recommended during the treatment period. The subjects were assessed at baseline and weeks 4, 8 and 12. The primary outcome was the percentage change in the total number of acne lesions between the baseline and week 12. Secondary outcomes were reduction in Global Acne Grading System score, inflammatory and non-inflammatory lesion count, patient satisfaction, and rate of adverse effects (erythema, burning, dryness, peeling, post-inflammatory hyperpigmentation, acne flare).

SPSS version 26.0 was used for data analysis. Continuous variables like age, acne duration, numbers of lesions, and Global Acne Grading System score were represented as mean ± standard deviation. Categorical variables (gender, skin type, response to treatment, and adverse effects) were presented as frequency and percentage. Paired t-test was used for within-group comparison (pretreatment vs. post-treatment) and independent sample t-test was used for between-group analysis. Categorial variables were compared using chi-square test. P-value ≤ 0.05 was considered statistically significant.

RESULTS

There was no significant difference between the two groups in the baseline demographic parameters or severity of acne, implying homogeneity of the study groups. The data are presented in Table-1.

Table No. 1: Baseline Characteristics

Variable	Group A (n=60)	Group B (n=60)	p-value
Age (years, mean ± SD)	22.6 ± 3.8	23.1 ± 3.5	0.48
Gender (Male/Female)	25 / 35	27 / 33	0.71
Duration of Acne (months)	14.2 ± 5.1	13.8 ± 4.7	0.62
Baseline TLC (mean ± SD)	29.4 ± 6.5	30.1 ± 6.2	0.54
Baseline GAGS Score	23.8 ± 4.2	24.1 ± 4.0	0.66

Both groups were statistically comparable at baseline ($p > 0.05$).

There was a gradual decrease in the total lesion count over time in both groups. Although both groups showed a reduction, salicylic acid group showed a faster response, especially in the initial visits. Table-2

Table No. 2: Reduction in Total Lesion Count (TLC)

Time Point	Group A (mean ± SD)	Group B (mean ± SD)	p-value
Baseline	29.4 ± 6.5	30.1 ± 6.2	—
Week 4	21.2 ± 5.8	18.4 ± 5.3	0.03
Week 8	13.6 ± 4.7	10.9 ± 4.2	0.02
Week 12	8.5 ± 3.9	6.7 ± 3.5	0.07

Within treatment groups, both treatments demonstrated significant reduction ($p < 0.001$) and between group comparison demonstrated early and superior efficacy of salicylic acid.

At the end of the study, both groups showed marked percentage reduction, with a slightly greater mean reduction with salicylic acid. Table-3

Table No. 3: Percentage Reduction in Lesion Count at Week 12

Group	Mean % Reduction	p-value
Glycolic Acid	71.1% ± 9.3	
Salicylic Acid	77.8% ± 8.7	0.01

Similarly, the acne severity scores were reduced in both groups, although slightly more in the salicylic acid group. Table-4

Table No. 4: Change in GAGS Score

Time Point	Glycolic Acid	Salicylic Acid	p-value
Baseline	23.8 ± 4.2	24.1 ± 4.0	—
Week 12	9.2 ± 3.1	7.6 ± 2.8	0.02

In terms of response levels, more patients in the salicylic acid group showed excellent response than those in the glycolic acid group. Table-5

Table No. 5: Treatment Response at Week 12

Response Category	Glycolic Acid (n=60)	Salicylic Acid (n=60)
Excellent (>75%)	28 (46.7%)	36 (60.0%)
Good (50–75%)	22 (36.7%)	18 (30.0%)
Moderate (25–50%)	10 (16.6%)	6 (10.0%)
Poor (<25%)	0	0

The products were well tolerated, with mild, transient side effects in some patients. Slightly more erythema and irritation were reported with glycolic acid. Table-6

Table No. 6: Adverse Effects

Side Effect	Group A	Group B
Erythema	11 (18.3%)	8 (13.3%)
Burning Sensation	13 (21.7%)	10 (16.7%)
Peeling	18 (30.0%)	15 (25.0%)
Post-inflammatory Hyperpigmentation	4 (6.7%)	3 (5.0%)

DISCUSSION

In this study, both glycolic acid and salicylic acid peels resulted in significant improvement in mild to moderate acne vulgaris; however, salicylic acid resulted in a faster and slightly better improvement in total lesion count and acne severity index (GAGS). This is physiologically justifiable, as salicylic acid is lipophilic and can better penetrate the pilosebaceous unit to exert comedolytic, keratolytic and anti-inflammatory effects. This is why we found the salicylic acid group improved earlier, at weeks 4 and 8.

Our results are in agreement with Manjhi et al. who used 35% glycolic acid and 30% salicylic acid in 120 patients and found better response with the latter in mild to moderate acne[10]. Their groups were comparable at baseline, similar to our study, and supports the conclusion that the response was due to the peeling agent. Garg et al also found superior improvement with 30% salicylic acid compared with 70% glycolic acid in active acne, supporting our finding that salicylic acid may be a better choice for active inflammatory acne[11].

Our findings also support Bhate et al, who reported that 70% glycolic acid and 30% salicylic acid were effective, but salicylic acid had a better clinical response in patients with mild to moderate acne[12]. Williams et al, also found good results with 30% salicylic acid and 50% glycolic acid and salicylic acid resulted in a quicker improvement of inflammatory lesions during early visits[13]. This is similar to our findings, where the effect was more evident in early follow-up visits and less evident at week 12.

The explanation of the early efficacy of salicylic acid is probably its oil-soluble nature and the ability to penetrate follicles. Acne is based on follicular occlusion, sebum retention and inflammation; thus, a drug that penetrates the sebaceous follicle can exert a more direct action on the site of inflammation. By contrast, glycolic acid is water-soluble and acts primarily via epidermal exfoliation, decreased corneocyte cohesion and improved skin texture. This accounts for why glycolic acid still had good improvement in acne, but more delayed improvement in inflammatory lesions.

Our findings differ slightly from studies which report similar efficacy of glycolic acid and salicylic acid peels. Almeman et al, using a split-face design, found improvement with both acids[14]. This may be explained by the split-face design, small sample size, short duration of follow-up, different concentrations, and low variability. In our parallel-group study, the individual factors including skin type, sebum production, sunscreen compliance and duration of acne may have contributed to the response.

Both groups had good safety profiles in our study. The most common side effects were mild erythema, burning, peeling and dryness, which were treated conservatively. This is in line with Li et al, who found superficial chemical peels to be safe if carefully chosen and monitored[15]. The marginally higher irritation in the glycolic acid group might be due to lower pH-dependent penetration into the epidermis, requiring

neutralization, while salicylic acid neutralises itself after crystallisation.

The rare incidence of post-inflammatory hyper-pigmentation in both groups is significant, as most of our Pakistani patients have Fitzpatrick skin types IV-V, for whom pigmentary complications are an important consideration. The recent focus on post-inflammatory hyperpigmentation in acne supports cautious use of superficial peels, e.g. glycolic acid and salicylic acid, in the right patients, particularly with photoprotection[16,17]. This may account for the low frequency of pigmentary complications in our study.

The results of our study must also be considered in the context of current acne guidelines. The 2024 American Academy of Dermatology guidelines place high value on evidence-based drug therapy as the cornerstone for acne treatment and view procedures like peels as adjunct to an acne treatment plan[18]. Therefore, the practical implication of our study is not that the salicylic acid peel should be used instead of the conventional acnes therapy, but rather that the salicylic acid peel can be a choice in patients with oily skin, comedonal acne, and active inflammatory lesions, whereas the glycolic acid one can be applied where post-acne pigmentation and texture irregularity are most evident.

In summary, the findings support the conclusion that both glycolic acid and salicylic acid peels are effective and well-tolerated in mild-to-moderate acne vulgaris, with quicker improvement from salicylic acid peel. The variability in studies is largely due to variations in the concentration of peels, number of peel sessions, severity of acne, skin phototypes, scoring systems used and whether peels were applied alone or in conjunction with topical treatment.

CONCLUSION

Glycolic acid and salicylic acid chemical peels were both effective and safe in decreasing the number of acnes lesions and the severity of acne in patients with mild to moderate acne vulgaris, but salicylic acid had a faster onset of action, higher percentage reduction of the total number lesions, and a higher proportion of excellent clinical response. Glycolic acid also showed a considerable improvement and could be a viable alternative especially in patients with post-acnes textural and pigmentary issues. Thus, salicylic acid could be the choice in cases of active inflammatory acne and both peels can be used as a supportive treatment in the right patients.

Author's Contribution:

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Drafting or Revising Critically:	Kashmala Asghar Khan, Nuzhat Naheed
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Impact of the Convalescent Rehabilitation Medical Hospital System on Functional Recovery in Stroke Patients: A Retrospective Cohort Study

Kyung-Sub Choi, Bong-Sik Woo and Dae-Hwan Lee

ABSTRACT

Objective: To investigate whether the implementation of the convalescent rehabilitation medical hospital system was associated with improved functional outcomes in stroke patients undergoing post-acute rehabilitation.

Study Design: A Retrospective cohort study

Place and Duration of Study: This study was conducted at the Rehabilitation department, IM Rehabilitation Hospital, from May 15, 2025, to December 22, 2025.

Methods: This study was a retrospective cohort study using electronic medical records (EMR). Stroke patients admitted to a rehabilitation hospital within 90 days after stroke onset were included. Participants were divided into two groups according to the implementation of the convalescent rehabilitation medical hospital system: patients treated before implementation (Group 1, n=107) and patients treated after implementation (Group 2, n=52). Functional outcomes were evaluated at admission, 4 weeks, and 8 weeks using the Mini-Mental State Examination (MMSE), Modified Barthel Index (MBI), and Hand Function Test (HFT).

Results: The improvement in activities of daily living was significantly greater in Group 2 than in Group 1 (MBI change: 12.39 ± 11.83 vs. 2.92 ± 4.87, $p < 0.001$; Cohen's $d = 1.21$). Upper limb function also showed greater improvement in Group 2 (HFT change: 2.59 ± 3.74 vs. 0.87 ± 2.58, $p = 0.004$; Cohen's $d = 0.57$). However, changes in cognitive function measured by MMSE did not differ significantly between the groups ($p = 0.055$).

Conclusion: The implementation of the convalescent rehabilitation medical hospital system was associated with greater improvements in activities of daily living and upper limb function in stroke patients. These findings suggest that structured intensive rehabilitation during the post-acute recovery phase may enhance functional outcomes after stroke.

Key Words: Stroke, Rehabilitation, Convalescent rehabilitation, Activities of daily living, Electronic medical records

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INTRODUCTION

Stroke is a major neurological disorder caused by an interruption of cerebral blood flow or rupture of cerebral vessels, leading to focal ischemic or hemorrhagic injury and subsequent neuronal damage. Stroke commonly results in persistent impairments across multiple domains, including motor and sensory function, cognition, language, swallowing, and emotional regulation. These deficits substantially limit functional independence and reduce quality of life [1].

A substantial proportion of stroke patients experience limitations in mobility and activities of daily living following the onset of the disease. Hemiparesis, a common sequela of stroke, causes motor and sensory impairments on the contralateral side of the body. In particular, upper limb dysfunction directly interferes with activities of daily living (ADL), including personal hygiene, dressing, and feeding. Impairments in finger control and object manipulation further restrict instrumental activities of daily living (IADL), such as meal preparation, community participation, and return to work [2]. Lower limb impairments are also common and often involve muscle weakness, spasticity, and impaired motor coordination. These deficits lead to asymmetric weight bearing, abnormal gait patterns, decreased postural stability, and an increased risk of falls. In addition, cognitive impairments frequently occur after stroke and may affect attention, memory, and executive function, thereby limiting participation in

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rehabilitation and delaying reintegration into independent living.

Early and intensive rehabilitation is considered essential for improving functional recovery after stroke. During the early recovery phase, neural plasticity is highly active, and repetitive, task-oriented training can facilitate reorganization of neural networks and enhance functional restoration[3,4]. Intensive rehabilitation programs can therefore contribute not only to improvements in motor performance but also to gains in balance, gait ability, cognitive function, and independence in daily activities.

However, the Korean healthcare system has historically been organized around acute medical care, which has limited the provision of continuous and structured rehabilitation during the post-acute recovery phase after stroke [5]. Following acute treatment, many patients are discharged from tertiary hospitals at an early stage, while the healthcare delivery system for post-acute rehabilitation has not been sufficiently established. As a result, access to intensive rehabilitation during the critical recovery phase after stroke has remained limited[3].

This policy was introduced to address these challenges. In 2017, the Korean Ministry of Health and Welfare established the convalescent rehabilitation medical hospital system under Article 18 of the Act on the Right to Health for Persons with Disabilities and Access to Medical Services [6]. The system was designed to provide intensive rehabilitation during the subacute recovery phase, particularly for patients with neurological conditions such as stroke. For stroke patients, the period between approximately 30 and 90 days after onset is considered a critical recovery phase during which neural plasticity is highly active. Intensive and task-oriented rehabilitation during this period is known to play a crucial role in promoting functional recovery. The convalescent rehabilitation medical hospital system therefore aims to provide structured multidisciplinary rehabilitation during this optimal recovery window. Within this system, patients can receive up to 16 units (approximately 4 hours) of rehabilitation therapy per day through coordinated services including physical therapy, occupational therapy, and speech therapy. These interventions are designed to improve motor function, cognitive function, communication ability, and independence in activities of daily living [6, 7]. By ensuring continuity of rehabilitation following acute hospital care, the system seeks to reduce gaps in rehabilitation services and enable stroke patients to receive intensive therapy during the most critical phase of recovery.

Despite the policy significance of this system, empirical evidence evaluating its clinical effectiveness remains limited. In particular, few studies have quantitatively examined functional recovery by comparing patient outcomes before and after the implementation of the convalescent rehabilitation system. Therefore, the purpose of this study was to investigate the impact of the convalescent rehabilitation medical hospital system on functional recovery in stroke patients by comparing changes in cognitive function, activities of daily living, and upper limb function between patients treated before and after the implementation of the system.

METHODS

This study was designed as a retrospective cohort study using electronic medical records(EMR) to compare functional recovery in stroke patients before and after the implementation of the convalescent rehabilitation medical hospital system. Clinical data were collected at three time points: at admission, 4 weeks after admission, and 8 weeks after admission. Changes in cognitive function, activities of daily living, and upper limb function were analyzed over time and compared between the two groups.

The study included patients who were admitted to IM Rehabilitation Hospital and diagnosed with stroke. Only patients who were admitted within 90 days after stroke onset and received inpatient rehabilitation treatment were considered for inclusion in the study. Participants were divided into two groups according to the implementation of the convalescent rehabilitation medical hospital system. Group 1 consisted of patients who received rehabilitation treatment before the implementation of the system, whereas Group 2 consisted of patients who were treated after the implementation.

Patients were eligible for inclusion if they met the following criteria: a confirmed diagnosis of stroke, admission within 90 days after stroke onset, hospitalization for at least 8 weeks, and availability of functional assessment data at three time points (at admission, 4 weeks after admission, and 8 weeks after admission). Patients were excluded if they had severe cardiovascular disease, progressive neurodegenerative disease, or psychiatric disorders that could affect rehabilitation outcomes. Patients were also excluded if they were unable to cooperate with the evaluation procedures, had a Glasgow Coma Scale score below 12, or were able to ambulate independently at the time of admission.

Both groups received multidisciplinary rehabilitation treatment. The rehabilitation program consisted of physical therapy, occupational therapy, speech therapy, and robot-assisted gait training. Physical therapy focused on lower extremity strengthening, balance training, gait training, mat exercises, and neurodevelopmental treatment. Occupational therapy was performed to improve upper limb function through grasping exercises, manipulation tasks, and activities of daily living training. Robot-assisted gait training was performed using devices such as Morning Walk, Lokomat, and Andago to facilitate early standing and

repetitive weight-shifting training. Group 1 received a total of 15 treatment units per day, with each unit consisting of 15 minutes of therapy. Group 2 received intensive rehabilitation treatment according to the convalescent rehabilitation medical hospital system.

Cognitive function was evaluated using the Mini-Mental State Examination (MMSE). Activities of daily living were assessed using the Modified Barthel Index (MBI). Upper limb function was evaluated using the Manual Function Test (HFT). Continuous variables were summarized as mean ± standard deviation.

All statistical analyses were performed using SPSS for Windows (version 25.0, IBM Corp., Armonk, NY, USA). Longitudinal changes in MMSE, MBI, and HFT across admission, 4 weeks, and 8 weeks were analyzed using linear mixed-effects models including group, time, and group-by-time interaction terms. In addition, analysis of covariance (ANCOVA) was performed to compare post-intervention (8-week) outcomes between groups after adjusting for baseline values. Baseline demographic and clinical variables were compared using the independent t-test, chi-square test, or Mann–Whitney U test, as appropriate.

RESULTS

The baseline characteristics of the participants are presented in Table 1. A total of 159 patients were included in the study, with 107 patients in Group 1 (before implementation) and 52 patients in Group 2 (after implementation). The mean age was significantly lower in Group 2 than in Group 1 (66.62 ± 15.77 vs. 73.41 ± 12.98 years, p = 0.008). There was no significant difference in sex distribution between the two groups (p = 0.113). The proportion of patients diagnosed with cerebral infarction was higher than that of cerebral hemorrhage in both groups, with no significant difference between groups (p = 0.276). The mean length of hospital stay was significantly shorter in Group 2 than in Group 1 (116.44 ± 48.68 vs. 318.42 ± 305.62 days, p < 0.001) (Table No.1).

Table No.1: General characteristics of subjects

Contents	Group 1 (n=107)	Group 2 (n=52)	*p*
Age	73.41 ± 7.43	66.62 ± 15.77	0.008*
Sex (male/female)	50 / 57	32 / 20	0.113
Diagnosis (ischemic/hemorrhage)	63 / 44	36 / 16	0.276
Length of stay (day)	318.42 ± 305.62	116.44 ± 48.68	< 0.001*

For cognitive function, MMSE scores were higher in Group 2 than in Group 1 at all times points. However, the difference between the groups reached statistical significance only at 8 weeks (p = 0.055). For activities of daily living, MBI scores were significantly higher in Group 2 than in Group 1 at admission, 4 weeks, and 8 weeks (all p < 0.001). The effect size increased over time, reaching a large effect at 8 weeks (Cohen's d = 1.21). Similarly, upper limb function measured by HFT was significantly higher in Group 2 than in Group 1 at all times points (p = 0.004 at admission, p = 0.002 at 4 weeks, and p = 0.004 at 8 weeks) (Table No.2).

Table No.2: Changes in functional outcomes at admission, 4 weeks, and 8 weeks

Measure	Time points	Group 1 (n=107)	Group 2 (n=52)	*p*	*Cohen' d*
MMSE (point)	Admission	17.05 ± 9.63	20.56 ± 7.67	0.090	0.33
	4 weeks	18.07 ± 10.35	21.46 ± 7.58	0.058	0.39
	8 weeks	18.81 ± 9.61	22.81 ± 6.87	0.055	0.45
MBI (score)	Admission	32.05 ± 24.91	51.90 ± 19.87	<0.001***	0.86
	4 weeks	32.84 ± 25.23	57.81 ± 21.83	<0.001***	1.02
	8 weeks	34.97 ± 25.33	64.29 ± 22.15	<0.001***	1.21
HFT (score)	Admission	10.68 ± 11.01	18.35 ± 7.60	0.004**	0.69
	4 weeks	10.94 ± 11.24	19.73 ± 7.19	0.002**	0.73
	8 weeks	11.55 ± 11.31	20.94 ± 6.46	0.004**	0.57

In the linear mixed-effects model, significant group-by-time interactions were observed for MBI and HFT scores, indicating that functional recovery trajectories differed significantly between the two groups over the

Table No.3: Linear mixed-effects model results for changes in MMSE, MBI, and HFT scores

Contents	Group effect β	*p*	Time effect β	*p*	Time x group β	*p*
MMSE	3.147	0.050	0.641	0.100	0.419	0.381
MBI	15.254	<0.001***	-3.267	<0.001***	4.730	<0.001***
HFT	6.887	<0.001***	-0.429	0.137	0.863	<0.001***

8-week follow-up period. In contrast, no significant group-by-time interaction was found for MMSE scores, suggesting that cognitive recovery patterns did not differ significantly according to implementation status (Table No.3).

Table No.4: ANCOVA results for post-intervention MMSE, MBI, and HFT scores adjusted for baseline value and age

Contents	Group effect			Adjust for baseline			Adjust for age		
	F	*p*	Partial η^2	F	*p*	Partial η^2	F	*p*	Partial η^2
8-week MMSE	1.167	0.282	0.007	931.218	<0.001***	0.857	4.539	0.035**	0.028
8-week MBI	44.453	<0.001	0.223	1173.540	<0.001***	0.883	2.618	0.108	0.017
8-week HFT	13.106	<0.001	0.078	1611.628	<0.001***	0.912	0.886	0.348	0.006

After adjusting for baseline MMSE and age using ANCOVA, no significant difference was observed between the groups in MMSE scores at 8 weeks ($F = 1.167$, $p = 0.282$, partial $\eta^2 = 0.007$). Baseline MMSE was a significant predictor of the 8-week outcome ($F = 931.218$, $p < 0.001$), and age also showed a significant but small effect ($F = 4.539$, $p = 0.035$). After adjusting for baseline MBI and age using ANCOVA, the post-implementation group showed significantly higher MBI scores at 8 weeks compared to the pre-implementation group ($F = 44.453$, $p < 0.001$, partial $\eta^2 = 0.223$). Baseline MBI was a significant predictor of the 8-week outcome ($F = 1173.540$, $p < 0.001$), whereas age was not significantly associated with MBI scores ($F = 2.618$, $p = 0.108$). After adjusting for baseline HFT and age using ANCOVA, the post-implementation group showed significantly higher HFT scores at 8 weeks compared to the pre-implementation group ($F = 13.106$, $p < 0.001$, partial $\eta^2 = 0.078$). Baseline HFT was a significant predictor of the outcome ($F = 1611.628$, $p < 0.001$), whereas age was not significantly associated with HFT scores ($F = 0.886$, $p = 0.348$) (Table No.4)

DISCUSSION

The present study investigated the impact of the convalescent rehabilitation medical hospital system on functional recovery in stroke patients using electronic medical record data. The main findings of this study were that patients who received rehabilitation treatment after the implementation of the convalescent rehabilitation system showed significantly greater improvements in activities of daily living and upper limb function compared with patients treated before the implementation of the system. However, improvements in cognitive function did not differ significantly between the two groups.

One of the most notable findings of this study was the significant improvement in activities of daily living measured by the MBI. The change in MBI scores was significantly greater in the post-implementation group than in the pre-implementation group, with a large effect size. This result suggests that the structured and intensive rehabilitation provided under the convalescent rehabilitation medical hospital system may contribute substantially to improving functional independence in stroke patients [5, 7, 8]. Activities of daily living are considered one of the most important indicators of functional recovery after stroke, as they directly reflect a patient's ability to perform essential self-care tasks and participate in daily life [8-10].

Upper limb function measured by the HFT also showed significantly greater improvement in the post-implementation group, with a moderate effect size. Recovery of upper limb function after stroke is often challenging due to complex motor control requirements and the high prevalence of persistent hemiparesis. The greater improvement observed in the post-implementation group may be associated with increased intensity and multidisciplinary rehabilitation approaches, including task-oriented occupational therapy and robot-assisted gait training, which may indirectly promote upper limb functional use during rehabilitation [6, 11].

In contrast, the change in cognitive function measured by the MMSE did not differ significantly between the two groups. Cognitive recovery after stroke is influenced by multiple factors, including lesion location, severity of brain injury, and premorbid cognitive status [12]. Furthermore, cognitive improvement often occurs over a longer period compared with motor recovery [13]. Therefore, the relatively short observation period of eight weeks in this study may not have been sufficient to detect significant differences in cognitive outcomes between the two groups.

Another important finding of this study was the significant reduction in the length of hospital stay observed after the implementation of the convalescent rehabilitation medical hospital system. This difference should be interpreted in the context of changes in the rehabilitation delivery system in Korea. Prior to the implementation of the convalescent rehabilitation system, inpatient rehabilitation often continued for prolonged periods without a standardized framework for intensive rehabilitation or structured discharge planning. In contrast, the convalescent rehabilitation system introduced a structured rehabilitation model with defined treatment intensity and a clearer transition pathway following the subacute rehabilitation phase [5-7]. These changes may have contributed to a more

efficient rehabilitation process and earlier discharge while maintaining functional recovery. By providing intensive rehabilitation during the critical recovery period after stroke, the system may facilitate earlier functional improvement and transition to community-based care [7, 14]. Therefore, the shorter length of hospital stay observed in the post-implementation group may reflect changes in healthcare policy, admission criteria, and discharge planning processes rather than rehabilitation efficiency alone.

In the linear mixed-effects model, significant group effects were observed for MBI and HFT, indicating overall superior functional performance in the post-implementation group. Significant group-by-time interactions were also identified for MBI and HFT, suggesting that improvements over time were greater in the post-implementation group. However, no significant group-by-time interaction was found for MMSE. To further control for baseline differences, ANCOVA was performed using the 8-week score as the dependent variable and adjusting for baseline values and age as covariates. After adjustment, MBI and HFT remained significantly higher in the post-implementation group, whereas MMSE did not differ significantly between groups [15]. Although significant baseline differences were observed between the groups, particularly in age and initial functional status, these were statistically controlled using ANCOVA. The persistence of significant group differences in MBI and HFT after adjustment suggests that the observed effects are unlikely to be solely explained by baseline imbalance.

Despite these findings, several limitations should be considered when interpreting the results of this study. First, this study was conducted using a retrospective design based on electronic medical records from a single rehabilitation hospital, which may limit the generalizability of the findings. Second, baseline differences between the two groups, particularly in age, may have influenced the observed outcomes. Third, the study evaluated functional outcomes over a relatively short follow-up period of eight weeks, which may not fully capture long-term recovery patterns after stroke.

Nevertheless, this study provides meaningful evidence regarding the potential clinical benefits of the convalescent rehabilitation medical hospital system for stroke patients. The findings suggest that structured and intensive rehabilitation during the post-acute recovery phase may play an important role in improving functional outcomes, particularly in activities of daily living and upper limb function.

CONCLUSION

The present study demonstrated that the implementation of the convalescent rehabilitation medical hospital system was associated with greater improvements in activities of daily living and upper limb function in stroke patients. These findings suggest that structured and intensive rehabilitation during the post-acute phase may play an important role in enhancing functional recovery after stroke. Further multicenter prospective studies are needed to confirm these findings.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Kyung-Sub Choi, Bong-Sik Woo, Dae-Hwan Lee
Drafting or Revising Critically:	Kyung-Sub Choi, Bong-Sik Woo, Dae-Hwan Lee
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Actual versus Predicted Overall Survival in Patients Treated Surgically for Metastatic Spinal Cord Compression

Zaid Sami Ullah, Oliver Bates, Namwa Wongkalasin, Jasmeet Dhir and Marcin Czyz

ABSTRACT

Objective: To compare the predicted survivals based on Tokuhashi and Tomita scores, as well as clinical estimates by the oncologist, with the actual observed survival

Study Design: A retrospective observational study

Place and Duration of Study: This study was conducted at the Queen Elizabeth Hospital, Birmingham, UK between 20th June 2025 to 19th October 2025.

Methods: This was a retrospective observational study was carried out at Queen Elizabeth Hospital, Birmingham, UK between 20th June 2025 to 19th October 2025 of 32 patients treated surgically for metastatic spinal cord compression.

Results: A Cox proportional hazards model found Tokuhashi and Tomita scores to have negative predictive values. Log-rank tests demonstrated p-values <0.05 in the comparison of outcomes with Tokuhashi, Tomita and oncological expert predictions, indicating significant differences between predicted and actual survival. Spearman's correlation coefficient showed a moderate positive correlation between Tokuhashi predictions and observed survival (p= 0.017), while Tomita predictions showed no correlation with observed survival (p = 0.893). The discriminatory predictive performance of the two scoring systems revealed areas under the curve of 0.57 and 0.369 for Tomita and Tokuhashi, respectively. Both showed slight non-specific agreement with actual survival outcomes, with kappa values of 0.04 and 0.07, respectively.

Conclusion: While both of these scoring system prognostic models can serve as guides to likely outcomes, they lacked predictive accuracy in our cohort. We recommend the development of more robust, individualised survival prediction tools for preoperative treatment planning in MSCC patients.

Key Words: Metastatic spinal canal compression, Prognostic assessment in oncology, Spinal metastasis, Survival estimation, Tokuhashi scoring system, Tomita scoring system

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INTRODUCTION

Metastatic spinal canal compression (MSCC) is a serious, devastating complication of advanced-stage malignancy with an established primary site that can present as severe back pain and neurological deficits. Surgical treatment in terms of decompression and stabilization helps to relieve the pain, halt further neurologic deterioration, and restore the baseline functionality.

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Pre-operative proper selection of patients for surgical intervention remains challenging to reduce the untoward risks of surgical morbidity and mortality.[1] Predicting the survival prognosis in MSCC patients is very crucial. For this, different prognostic prediction tools remain familiar to the Neurosurgeons, including Modified Tokuhashi, Tomita, and Bauer scoring systems, each incorporating variable characters and interpretation for survival predictions.[2] Although the old prognostic classification models for MSCC prognosis give an idea in preoperative decision making for management strategies for their continued correlation with actual observed survival needs revalidations and refinements to guide a more realistic prognosis.[3-5]

The purpose this study is to compare the survival predictions in surgically managed MSSC patients provided by the prognostic tools like Tokuhashi and Tomita, as well as by the oncological clinical estimates, with the actual observed survival, i.e., from the time of intervention till last follow-up or death. In this way, we also want to pinpoint the factors that could cause the discrepancies in prediction and reality and recommend

the further incorporation of broader parameters in these models to improve the survival predictions in MSCC patients.

METHODS

This retrospective study was at the Queen Elizabeth Hospital, Birmingham, UK, between November 2019 to December 2024 vide letter CPSP/REU/NSG-2023-250-964 dated June 16, 2025 and 32 adult patients who underwent surgery for metastatic spinal canal compression consecutive non-probability sampling was used. The clinical data of the patients were recorded. The Tokuhahsi and Tomita scores were calculated for all patients based on the individual parameters of the respective models. Pre- and postoperative neurological examination findings were recorded for Frankel grading.[6] Oncological estimates were recorded from oncology clinic letters, but they varied in format. Some of the patients had no documented oncological prognosis. Actual survival was defined as the time from surgery to death was recorded in months. Data were analysed using the SPSS-2025. The Cox's proportional hazards model to evaluate the predictive value of the scoring systems was used. Spearman's rank correlation coefficient to determine the correlations between the predictive approaches and the outcomes and Cohen's kappa to establish the level of agreement and Kaplan–Meier curves and the log-rank test to graphically plot survival distribution over time. The discriminatory performance of the prediction models by plotting the receiver operating characteristic (ROC) and area under the curve (AUC) values. *P*-values ≤0.05 were considered statistically significant.

RESULTS

The mean age was 59.9±11.8 years and 19 (59.4%) of the 32 patients were male. The most common primary cancer was renal cell carcinoma, accounting for 21.88% of cases, followed by prostate and rectal cancer. Preoperative neurological function was assessed using the Frankel scale. There were 18 (56.25%) of the cases had Frankel grade E, 7 (21.88%) had Frankel grade D, 4 (12.5%) had Frankel grade C and 3 (9.38%) had Frankel grade B. The mean postoperative survival time was 9.73±10.6 months. At the mean final follow-up of 6-12 months, 50% of the patients were alive and 50% were deceased. (Tables 1-2).

Table No. 1: Demographic and clinical characteristics of the cohort (n = 32)

Variable	No.	%
Gender		
Male	19	59.40
Female	13	40.63
Visceral metastasis		
Present	15	46.90
Absent	17	53.13
Preoperative Frankel grade		
Grade B	3	9.38
Grade C	4	12.50
Grade D	7	21.88
Grade E	18	56.30
Postoperative Frankel grade		
Grade C	5	15.63
Grade D	9	28.13
Grade E	18	56.25
Survival status at last follow-up		
Alive	16	50.00
Deceased	16	50.00
Primary cancer site		
Renal cell carcinoma	7	21.88
Prostate	4	12.5
Colorectal	4	12.5
Thyroid	3	9.38
Lung	2	6.25
Other (each <5%)*	12	37.49

Cox proportional hazards modelling revealed a regression coefficient of −1.82 and a hazard ratio (HR) of 0.16 (p = 0.205) for the Tokuhashi predictions. The Tomita predictions had a regression coefficient of 0.42 and an HR of 1.52 (p= 0.759). Both demonstrated negative prognostic predictive value. Log-rank tests found p-values of <0.001, 0.01 and 0.04 for the Tokuhashi, Tomita and oncological expert predictions and therefore rejected the null hypothesis that there was no difference between the survival predictions of these model groups. However, it should be borne in mind that there was some bias in the oncology predictions due to variations in the data format used in the medical records and our arbitrary selection of the values (some patients had no documented oncological prognosis) Figures.1-2. Spearman's rank correlation coefficients showed a moderate, positive correlation between Tokuhashi scores and real survival outcomes (r[30] = 0.38, p = 0.017). Tomita predictions were negatively correlated with survival outcomes (r[30] = −0.02, p = 0.893) Figures. 3-4.

Table No. 2: Patient variables, predictive system scores and survival outcomes

Variables	Mean±SD	Median	Range (min–max)
Age (years)	59.9±11.77	61	31–82
No. of spinal levels affected	2.09±1.35	2	1–6
Tokuhashi score	9.53±2.63	9	4–15
Tomita score	5.75±2.62	6	2–10
Postoperative survival time (months)	9.73±10.6	7	1–51

The discriminatory performance of each prediction system revealedthe Tokuhashi system to have higher

sensitivity and specificity (93% each) for survival predictions <6 months (AUC = 0.369). Comparatively, the Tomita system showed better sensitivity (81%) and specificity (93%) in predicting survival >24 months (AUC = 0.57) [Figs. 5-6]. Higher AUC values based on ROC curves indicate a better overall classification model.

Cohen's kappa revealed slight non-specific agreement for Tokuhashi and Tomita scores, with kappa values of 0.05 (p= 0.415) and 0.07 (p= 0.256), respectively. However, the non-significant p-values indicate that the observed concordance is likely attributable to chance.

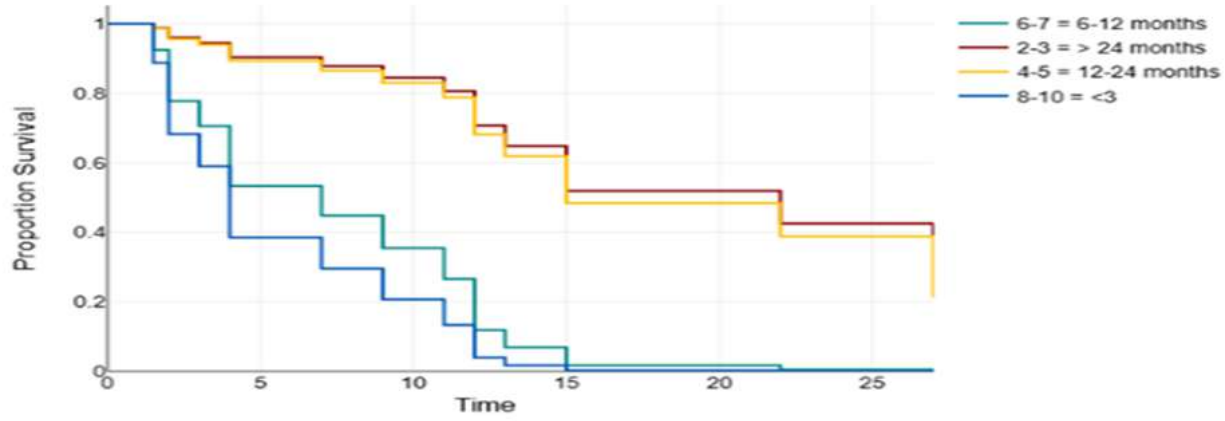

Figure No. 1: Kaplan–Meier curves showing Tomita system survival predictions for surgically-treated patients with metastatic spinal cord compression

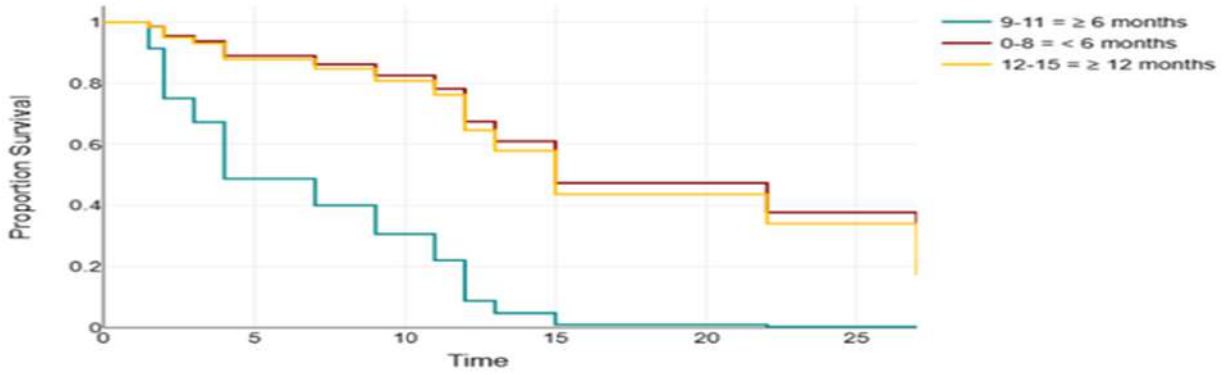

Figure No. 2: Kaplan–Meier curves showing Tokuhashi system survival predictions for surgically-treated patients with metastatic spinal cord compression

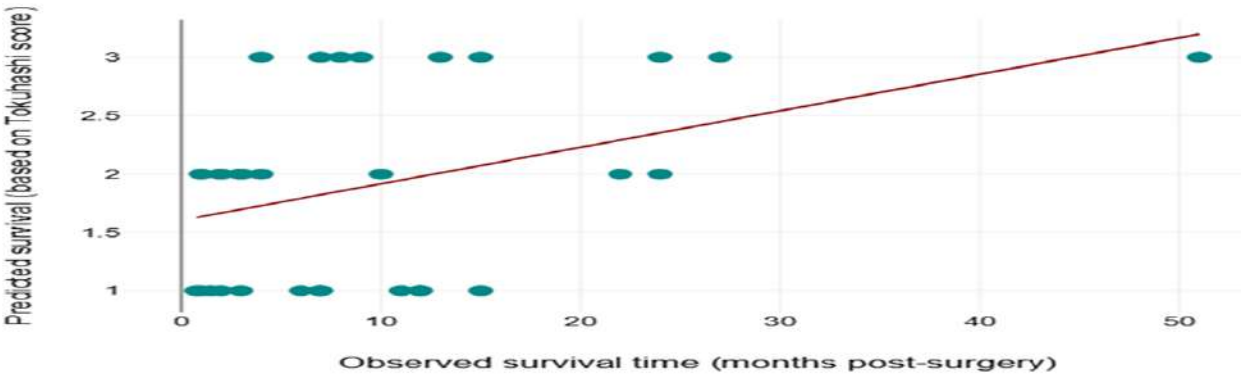

Figure No. 3: Spearman's rank correlation coefficients showing a moderate positive correlation between postoperative survival outcomes and Tokuhashi system survival predictions for surgically-treated patients with metastatic spinal cord compression

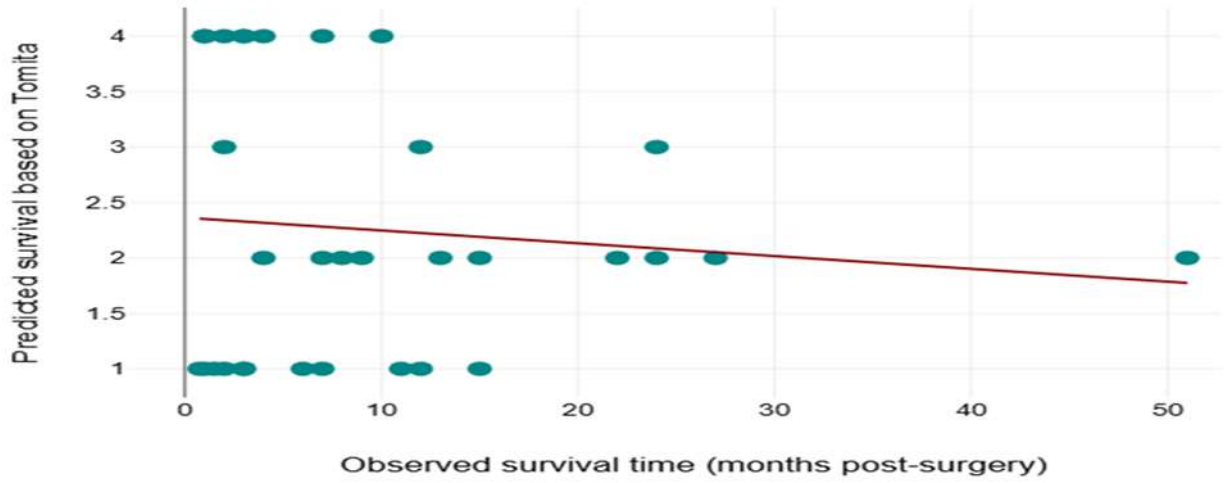

Figure No. 4: Spearman's rank correlation coefficients showing a negligible negative correlation between postoperative survival outcomes and Tomita system survival predictions for surgically-treated patients with metastatic spinal cord compression

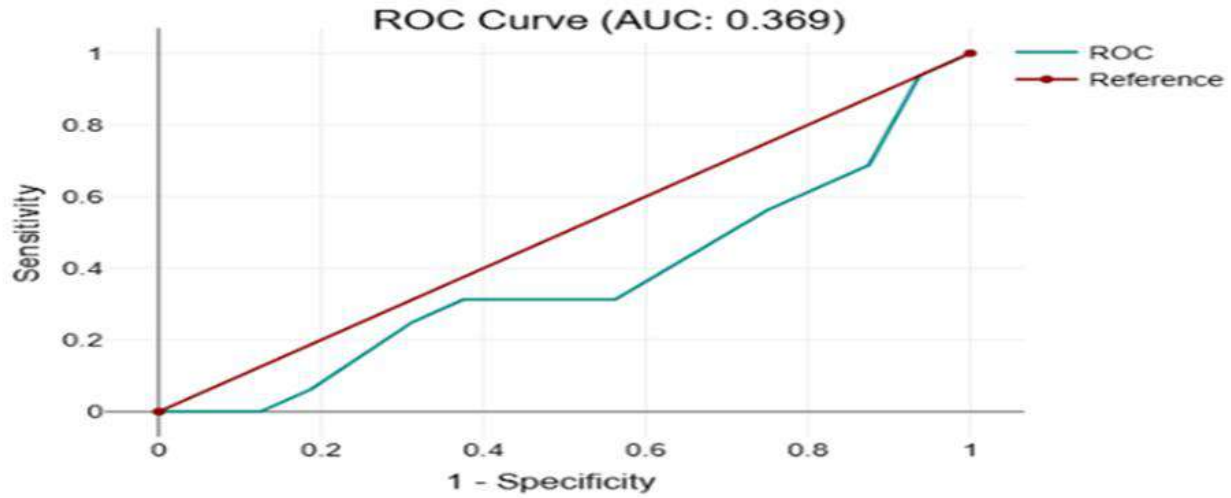

Figure No. 5: Discriminatory performance of Tokuhashi score survival predictions for surgically-treated patients with metastatic spinal cord compression AUC, area under the curve; ROC, receiver operating characteristic.

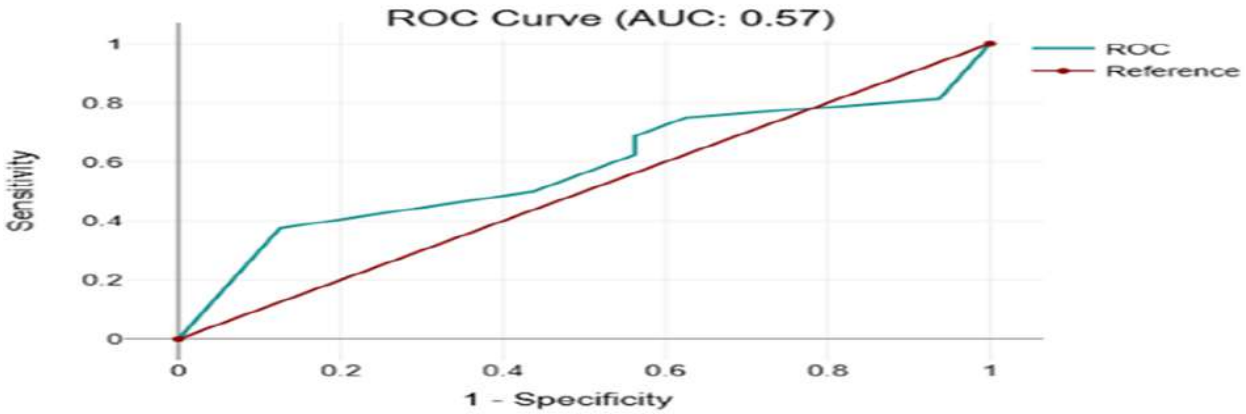

Figure No. 6: Discriminatory performance of Tomita score survival predictions for surgically-treated patients with metastatic spinal cord compression AUC, area under the curve; ROC, receiver operating characteristic

DISCUSSION

The comparisons of real survival outcomes with the predictive approaches used indicated that the Tokuhashi system had negative predictive value in our cohort. This conflict with the findings of Aoude et al[7] and Papastefanou et al[8], they found that, for patients with favourable prognoses, the modified Tokuhashi score demonstrates superior accuracy in survival duration prediction over the Tomita score. However, like us, Park et al[9], Quraishi et al[10] and Wang et al[11] found the predictive accuracy of the Tokuhashi system to be suboptimal (57.2%). They recommend the refinements of this system through the inclusion of more predictive parameters.

Tan et al[12,] Dardic et al[13] and Wibmer et al[14] compared four scoring systems and found the modified Tokuhashi score to exhibit the greatest predictive accuracy for survival. In the present study, both Tokuhashi and Tomita scores had negative predictive value but showed moderate, statistically significant correlations with actual survival. However, its overall discriminatory power was low (AUC = 0.369).[15,16]

We found that the survival estimates of attending oncologists lacked standardisation and were poor predictors of real-world outcomes. This contrasts with the findings of a previous report in which the prognostic assessments of oncologists accurately reflected the survival outcomes of consecutive MSCC patients.[17]

In concordance with our observations, Majeed et al[18] and Popovic et al[19] reported that prognostic scoring systems like Tokuhashi and Tomita are not uniformly accurate across all primary tumour types. Nevertheless, their integration of critical factors such as patient age, tumour type and stage and general health can facilitate surgical decision-making. In the present era of targeted therapies and immunotherapies, the variable performance of existing scoring systems observed in the present study highlights the need for more refined prognostic tools for use with this patient population.

CONCLUSION

While the Tokuhashi and Tomita prediction models offer reasonable general frameworks for preoperative survival predictions in surgically-treated patients with metastatic spinal canal compression, we found both to lack predictive accuracy in our cohort. We recommend re-auditing, ongoing refinement and standardisation of these approaches. Future research should focus on the development of more robust and accurate survival prediction tools, incorporating recent oncological treatment advances to optimise the selection of metastatic spinal canal compression patients for surgery.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Zaid Sami Ullah, Oliver Bates
Drafting or Revising Critically:	Namwa Wongkalasin, Jasmeet Dhir, Marcin Czyz
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Ethical Approval: No. CPSP/REU/NSG-2023-250-964 dated 16.06.2025

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Original Article

Vulvovaginal Candidiasis During Pregnancy: An Integrated Analysis of Hormonal and Immunological Interplay

Hormonal and Immunological Interplay in VVC

Ali Fayez Noor[1], Abdulameer Jasim Mohammed[1] and Omar Sadik Shalal[1]

ABSTRACT

Objective: To investigate the combined immunological and hormonal alterations associated with pregnancy-associated vulvovaginal candidiasis (VVC).

Study Design: A case control study

Place and Duration of Study: This study was conducted at the College of Health and Medical Technology, Middle Technical University, from April to September 2025.

Methods: From each participant, blood and vaginal swab samples were collected prior analysis, involving 90 pregnant women, including 47 patients diagnosed with VVC and 43 healthy controls. Sabouraud dextrose agar (SDA) and CHROMagar *Candida* media were used for fungal cultivation for the detection of Candida. Enzyme-linked immunosorbent assay (ELISA) was used to evaluate serum levels of estradiol, progesterone, IL-10, and cortisol.

Results: The findings showed that significant differences were observed between patients and controls ($p < 0.001$), with patients showing considerably higher levels of cortisol and IL-10 along with reduced levels of progesterone and estradiol.

Conclusion: Overall, the current study suggests that VVC in pregnant women is associated with hormonal disturbance, immunological dysregulation, and neuroendocrine alteration. This study highlights the combined role of immunological and hormonal factors in the pathogenesis of VVC.

Key Words: Vulvovaginal candidiasis, Pregnancy, IL-10, Immune dysregulation, Cortisol, Estrogen

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INTRODUCTION

Vulvovaginal candidiasis (VVC) is considered one of the widely frequent fungal infections that affect women in their reproductive years[1] . *Candida* albicans is an opportunistic commensal microorganism that infect the vaginal microbiome and may associate to the development of vaginal infection[2]. Pregnancy is one of several factors that contribute to increased susceptibility to Vulvovaginal candidiasis due to hormonal and immunological alteration[3]. Studies suggest that estrogen may elevate glycogen storage within vaginal epithelial cell**.** which may create a nutrient-rich environment that could encourage colonization and pathogenicity of *Candida* infection[4]. Additionally, progesterone may have an impact on immunological responses and epithelial integrity, even though, compared to estrogen, its role is limited and poorly understood[5]. In addition, Interleukin-10 (IL-10), one of the primary cytokines that is particularly significant because of its anti-inflammatory effects and function in maintaining immunological homeostasis[6]. Notably, Cortisol is a significant stress hormone with immunosuppressive properties, has been linked to an increased risk of genitourinary infections and alteration of vaginal immunological homeostasis. Elevated cortisol levels during pregnancy could weaken host defenses and worsen vaginal dysbiosis, which would promote opportunistic infections like *Candida*[7]. Limited studies have investigated the combined hormonal and immunological alterations associated with pregnancy-related VVC, highlighting an important gap in current knowledge. Therefore, this study aimed to evaluate serum estradiol, progesterone, IL-10, and cortisol levels in pregnant women with VVC and healthy controls.

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METHODS

The present study was performed in the obstetrics and gynecology and microbiological laboratory department

of Baghdad Teaching Hospital in Baghdad, Iraq, during the period from March to August 2025. Among the 90 pregnant women aged between 16 and 45 years were participated in the research, there were 47 cases and 43 controls. During morning visits, blood and vaginal swab samples were collected. Each patient underwent a speculum examination by a gynecologist who documented clinical signs and symptoms. Demographic informations of all participants was recorded, including, age, gestational age, number of pregnancies, history of abortions, and chronic disease.

Inclusion and exclusion criteria: Pregnant women with vaginal candidiasis and healthy controls were included, while those with immune disorders, prior antimicrobial treatment, vaginal bleeding or other vaginal infections were excluded.

Ethical Approval: The ethical approving was obtained from the Medical Ethics Committee of Middle Technical University (MEC: 72; 11 January 2025). All procedures followed the Declaration of Helsinki, and all participants provided written informed consent. All participants took part voluntarily, and all data were anonymized and kept confidential.

Laboratory analysis: Venous blood samples were obtained from the patient and control groups using standardized protocols. Estradiol (E2), progesterone, cortisol, and interleukin-10 (IL-10) Levels were assessed using the enzyme-linked immunosorbent assay (ELISA) as it provides a sensitive and quantitative method for measuring hormonal and cytokine concentration[8]. Following the manufacturer-provided instructions ELK Biotechnology **(**China), ELISA absorbance was determined using HumaReader HS microplate reader (Germany). In addition, vaginal swabs were aseptically collected by a qualified gynecologist using sterile techniques, using sterile cotton swabs for the isolation of *Candida* species. The samples were later inoculated into Sabouraud dextrose agar (SDA) and CHROMagar (India), media for fungal detection. The inoculated plates were incubated at 37°C for 24–48 hours. Subsequently, the resulting colonies were examined microscopically to confirm the characteristic morphology of *Candida* species.

Statistical Analysis: SPSS version 26 was used to statistically analyze all of the data. For categorical parameters, the chi-square (χ^2) test was performed, and group means were compared using independent samples t-tests. Sensitivity, specificity, and ideal cut-off values were examined using ROC curve analysis. A p-value below 0.05 was considered statistically significant, while a p-value below 0.01 was considered highly significant..

RESULTS

Demographic characteristics: Table 1 represents the demographic and clinical characteristics of the study groups, it shows no significant differences between the negative and positive groups in age ($p = 0.136$), trimester ($p = 0.75$), number of previous pregnancies ($p = 0.726$), history of abortion ($p = 0.372$), or chronic diseases ($p = 1.000$), indicating that the groups were comparable.

Estimation of Biomarkers: Biomarker levels are represented in Table 2. Including the mean and standard deviation of immunological and hormonal biomarkers between patients and controls. The results showed significant differences between patients and controls ($p < 0.001$). Patients exhibited lower levels of estradiol (337.99 ± 59.67 vs 736.79 ± 192.81), and progesterone (8.85 ± 2.39 vs 20.13 ± 7.08), along with higher levels of IL-10 (126.66 ± 18.62 vs 62.20 ± 14.97), and cortisol (41.95 ± 13.81 vs 22.81 ± 5.37).

Table No. 1. Demographic characteristics among patients and control.

Parameter		**Patient** N. (%)	**Control** N. (%)	**Total**	**p-value**
Age group	18-25	18 (38.3)	12 (27.9)	30 (33.3)	0.136 (NS)
	26-35	27 (57.4)	24 (55.8)	51 (56.7)	
	36-45	2 (4.3)	7 (16.3)	9 (10)	
Trimesters	First	2 (4.3)	0 (0)	2 (2.2)	0.208 (NS)
	Second	3 (6.4)	6 (14)	9 (10)	
	Third	42 (89.4)	37 (86)	79 (87.8)	
Previous Pregnancies	1-2	16 (34)	18 (41.9)	34 (37.8)	0.726 (NS)
	3-4	22 (46.8)	17 (39.5)	39 (43.3)	
	>5	9 (19.1)	8 (18.6)	17 (18.9)	
Previous abortion		18 (38.3)	12 (27.9)	30 (33.3)	0.296 (NS)
Chronic disease		13 (27.7)	11 (25.6)	24 (26.7)	0.824 (NS)

Data are shown as number (percentage). Group differences were analyzed using the chi-square (χ^2) test. NS, not significant.

Receiver operating characteristic (ROC) analysis: ROC analysis demonstrated a high discriminative ability of IL-10 (AUC = 1.000). With an ideal cutoff value of 72.85 pg/mL achieving 100% sensitivity and specificity. However, this result should be viewed with caution given the relatively small number of participants and lack of external validation. Cortisol also showed moderate to high discriminative

performance (AUC = 0.910), with a cutoff value of 22.5 ng/mL yielding 95.7% sensitivity and 65.1% specificity. In contrast, estradiol and progesterone exhibited inverse diagnostic patterns, with lower levels associated with the positive group ($p < 0.001$ for all biomarkers), as shown in Figure No. 1.

Table No. 2. determination of biomarker levels of the study groups

biomarker	Mean ± SD		p-value
	patient	control	
Estradiol (E2) (pg/ml)	337.99 ± 59.67	736.79 ± 192.81	p < 0.001
Progesterone (ng/ml)	8.85 ± 2.39	20.13 ± 7.08	p < 0.001
IL-10 (pg/ml)	126.66 ± 18.62	62.20 ± 14.97	p < 0.001
Cortisol (ng/ml)	41.95 ± 13.81	22.81 ± 5.37	p < 0.001

Values are reported as mean ± standard deviation (SD). IL-10 stands for interleukin-10. A p-value below 0.05 was considered significant.

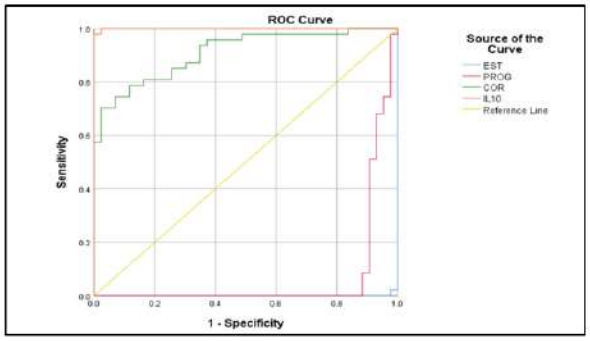

Figure No. 1: (ROC) analysis of Estrogen, Progesterone, IL-10, and Cortisol among Patients and Controls.

DISCUSSION

The present study provides new insights through a combined evaluation of immunological and hormonal alterations in pregnancy-associated vulvovaginal candidiasis, this multifactorial approach has been insufficiently addressed in previous studies, which have largely focused on individual factors. Our study demonstrated substantial differences in immunological and hormonal parameters within pregnant women with vulvovaginal candidiasis, it showed a significant increase in IL-10 levels and cortisol as well as decreased estradiol and progesterone. The two groups were similar in their demographic characteristics, indicating a fair baseline comparability, supporting that the observed alterations in IL-10, cortisol, estradiol, and progesterone are likely due to disease-related mechanisms rather than confounding elements. According to some studies that are in line with our findings, showed no statistically meaningful differences in some demographic and clinical factors between groups, indicating that disease occurrence may be more strongly associated with biological and immunological regulations rather than baseline characteristics[9]. Notably, Pregnancy-related changes may enhance immune tolerance, making an optimal condition for the growth and persistence of *Candida* species[10,11]. The present study found that pregnant women with vulvovaginal candidiasis exhibited significantly lower blood levels of estradiol (E2) and progesterone compared to healthy controls. Studies indicated that estrogen may promote *Candida* growth by increasing glycogen availability and modifying local immune responses, which would facilitate fungal persistence.[12]. Consequently, these findings are in line with previous reports revealed that women with recurrent vulvovaginal candidiasis had significantly lower serum progesterone levels than healthy controls. This suggests that hormonal alterations could possibly affect the pathogenesis of VVC[13]. According to experimental models, progesterone had no apparent effect on the susceptibility to vaginal *Candida* infection, whereas estrogen was the main hormone that contributed to persistent infection[14]. Notably, limited studies have directly measured blood progesterone levels in patients with VVC. Numerous factors might account for the differences between our results and previous studies. First of all, pregnancy is characterized by notable immunological and endocrine changes were the subject of the current study. Furthermore, determination of systemic hormone levels could not accurately represent local vaginal hormonal activity and concentrations[15]. The majority of studies have examined hormonal levels in the vaginal fluid, interestingly, the elevated cortisol levels observed in the present study may contribute to reduced gonadotropin secretion, that could influence estrogen and progesterone production[16]. According to reports elevating cortisol during chronic stress can decrease estrogen production[17]. This may represent another reason why estrogen levels have been decreased in the current study. Also, Inflammatory reactions linked to infections could lower hormone levels by changing endocrine regulations[18]. Our results may also be affected by differences in sample size, gestational age, laboratory measurement methods, and demographics. Our study revealed that IL-10 levels were markedly increased in women with VVC. These findings are in line with previous studies that suggest women with VVC have elevated IL-10 levels. Studies indicated that IL-10 levels are increased in recurrent vulvovaginal candidiasis. As experimental studies reported, higher IL-10 expression during recurrent *Candida* infection may promote fungal persistence and reduction in fungal clearance[19]. Therefore, these findings are consistent with the idea that, increased IL-

10 levels in VVC may reflect immunological imbalance, although IL-10 also has protective anti-inflammatory roles. The significant elevation of IL-10 observed suggests a shift toward an anti-inflammatory immune dysregulation that could restrict effective antifungal defense. Although, IL-10 plays a protective function in reducing tissue damage. Women with VVC in the current study had considerably higher serum cortisol levels than controls. A clinical study indicates that Women with VVC had considerably lower early-morning cortisol levels, which may indicate long-term stress**,** that could compromise immunological control and increase the persistence of the disease[20]. Stress-induced cortisol release may be associated with alterations in vaginal microbial balance, weaken estrogen-dependent vaginal immunity thus increases the risk of vulvovaginal infection[21]. The elevated cortisol levels observed in the present study are inconsistent with some previous studies. This lack of agreement may be partly explained by differences in sample type, as serum and salivary cortisol levels may differ significantly, particularly under pathological conditions. In this context, serum cortisol represents total hormone levels in circulation, whereas salivary cortisol reflects the unbound, biologically active fraction, which can provide a more functionally relevant measure in clinical and research settings[22]. Based on ROC analysis, IL-10 showed particularly high accuracy, whereas cortisol exhibited high sensitivity with moderate specificity, indicating that susceptibility to VVC is not determined by a single element, but complex interactions between host immunity and endocrine interactions. Our findings should be interpreted in light of several limitations, including the relatively small sample size and the fact that the study was conducted at a single center, and the use of serum rather than local vaginal measurements. In addition, the study's cross-sectional design limits causal interpretation.

CONCLUSION

Vulvovaginal candidiasis (VVC) during pregnancy is influenced by several factors including immunological and hormonal dysregulation. Women who were infected showed low levels of estradiol and progesterone, along with significantly elevated levels of IL-10 and cortisol when compared to healthy controls, as a result, these findings may indicate a disturbance in the immuno-endocrine balance. The present findings support the concept that VVC is predominantly an immunopathological condition influenced by host immune regulation and the hormonal environment. Moreover, IL-10 and cortisol may also have potential diagnostic value. Overall, the present investigation suggests a potential interaction between hormonal and immunological factors in pregnancy-associated VVC and may provide more development of diagnostic and therapeutic strategies.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Ali Fayez Noor, Abdulameer Jasim Mohammed
Drafting or Revising Critically:	Ali Fayez Noor, Omar Sadik Shalal
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Risk Factors for Myopia in Pediatric Age Group Presenting at Tertiary Care Hospital

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ABSTRACT

Objective: To evaluate the risk factors associated with myopia in the pediatric age group presenting to a tertiary care hospital.

Study Design: A descriptive cross-sectional study

Place and Duration of Study: This study was conducted at the Ophthalmology unit, Hayatabad Medical Complex, from January 2025 to June 2025.

Methods: Non-probability consecutive sampling was used to include 1534 children aged 5-16 years with a diagnosis of myopia. Myopia was considered to be a sphere equivalent of 0.50 diopters and below in either eye. A structured proforma was used to gather data on demographic characteristics, family history, near work, screen time and outdoor activity. Visual acuity, cycloplegic refraction, subjective refraction, and fundus examination were conducted on all subjects. The analysis of data was conducted with SPSS 26.

Results: The mean age was 11.2 ± 3.1 years. Positive family history of myopia was present in 612 (39.9%) children, near work >2 hours/day in 1018 (66.4%), screen time >2 hours/day in 874 (57.0%), and outdoor activity >2 hours/day in 412 (26.9%). Myopia severity was greatly linked to family history, prolonged near work and more screen time whereas outdoor activity was considered to have a protective link.

Conclusion: Family history, a longer duration of near work, more screen time, and less outdoor activity were found to have a significant association with pediatric myopia. Early screening, parental education, near work and screen time regulation, decreased screen time and encouragement of outdoor activities can be used to alleviate the burden of myopia among children.

Key Words: Myopia, Paediatric, Risk factors, Screen time, Near work, Outdoor activity.

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INTRODUCTION

One of the most frequently seen refractive errors in children is myopia or shortsightedness. It has become a significant public health issue in the world, with its growing incidence and chronic ophthalmological complications[1]. Nearly half of the world's population is predicted to have myopia by 2050, with a sizable portion of the population getting extreme myopia, which increases their chance of developing vision-threatening conditions such retinal detachment, glaucoma, and myopic maculopathy[2]. Myopia usually develops at the school-going age and in this case, early detection of risk factors would be essential in preventing and controlling this condition.

Myopia etiology is multifactorial because it is a complex interaction of genetic predisposition and environmental exposures[3]. There is solid evidence that children born to myopic parents face a much greater risk and it becomes even more likely when both parents have the condition[4,5]. However, genetic predisposition cannot be used to explain the recent increase in prevalence alone, and the relevance of modifiable environmental determinants.

Among environmental influences, there is a consistent finding that a greater involvement in near-work activities, including longer reading, writing, and screen time, is correlated with increased risk of developing myopia[6,7]. The decreased outdoor activity has become also a critical factor and various studies have shown the protective effect of more time spent outdoors which could be explained by the higher level of light and less accommodative stress[8,9]. Moreover, the contemporary changes in lifestyle, such as the overuse of digital devices and reduced physical activity also add to the increasing burden of pediatric myopia[10].

The other risk factors are age, ethnicity, level of education, sleep habit, and nutritional status, all of which have demonstrated the different levels of

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association with the development of myopia[11,12]. Children who are referred to tertiary care hospitals are usually more progressive or symptomatic, and such a setting would be useful in understanding the relative contribution of these risk factors in clinical populations. These determinants should be well comprehended to implement specific preventive measures and inform successful clinical management. However, although the worldwide burden of pediatric myopia is steadily rising, local statistics on its risk factors are scarce, especially those concerning tertiary care hospitals in Khyber Pakhtunkhwa. The bulk of available evidence is based on school-based or international research which is not necessarily representative of the clinical profile, lifestyle patterns and environmental exposures of children presenting to hospitals in this region. Thus, the purpose of this study was to evaluate the risk factors related to myopia in children who are admitted to a tertiary care hospital.

METHODS

This descriptive cross sectional study was conducted at Department of Ophthalmology, Hayatabad Medical Complex, Peshawar from January 2025 to June 2025. Thus, the sample size formula of WHO was used to calculate a single population proportion with a 95% confidence level, a margin of error of 2.5%, and an estimated prevalence of 30% for pediatric myopia as shown in published literature [13]. The sample size needed was around 1291. Given the large number of patients in the outpatient department during the study period and to enhance accuracy of estimates, the final sample size was expanded to 1534 children.

A non-probability consecutive sampling was used to enroll children aged 5–16 years that visited outpatient ophthalmology department. Children with a diagnosis of myopia (spherical equivalent of -0.50 D or less in both eyes) were all studied. Children with pathological myopia, congenital or acquired ocular diseases (cataract, glaucoma, retinal disease) or history of ocular trauma or previous ocular surgery and systemic disease that affects vision were excluded.

Ethical approval was obtained from the hospital institutional review board before collection of data began, and informed consent was obtained from all children's parents/guardians in the form of a written consent. A pre-tested proforma was used to collect the data. Demographic data was collected such as age, gender and place of residence. The duration and kind of near work (reading and screen time), amount of time spent outdoors, degree of education, and family history of myopia were all noted as potential risk factors.

A detailed ophthalmic assessment was carried out on all children's. Snellen chart was used to measure visual acuity. Cycloplegic refraction was performed using cyclopentolate (1%) and then retinoscopy and subjective refraction were used to ascertain the final refractive error. The funduscopic examination was carried out to rule out any underlying pathological causes of myopia.

The operational definition of near work was defined as working within a range of less than 3040 cm and doing so for at least two hours every day. The operational definition of outdoor activities was defined as spending time outside during the day. The data was entered and analyzed using the Statistical Package of Social Sciences (SPSS) version 26. Frequencies and percentages were used to describe qualitative factors, whereas mean ± standard deviation was used to express quantitative data like age and time spent near work. The relationship between different risk factors and myopia was examined using the Chi-square test. Significant importance was defined as a p-value of less than 0.05.

RESULTS

Mean age of participant was 11.2 ± 3.1 years (ranged 5-16 yeras). There were 692 (45.1%) females and 842 (54.9%) males. 38.7% of participants were from rural areas, whilst 61.3% of participants were from metropolitan areas.

Table No. 1: Demographic Characteristics of Study Population (n = 1534)

Variable	n (%)
Age Group (years)	
5–8	402 (26.2%)
9–12	648 (42.3%)
13–16	484 (31.5%)
Gender	
Male	842 (54.9%)
Female	692 (45.1%)
Residence	
Urban	941 (61.3%)
Rural	593 (38.7%)

A positive family history of myopia was observed in 612 (39.9%) children. Regarding behavioral factors, near work for more than 2 hours/day was reported in 1018 (66.4%) participants, while screen time exceeding 2 hours/day was noted in 874 (57.0%) children. Only 412 (26.9%) children reported outdoor activity of more than 2 hours/day. Table-2

Table No. 2: Distribution of Risk Factors Among Participants (n = 1534)

Variable	n (%)
Family History of Myopia	
Present	612 (39.9%)
Absent	922 (60.1%)
Near Work (>2 hours/day)	
Yes	1018 (66.4%)
No	516 (33.6%)
Screen Time (>2 hours/day)	

Variable	n (%)
Yes	874 (57.0%)
No	660 (43.0%)
Outdoor Activity (>2 hours/day)	
Yes	412 (26.9%)
No	1122 (73.1%)

On stratification, family history of myopia, prolonged near work, and increased screen time showed a statistically significant association with myopia severity ($p < 0.05$). Conversely, increased outdoor activity demonstrated a protective effect, with children spending more than 2 hours outdoors showing lower severity of myopia ($p = 0.01$). Table-3

Table No. 3: Association of Risk Factors with Myopia Severity (n = 1534)

Risk Factor	Mild Myopia	Moderate Myopia	High Myopia	p-value
Family History				
Present	248 (40.5)	262 (42.8)	102 (16.7)	0.02
Absent	462 (50.1)	356 (38.6)	104 (11.3)	
Near Work >2 hrs/day				
Yes	438 (43.0)	438 (43.0)	142 (14.0)	0.01
No	272 (52.7)	180 (34.9)	64 (12.4)	
Screen Time >2 hrs/day				
Yes	364 (41.6)	380 (43.5)	130 (14.9)	0.03
No	346 (52.4)	238 (36.1)	76 (11.5)	
Outdoor Activity >2 hrs/day				
Yes	244 (59.2)	130 (31.6)	38 (9.2)	0.01
No	466 (41.5)	488 (43.5)	168 (15.0)	

DISCUSSION

These results of our study are mostly in line with the multifactorial model of myopia where inherent predisposition and adjustable environmental exposures both play a role in the development and progression of myopia.

Family history was found to be extremely related with severity of myopia in our study. This observation agrees with Ha et al[14] who found parental myopia as a significant non-modifiable risk factor, but its impact can be altered by the environmental exposures as near work and outdoor time. Similarly, Holden et al[15] defined myopia as a disorder that is brought about by genetic and environmental factors. This association in our population might be more pronounced since children who attend a tertiary care hospital will tend to represent symptomatic or clinically identified cases but not a population screened at schools.

In our study, prolonged near work was also found to have a significant relationship with the severity of myopia. This is in line with Pan et al[16] who established a strong relationship between near-work activities and myopia in children. Tideman et al[17] also established that the duration of homework and pressure to study in school were linked to myopia in school going children. Similar educational pressures, excessive reading hours and fewer visual breaks may be reflected in our findings among school going children in our environment. Myopia was significantly correlated with increased screen time in our study. Zhao et al.[18] have shown that increased screen time leads to myopia in children and adolescents, particularly computer-based screen time. Alshamlan et al[19] recently reported a dose-response effect between digital screen time and myopia, with each additional hour of daily screen time raising the risk of myopia. The similarity of our findings to these studies could be attributed to the growing adoption of smartphones, tablets, and online learning platforms by children. But the precise extent might vary since our research involved parent/child-reported screen time which could be influenced by recall bias.

The results of our study suggest that outdoor activities are protective against myopia and that the duration of outdoor time and the severity of myopia are inversely correlated. This is in line with the results from the IMI risk factor analysis by Chen et al.[20] who found that one of the most consistent environmental factors that protect against myopia is outdoor exposure. Another study by Alrasheed et al[21] also revealed that more outdoor activities on weekdays and weekends were linked with decreased risk of myopia. The protective effect can be associated with increased light intensity in the outdoors and decreased sustained accommodative requirement.

A number of differences with international studies can be attributed to the differences in the study setting, age group, diagnostic method, lifestyle, ethnicity, and the educational environment[22,23]. Our research was a hospital based study whereas most of the earlier studies were either school based or population based. Thus, children with more symptomatic or clinically significant refractive error may be part of our sample. Besides this, cycloplegic refraction in our study enhances the accuracy of the diagnosis as compared to other works in which non-cycloplegic autorefraction or

self-reported myopia was used. The results on the whole substantiate the importance of early screening, parental counselling, decreased exposure to continuous near work and screen time, and encouragement of frequent outdoor play in children.

There are certain limitations to this study that must be noted. The study was a single-center, hospital-based study, which might not be applicable in the general population of children because those who presented with refractive errors to a tertiary care hospital are more likely to have symptomatic or advanced refractive errors. The cross-sectional design does not allow determining the causal relationship between the identified risk factors and myopia but only assesses associations. Also, information about screen time, near work, outdoor activity, and family history were parentally or participant-reported, and thus there was a possibility of recall bias. Other vital variables like socioeconomic status, parental education, lighting conditions, nutritional status, sleep patterns and academic workload were not delved into in details and may affect the observed associations..

CONCLUSION

Positive family history, extended near work and less outdoor activity were significantly associated with pediatric myopia. The results of this study clearly show the synergistic effect of genetic susceptibility and environmental risk factors in the development and progression of myopia in children. In children, early screening, parent awareness, limiting continuous near work and screen time, and encouraging regular outdoor activity may be helpful for preventing or slowing myopia progression.

Author's Contribution:

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Drafting or Revising Critically:	Muhammad Ashraf, Noor ul Hussain
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Relationship Between Interleukin Levels and Bacterial Dental Caries in Autistic Children in Baghdad Governorate

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ABSTRACT

Objective: To investigate the relationship between salivary interleukin levels and dental caries in autistic children in Baghdad, given the higher burden of caries in this population and emerging evidence of immune dysregulation in Autism Spectrum Disorder (ASD).

Study Design: A case-control study.

Place and Duration of Study: This study was conducted at the Department of Conservative Dentistry/ College of Dentistry/Ashur University, Baghdadad, Iraq between July and October 2025.

Methods: This case-control study enrolled 55 children with ASD and 55 neurotypical controls, aged 5-12 years. Dental caries experience was assessed using the dmft /DMFT indices. Salivary levels of interleukin (IL)-1β, IL-6, IL-10, and IL-17A were quantified using enzyme-linked immunosorbent assay (ELISA), alongside bacterial culture analysis.

Results: Children with ASD had significantly higher mean dmft/DMFT scores (6.8 ± 3.5) than controls (3.2 ± 2.4). They exhibited a pro-inflammatory salivary profile characterized by elevated IL-1β and IL-6, and reduced IL-10 levels ($p < 0.01$). Strong positive correlations were observed between caries experience and IL-1β ($r = 0.68$) and IL-6 ($r = 0.59$). Regression analysis identified IL-1β and poor oral hygiene as significant predictors of dental caries.

Conclusion: Autistic children in Baghdad experience a greater dental caries burden associated with a pro-inflammatory salivary cytokine profile, indicating that immune dysregulation may be a significant biological contributor to oral health disparities in this population.

Key Words: autism spectrum disorder; dental caries; interleukins; saliva; oral health.

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INTRODUCTION

Autism spectrum disorder (ASD) is a complex neurodevelopmental condition characterised by persistent challenges in social communication, interaction, and restricted, repetitive patterns of behaviour[1.] The global prevalence of ASD has been steadily increasing, making it a significant public health concern. Beyond its core symptoms, ASD is frequently associated with a range of co-morbidities, among which oral health disparities, particularly a higher burden of dental caries, are notably prevalent[2.]

The aetiology of dental caries is multifactorial, involving dynamic interactions among cariogenic bacteria, fermentable carbohydrates, salivary factors, and the host's immune response. Cariogenic bacteria, such as Streptococcus mutans and Lactobacillus species, metabolise fermentable carbohydrates to produce acids that demineralize tooth enamel. Autistic children represent a high-risk population for caries due to a convergence of behavioural and physiological factors, including dietary preferences for cariogenic foods, medication-induced xerostomia, and profound challenges in maintaining effective oral hygiene. This combination fosters an oral environment conducive to the proliferation of pathogenic bacterial biofilms, establishing a direct microbiological basis for their increased caries burden. In autistic children, several risk factors converge to elevate the caries risk, including dietary preferences for soft, sugary foods, medication-

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induced xerostomia, oral aversions, and behavioral challenges that complicate the performance of effective oral hygiene and access to dental care[3].

Recent research has shifted focus towards understanding the role of systemic inflammation as a potential biological link between ASD and its associated co-morbidities. A growing body of evidence indicates that immune dysregulation and a chronic pro-inflammatory state are key features of ASD[4,5]. Central to this inflammatory response are interleukins (ILs), which are cytokines that mediate communication between immune cells and can influence peripheral systems, including oral health. Altered levels of specific interleukins, such as the pro-inflammatory IL-6, IL-17, and IL-1β, have been consistently reported in the serum and brain tissue of individuals with ASD, suggesting their involvement in the disorder's pathophysiology[5,6].

Within the oral cavity, the levels of these signalling molecules in saliva and gingival crevicular fluid reflect the local immune and inflammatory status. In the context of dental caries, the carious process itself can provoke an immune response, potentially altering local interleukin profiles. However, it is hypothesised that the systemic inflammatory milieu in autistic children may predispose them to a more pronounced or dysregulated oral inflammatory response, thereby modifying their susceptibility to caries(7). While studies have begun to explore salivary cytokines in various conditions, the specific relationship between interleukin levels and the dental caries experience in autistic children remains an area requiring significant investigation, particularly in particular populations.

In Baghdad Governorate, there is a recognized need to understand the unique health challenges faced by autistic children. To date, no study has investigated the potential interplay between systemic or salivary interleukin concentrations and the high prevalence of dental caries in this vulnerable demographic. Therefore, this study aims to determine the relationship between levels of key interleukins (e.g., IL-1β, IL-6, IL-10, IL-17) and the prevalence and severity of dental caries in autistic children residing at the Iraqi Centre for Autism in Baghdad, Elucidating this relationship could provide crucial insights into the biological mechanisms underlying oral disease in ASD and pave the way for novel preventive or therapeutic strategies.

METHODS

1. Study Design and Setting: A case-control study was conducted at Department of Conservative Dentistry/ College of Dentistry/Ashur University, Baghdadad, Iraq between July and October 2025. The study participants were recruited from several governmental and private special needs centres and pediatric dental clinics across the Iraqi Centre for Autism in Baghdad, Iraq.

2. Sample size: total sample size of 110 participants (55 per group)**.**

3. Study Participants: A total of 110 children, aged 5-12 years, were enrolled and divided into two groups:

- Group I (Case Group): 55 children with a confirmed diagnosis of Autism Spectrum Disorder (ASD).
- Group II (Control Group): 55 neurotypical children, matched for age and sex, with no clinical diagnosis or family history of ASD.

3.1. Inclusion Criteria: For the Case Group: A formal diagnosis of ASD by a specialist psychiatrist based on the Diagnostic and Statistical Manual of Mental Disorders.

3.2. Exclusion Criteria:

- Children with other systemic diseases known to affect immune function (e.g., autoimmune disorders, diabetes, recent febrile illness).
- Use of anti-inflammatory drugs, antibiotics, or immunosuppressants within the last one month.
- Children who had undergone any dental treatment (e.g., fillings, extractions) or professional cleaning in the preceding three months.
- Presence of severe gingivitis or periodontitis that could significantly alter local cytokine levels.

4. Data Collection and Clinical Examination

4.1. Questionnaire and Interview: A pre-designed questionnaire was used to collect data from parents/guardians on:

- Demographic details (child's age, sex).
- Medical history and medication use.
- Dietary habits, specifically the frequency of sugary food and drink consumption per day.
- Oral hygiene practices (toothbrushing frequency and assistance).

4.2. Dental Caries Assessment: A single, calibrated examiner (Kappa score >0.85 for intra-examiner reliability) performed all oral examinations using a disposable mouth mirror and a World Health Organisation (WHO) community periodontal index (CPI) probe under adequate artificial light. The examination took place in a quiet, well-lit room at the participating centres to ensure the comfort of the autistic children.

Dental caries was recorded using the dmft/DMFT index (decayed, missing, and filled teeth for primary and permanent dentitions, respectively) following the WHO criteria. A tooth was recorded as decayed at the cavitation level (d/D). The total dmft/DMFT score for each child was calculated.

4.3. Saliva Sample Collection: Unstimulated whole saliva (approximately 2-3 ml) was collected from each child between 9:00 and 11:00 a.m. to minimise diurnal variation. For autistic children, collection was performed using the passive drool method or with a sterile plastic syringe, allowing breaks as needed to accommodate behavioural challenges. Children were instructed not to eat or drink for at least one hour before sampling.

Saliva samples were immediately transferred into sterile, pre-labeled Eppendorf tubes and placed on ice. Within two hours, they were transported to the laboratory and centrifuged at 3000 rpm for 15 minutes at 4°C to remove cells and debris. The clear supernatant was aliquoted and stored at -80°C until used.

4.4. Bacteriological test: Using a clean toothpick, samples of their dental plaque were collected from the buccal surfaces and stored in normal saline (1 ml), then dispersed using a Vortex mixer for 30 seconds. Serial dilutions were performed, and cultures were incubated in selective media; bacterial counts were determined by CFU enumeration using a dissecting microscope (×15).

4.5. Estimation levels of Interleukins: The concentrations of interleukins (IL-1β, IL-6, IL-10 and IL-17A) in the saliva samples were measured using commercial, specific Enzyme-Linked Immunosorbent Assay (ELISA) kits (e.g., from Ela Science or R&D Systems).

5. Statistical Analysis: Data were analyses using the Statistical Package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). The normality of data distribution was checked using the Shapiro-Wilk test. Descriptive statistics were presented as mean ± standard deviation (SD) for continuous variables and as numbers and percentages for categorical variables.

- An independent samples t-test (for parametric data) or Mann-Whitney U test (for non-parametric data) was used to compare the mean levels of interleukins and dmft/DMFT scores between the two groups.
- The Chi-square test was used to compare categorical variables like sex and brushing frequency.
- The correlation between interleukin levels and dmft/DMFT scores was assessed using Spearman's rank correlation coefficient (rho).

A multiple linear regression analysis was performed to identify the significant predictors of the dmft/DMFT score, including interleukin levels, age, sugar frequency, and oral hygiene status as independent variables.

A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 120 children were initially recruited for this study. After applying the exclusion criteria, 110 children were included in the final analysis, comprising 55 children with autism spectrum disorder (ASD) and 55 neurotypical children.

1. Demographic and Baseline Characteristics: The two groups were comparable in terms of age and sex distribution ($p > 0.05$), indicating successful matching. However, significant differences were observed in oral health behaviours. Children with ASD had a significantly higher frequency of daily sugar consumption ($p < 0.01$) and a lower frequency of supervised toothbrushing ($p < 0.001$) compared to the control group (Table 1).

2. Dental Caries Experience: The dental caries experience, as measured by the dmft/DMFT index, was significantly higher in the ASD group (6.8 ± 3.5) compared to the control group (3.2 ± 2.4), and this difference was statistically significant ($p < 0.001$).

Table No. 1: Demographic and Behavioural Characteristics of the Study Participants

Characteristic	ASD Group (n=55)	Control Group (n=55)	p-value
Age (years), Mean ± SD	8.2 ± 2.1	8.0 ± 2.3	0.621
Sex, No.(%)			0.854
Male	42 (76.4%)	41 (74.5%)	
Female	13 (23.6%)	14 (25.5%)	
Sugar Intake >2x/day, No.(%)	38 (69.1%)	22 (40.0%)	<0.01
Supervised Brushing, No.(%)	15 (27.3%)	45 (81.8%)	<0.001

3. Salivary Interleukin Levels: The analysis of salivary interleukin levels revealed a distinct pro-inflammatory profile in children with ASD. As shown in Table 2, the ASD group had significantly higher concentrations of the pro-inflammatory cytokines IL-1β and IL-6 compared to the control group ($p < 0.001$ for both). In contrast, the levels of the anti-inflammatory cytokine IL-10 were significantly lower in the ASD group ($p < 0.01$). No significant difference in IL-17A levels was found between the two groups ($p = 0.085$).

Table No. 2: Salivary Interleukin Levels (pg/ml) in the Study Groups

Interleukin	**ASD Group (n=55)**	**Control Group (n=55)**	**p-value**
(Mean ± SD)			
IL-1β	45.3 ± 15.2	22.1 ± 8.7	<0.001
IL-6	12.5 ± 4.8	5.9 ± 2.5	<0.001
IL-10	8.2 ± 3.1	11.5 ± 4.0	<0.01
IL-17A	5.5 ± 2.3	4.8 ± 1.9	0.085

A multiple linear regression model was constructed to predict the dmft/DMFT score, controlling for age, sugar frequency, and brushing habits. The model indicated that elevated levels of IL-1β ($\beta = 0.42$, $p < 0.001$) and poor oral hygiene ($\beta = 0.38$, $p < 0.01$) were the strongest independent predictors of a higher caries experience in children with ASD.

In the ASD group, strong positive correlations were observed between the pro-inflammatory cytokines (IL-

1β and IL-6) and the loads of both *S. mutans* and *Lactobacillus* spp., suggesting that higher bacterial colonisation is associated with increased inflammatory response. Additionally, negative correlations were observed between the anti-inflammatory cytokine IL-10 and bacterial load in the ASD group, suggesting that lower IL-10 levels are associated with greater bacterial colonisation.

Regarding IL-17A, no significant correlations with bacterial load were observed in either group, consistent with the non-significant difference reported in Table -3.

Table No. 3: Correlation Between Cariogenic Bacterial Load and Salivary Interleukin Levels in Autistic and Neurotypical Children

Parameter	IL-1β	IL-6	IL-10		IL-17A
S. mutans (CFU/ml x 10^5)	(pg/ml) Mean ± SD				
ASD Group (n=55)	45.3 ± 15.2	12.5 ± 4.8	8.2 ± 3.1		5.5 ± 2.3
Control Group (n=55)	22.1 ± 8.7	5.9 ± 2.5	11.5 ± 4.0		4.8 ± 1.9
p-value		<0.001	<0.001	<0.01	0.085
Lactobacillus spp. (CFU/ml x 10^4)					
ASD Group (n=55)	45.3 ± 15.2	12.5 ± 4.8	8.2 ± 3.1		5.5 ± 2.3
Control Group (n=55)	22.1 ± 8.7	5.9 ± 2.5	11.5 ± 4.0		4.8 ± 1.9
p-value	<0.001		<0.001	<0.01	0.085
Correlation with *S. mutans* (r)					
ASD Group	r = 0.62*	r = 0.55*	r = -0.41*		r = 0.15
Control Group	r = 0.48*	r = 0.39*	r = 0.21		r = 0.12
Correlation with *Lactobacillus* (r)					
ASD Group	r = 0.58*	r = 0.51*	r = -0.38*		r = 0.11
Control Group	r = 0.42*	r = 0.35*	r = 0.18		r = 0.09

*Note: Values represent mean ± standard deviation. Correlation coefficients (r) indicate Spearman's rank correlation between bacterial load and interleukin levels. Indicates statistical significance ($p < 0.05$).

DISCUSSION

This case-control study provides novel evidence of a significant relationship between altered salivary interleukin levels and the high prevalence of dental caries in autistic children residing in Baghdad Governorate. Our findings underscore that the oral health disparity in ASD is not merely behavioural but is likely underpinned by a distinct biological component involving immune dysregulation.

The core finding of this study is the significantly elevated levels of pro-inflammatory interleukins, specifically IL-1β and IL-6, in the saliva of autistic children compared to their neurotypical peers. This aligns with the growing body of literature characterising ASD as a condition of systemic immune dysregulation and chronic low-grade inflammation[3,4]. A recent study by Saresella et al. (2023) similarly reported elevated pro-inflammatory cytokines in the peripheral blood of autistic children, suggesting a pervasive inflammatory state[5]. Our research extends this concept to the oral environment, proposing that the mouth serves as a mirror of systemic immune status in ASD. The potent pro-inflammatory nature of IL-1β and IL-6 can disrupt the normal homeostasis of the oral microbiome and the mineral balance of the tooth structure, potentially creating a more cariogenic environment[8].

We found a significant positive correlation between pro-inflammatory cytokines (IL-1β, IL-6) and caries severity (dmft/DMFT) in the ASD group, suggesting a dose-response relationship. This could mean either that systemic inflammation in ASD primes oral tissues for an exaggerated response to cariogenic bacteria or that high caries levels perpetuate local inflammation. However, regression analysis showing IL-1β as a strong independent predictor—even after accounting for behaviour—supports the first interpretation[7,9].

Interestingly, we observed significantly lower levels of the anti-inflammatory cytokine IL-10 in the ASD group. IL-10 plays a crucial role in dampening inflammatory responses and maintaining immune tolerance. A deficiency in IL-10 could lead to an unchecked pro-inflammatory state, failing to counterbalance the effects of IL-1β and IL-6[10]. This imbalance between pro-inflammatory and anti-inflammatory forces likely creates an oral environment highly susceptible to chronic inflammatory diseases such as caries.

The lack of a significant difference in IL-17A levels between groups is noteworthy. While IL-17 is implicated in the pathogenesis of autoimmune and chronic inflammatory diseases, its role in caries, specifically in ASD, appears to be less pronounced than that of the IL-1β/IL-6 axis. This finding suggests that the specific inflammatory pathways involved in oral

health disparities in ASD may be unique and require further delineation.

Behavioural data confirm higher sugar intake and poorer oral hygiene in this population, which contribute to high caries rates[3,11]. However, our study shows that biological immune factors are independently associated with disease outcome, highlighting the need for a dual approach: tailored preventive programmes addressing behaviour, and management of underlying inflammation.

CONCLUSION

In conclusion, autistic children in Baghdad show higher caries rates and a pro-inflammatory cytokine profile (high IL-1β and IL-6, low IL-10). The strong association between interleukins and caries severity suggests that immune dysregulation drives oral health disparities.

Author's Contribution:

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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Investigating the Relationship Between Osteoporosis and Tooth Loss in Postmenopausal Women

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ABSTRACT

Objective: This case-control study aimed to determine whether osteoporosis is associated with tooth loss in postmenopausal women.
Study Design: A case-control study.
Place and Duration of Study: This study was conducted at the Al-Farahidi University / College of Dentistry, Baghdad Iraq between January and September 2024.
Methods: A total of 400 postmenopausal women aged 50–75 years were enrolled, including 200 with osteoporosis (bone mineral density T-score < -2.5) and 200 without osteoporosis (T-score > -1.0). Data on age, body mass index, cigarette use, diabetes, and dental hygiene were collected, and clinical dental examinations were conducted.
Results: Women with osteoporosis had a significantly higher rate of severe tooth loss (<20 teeth) compared to those without osteoporosis (77.5% vs. 40.0%; $p < 0.001$) and a considerably lower number of remaining teeth (14.2 ± 7.5 vs. 20.8 ± 5.9; $p < 0.001$). After adjusting for confounding factors, osteoporosis remained a robust independent predictor of severe tooth loss (adjusted odds ratio: 3.15, 95% CI: 1.98–5.01, $p < 0.001$). Periodontitis was identified as the primary cause of tooth extractions in osteoporotic women.
Conclusion: A strong correlation exists between osteoporosis and tooth loss in postmenopausal women, highlighting the need for integrated medical and dental care.
Key Words: Osteoporosis; Tooth loss; Postmenopausal women; Periodontitis; Dental health; Risk factors.

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INTRODUCTION

A major worldwide public health problem, osteoporosis affects mostly postmenopausal women and is defined by reduced bone mass and microarchitectural degradation of bone tissue[1]. After menopause, estrogen levels drop, which speeds up bone remodelling, causes more bone to be resorbed than formed, and makes bones more brittle and prone to fractures[2].

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A large percentage of the elderly female population is at risk for osteoporosis, according to the WHO, which is defined as a bone mineral density (BMD) T-score of -2.5 or below[3].

As people age, tooth loss becomes more common, which is an indicator of poor dental and overall health. Periodontal disease and periapical pathology are the main reasons why people lose their teeth. The health of the alveolar bone has a role in both of these conditions[4]. Osteoporosis may accelerate the degradation of this metabolically active and sensitive bone, thereby increasing the risk of periodontal disease and, eventually, tooth loss[5].

Given the strong correlation between the jawbone and total bone mineral density, which may serve as an indicator of the overall health of the skeleton, this link makes biological sense[6]. Vitamin D insufficiency, RANKL-mediated bone resorption, and chronic inflammation are shared pathophysiological pathways between tooth loss and osteoporosis, which are still being studied[7, 8].

Results have often been contradictory owing to methodological discrepancies, sample characteristics, or confounding variables, including smoking, diabetes, and dental care availability, despite the long history of research on the link between systemic osteoporosis and oral bone loss[9]. The evidence for this connection has

been strengthened by subsequent investigations that have used improved diagnostic methods such as DXA and CBCT[10,11]. Instead of being limited to tooth loss in older women, recent longitudinal studies have shown that low BMD may predict it[12].

The main aim of this research is to assess, after controlling for important confounding factors, the correlation between tooth loss and osteoporosis, as measured by BMD T-scores, in postmenopausal women. Because panoramic radiographs and dental status can serve as screening tools for osteoporosis, this association is clinically relevant. Women at high risk might benefit from earlier detection and treatment if dental and medical professionals worked together[13].

METHODS

The study was conducted at the Al-Farahidi University / College of Dentistry, Baghdad Iraq between January and September 2024. All participants provided written informed consent.

2. Study Population and Participant Selection: Participants ranged in age from 50 to 75 and were all women who had gone through menopause. After a woman has gone menstrual-free for twelve months, she is considered to have entered menopause.

Inclusion Criteria: Naturally postmenopausal women aged 50-75 years; able and willing to provide informed consent; recent (within 6 months) dental panoramic radiograph or willingness to undergo one.

Exclusion Criteria: History of surgical menopause or current use of hormone replacement therapy (HRT); Medical conditions known to severely affect bone metabolism (e.g., hyperparathyroidism, Paget's disease, renal osteodystrophy); Current or recent (within the past year) use of medications affecting bone density (e.g., bisphosphonates, corticosteroids, teriparatide; History of head and neck radiation therapy; Edentulism (complete tooth loss) prior to menopause (as recalled by the patient); Active, severe periodontal disease requiring immediate surgical intervention.

3. Sample Size Calculation

Sample size was calculated using [e.g., G*Power software, version 3.1]. Based on a previous study, an odds ratio of 2.5 for tooth loss in osteoporotic women was assumed. With 80% power and a 5% two-sided alpha error, at least 178 participants (89 per group) were required. Four hundred participants were recruited to allow for dropouts and subgroup analyses.

4. Group Allocation (Case-Control)

Based on the assessment of bone mineral density (BMD), the participants were separated into two groups:

- **Case Group (Osteoporotic):** Women with a BMD T-score of ≤ -2.5 at either the lumbar spine (L1-L4) or the femoral neck (n=200).
- **Control Group (Non-Osteoporotic):** Women with a BMD T-score of > -1.0 at both sites (n=200).

To ensure clear separation of groups, our study excluded women with osteopenia, defined as a T-score between -1.0 and 2.5.

5. Data Collection and Measurements

A. Primary Exposure Variable: Osteoporosis Diagnosis

The left femoral neck and lumbar spine (L1-L4) were imaged using dual-energy X-ray absorption (DXA) to measure bone mineral density (BMD) in g/cm². All photos were evaluated by a single board-certified radiologist. The findings were presented as T-scores, which indicate the number of standard deviations above or below the average bone density of a healthy young adult female.

B. Primary Outcome Variable: Tooth Loss: A single calibrated dentist who was not informed of the subjects' BMD status conducted a full-mouth oral examination. The evaluation used a mouth mirror, a WHO periodontal probe, and conventional clinical illumination.

Tooth Count: We counted all the normal teeth (but excluding the third molars, often called wisdom teeth). Two techniques were used to represent the outcome:

The average number of teeth lost is 28 minus the current tooth count.

In epidemiological research, a severe case of tooth loss is defined as the presence of fewer than twenty natural teeth.

C. Covariates and Confounding Factors: A structured interview and evaluation of medical and dental records were used to gather data on possible confounders:

- Sociodemographic factors include gender, years since menopause, educational attainment, and family income.
- **Anthropometric:** Body mass index (BMI) (kg/m²) was determined by measuring height and weight.
- Past medical conditions include diabetes, high blood pressure, rheumatoid arthritis, and use of calcium and vitamin D supplements.
- **Lifestyle Factors:**
  - **Smoking Status:** Categorised as never, former, or current smoker.
  - **Physical Activity:** Assessed using the International Physical Activity Questionnaire (IPAQ) short form.
- **Dental and Oral Health Variables:**
  - The main cause for extracting each tooth was documented as either periodontitis-related or caries-related, depending on the patient's recollection and the dental records that were accessible. Keep in mind that this is a restriction since memory isn't always reliable.

- **Proper Oral Hygiene Practices:** How often (in minutes) you wash your teeth and how often you see the dentist.

6. Statistical Analysis

Using SPSS Statistics 28.0 (IBM Corp., Armonk, NY, USA), the data were critically examined. It was deemed statistically significant if the p-value was less than 0.05.

- **Descriptive Statistics:** The mean ± standard deviation (SD) was used to display continuous data, and the case and control groups were compared using either the independent-samples t-test or the Mann-Whitney U test, depending on whether the variables were normal. We used the Chi-square test or Fisher's exact test to compare categorical variables, which were given as frequencies (percentages).
- **Univariate Analysis:** The association between osteoporosis and tooth loss was assessed using logistic regression for severe tooth loss and linear regression for the number of teeth lost.
- **Multivariate Analysis:** The aOR and 95% CI for the link between osteoporosis and severe tooth loss were estimated using multiple logistic regression, which allowed us to account for possible confounders. The relationship with tooth loss, a continuous variable, was evaluated using multiple linear regression. Covariates included in the final models were those with p-values < 0.1 in the univariate analysis or deemed clinically relevant.

RESULTS

A total of 458 women who had gone through menopause were examined. Table 1 shows that 400 participants were recruited and ultimately completed the trial, with 200 belonging to the osteoporotic group and 200 to the non-osteoporotic group.

Table 1. Baseline Characteristics of the Study Participants.

Characteristic	Osteoporotic Group (No. =200)	Non-Osteoporotic Group (No.=200)	p-value
	(mean ± SD)		
Age (years)	65.4 ± 6.1	60.1 ± 5.3	**<0.001**
Years since menopause	18.2 ± 7.5	12.5 ± 6.2	**<0.001**
Body Mass Index (kg/m²)	22.1 ± 2.8	26.5 ± 3.4	**<0.001**
Smoking Status No. (%)			
Never Smoker	160 (80.0)	170 (85.0)	0.215
Former Smoker	35 (17.5)	25 (12.5)	
Current Smoker	5 (2.5)	5 (2.5)	
Diabetes Mellitus No.(%)	30 (15.0)	22 (11.0)	0.245
Calcium Supplement Use No.(%)	85 (42.5)	78 (39.0)	0.482
Regular Dental Visits No.(%)	70 (35.0)	125 (62.5)	**<0.001**
Tooth Brushing (times/day) (mean ± SD)	1.6 ± 0.7	1.9 ± 0.6	**<0.001**

Table 2. Dental Status and Tooth Loss Comparison

Dental Variable	Osteoporotic Group	Non-Osteoporotic Group	p-value
Number of Remaining Teeth (Mean ± SD)	14.2 ± 7.5	20.8 ± 5.9	**<0.001**
Number of Teeth Lost (Mean ± SD)	13.8 ± 7.5	7.2 ± 5.9	**<0.001**
Severe Tooth Loss (<20 teeth) No. (%)	155 (77.5%)	80 (40.0%)	**<0.001**
Primary Reason for Loss (Patient-Reported) No. (%)			0.002
Periodontitis	115 (57.5)	85 (42.5)	
Caries	85 (42.5)	1. 7.5)	2.

The two groups were similar in smoking status and diabetes prevalence. The osteoporotic group, on the other hand, was somewhat older, had been menopausal for longer, and had a lower average body mass index. The control group reported better oral hygiene practices, such as more frequent brushing and dental checkups (Table 1).

Dental status analysis showed significant differences between groups. The osteoporotic group had fewer remaining teeth (14.2 ± 7.5 vs 20.8 ± 5.9, p<0.001) and more teeth lost (13.8 ± 7.5 vs 7.2 ± 5.9, p<0.001). Severe tooth loss was more common in the osteoporotic group (77.5% vs. 40.0%, p<0.001). Periodontitis was the main cause of tooth loss in the osteoporotic group, while caries was more common in the control group (Table 2).

Multiple regression analyses were conducted to control for confounders. After adjusting for age, years since menopause, BMI, smoking status, diabetes, and dental

visit frequency, osteoporosis remained a significant independent predictor of severe tooth loss.

The multivariate logistic regression model showed that women with osteoporosis had more than 3 times the odds of severe tooth loss compared to their non-osteoporotic counterparts (aOR: 3.15, 95% CI: 1.98-5.01, p<0.001). Increasing age. Multivariate logistic regression showed that women with osteoporosis had over three times the odds of severe tooth loss compared to non-osteoporotic women (aOR: 3.15, 95% CI: 1.98-5.01, p<0.001).

Table No. 3. Multiple Regression Analysis for Severe Tooth Loss (<20 teeth)

Variable	Adjusted Odds Ratio (aOR)	95% Confidence Interval (CI)	p-value
Osteoporosis (Yes vs. No)	3.15	1.98 - 5.01	**<0.001**
Age (per 1-year increase)	1.05	1.01 - 1.10	0.028
BMI (per 1-unit increase)	0.92	0.87 - 0.98	0.007
Regular Dental Visits (Yes vs. No)	0.48	0.30 - 0.76	0.002

Increasing age and lower BMI were also significant risk factors, while regular dental visits were protective (Table 3). fewer remaining teeth, a higher prevalence of severe tooth loss, and are over three times more likely to have lost a critical number of teeth (<20), even after accounting for major confounding factors such as age, BMI, and dental care habits.

DISCUSSION

The greater mean number of teeth lost in the osteoporotic group (13.8 vs. 7.2) supports the idea that systemic bone loss may also affect the alveolar bone supporting the teeth[13]. mandible and maxilla, like the spine and hip, are composed of trabecular bone, which is highly metabolically active and particularly susceptible to estrogen deficiency and increased osteoclastic activity in osteoporosis. This bone resorption can reduce alveolar bone density and height, compromise tooth support and increase the risk of loss[14,15].

The significance of professional preventive treatment, especially in the early management of periodontitis and caries, is underscored by the fact that frequent dental visits emerged as a substantial protective factor.

Several limitations are included in this investigation. Only correlation, not causation, can be established using the case-control approach. Patient recollection, which may be biased, was used to determine the causes of tooth loss. The findings would be stronger with a prospective cohort study. Even after controlling important confounders, unmeasured variables, such as genetics, food history, and socioeconomic position, may still lead to residual confounding. Additionally, generalizability may be limited due to single-central recruitment[16,19].

Notwithstanding these caveats, the research has significant merits. There was strict grouping; the gold standard for osteoporosis diagnosis was DXA; a qualified dentist who was unaware of the patients' bone state performed the dental examinations; and all other confounding variables were thoroughly controlled for in the analysis[20,21].

These results have important consequences for clinical practice. One possible symptom of systemic bone fragility in postmenopausal women is tooth loss. For postmenopausal women presenting with significant tooth loss or rapidly advancing gum disease with no apparent aetiology, dentists may consider suggesting bone mineral density tests. In comprehensive treatment, physicians addressing osteoporosis should stress the need to maintain good oral hygiene and to attend frequent dental appointments. These findings emphasise the need for dental and medical experts to work together to reduce the risk of osteoporosis and tooth loss in women after menopause, and the tight connection between systemic and oral bone health[21].

CONCLUSION

A strong correlation exists between osteoporosis and tooth loss in postmenopausal women, highlighting the need for integrated medical and dental care.

Author's Contribution:

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Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Scar Tenderness at Repeat C. Section

Evaluation of Scar Integrity in Patients Having Scar Tenderness at Repeat Caesarean Section in Term Pregnancy at a Tertiary Care Hospital

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ABSTRACT

Objective: To evaluate scar integrity in patients having scar tenderness at repeat caesarean section in term pregnancy at a tertiary care hospital, Peshawar.

Study Design: A cross sectional study.

Place and Duration of Study: This study was conducted at the Department of Obstetrics & Gynaecology, Lady Reading Hospital, Peshawar from 1st July 2023 to 31st December 2023.

Methods: A total of 142 term pregnant women with previous one caesarean section presenting with caesarean scar tenderness were included. Scar integrity was assessed as either the presence or absence of scar dehiscence. Data was analyzed using SPSS. Quantitative variables were presented as mean ± standard deviation (SD) and categorical variables as frequency and percentage. Association was determined using chi-square test and a p-value of ≤0.05 was regarded as statistically significant.

Results: The mean age of the patients was 29.37 ± 6.14 years, mean gestational age was 38.47 ± 1.17 weeks, and mean BMI was 23.29 ± 2.58 kg/m². 41 patients had scar dehiscence (28.9%) and 101 patients did not have any scar dehiscence (71.1%). No statistically significant association was found between scar dehiscence and educational status (p=0.181), socioeconomic status (p=0.571), residence (p=0.219), age group (p=0.763), gestational age (p=0.119), BMI (p=0.736), or parity (p=0.571).

Conclusion: A significant percentage of term pregnant women with previous 1 caesarean section had scar tenderness with scar dehiscence being observed in over one-third of them. None of the demographic or obstetric variables were found to be significantly related to scar dehiscence, but scar tenderness is a clinical sign that needs attention and prompt obstetric treatment.

Key Words: Scar dehiscence; scar tenderness; previous caesarean section; scar integrity; term pregnancy; repeat caesarean section.

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INTRODUCTION

Cesarean section has emerged as one of the most common obstetric procedures in the world, and it has been increasing in the last few decades[1].

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While caesarean delivery can be lifesaving for mother and child, the growing proportion of women with an older caesarean scar has brought with it new clinical challenges when women become pregnant again, such as safety of repeat caesarean section, trial of labour after caesarean and risk of caesarean scar-related complications[2]. Therefore, it is necessary to assess the previous uterine scar correctly in terms of antenatal and intrapartum decision making in term pregnancy.

The integrity of the lower uterine segment scar is significant because if healing is inadequate, the scar will thin, open up, or in rare cases, the uterus may rupture. Caesarean scar defects are also now known to be part of a spectrum of abnormal scar healing and have been linked to gynecological symptoms, obstetric complications and to the technical difficulty of subsequent caesarean section[3]. In women who present at term with a previous caesarean section, scar tenderness is regarded as a clinical warning sign, particularly if accompanied by lower abdominal pain,

uterine irritability and/or maternal discomfort. The accuracy of clinical judgement, however, is not always reliable in predicting the actual intraoperative scar weakness, and the tenderness of the scar does not accurately predict the weakness of the scar[4,5].

Scar dehiscence may occur in a significant number of women with previous caesarean section and scar tenderness as reflected by recent regional data, which would highlight the importance of thorough assessment prior to and during repeat caesarean delivery[6]. Lower uterine segment thickness also has been investigated as a non invasive predictor of scar integrity, and systematic reviews indicate a relationship between lower thin measurements of the lower uterine segment and scar defects[7,8].

Simple clinical parameters like scar tenderness are still very relevant in resource-limited tertiary care hospitals where women often present late in pregnancy and information about previous operations may be incomplete[9]. In more recent analyses, categories of risk were created using the measure of thickness of the lower segment of the uterus, and local validation is needed before this threshold is applied in general[10]. Therefore, in term pregnancy, assessment of the relationship between scar tenderness and intraoperative scar integrity at repeat caesarean section can be used clinically as evidence to enhance maternal safety, surgical preparedness and decision making in tertiary obstetric care.

METHODS

This was a cross-sectional study carried out in the Department of Obstetrics & Gynaecology, Lady Reading Hospital, Peshawar, from 1st July, 2023 till 31st December 2023. The study was conducted using non-probability consecutive sampling technique in which 142 patients were included. Eligibility criteria included having had a single lower-segment caesarean section, singleton term pregnancy (gestional age ≥ 37 weeks), and scar tenderness during trial of labour or antenatal assessment. Localized tenderness to the previous caesarean scar/lower uterine segment on clinical examination, with or without lower abdominal pain, was classified as scar tenderness. The patients with more than one caesarean section, previous classical caesarean section, history of uterine surgery other than caesarean section, multiple pregnancy, placenta previa, placenta accreta spectrum, intrauterine fetal death, known fetal anomaly and incomplete clinical record were excluded from the study.

Detailed history was taken after informed consent from each patient including age, parity, gestational age, booking status, indication for previous caesarean section, duration since previous caesarean section, onset of labour pain, associated symptoms. A general physical examination and obstetric examination was conducted. Particular attention was given to the presence and severity of scar tenderness. All cases had a standard obstetric assessment, fetal monitoring and an ultrasound abdomen performed. The lower uterine segment was evaluated by ultrasound for the presence of a scar, scar thinning, scar discontinuity, bulging of membranes, or any abnormality indicative of scar dehiscence.

Those who reported scar tenderness were treated as per departmental protocol and delivered by a repeat cesarean section. Before the uterine incision, the prior uterine scar was carefully examined during surgery. Adequacy of the scar was determined intraoperatively and documented as either an intact scar or scar dehiscence. Separation or thinning of the previous uterine scar with intact serosa and/or fetal membranes without complete uterine rupture was considered scar dehiscence. If there was complete uterine rupture, it is to be noted separately.

A predesigned proforma was used to record all relevant information. The primary outcome variable was scar integrity, defined as dehiscence or no dehiscence of the scar. Data were entered and analyzed using SPSS. The quantitative variables (age, gestational age, parity and interpregnancy interval) were expressed as mean ± standard deviation. Qualitative variables like booking status, previous caesarean section, the ultrasound results and scar integrity were presented as frequency and percentages. Stratification was done where appropriate to assess the distribution of scar dehiscence according to important clinical variables.

RESULTS

A total of 142 women with previous one caesarean section and scar tenderness at term pregnancy were included in the study. The mean age was 29.37 ± 6.14 years, mean gestational age was 38.47 ± 1.17 weeks, and mean BMI was 23.29 ± 2.58 kg/m². Baseline clinical characteristics are summarized in Table 1.

Table No. 1. Baseline clinical characteristics of study participants

Variable	Frequency (%) / Mean ± SD
Age, years	29.37 ± 6.14
Gestational age, weeks	38.47 ± 1.17
BMI, kg/m²	23.29 ± 2.58
Age 18–30 years	79 (55.6%)
Age 31–40 years	63 (44.4%)
Gestational age 37–38 weeks	70 (49.3%)
Gestational age 39–40 weeks	72 (50.7%)
Healthy BMI, 18–25 kg/m²	110 (77.5%)
Overweight/obese BMI, >25 kg/m²	32 (22.5%)
Para 1	78 (54.9%)
Para >1	64 (45.1%)

Sociodemographic characteristics of the study population are presented in Table 2. Most patients were from rural areas 94 (66.2%).

Scar dehiscence was observed in 41 patients (28.9%), while 101 patients (71.1%) had no scar dehiscence, as shown in Table 3.

Table No. 2. Sociodemographic characteristics of study participants

Variable	Frequency (%)
Educational status	
Illiterate	45 (31.7%)
Secondary education	51 (35.9%)
Higher education	46 (32.4%)
Socioeconomic status	
Rich	51 (35.9%)
Middle	40 (28.2%)
Poor	51 (35.9%)
Residence	
Rural	94 (66.2%)
Urban	48 (33.8%)

Table No. 3. Frequency of scar dehiscence among study participants

Scar dehiscence	Frequency (%)
Yes	41 (28.9%)
No	101 (71.1%)
Total	142 (100.0%)

The association of scar dehiscence with sociodemographic variables is shown in Table 4. No statistically significant association was observed with educational status, socioeconomic status, or residence.

Table No. 4. Association of scar dehiscence with sociodemographic variables

Variable	Scar dehiscence Yes n (%)	Scar dehiscence No n (%)	Total	p-value
Educational status				
Illiterate	16 (35.6%)	29 (64.4%)	45	**0.181**
Secondary education	10 (19.6%)	41 (80.4%)	51	
Higher education	15 (32.6%)	31 (67.4%)	46	
Socioeconomic status				
Rich	12 (23.5%)	39 (76.5%)	51	**0.571**
Middle	13 (32.5%)	27 (67.5%)	40	
Poor	16 (31.4%)	35 (68.6%)	51	
Residence				
Rural	24 (25.5%)	70 (74.5%)	94	**0.219**
Urban	17 (35.4%)	31 (64.6%)	48	

The association of scar dehiscence with clinical and obstetric variables is presented in Table 5. Scar dehiscence was more frequent at 39–40 weeks of gestation 25/72 (34.7%) than at 37–38 weeks 16/70 (22.9%), but the difference was not statistically significant.

Table No. 5. Association of scar dehiscence with clinical and obstetric variables

Variable		Scar dehiscence Yes n (%)	Scar dehiscence No n (%)	Total	p-value
Age group:	18–30 years	22 (27|.8%)	57 (72.2%)	79	**0.763**
	31–40 years	19 (30.2%)	44 (69.8%)	63	
Gestational age:	37–38 weeks	16 (22.9%)	54 (77.1%)	70	**0.119**
	39–40 weeks	25 (34.7%)	47 (65.3%)	72	
BMI: Healthy, 18–25 kg/m²		31 (28.2%)	79 (71.8%)	110	**0.736**
Overweight/obese, >25 kg/m²		10 (31.3%)	22 (68.8%)	32	
Parity:	Para 1	21 (26.9%)	57 (73.1%)	78	**0.571**
	Para >1	20 (31.3%)	44 (68.8%)	64	

P-values were calculated using Pearson chi-square test

DISCUSSION

This study aimed at the assessment of the integrity of scars of term pregnant women with previous one Caesarean section (CS) presented with scar tenderness. Nearly one-third (28.9%) of symptomatic women were found to have scar dehiscence, or a weak scar. This finding suggest that scar tenderness may be a significant warning sign in women who have had a prior caesarean section, especially at term or at the time of trial of labour. Our finding was similar to a study who reported that 23.75% of women with tenderness after their first caesarean section had scar dehiscence. His study also revealed that there were no significant relationships between age, gestational age, BMI or

parity with scar dehiscence, consistent with our findings. The slightly higher incidence of our study could be related to only considering term pregnancies, as progressive thinning of the lower uterine segment and uterine contractions could possibly result in increased risk for scar compromise.[11]

Conversely, Rozenberg et al experienced scar dehiscence in 14.9% of patients with a previous one CS and scar tenderness[12]. This lower frequency might account for different inclusion criteria, diagnostic methods and gestational age distribution. Their study comprised of patients beyond 28 weeks gestation, while our study involved pregnant women at term. The lower portion of the uterus is more stretched at term, increasing the likelihood of the presence of scar thinning or dehiscence. Interpretation of the ultrasound and the threshold for the diagnosis of dehiscence can also create some variation in the frequency reported.[13]

Our study also has a higher frequency than in large, general populations having elective repeat caesarean section. In a study by Bujold et al, 4.6% of women undergoing elective repeat caesarean delivery had uterine scar dehiscence[14]. The much lower rate in their study is understandable because they included an elective repeat caesarean population rather than a symptomatic group with scar tenderness. They reported that maternal age and parity were not significant factors influencing dehiscence, which is consistent with our results, and therefore does not allow for consistent prediction of scar integrity based on maternal age and parity alone.[15]

We found no significant relationship between scar dehiscence and age, parity, BMI, education, socioeconomic status or residence; these variables may be more clinically important than demographic variables for the identification of women at risk. There was no statistical difference in the rate of scar dehiscence between 39–40 weeks and 37–38 weeks, although the dehiscence rate was higher at 39–40 weeks, numerically. This may be because of the small gestational age range and small sample size of the subgroups. However, like BMI, there was no significant relation observed, likely due to the fact that the integrity of the uterus scar is modified by a variety of factors related to the scar, such as previous surgical technique, method of uterine closure, post-surgical infection, interpregnancy interval, lower uterine segment thickness, and duration of labour[16,17].

Lower uterus segment thickness has been investigated as a useful ultrasound parameter to predict scar defects in our study. In a study by Kandregula et al, found that lower uterine segment thickness was associated with a higher risk of uterine dehiscence or rupture, but they did not standardize the measurement techniques or cut-off values. Thus, ultrasound is a tool to assist in the clinical decision-making process, but should not be used as a substitute for clinical evaluation. Ramadan et al, further demonstrated that ultrasound-based management alone did not result in any significant decrease in adverse maternal-fetal outcomes, and thus ultrasound should be combined with clinical symptoms, such as scar tenderness and labour status.[18]

The results of this study are in agreement with published literature, indicating that in women with previous caesarean section, tenderness of the scar is an important clinical sign. The increased frequency of scar dehiscence in our study may be due to the study population (symptomatic), term gestation, tertiary care center, and potential referral bias. However, there is no significant association with any of the variables studied, suggesting that routine obstetric variables are not sufficient to predict scar dehiscence.

This study has certain limitations which needs to be addressed. It was a single centre cross sectional study with possible limitations in generalizability. A group of women who were not tender to scar was not available for comparison, so the predictive value of scar tenderness was not available. Important variables such as time to conception, reason for previous cesarean section, method of uterine closure, infection following surgery and length of labour were not assessed. Furthermore, the assessment of the integrity of scar with ultrasound is operator-dependent and no common lower uterine segment thickness cut-off value was used.

CONCLUSION

Scar dehiscence was observed in a considerable proportion of term pregnant women with previous caesarean section presenting with scar tenderness. Although no significant association was found with age, gestational age, BMI, parity, education, socioeconomic status, or residence, scar tenderness remains an important clinical warning sign. Therefore, women with previous caesarean section who present at term with scar tenderness should be carefully evaluated and managed promptly to reduce the risk of maternal and fetal complications..

Author's Contribution:

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Drafting or Revising Critically:	Sadia Baig, Arsh 5. Ilham
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Original Article

Structured Educational Program for Mothers: Addressing Febrile Seizures and Associated Stress

Asima Bibi, Madiha Mukhtar and Sarfraz Masih

ABSTRACT

Objective: To assess and enhance structured educational program for mothers and reducing stress regarding febrile seizures before and after implementation of structured educational program.

Study Design: Quasi experimental study

Place and Duration of Study: This study was conducted at the Medical Department, Children Hospital Lahore from 1st June 2025 to 30th November 2025.

Methods: Eighty two mothers of children with febrile seizures, aged 6 months to 6 years were enrolled. A structured close ended questionnaire was used to evaluate the pre-post data that contained 20 knowledge questions statements and 18 items practice based statements and stress related 18 statements containing Likert scale were used to assess the level of knowledge, practices and stress of mothers before and after guidelines-based educational intervention.

Results: The mean knowledge percentage score was 48±4.46 and the mean practice percentage score was 50±4.42, indicating poor baseline knowledge and practices. After the educational intervention, the mean knowledge score increased to 60±4.01 and the practice score increased to 64±3.75. At follow-up, knowledge and practice scores remained improved at 58±4.12 and 62±3.89, respectively. Parental stress decreased from 57±4.17 before the intervention to 46±4.49 after the intervention and 45±4.51 at follow-up. These changes were statistically significant ($p = 0.001$).

Conclusion: Structured intervention was highly effective in enhancing knowledge and practices of mothers while reducing stress among mothers of children with febrile seizures.

Key Words: Febrile seizures, Knowledge, Practice, Stress, Management

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INTRODUCTION

Febrile seizures are common childhood seizures associated with fever and no underlying intracranial infection or prior afebrile seizures.[1] The symptoms are primarily seen in children between 6 months and 5 years of age; prevalence rates are approximately 2-5% worldwide, but vary by region. They are the most common reason for pediatric hospitalization in Pakistan, and are most likely to occur in children under 3 years of age, particularly 6-12 months of age, and usually resolve over a few minutes.[2] Although febrile seizures are generally harmless, they cause a great deal of stress and anxiety for both the caregivers and especially the mother.[3]

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It is well documented that parents are frightened by febrile seizures and over 90% of parents have reported a high level of fear during febrile seizures.[4] This lack of confidence is often due to lack of knowledge and misconceptions about serious consequences that result in unsafe first aid practices and unnecessary delays in medical treatment.[5]

Ongoing caregiver worry can also impact the response to subsequent outbreak(s). While effective home management, including the recognition of a fever and how to manage it, as well as the knowledge of when to seek medical attention, is crucial, there is significant knowledge gaps as many parents have limited knowledge of the signs of fever and how to recognise it, as well as suitable first-aid.[6] Education is key in bridging the gap in knowledge that caregivers have about febrile seizures. Specific instructions to mothers as primary caregivers boost confidence, improve initial management of seizures, and minimize long-term psychological distress.[7] The interventions have demonstrated benefits for family well-being, a decrease in unnecessary hospitalizations and unnecessary healthcare expenses caused by suboptimal family care, an improvement in caregiver responses, and decreased anxiety.[8-10] More especially this study is relevant in Pakistan, where parents' poor knowledge is leading to

unnecessary hospital visits, delay in seeking care, and higher levels of emotional stress.[11] There is evidence that informed caregivers are better prepared to respond to seizures, keeping them safe and cool, and obtaining prompt medical attention, and that they experience less anxiety and better coping during seizures.[12,13] International research also confirms that formal education has a great impact on parental knowledge, stress levels and safer management practices.[14,15] Hence, the purpose of this study is to improve maternal knowledge and decrease maternal stress by providing a structured education program about febrile seizure management and the psychological impact of febrile seizures.

METHODS

This quasi-experimental single group pre-test and post-test study was conducted at Department of Pediatrics at Children's Hospital Lahore from 1st June to 30th November 2025 vide letter No. UOL/IREB/25/09/003 dated 30.06.2025. Eighty two mothers of children aged 6 months to 6 years who were admitted with febrile seizures were enrolled. Those mothers who were the main caregivers of the child, lived within the study area defined, or registered at the participating healthcare facilities, were willing to give informed consent, could understand the educational content and were able to attend the educational sessions and follow up assessments were included. Those mothers who were not the primary caregivers, lacked previous specialized training or knowledge about management of febrile seizures, and who had children with chronic neurological disorders, severe systemic illnesses, developmental disabilities, or other significant medical conditions that could affect participation were excluded. Structured demographic questionnaire and standardized assessment instruments measuring mothers' knowledge, home management practices and stress concerning febrile seizures were used to gather baseline information. Demographic data, including the maternal age, level of education, occupation, socioeconomic status, family type, previous history of febrile seizures, and clinical data related to the child, was collected in the demographic questionnaire.

A 20 item close-ended questionnaire was used to check the knowledge of mothers about febrile seizures. All correct answers received a mark of 1 and all incorrect answers received a mark of 0, thus giving a total mark of 0-20. The knowledge scores were classified as poor (0-7), moderate (8-13) and good (14-20). An 18 item questionnaire with dichotomous responses (Yes = 1, No = 0) was used to evaluate home management practices. The range of total practice scores was 0 to 18 with poor (0-9), moderate (10-13) and good (>13). The Parental Stress Scale (18 items, 5 point Likert scale) was used to assess parental stress. Stress levels were categorized as low (18–39), moderate (40–59), and high (60–90). The structured educational program consisted of content on the causes, symptoms, management of fever, first aid for seizures, when to seek medical help, preventing complications of a seizure and coping psychologically as a caregiver. Lectures, discussion, demonstrations and distribution of informational material were used to conduct educational sessions. The study instruments were also validated based on the content, the Content Validity Index (CVI) of the instruments of knowledge, practice and stress were 0.82, 0.84 and 0.81 respectively. The instruments were found to have good internal consistency in reliability testing. Data was inputted and analysed within SPSS version 26. Paired t-test was used to compare the mean knowledge and practice and stress scores before and after the intervention. The $p \leq 0.05$ was considered statistically significant.

RESULTS

Most mothers were aged 25-35 years (63.4%), and all participants were female, as the study included mothers only.

Table No. 1: Distribution of demographic variables (n=82)

Variable	No.	%
Mothers' age (years)		
18-24	21	25.6
25-35	52	63.4
> 35	9	11.0
Education		
Illiterate	27	32.9
Primary	16	19.5
Middle	16	19.5
High	13	15.9
Intermediate/above	10	12.2
Number of children		
One	22	26.8
Two	26	31.7
Three or more	34	41.5
Child's age		
6 months to 2 years	45	54.9
3–5 years	37	45.1
Residence		
Rural	37	45.1
Urban	36	43.9
Semi-urban	9	11.0
Occupation		
Homemaker	44	53.7
Daily wage worker	10	12.2
Salaried employee	17	20.7
Self-employed	11	13.4
Family type		
Joint	58	70.7
Nuclear	24	29.3

About one-third was illiterate 32.9%, while the remaining participants had education ranging from

primary to intermediate/above. Regarding family and living characteristics, 41.5% had three or more children, and more than half of the children were aged 6 months to 2 years (54.9%). Residence was nearly equally distributed between rural (45.1%) and urban (43.9%) areas. Most mothers were homemakers (53.7%) and lived in joint family systems (70.7%) [Table 1]..

The mean knowledge percentage score increased from 48±4.46 before the intervention to 60±4.01 after the intervention and remained improved at follow-up 58±4.12. Similarly, the mean practice percentage score improved from 50±4.42 before the intervention to 64±3.75 after the intervention and was sustained at follow-up 62±3.89. The improvements in both knowledge and practices were statistically significant (p=0.001), indicating the effectiveness of the structured educational intervention (Table 2).

Mothers had a moderate level of stress before the intervention, with a mean score of 57±4.17. After the educational program, the mean stress score decreased to 46±4.49 and remained reduced at follow-up 45±4.51. This indicates a sustained reduction in parental stress after the structured educational intervention (Table 3).

Table No. 2: Comparison of pre-, post- and follow-up percentage scores of mothers' knowledge and practices regarding febrile seizures

Variable	Pre-intervention percentage score	Post-intervention percentage score	Follow-up percentage score	t-test	p-value
Knowledge	48±4.46	60±4.01	58±4.12	18.10	0.001
Practice	50±4.42	64±3.75	62±3.89	30.73	0.001

Table No. 3: Mean parental stress scores across three time points regarding febrile seizure management (n = 82)

Measurement time	Mean±SD	Stress category
Pre-intervention	57±4.17	Moderate stress
Post-intervention	46±4.49	Moderate stress
Follow-up	45±4.51	Moderate stress

DISCUSSION

This quasi-experimental study aimed to assess and improve mothers' knowledge of febrile seizures across pre-intervention, post-intervention, and follow-up phases. Prior to the intervention, 58% of participants had poor knowledge. The educational intervention increased good knowledge to 73% and 71% of participants at follow-up which was statistically significant (p<0.05). This is consistent with studies demonstrating comparable impact of specific learning on knowledge, attitudes, and practices of parents of febrile seizures.[16] Misconceptions like febrile seizures being equally epilepsy, always needing anticonvulsants or causing brain damage were significantly reduced post intervention, consistent with what is found in the literature; that misconceptions are common among uneducated parents.[17] Follow-up assessments showed sustained improvement in knowledge, indicating that correcting misconceptions and providing evidence-based education leads to lasting retention over time.[18] Mothers frequently misunderstand febrile seizures, often conflating them with epilepsy or believing they cause brain damage. In Saudi Arabia, recent study found that 73.3% of parents incorrectly believed febrile seizures are a form of epilepsy.[19] This is also observed globally surveys that inadequate parental knowledge and high levels of concern are common and contribute to fear and inappropriate first-aid responses.[20]

Interventions such as structured educational sessions, pamphlets, or empowerment programs significantly improve parental knowledge, attitudes, and practices. This study aligns with a clinical trial showed significant increased knowledge, attitude, and practice scores one month after structured educational sessions compared to controls.[21] Another quasi-experimental study is consistent with it that empowerment programs significantly (p<.001) elevated knowledge and home management practices.[18] Health education also improves parents' confidence and attitude toward emergency handling of febrile seizures.[22]

In the present study, before the intervention, a majority of participants demonstrated poor home management practices. Only 17 participants exhibited moderate practices, while 15 participants (18%) demonstrated good practices. This indicates that the overall level of home management was relatively low prior to the intervention. Following the intervention, there was a marked improvement in home management practices. There was a significant rise in the number of participants that reported having good practices: 64 (78%) compared to 10 (12%) for poor practices. Slightly less of those with moderate practices, 8 (10%), increased. The findings indicate that the intervention had a positive impact on the improvement of home management behaviors. Of the 62 participants (76%) who followed good practices at follow-up, there was evidence of continued improvements with time. The short-term intervention benefits are consistent with previous studies that have found education that is targeted to reduce febrile seizures to be effective in

improving caregiver knowledge and home management.[18] The high response rates at follow-up indicate that parents remembered important points about recognising fever, effective management and not performing harmful practices like shaking or mouth-to-mouth resuscitation. The results are also consistent with previous studies that have reported that structured maternal education has a significant effect on knowledge, attitude and practice about febrile seizure prevention and care.[17] Although this study demonstrates improvement of knowledge across populations, recent studies have shown that there remain significant parent misconceptions and concerns about febrile seizures, and that additional education and reinforcement strategies are needed.[23]

Similarly, many mothers monitor fever and have access to thermometers, misunderstandings about seizure management remain reinforcing that basic informational interventions can reduce 'fever phobia' and unsafe practices in community settings.[1] The study results are consistent with international evidence demonstrating that educational and psychosocial interventions significantly reduce parental stress in cases of febrile seizures.[23] A study by Simbolon et al[24] reported high levels of anxiety among parents of children with febrile seizures, primarily due to inadequate knowledge and fear of epilepsy. The current study extends this literature by demonstrating that a structured intervention can effectively reduce parental stress and improve long-term coping.

CONCLUSION

The structured educational interventional program had an encouraging effect on improving the knowledge, practices and maternal stress scores of mothers regarding Febrile Seizures management. The structured intervention was highly effective in reducing stress among mothers of children with febrile seizures. Stress levels significantly decreased from pre-intervention to post-intervention and remained stable (moderate stress) at follow-up. These findings emphasize the importance of parental education and psychosocial support in managing febrile seizures and highlight the vital role of nurses in delivering family-centered care.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Asima Bibi, Madiha Mukhtar
Drafting or Revising Critically:	Asima Bibi, Sarfraz Masih
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Evaluation of Lactation Support Education among Primiparous Post-Cesarean Mothers

Lactation Support Education among Primiparous Post-Cesarean Mothers

Nasreen Asghar, Madiha Mukhtar and Sarfraz Masih

ABSTRACT

Objective: To evaluate the effects of Lactation Support education on mother's knowledge regarding breastfeeding and breast engorgement in primiparous post cesarean women.

Study Design: Quasi-experimental study

Place and Duration of Study: This study was conducted at the Sharif Medical Hospital Lahore from 1st July 2025 to 30th November 2025.

Methods: This study was conducted among 90 primiparous mothers. A questionnaire regarding breastfeeding knowledge and Hill & Humenick six-point breast engorgement scale was used to collect the data. The participants' baseline breastfeeding knowledge scores was initially obtained through pre-assessment. The intervention group took part in prenatal lactation support education two weeks earlier to their planned cesarean section. The intervention group received lactation support education. After intervention the knowledge and breast engorgement was assessed to see the effect of the intervention.

Results: The intervention group showed a noticeable improvement following the intervention. Their mean rank knowledge score increased significantly to 66.59±2.256 from the control group's mean of 24.41±1.876 (z= –7.724, p=0.000). Similarly there was a statistically significant difference in breast engorgement outcomes between the control and intervention groups, where the control group had a substantially higher mean rank 56.37±1.252 as compare to the intervention group 34.63±0.919, indicating less engorgement symptoms (p-value of 0.000)

Conclusion: The lactation support education improved breastfeeding knowledge and reduced breast engorgement among primiparous mothers. Following the instructional session, mothers in the intervention group shown a notable improvement in their breastfeeding knowledge from poor to good, but the control group showed little change.

Key Words: Lactation education, Breast feeding support, Breast feeding knowledge, Breast engorgement

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INTRODUCTION

Breastfeeding is vital for the health and development of both mother and child, providing essential nutrition and strengthening maternal-infant bonding.[1] Lactation changes in the mammary glands brought about by pregnancy and delivery are essential for successful breastfeeding, which is vital to the survival of the newborn.[2,3] However, breastfeeding issues like engorgement, low milk supply, and delayed lactation can make exclusive breastfeeding difficult, especially for first-time mothers C-sections are becoming more common worldwide, with more than 1.8 million being performed every year, and rates that are even higher than the WHO recommendation of 10-15%.[4]

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The rapidly increasing population of Pakistan and lack of adequate health care facilities also contribute to maternal and neonatal health issues.[5]

Post-cesarean mothers experience extra complications such as pain, delayed lactation and challenges to self-care during recovery that may have a negative effect on breastfeeding.[6] The discomfort, pain and decreased milk production caused by breast engorgement are among the main obstacles to exclusive breastfeeding[7] and are the result of hormonal feedback mechanisms.[8] Early lactation is especially vulnerable[9] owing to delayed responses of prolactin and oxytocin, and incomplete ductal emptying.[10] Other factors such as misconceptions, work-related constraints and environment also cause mothers to supplement with formula or water, reducing exclusive breastfeeding rates.[11] Breastfeeding interventions, such as lactation empowerment programs, are needed to enhance breastfeeding outcomes.[12] These programs, delivered by trained nurses, focus on educating mothers about breastfeeding techniques[13], managing engorgement, and promoting adequate milk supply.[14] Addressing gaps in knowledge and support can enhance lactation initiation, reduce breast engorgement, and promote exclusive breastfeeding[15], ultimately improving maternal and

infant health and reducing long-term economic and cognitive losses at the national level.[16]

METHODS

This two groups cases and control quasi experimental study was conducted at Department of Gynecology & Obstetrics, Sharif Medical City Hospital Lahore, Pakistan from 1st July 2025 to 30th November 2025 vide letter No. UOL/IREB/25/09/0016 dated 30th June 2025. The study population consisted of primiparous prenatal women. A purposive sample of 90 participants was recruited based on the inclusion criteria. Sample size was calculated while using Openepi version 3 with 95% confidence interval, 5% margin of error by using formula. Only first-time mothers with no prior breastfeeding experience, participants had an elective caesarean section, mothers ages of 18 and older-the typical range for new mothers accepted and women are eligible if they do not have any medical illnesses that prevent them from nursing, such as active breast infections etc were included. Mothers with prior pregnancies and breastfeeding experiences, unable to participate in breastfeeding or postnatal care due to severe postpartum mental health issues and serious pre-existing diseases, such as uncontrolled diabetes, severe cardiovascular disease were excluded.

Intervention group took part in prenatal lactation support education two weeks earlier to their planned cesarean section. A group comprising of 5-6 individuals received lactation support education, where a researcher delivered a detail education on the anatomy and physiology of the breast, the importance of breastfeeding methods, strategies for appropriate breastfeeding and challenges in post cesarean women. various breastfeeding positions were discussed like sitting & standing positions, football hold, cross-over hold, and side-lying position. Additional topics were covered the role of breastfeeding in breast engorgement prevention. While control group received only routine care no additional knowledge provided to them. The data was entered and analyzed through SPSS-25.

RESULTS

The demographic characteristics of participants were similar in both control and intervention groups. Most were aged 26–30 years (40% control, 42.2% intervention) and married (95.6%), with the majority being housewives (93.3% control, 86.7% intervention). The control group had more urban residents (57.8%), while the intervention group had a higher proportion with university education (37.8%) and rural residency (48.9%). Most participants belonged to extended families, and around two-thirds in both groups reported insufficient household income (Table 1).

The intervention significantly enhanced participants' knowledge. Before the intervention, 73.3% had poor knowledge, 26.7% had fair knowledge, and none had good knowledge. After the intervention, 64.4% achieved good knowledge, 35.6% fair knowledge, and no participants remained in the poor knowledge category, demonstrating a marked shift from low to high knowledge levels (Table 2).

Table No. 1: Demographic findings of the participants (n=90)

Variable	Control Group	Intervention Group
Age (years)		
<20	2 (4.4%)	5 (11.1%)
21-25	12(26.7%)	11(24.4%)
26-30	18(40%)	19(42.2%)
31- 35	13(28.9%)	10(22.2%)
Residence		
Rural	19 (42.2%)	22 (48.9%)
Urban	26(57.8%)	23(51.1%)
Education Level		
Basic	16 (35.6%)	8 (17.8%)
Secondary	19 (42.2%)	20 (44.4%)
University and above	10 (22.2%)	17 (37.8%)
Occupation		
Working Women	3 (6.7%)	6 (13.3%)
Housewife	42 (93.3%)	39 (86.7%)
Type of family		
Housewife	42 (93.3%)	39 (86.7%)
Nuclear	18(40%)	17(37.8%)
Extended	27(60%)	28(62.2%)
Monthly Income		
Enough	15(33.3%)	17(37.8%)
Not enough	30(66.7%)	28(62.2%)
Enough and saving	-	-
Marital Status		
Married	43(95.6%)	43(95.6%)
Divorced	2(4.4%)	2(4.4%)
Widow	-	-

Table No. 2: Knowledge of breast feeding among primi-parous women intervention group (n=45)

Knowledge Level	Pre-Intervention	Post Intervention
Poor Knowledge	33 (73.3%)	-
Fair Knowledge	12 (26.7%)	16 (35.6%)
Good Knowledge	-	29 (64.4%)

The intervention significantly reduced breast engorgement. In the intervention group, 73.3% reported no engorgement compared to 17.8% in the control group. Mild, moderate, and severe engorgement was higher in the control group (33.4%, 13.6%, 17.8%) than in the intervention group (8.9%, 8.9%, 4.4%). These results show the intervention effectively lowered both the frequency and severity of breast engorgement (Fig. 1).

At baseline, there was no significant difference in breastfeeding knowledge between the control (44.26±2.003) and intervention groups (46.74±1.694; p=0.640). After the intervention, the intervention group showed a significant improvement (66.59±2.256) compared to the control group (24.41±1.876; z = –7.724, p=0.000), demonstrating the effectiveness of the educational program (Table 3). Post-intervention, the intervention group showed significantly lower breast engorgement (34.63±0.919) than the control group (56.37±1.252), with the difference being statistically significant (Z = –4.260, p=0.000, p<0.05) [Table 4].

Table No. 3: Knowledge of breast feeding control versus intervention (n=90)

Breast Engorgement	Control (Mean Rank±SD)	Interventional (Mean Rank±SD)	Z test	P-value
Pre Intervention	44.26±2.003	46.74±1.694	-.468	0.640
Post Intervention	24.41±1.876	66.59±2.256	-7.724	0.000

Mann Whitney U test with p<.05 value as significant

Table No. 4: Effect of intervention on breast engorgement

Breast Engorgement	Control (Mean Rank±SD)	Interventional (Mean Rank±SD)	Z test	P-value
Post-Intervention	56.37±1.252	34.63±.919	-4.260	0.000

Mann Whitney U test with p<.05 value as significant

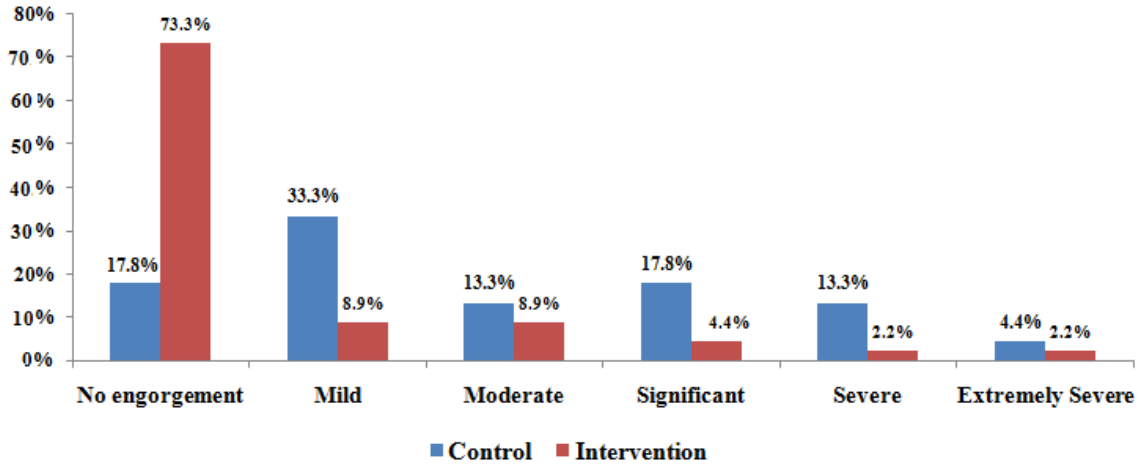

Figure No. 1: Breast engorgement levels among control and intervention groups

DISCUSSION

The demographic data found in this study was relatively similar between the intervention and control group, suggesting homogeneity and encouraging the internal validity for the intervention provided. In terms of age distribution, the majority of mothers in both groups were between the ages of 26 and 30 (40% in the control group and 42.2% in the intervention group), followed by those between the ages of 31 and 35. There were fewer women under the age of twenty in both groups, indicating that the study population did not adequately represent teenage pregnancies. The majority of moms had inadequate monthly income (66.7% control, 62.2% intervention), lived in extended families (60% control, 62.2% intervention), and were housewives (93.3% control, 86.7% intervention). The control group had a somewhat larger percentage of urban residents (57.8%) than the intervention group (51.1%). In terms of education, the majority of women had completed secondary school, while the intervention group had a greater percentage of moms with a university degree (37.8% vs. 22.2%). 95.6% of them were married. These results are in strong agreement with Awad et al[17] in Egypt, the average mother's age was 26.3 years, that 78% of moms were housewives, and that almost 40% had a university degree. Similar to the prenatal profile of the current study, another comparable study carried out in Egypt found that the majority of participants were primigravida (80%) with a mean gestational age of 32 weeks.[18] In similar way, another study from Egypt found supporting findings to this current study where 75% of the participants were married, living in rural areas, having low incomes.[19] Furthermore another such research conducted in India found similar findings, where a large number of mothers were living in joint families and more that 50% of the mothers were having secondary education, suggesting very similar pattern of home and residential pattern to the current study.[20]

Inconsistent to the findings of this current study, some differences in demographics were observed in a

previous study conducted by Velioğlu and Demirci2[1], the experimental and the control group had varied demographics especially in term of education status, employment and gestational age among mothers. Such differences in the groups may be because of the regional variations and differences in healthcare services. Amin et al[19] also observed a largely working maternal population, demonstrating diversity in female labor involvement across cultural and national contexts, whereas the majority of participants in the current study were housewives. Such differences may influence breastfeeding continuity and maternal exposure to health education.

Furthermore, the current study's control and intervention groups' similar demographics support causal inference by guaranteeing that post-intervention gains in knowledge and breast engorgement were mainly attributable to the educational intervention rather than demographic confounders. According to health literacy theory, the intervention group's increased percentage of educated moms may have improved information retention and implementation. According to the current study, no moms attained good knowledge after the intervention, and only a slight improvement in knowledge was seen in the control group, with poor knowledge declining from 68.9% to 53.3% and fair knowledge risings from 31.1% to 46.7%. On the other hand, the intervention group showed a significant improvement, with fair knowledge reaching 35.6%, good knowledge rising from 0% to 64.4%, and poor knowledge falling from 73.3% to 0%. This demonstrates the lactation support educational intervention's high efficacy. These results are consistent with a prior study that found that strong knowledge rose to 83% ($p<0.001$) while poor knowledge decreased from 41% to 17%.[17] More consistently, during a past study the good knowledge score among the mothers raised from 14.3% during the pre-intervention phase to 80% during the post-intervention period.[18] In another study conducted by Amin et al[19] was found that during post intervention period, good knowledge score among the participants increased to 85% and on the other hand the poor knowledge score decreased from 95% at pre intervention to 16% during the post intervention assessment. According to Tak and Chaturvedi[20], mean knowledge rose from 11.0±2.77 to 20.96±1.24 ($p=0.001$).

Breastfeeding Knowledge scores among mothers at baseline assessment in this present study were very similar between the control and intervention group ($p = 0.640$), showing homogeneity between the groups. Following the intervention, there was a highly significant difference ($Z=-7.724$, $p=0.000$), with the intervention group's mean rank being 66.59 as opposed to the control group's 24.41. Prior to study consistently showed that following the implementation of the supportive educational intervention, primiparous women's understanding of breastfeeding and breast engorgement greatly improved, with a highly significant difference at ($P<0.01\%$) (18). In a similar way, Amin et al[19] found a positive correlation between knowledge and less breast problems, as well as notable gains in mother self-care habits and knowledge. Tak and Chaturvedi[20] found that among primiparous moms participating in a structured educational program, mean post-test knowledge levels were significantly higher than pre-test values. The report claims that the significant increase in breastfeeding knowledge seen in this study is consistent with results from a number of recent investigations.

Furthermore, Devasia et al[22] found that educational interventions resulted not a significant improvement in participants' knowledge, where mothers were still found having inadequate knowledge regarding breastfeeding. The need and significance of a well-integrated multimodal and interactive therapy for primiparous mothers is highlighted to bring the difference.

This current study revealed that 73.3% participants from the intervention group had no breast engorgement, while in the control group only17.8% participants had no breast engorgement. Moreover 18% participants in the control group developed severe breast engorgement. These findings suggest that the education intervention decreased the incidence of breast engorgement among the participants in the intervention group.

CONCLUSION

The structured lactation support intervention is likely to be effective in enhancing knowledge about breastfeeding and decreasing breast engorgement in primiparous mothers. There were significant improvements in knowledge for the mothers in the intervention group, and in the incidence and severity of engorgement, compared with the control group. The results indicate that breastfeeders who received skill-based breastfeeding counseling in a targeted manner were more comfortable, had better feeding outcomes, and were more successful in breastfeeding, thus emphasizing the need to incorporate targeted, skill-based breastfeeding education into routine postpartum care.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Nasreen Asghar, Madiha Mukhtar
Drafting or Revising Critically:	Nasreen Asghar, Sarfraz Masih
Final Approval of version:	All the above authors
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Original Article

microRNA-145 Gene Expression Levels in the Blood of Breast Cancer

Evaluation of Circulating miRNA-145 Gene Expression as a Potential Biomarker in Breast Cancer: A Comprehensive Correlational Study with Hormonal Receptors, Clinical Parameters and Therapeutic Response

Intisar Mohammed Kashash, Kiaser Abdulsajjad M. Hussain and Alaa Hussein Mahdi

ABSTRACT

Objective: To investigate microRNA-145 gene expression levels in the blood of breast cancer patients versus healthy subjects and examine its relationship with molecular, clinical, and therapeutic features.

Study Design: Case-control study

Place and Duration of Study: This study was conducted at the Imam Hussein (AS) Center for Oncology and Hematology, Karbala, Iraq, from 1st December 2024 to 31st July 2025.

Methods: The samples comprised two groups of women (patients and a control group). The gene expression levels were quantified using quantitative reverse transcription-polymerase chain reaction, with U6 being the normalization gene. Statistical analysis was conducted to establish the correlation between gene levels and hormone receptors (estrogen receptor, progesterone receptor, human epidermal growth factor receptor 2), histological features (tumor size, metastasis) and treatments (chemotherapy, biological, radiation).

Results: Significant differences were evident in the microRNA-145 expression levels between patients and controls (0.37 vs. 1.00; p=0.0001). A significant difference existed between the expression level and the hormone receptor status (estrogen receptor, progesterone receptor, human epidermal growth factor receptor 2), tumor size and lymph node invasion. The radiation group exhibited the lowest expression levels of the gene (0.361) as opposed to the chemotherapy and biological groups.

Conclusion: The reduced microRNA-145 expression in breast cancer patients and supports its role as a diagnostic and prognostic biomarker.

Key Words: Breast cancer, MicroRNA-145, Hormone receptor, Chemotherapy

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INTRODUCTION

The issue of breast cancer development is one of the biggest challenges that affect the health of women today, because the frequency of developing such tumors and mortality rate are high and lead among all other cancer.[1]

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With advances in diagnostics and treatment approaches, there is still a necessity to develop non-invasive biomarkers which will be able to detect breast cancer in early stages predict the disease course, and evaluate the effectiveness of treatment. Traditional biomarkers do not fully explain tumor progression, increasing interest in molecular biomarkers such as microRNAs.[2]

MicroRNAs are small nucleic acids that are involved in post-transcriptional regulation of gene expression in physiological and pathological conditions associated with cell division, differentiation, and apoptosis. These molecules can be divided into two groups, oncogenic miRNAs and tumor suppressor miRNAs. MiRNA-145 is known as a tumor suppressor gene, whose decreased expression contributes to the development of aggressive breast cancer due to increased proliferation and metastatic capacity of tumor cells. While most previous works were devoted to investigating the role of miRNA-145 at tissue level, the analysis of its

concentration in circulating blood samples (circulating miRNA) is an underdeveloped aspect that deserves further exploration in combination with clinical data on breast cancer patients.[3-5]

Breast cancer pathology is characterized by the interconnection of multiple factors: hormonal background (ER, PR, HER2 receptor), pathology features, medical and reproductive history of patients, and treatment types (chemotherapy, biological therapy, and radiotherapy).[6] Thus, understanding the interaction of miRNA-145 with these aspects could help to identify molecular mechanisms of breast cancer and the effect of different treatments on this process.[7] This research aims to address the problem and examine the expression of miRNA-145 gene in blood samples of breast cancer patients in comparison with control healthy samples. Specifically, we plan to analyze the correlation of this gene level with hormone receptors and other features described above. The expected results of the study may contribute to the use of miRNA-145 as a biomarker.

METHODS

This case-control study was conducted at the Imam Hussein (AS) Center for Oncology and Hematology, Karbala, Iraq, from 1st December 2024 to 31st July 2025 vide letter 2024/Issue 3783/Approval/JSDJNEHU Dated November 22, 2024. A total of 100 women were enrolled and stratified into two groups; case group (n=60) with histopathologically confirmed breast cancer, and control group (n=40) age-matched healthy women with no personal or family history of malignancy.

Venous blood samples (2 mL) were collected from each participant into EDTA-containing tubes to preserve RNA integrity. Samples were immediately mixed with TRIzol® Reagent (TransGen, China). At a 1:1 (v/v) ratio, vortexed thoroughly, incubated at room temperature for 5 min, and stored at −80°C until RNA extraction. Total RNA, including microRNAs, was isolated following the manufacturer's protocol with minor modifications: samples were phase-separated with chloroform, RNA was precipitated with isopropanol, washed with 75% ethanol, and resuspended in RNase-free water. RNA concentration and purity were assessed using a UV-Vis Spectrophotometer (Shimadzu, Japan) ; only samples with A260/A280 ratios between 1.8–2.0 were included in downstream analyses.

One-Step RT-qPCR for miRNA-145 Quantification: Relative expression of miRNA-145 was quantified using the GoTaq® 1-Step RT-qPCR System (Promega, USA) on an Analytik Jena Real-Time PCR System (Germany). The small nuclear RNA (U6)was selected as the endogenous reference gene based on its stable expression across blood samples.[4,5] Primer sequences (5'→3') were: miRNA-145 Forward:ACACTCCAGCTGGGCAGGTCAAAAGGG TCC, Reverse: GGTGTCGTGGAGTCG) and U6 (Forward: CCTTGTCCTCACGGTCCAGT, Reverse: AACCATGACCTC AAGAACAGTATTT) (Macrogen, South Korea) Each 20 µL reaction contained: 10 µL GoTaq® qPCR Master Mix (2X), 0.4 µL GoScript™ RT Mix (50X), 300 nM each primer, 1.6 µL $MgCl_2$ (25 mM), 100 ng RNA template, and nuclease-free water to volume. Thermal cycling conditions were: reverse transcription at 37°C for 15 min; initial denaturation at 95°C for 10 min; followed by 45 cycles of denaturation at 95°C for 10 s, annealing at 58°C for 30 s, and extension at 72°C for 30 s. All reactions were performed in triplicate, and amplification specificity was confirmed by melting curve analysis.

Relative quantification of miRNA-145 expression was calculated using the comparative Ct ($2^{-\Delta\Delta Ct}$) method.[6] Normalization was performed as: $\Delta Ct = Ct(miRNA\text{-}145) - Ct(U6)$; calibration as: $\Delta\Delta Ct = \Delta Ct(case) - \Delta Ct(control)$; and fold change as: Relative Quantity (RQ) = $2^{-\Delta\Delta Ct}$. Expression levels were expressed as fold change relative to the control group.

Data analysis was done with SPSS-23. Comparisons among groups were done through independent t-test or Mann Whitney U test where appropriate. Association between miRNA-145 level and other clinicopathological variables was studied by applying Pearson and/or Spearman correlation coefficient. Significance level was set at two-tailed $p<0.05$.

RESULTS

The decrease in the relative expression level of miRNA-145 in breast cancer patients compared to the control group, with an average expression of 0.37 in the patient group versus 1.00 in the control group, which served as the reference value (Fig. 1). A significant decrease in the relative expression level of miR-145 was observed in breast cancer tissue compared to the control. This indicates reduced gene expression of this microRNA in tumor tissue (Fig. 2).

Table 1 showed significant differences in miRNA-145 gene expression levels between the control group and the groups associated with hormone receptor status (ER and PR) and HER2 receptor status. The mean concentration in the control group was 1.359±0.232, with an LDS of 0.193 and a significance level of p =0.0001. In patients with HER2-positive receptors, the mean concentration was 0.400 ± 0.244, while in patients with HER2-negative receptors it was 0.327±0.124. This confirms a significant difference in miRNA-145 gene expression levels between the groups. Additionally, the results for the ER receptor in the table show that the mean concentration in the control group was 1.378±0.264, with an LDS of 0.308 and a significance level of p=0.0021, while the concentration in patients with ER-positive receptors

was 0.328±0.328. The concentration of miRNA-145 was 0.160 and rose relatively to 0.545±0.247 in ER-negative patients. For the PR receptor, the concentration in the control group was 1.358±0.214 with an LDS of 0.189 and a p-value of 0.0001. The concentration level in the positive PR receptor was 0.257±0.123, and in the negative PR receptor it reached 0.523±0.256.

Figure 3 showed negative correlations between the control group and both HER2-positive (r=-0.324) and HER2-negative groups (r=-0.456), while a weak positive correlation was observed between HER2-positive and HER2-negative groups (r=0.218). Figure 4 demonstrated a strong negative correlation between the control group and ER-positive patients (r=-0.734), and a weak negative correlation with ER-negative patients (r=-0.263). A weak positive correlation was observed between ER-positive and ER-negative groups (r=0.262). Figure 5 showed a weak positive correlation between the control group and PR-positive patients (r=0.104), whereas a weak to moderate negative correlation was observed with PR-negative patients (r=-0.403). In addition, a weak inverse correlation was found between PR-positive and PR-negative groups (r=-0.170).

Table 2 showed the significant differences in the expression level of miRNA-145 between the control group and breast cancer patients based on certain clinical and pathological characteristics. The gene expression concentration in the control group was 0.214±1.358, while this level was lower in breast cancer patients. Analysis of the relationship between tumor size and gene expression level revealed that patients with tumors larger than 5 cm had a level of 0.82±0.66, while patients with tumors smaller than 5 cm had a lower level of 0.372±0.168 compared to the control group. The p-value was 0.00001, and the LSD value was 0.161. Regarding lymph node metastasis, the results showed a significant increase in gene expression levels in patients with positive lymph node metastasis (0.241±0.466), while a significant decrease was observed in patients without lymph node metastasis compared to the control group. The lymphatic system, where the value was 0.114±0.357 and the p-value was 0.0001 and the LSD value was 0.228. When comparing the type of surgical excision, a significant increase in the level of gene expression was found in cases of total tumor removal, where it reached 0.291±0.786, and a significant decrease was recorded in partial tumor removal, where it reached 0.121±0.288, compared to the control group, whose mean was 0.214±1.358, and the p-value was 0.00001 and the LSD value was 0.161.

Table No. 1 Gene expression level for miRNA145 and its relationship to the condition of HER2, ER and PR receptors in breast cancer patients compared to the control group

Variables	Parameters	Mean±SD	p-value	LDS value
miRNA145	Control	0.232±1.359	0.0001	0.193
	Her 2 Positive	0.244±0.400		
	Her 2 Negative	0.124±0.327		
	Control	0.246±1.378	0.0021	0.308
	ER Positive	0.160±0.328		
	ER Negative	0.247±0.545		
	Control	0.214±1.358	0.0001	0.189
	PR Positive	0.257±0.123		
	PR Negative	0.256±0.523		

Table No. 2: Comparison of miR-145 gene expression levels according to tumor size, lymph node involvement, and type of surgical resection in breast cancer patients

Variables	Parameters	Mean±SD	p-value	LDS value
miRNA145	Control	0.214±1.358	0.0001	0.161
	Tumor size >5 cm	0.66±0.82		
	Tumor size <5 cm	0.168±0.327		
	Control	0.214±1.358	0.0001	0.228
	Lymph node positive (positive lymph node involvement)	0.241±0.466		
	Lymph node negative (negative lymph node involvement)	0.114±0.355		
	Control	0.214±1.358	0.0001	0.161
	Total tumor resection	0.291±0.786		
	Partial tumor resection	0.121±0.288		

Table No. 3: Impact of various forms of treatment on the levels of miRNA in women suffering from breast cancer as compared to the control group

Variables	Parameters	Mean±SD	p-value	LDS value
miRNA145	Control	0.214±1.358	0.0001	0.294
	Chemotherapy	0.339±0.643		
	Biological treatment	0.186±0.467		
	Radiotherapy	0.340±0.631		

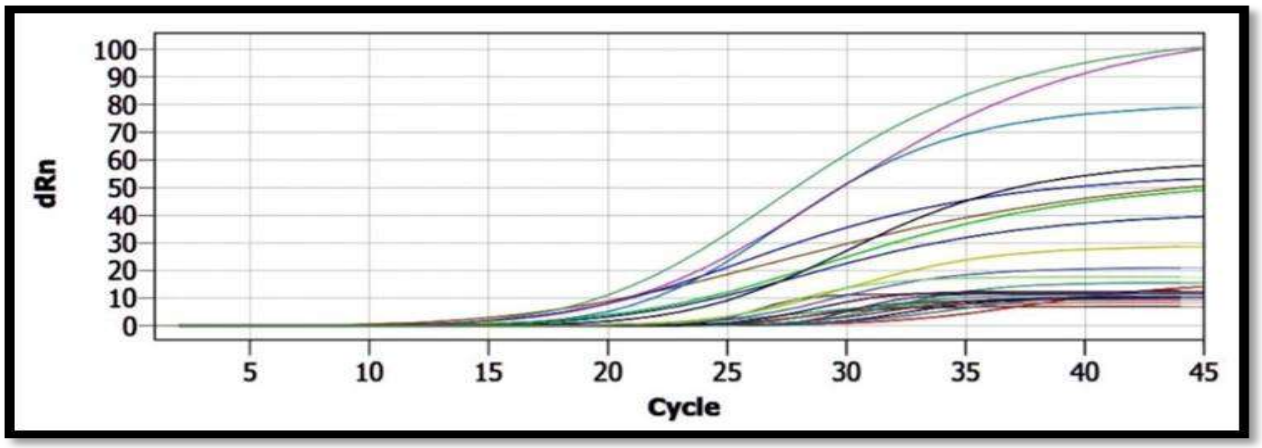

Figure No. 1: Amplification Curves for qPCR analysis of miRNA-145 expression in breast cancer patient samples and control group, and the CT value for both miRNA145 and U6 genes

Table 3 showed that the average level of miRNA gene expression in the control group was (1.358±0.214), which is higher than the values recorded in the treated groups.

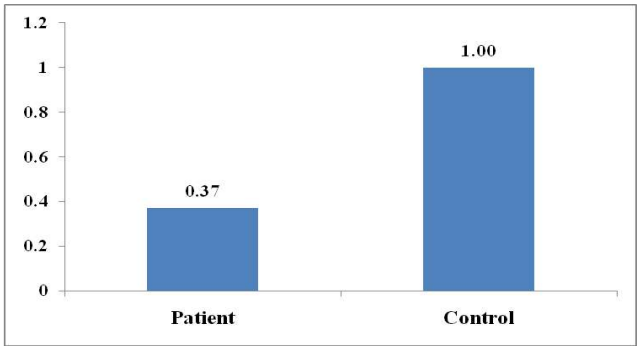

Figure No. 2: Relative expression level of miRNA-145 in the patient group compared to the control group

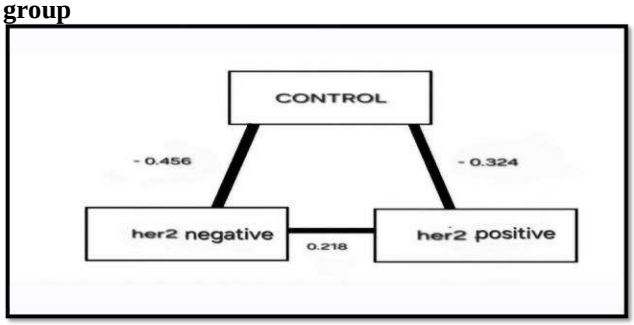

Figure No. 3: Relationships between the three miRNA-145 levels in the control group and breast cancer patients according to HER2 receptor status

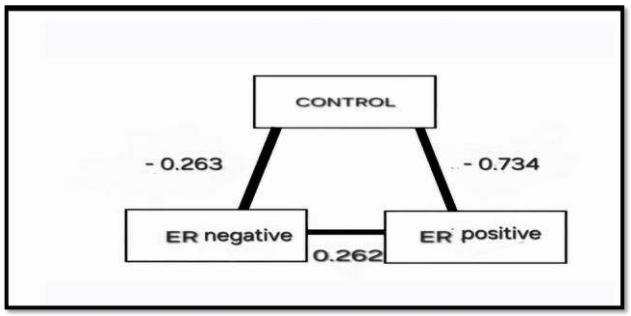

Figure No. 4: Relationships between the three miRNA-145 levels in the control group and breast cancer patients according to ER receptor status

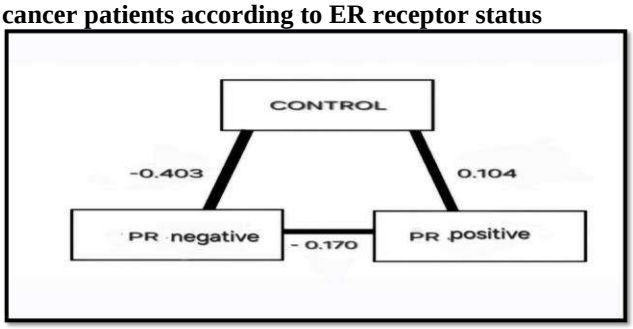

Figure No. 5: Relationships between the three miRNA-145 levels in the control group and breast cancer patients according to PR receptor status

The chemotherapy group recorded (0.634±0.339), while the biological therapy group recorded (0.467±0.186), and the radiotherapy group recorded (0.361±0.234). Statistical analysis revealed highly significant differences between the groups at a significance level of

($p \leq 0.0001$). The lowest significant difference (LSD=0.294) indicates that the differences between the group means are real and not random. It is clear that the control group differs significantly from all treatment groups. Significant differences were also found between chemotherapy and both biological and radiotherapy, as well as between biological and radiotherapy.

DISCUSSION

In the present study, the decrease in the gene expression of miRNA-145 in breast cancer tissue, suggesting a possible loss of its regulatory role in inhibiting cell growth. The findings are consistent with Zheng et al8 and Campos-Parra & Sánchez-Marín[9] that have suggested miR-145 acts as tumor suppressor microRNA in breast cancer, where it was expressed at lower levels in cancerous tissue compared to normal tissue.

This study showed that the mean concentration in the control group was 1.359±0.232. In patients with HER2-positive receptors, the mean concentration was 0.400±0.244, while in patients with HER2-negative receptors it was 0.327 ± 0.124. The mean concentration of ER receptor in control group was 1.378±0.264, while the concentration in patients with ER-positive receptors was 0.328±0.328. PR receptor, the concentration in the control group was 1.358±0.214. The concentration level in the positive PR receptor was 0.257±0.123, and in the negative PR receptor it reached 0.523±0.256. These results show a clear decrease in the gene expression level of miRNA-145 in breast cancer patients compared to the control group, with some differences related to the status of hormone receptors and the HER2 receptor. This indicates the regulatory role of this gene in tumor development and progression.[10-13]

In the current study, negative correlations between the control group and both HER2-positive and negative groups, while a weak positive correlation was observed between HER2-positive and negative groups. The strong negative correlation between control group, ER-positive was in patients group and weak negative correlation with ER-negative patients. A weak positive correlation was observed between ER-positive and ER-negative groups. The weak positive correlation between the control group and PR-positive patients, whereas a weak to moderate negative correlation with PR-negative patients. When its expression is reduced, the activity of signaling pathways associated with receptor family increases, leading to increased proliferation of cancer cells and their ability to invade and spread.[14-16]

The results of the present study support the findings of other studies showing that miRNA-145 plays a crucial role in inhibiting cancer cell migration and metastasis, and that its reduced levels may contribute to tumor progression and increased aggressiveness.[17-21] The results of this study show that low levels of miRNA-145 in breast cancer patient samples are associated with tumor metastasis to lymph nodes. This association is based on the molecular targets of this miRNA, most notably SOX2 (Sex Determining Region Y-Box[2]) and FSCN1 (Fascin Actin-Bundling Protein 1). miRNA-145 normally acts as an inhibitor of SOX2 expression, a transcription factor that promotes stem cell characteristics and proliferative capacity, and also prevents apoptosis. Therefore, low levels of miRNA-145 lead to increased SOX2 expression, which facilitates tumor growth. Moreover, miRNA-145 also targets the FSCN1 protein, which is involved in the control of cell architecture and motility. High concentrations of FSCN1 due to the reduction of miRNA-145 contribute to increased capacity of tumor cells to penetrate and migrate to lymph nodes.[22] The results obtained in the current study correspond to the data obtained previously.[23] This paper shows that reduction of miRNA-145 leads to increased proliferation through increased expression of SOX2 and FSCN1 genes, thus emphasizing the importance of the considered miRNA as a marker of breast cancer progression and metastasis.

CONCLUSION

There is a statistically significant decrease in circulating miRNA-145 in breast cancer patients in comparison with the healthy control group. Circulating miRNA-145 expression levels correlated significantly with hormonal receptors, clinical parameters of tumors, lymph node invasion, and methods of therapy used. The reduction in expression of miRNA-145 was associated with higher aggression in tumor development and various responses to therapies. In general, circulating miRNA-145 can be considered a promising biomarker for the diagnosis, prognosis, and monitoring of breast cancer patients.

Author's Contribution:

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Final Approval of version:	All the above authors
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Original Article

Evaluation of Urea, Creatinine, and Total Protein in Iraqi Women with Breast Cancer Patients in Pre- and Postmenopausal

Nasr Afit Alobaidy[1], Zaid Ahmed Hameed[2] and Baraa Qassim Dawood[2]

ABSTRACT

Objective: To evaluate the relationship between Iraqi women subjected to breast cancer and their serum levels of urea, creatinine, total protein and body mass index.

Study Design: Descriptive study

Place and Duration of Study: This study was conducted at the Anbar Cancer Center, Iraq from 1st October 2023 to 30th June 2024.

Methods: One hundred women's (60 women's with breast cancer and 40 women healthy) were enrolled. They were divided in to two groups (pre-menopausal and post-menopausal). Concentration of serum urea, creatinine and total protein were determined by enzymatic colorimetric method using Semi-Auto Analyzer instrument (spectrophotometry).

Results: The Urea and creatinine concentrations showed significant differences between the breast cancer patients and healthy controls, while total protein and body mass index did not show a significant difference compared to the control group at premenopausal. At post-menopausal all parameter showed a significant difference compared to the control groups. The parameters were compared based on the body mass index and significant differences were observed compared to the control group in pre- and post-menopausal status.

Conclusion: Renal functions test can be considered as risk factors for women's with breast cancer.

Key Words: Serum urea, Serum creatinine, Serum total protein, Breast cancer, Body mass index

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INTRODUCTION

Breast cancer (BC) is the most prevalent malignancy among women and one of the leading causes of cancer-related mortality in Iraq.[1] Breast cancer is the second most common cancer globally, after lung cancer.[2] Tumors come in two primary varieties: benign and malignant.[3] Metastasis is the process by which malignant tumors spread to other parts of the body. This method allows tumors to spread to different areas of the body. Another name for tumours that are cancerous is malignant tumours.

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Unlike many other malignancies, blood cancers like leukemia typically do not develop into solid tumors. Noncancerous tumors don't invade other tissues which are known as metastasis.[4] Cancer cells that enter the blood or lymphatic system have the potential to metastasis, or spread, to other areas of the body. One component of the immune system in your body is the lymphatic system. Lymph nodes are microscopic glands about the size of beans that are a part of a system of tubes and organs that collect and move clear lymph fluid from the body's tissues into the bloodstream. Waste materials from tissues and immune system cells are present in the clear lymph fluid that fills the lymphatic tubes. The breast is drained of extra lymph fluid by the lymph vessels. Breast cancer may result from the facilitation of cell entrance and proliferation in lymph nodes by lymph veins.[5]

In 2016, about 650 million adults were obese and approximately 1.9 billion were overweight. Obesity and the risk of breast cancer are significantly correlated. Because adipose tissue serves as the primary reservoir for estrogen production after menopause, premenopausal obesity and premature menopause reduce the risk, whereas postmenopausal obesity increases it. In postmenopausal women who are overweight, elevated blood estrogen levels and

enhanced peripheral estrogen generation have been identified as important risk factors for breast cancer.[6]

The blood chemistry panel (BCP) is a routine test used to assess a range of chemical components created during the breakdown or metabolism of certain substances or discharged from bodily tissues. The BCP quantifies the blood's concentrations of chemicals, enzymes, and organic waste products. It assesses the condition and appropriate operation of different organs throughout chemotherapy. According to the aberrant blood chemistry results, breast cancer may have progressed to the liver, kidney, or bone. Few studies have examined the relationships between kidney function tests (KFTs) and liver function tests (LFTs) and breast cancer mortality.[7]

A patient with BC who has normal kidney function runs the risk of developing renal failure because of hypercalcemia, tumor lysis syndrome (TLS), and paraneoplastic syndromes.[8]

Many chemotherapy drugs must be metabolized and eliminated by the kidneys in good functioning order.[9] A common consequence for patients with solid tumors is renal impairment. Approximately 50-60% of individuals with solid tumor malignancies are thought to have a glomerular filtration rate (GFR) that is below normal, with creatinine clearance typically falling between 60 and 90 mL/min.[10]

Breast cancer may have a variety of effects on renal function. These processes are closely linked to paraneoplastic syndrome. Antigen antibody complex accumulation in tubular and glomerular structures, fluid and electrolyte imbalance, and ectopic hormone release can all contribute to renal impairment in paraneoplastic disorders.[11]

Proteins are known to be the fundamental building blocks of all living cells and to be present in a wide range of chemicals, such as hormones, enzymes, and antibodies. Serum protein concentration variations have been linked to the progression of cancer and may be a sign of health issues that could yield crucial diagnostic data.[12] The equilibrium between the rates of protein synthesis and catabolism or loss determines the amount of protein in the serum. The amount of albumin, globulin, fibrinogen, and total protein in the plasma are all measured by a total plasma protein test[13], which also demonstrates how an organism is really operating.[14]

The body mass index (BMI) is a measurement of body fat based on height and weight. According to the International Association for the Study of Obesity, the International Obesity Task Force, and the regional office of the World Health Organization for the Western Pacific Region, normal weight for Asian adults is defined as BMI 18.5 to 22.9 kg/m^2, overweight as BMI 23 to 24.9 kg/m^2, and obesity as BMI 25 kg/m^2 or higher.[15] Mortality increases by 20% for males and 10% for women when body weight is more than 20% over average. Compared to non-obese people, obese individuals with a BMI of more than 30 kg/m^2 are more likely to die young.[16] Globally, being overweight or obese ranks as the fifth most common preventable cause of death.[17] According to WHO estimates, problems from overweight and obesity were responsible for 4.5 million deaths globally in 2013.[18]

METHODS

This descriptive study was conducted at Anbar Cancer Center, Iraq from 1st October 2023 to 30th June 2024 vide letter 43egr/QM/Approval/rgEEUI3 date 24th September 2023. One hundred women (60 patients and 40 healthy) divided into two groups: group 1 (premenopausal) comprised 25 patients and 23 healthy; and group 2 (postmenopausal) comprised 35 patients and 17 healthy. The venous blood sample was collected and placed in a gel tube for the serum separation (centrifugation at 3000 rpm for 10 min.). Serum samples were stored in the freezer at -20°C until use. Serum urea, creatinine, and total protein were measured using a Semi-Auto Analyzer kit (AGAPPE, Switzerland). The data was analyzed through SPSS-26. A p-value <0.05 was considered significant.

RESULTS

There was a significant increase in serum levels (urea and creatinine) in BC pre- and post-menopausal women as compared to controls ($p \leq 0.001$). There was also an increase in serum level of total protein in BC pre-menopausal but no significant difference ($p > 0.05$), while serum level of total protein in BC post-menopausal showed a significant increase as compared with controls ($p \leq 0.01$). For BMI, there was no significant difference in both pre- and post-menopausal stages compared to the control group ($p > 0.05$) [Table 1].

There was a significant increase in serum levels (urea and creatinine) in BC post-menopausal women as compared to BC pre-menopausal women ($p \leq 0.001$ and $p \leq 0.05$, respectively), while there was an increase in serum levels of total protein in BC post-menopausal women but no significant difference compared to BC pre-menopausal women ($p > 0.05$). Regarding BMI, no significant difference was observed between the two states ($p > 0.05$) [Table 2).

There was a significant increase in serum levels (urea, creatinine, and total protein) in BC premenopausal women as compared to controls ($p \leq 0.05$, $p \leq 0.001$, and $p \leq 0.05$, respectively). Also, there was a significant increase in serum levels (urea and creatinine) in BC postmenopausal women as compared to controls ($p \leq 0.01$, $p \leq 0.05$, respectively), while serum total protein levels showed an increase but no significant difference compared to controls ($p > 0.05$) at BMI 18-24 kg/m^2. At BMI of 25-29 kg/m^2, there was a significant increase in serum levels (urea, creatinine, and total protein) in BC premenopausal women as compared to

controls ($p \leq 0.001$, $p \leq 0.001$, and $p \leq 0.05$, respectively), while serum levels (urea and creatinine) showed a significant increase in BC postmenopausal women as compared to controls ($p \leq 0.001$ and $p \leq 0.05$, respectively), except serum total protein level showed an increase compared with the control but was not significant ($p > 0.05$). At BMI of 30-40 kg/m^2, there was a significant increase in serum levels (urea and creatinine) as compared to controls ($p \leq 0.001$ and $p \leq 0.05$, respectively), while serum total protein levels showed an increase compared with control but without significance ($p > 0.05$). In BC pre-menopausal women and in BC post-menopausal women, all parameters showed a significant increase as compared to controls ($p \leq 0.001$, $p \leq 0.001$, and $p \leq 0.01$, respectively) [Table 3].

Table No. 1: Comparison of serum of pre- and post-menopausal patients with control group

Groups		Urea (mg/dL)	Creatinine (mg/dL)	Total protein (g/dL)	BMI (kg/m^2)	Age
Pre-menopausal	Control (n=23)	21.870±2.321	0.804±0.114	6.354±0.436	28.458±5.063	37.80±5.12
	Case (n=25)	31.346±8.634	1.158±0.174	6.576±0.481	27.948±4.332	38.42±5.20
	P-Value	0.000***	0.000***	0.10^{NS}	0.71^{NS}	0.11^{NS}
Post-menopausal	Control (n=17)	30.167±3.974	1.00±0.118	6.844±0.564	27.832±5.231	56.12±7.33
	Case (n=35)	42.800±6.676	1.304±0.264	7.490±0.623	27.840±5.048	57.50±8.18
	P-Value	0.000***	0.000***	0.00**	1.00NS	0.244NS

*P<0.05, **P<0.01, ***P<0.001, NS = Not-significant (P>0.05)

Table No. 2: The differences between studied parameters in premenopausal and postmenopausal states

Groups	Urea (mg/dL)	Creatinine (mg/dL)	Total protein (g/dL)	BMI (Kg/m^2)	Age
Pre-menopausal (n=25)	31.346±8.634	1.158±0.174	6.576±0.481	27.948±4.332	38.42±5.20
Post-menopausal (n=35)	42.800±6.676	1.304±0.264	7.490±0.623	27.840±5.048	57.50±8.18
P-Value	0.000***	0.017*	0.930NS	0.33NS	0.000***

*P<0.05, **P<0.01, ***P<0.001, NS = Not-significant (P>0.05)

Table No. 3: The serum parameters in pre- and post-menopausal patients and the control group according to body mass index

BMI (kg/m^2)	Groups		Urea (mg/dL)	Creatinine (mg/dL)	Total protein (g/dL)
18 – 24	Pre-menopausal patients	Control (n=7)	21.428±2.070	0.857±0.097	6.147±0.434
		Case (n=8)	33.125±11.494	1.225±0.138	6.698 ±0.534
		P-Value	0.020*	0.000***	0.046*
	Post-menopausal patients	Control (n=6)	32.333±1.861	1.050±0.083	6.908±0.502
		Case (n=11)	45.090±9.016	1.313±0.289	7.214±0.512
		P-Value	0.004**	0.048*	0.251NS
25 – 29	Pre-menopausal patients	Control (n=7)	22.285±2.058	0.814±0.089	6.554±0.446
		Case (n=9)	31.555±7.535	1.122±0.192	6.742±0.558
		P-Value	0.000***	0.000***	0.03*
	Post-menopausal patients	Control (n=6)	32.1667±4.262	1.066±0.121	7.333±0.294
		Case (n=12)	44.666±4.559	1.341±0.227	7.604±0.774
		P-Value	0.000***	0.014*	0.426NS

30 – 40	Pre-menopausal patients	Control (n=9)	21.888±2.842	0.775±0.133	6.336±0.257
		Case (n=9)	29.555±7.333	1.258±0.290	6.351±0.399
		P-Value	0.01*	0.007**	0.928NS
	Post-menopausal patients	Control (n=6)	26.000±0.894	0.883±0.040	6.290±.274
		Case (n=12)	38.833±4.108	1.133±0.187	7.629±0.512
		P-Value	0.000***	0.000***	0.002**

*P<0.05, **P<0.01, ***P<0.001, NS = Not-significant (P>0.05)

DISCUSSION

According to the current study, premenopausal and postmenopausal BC women had significantly higher urea levels than healthy women. The results of the current study are consistent with those of Al-Hussein[19] and Chauhan et al[20], whose results showed a significant rise in the concentration of urea in BC, and urea is an important chemical parameter for cancer monitoring, while the results of the current study disagreed with Al-Saeedi et al[21] and Devi et al[22], who indicated that there was no difference in urea concentrations when comparing women with breast cancer with healthy people where they are within the normal range, as shown by the results of the study by Abou Zaid et al[23] a small increase in urea concentration in the affected group compared to the healthy group. One possible explanation for the higher urea levels in BC compared to the healthy group is an increase in cellular protein metabolism brought on by chemotherapy's increased death of cancer cells and some healthy cells.[21]

Serum creatinine levels are thought to be a more sensitive indicator of renal function than urea. Since elevated creatinine can only be caused by renal dysfunction. In this study, creatinine levels throughout premenopausal and premenopausal status were found to be statistically significantly higher in BC women than in healthy women. Devi et al[22] found that creatinine levels between 1.0 and 2.0 mg/dl were higher than the typical reference range; this finding is consistent with our study. In contrast to our investigation, Abdallah et al[24] discovered that BC cases had lower creatinine levels when compared to control. Creatinine levels rise in BC patients in both pre-menopausal and post-menopausal states, according to several studies.[25] The glomerulus mostly filters creatinine, although between 10% and 40% of creatinine clearance depends on active tubular secretion that is mediated by several solute-carrier transporters, including MATE2-K, organic cation transporter (OCT2), and multidrug and toxin extrusion protein MATE1. The proximal tubule cells' basolateral membrane contains an organic cation transporter that takes up cations from the blood and transports them into the cells. On the other hand, MATE1 and MATE2-K are located on the apical membrane and mediate the efflux of organic compounds, including toxins and drugs, from the cells to the urine.[26] Inhibition of these particular solute-carrier transporters can therefore result in a substantial reduction in creatinine clearance, which will raise serum creatinine levels.[27]

However, our research revealed that premenopausal and postmenopausal BC women had significantly higher levels of total protein than the control group. The present study is consistent with a Jordanian study that found elevated serum total protein in BC[28] and with multiple investigations that found elevated serum total protein in brain tumors.[29] The fact that albumin and other proteins, collectively referred to as globulins, make up total serum protein may be the cause of this rise in concentration. It is well known that oxidative stress, such as that caused by cancer, can alter the concentration of serum albumin.[30]

The findings demonstrated that postmenopausal women had considerably greater levels of urea, creatinine, and total protein than premenopausal women. These findings concurred with those of Omon et al.[31] For both pre-menopausal and post-menopausal women with BC, there was a significant correlation between increased BMI and elevated levels of urea, creatinine, and total protein. The increased BMI might affect metabolic indicators and renal function in this patient population, our study points to a connection between obesity, metabolic dysfunction, and BC. These results are consistent with literature.[32,33]

CONCLUSION

The difference in the levels of urea, creatinine, and total protein between women before and after menopause, as the levels of urea, creatinine, and total protein in women after menopause were higher than before menopause and found differences in urea, creatinine, and total protein level based on BMI in women with BC who were premenopausal and postmenopausal.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Nasr Afit Alobaidy, Zaid Ahmed Hameed
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Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Pes Anserinus Syndrome, Exploring Factors that Might Increase its Occurrence: Cross-Sectional Descriptive Study

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ABSTRACT

Objective: To explore and determined conditions that might be associated with increasing incidence of Pes anserine syndrome.

Study Design: Cross sectional descriptive study

Place and Duration of Study: This study was conducted at the Orthopedic Surgeons, Department of Surgery, Iraqia Medical School, Iraq from 1st August 2023 to 31st October 2025.

Methods: 108 patients diagnosed with Pes anserine syndrome based on clinical and ultrasonigraphic findings, the patients having a carful detailed history and examination in addition and age range 22-71 years were enrolled. Osteoarthritis grade has been graded centered upon the radiographic classification of the Kellgren-Lawrence classification knee.

Results: There were 25 (23.2%) males and 83 (76.8%) females with average age was 45.0±13.4 years for males, of them 16 (64%) were more than 40 years old, and 54±9.6 years for females, 69(86%) being more than 40 years old. 62 (58%) had history of primary osteoarthritis, 67% of them (42 patients) with the Kellgren-Lawrence classification of III or more. 41 (38%) patients were diabetics.73 (68%) patients had body mass index of more than 25. (26%) patients had a positive immunoglobulin M level in their blood, only 7of them with concomitant osteoarthritis. 13% patients had history of surgery of less than 3 month. 9% patients had recent history (<1 month) of corticosteroids knee intra-articular injections, 8 patients for knee osteoarthritis and one for a recent knee trauma.

Conclusion: Because the contributing factors for Pes anserine syndrome has yet to be clarified and in order to ensure adequate treatment.

Key Words: Pes anserinus syndrome, Effect, Factors, Occurrence

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INTRODUCTION

Pes anserine syndrome (PAS) is a common soft tissue pain syndrome of the knee and induces pain in knee and subsequently affects the patient's quality of life with OA.[1,2] The conjoined tendons of the gracilis, sartorius and semitendinosus constitute the pes anserine tendon which attaches to the anteromedial proximal tibia 5 cm distal from the medial tibial joint line.

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Pes bursa anserine is located deep to the pes anserinus tendon and medial collateral ligament.[3] These muscles are predominantly primary flexors of the knee with secondary internal rotation of the tibia, providing a varus and rotational conservation for the knee.[4] The anserine bursa is one of 13 bursae situated around the knee, located just beneath the pes anserinus.

Pathological processes which affect the PA, especially pes anserine bursitis (PAB), are frequent causes of medially-located knee ache. PAB consists of inflammation of bursa around the PA tendons and the medial collateral ligament.[5] The name "tendinopathy" now embraces entire conditions where there are chronic clinical conditions that are associated to the presence of pain, swelling and functional limitation, affecting tendons along with adjacent structures.[6,7] In particular age, sex-gender and body mass are important un-amendable factors while inappropriate too much loading disuse, drugs and smoking have been considered highly modifiable factors.[80] Even if the term "tendinitis" is usually linked to the concept of tendinopathy, in recent years it has been demonstrated

that inflammation plays a key role only during the early phases of the illness, whereas degenerating and apoptotic phenomena were prevalent several times due to chronic overuse condition correlates with work and/or sports.[7,9]

The adjacent nature of the tendon and bursa also causes separation of PAT from PAB to be challenging on physical exam. A clear differentiation between PAB and PA tendinopathy (PAT) is difficult and the proposed treatment of the studies in present literature is similar for both entities. Furthermore, the pain-related structures in PA area are still not clearly identified: here are some doubts on when say that the PA is an effectively chronic degenerative or inflammatory bursitis and/or tendinopathy.[10] Therefore, it may be more appropriate simply to refer to this entity as "pes anserinus syndrome" rather than PAB or PAT.

There is a history of repetitive mechanical stress or trauma to the Pes anserinus bursa in most cases. If the hamstrings are tight, they help create added tension on the bursa which causes direct mechanical and frictional irritation. Physical trauma or infection may be a triggering factor for the inflammation.[11] The disease entity is also often linked with other knee pathologies, including Osgood-Schlatter's disease, suprapatellar plical irritation and medial compartment or patellofemoral arthritis that can lead to hamstring spasm.[12] Obesity and valgus deformity of the knee (which particularly affects middle-aged women) add to the risk.[13]

Flat feet (pes planus) also place patients at risk for developing bilateral pes anserine bursitis secondary to abnormal lower extremity alignment causing an increase in medial dictating pressure on the knee. Local trauma, bony exostosis and tendon tightness are also contributing factors.[14] Bio-psycho-social elements lead to pes anserine bursitis development.[15] Mechanical problems of the knee, obesity and athletic activities with high degree of lateral move as basketball and racquet sports are major causes.[16]

The disease also frequently occurs in persons with early-stage medial knee osteoarthritis and in a large proportion of persons with diabetes mellitus. Pes anserine bursitis was observed in 34 of these patients. A marked gender gap was also apparent with 91% of cases being females and 9% males. In contrast, bursitis did not develop in any of the control patients without diabetes.

Meniscal lesions are more frequently found in OA, could possibly contribute to pain generation of the advantageous medial sensitive area of the knee[17] and should be ruled out by good differential diagnosis from other pathologies that can mimic PAS. One of the underestimated possible causes of PAS is viral infection especially after COVID pandemic as many researches had identified musculoskeletal sequelae associated with this disease which prompt the need to be considered for PAS causation.[18]

METHODS

This cross sectional descriptive was conducted at Orthopedic Surgeons, Department of Surgery, Iraqia Medical School, Iraq from 1st August 2023 to 31st October 2025 vide letter No. 1332 dated 6-3-2023 and 108 patients diagnosed with PAS based on clinical and ultrasonigraphic findings were enrolled. Although clinical examination is simple, the use of ultrasonography as a supplemental diagnostic measure has previously been advocated.[19] Patients with neuromuscular diseases, malignancy, stroke and rheumatoid disease were excluded.

After having informed consent, all affected were having a carful detailed history and examination in addition all were sent for blood test of CBC (complete & differential blood count) plus ESR, CRP and IgM assessment for a recent viral infection. Osteoarthritis grade has been graded centered upon the radiographic taxonomy of the Kellgren-Lawrence classification knee.[20] The findings were noted down along with the demographic data (gender and age) and body mass index of the case persons in the list of gathering data. The data was entered and analyzed through SPSS-20.

RESULTS

There were 25 (23.2%) males and 83 (76.8%) females with average age was 45±13.4 years for male, of them 16 (64%) were more than 40 years old, and 54±9.6 years for female, of them 69(86%) being more than 40 years old (Table 1).

Sixty (57.4%) patients had history of primary OA, 67% of them (42 patients) with The Kellgren-Lawrence classification of III or more (Table 2).

Forty one (37.9%) patients were diabetics, 73 (67.6%) patients had BMI of more than 25.

Table No. 1: Demographic information of the patients (n=108)

Variable	No.	%
Gender		
Male	25	23.2
Female	83	76.8
Age (years)		
22-40	39	36.1
41-72	69	63.9

Table No. 2: History of primary osteoarthritis

Variable	No.	%
Osteoarthritis	60	57.4
\Kellgren-Lawrence classification of III or more	42	67.0

Twenty eight (25.9%) patients had a positive IgM level in their blood, only 7of them with concomitant OA.

Fourteen (12.9%) patients had history of surgery of less than 3 month, 12 patients underwent total knee replacement, one ACL reconstruction with gracillis tendon grafting and one for corrective mal-united proximal-tibial fracture.

Nine (8.4%) patients had recent history (<1 month) of corticosteroids knee intra-articular injections, 8 patients for knee OA and one for a recent knee trauma. One patient was teenager (15 years old) involved in runner sport activity.

DISCUSSION

Despite being common however, this entity is commonly overlooked. The exact incidence is unknown. In a study, 600 patients attending an outpatient clinic, the diagnosis of "soft tissue rheumatism" was given to 108; with 43 had anserine bursitis.[21] Average mean age of the total study population was 51.9± 11.37. The average age is in the range of previously reported by Helfenstein & Kuromoto[22] was 55.6, and Uysal et al[23] was 58.9±9 hence being in a middle age could be considered the most ummodifiable risk factor for having PAS.

Nevertheless, it is more frequent that anserine bursitis/tendinitis syndrome occurs in obese women with osteoarthritis of the knee.[24] This discrepancy could be explained by being a consequence of the fact that females have slightly wider pelvis and the knee is angled more, causing greater pressure on the area of attachment of pes anserinus and this finding also been observed in our study.

Regarding OA, a recent study included 245 patients with osteoarthritis attending the clinic complaining from knee pain. On the basis of clinical features and sonographic scan, 175 cases (71.4%) suffered from true diagnosis of pes anserine bursitis. Bursitis was bilateral in 72 cases (41.1%). Right bursitis was observed in 28 patients (16%) and left bursitis in 75 patients (42.8%)[25], another study of Kang et al[26] was 46.8%, which our findings of 68% of patients in the study had history of OA is agreed with and it is relatively more common with increasing OA grade.

Metabolic comorbidities including diabetes mellitus, in some cross-sectional studies type-II DM has been found to be linked with PAS when contrasted with a non-diabetic persons.[27] The observed relation of PAS to BMI in our findings was been also documented as there was a significant relationship with high BMI and the rate of anserine bursitis.[25]

The fact that PAS could be due to viral event is neither been well established nor well estimated with lack of studies focusing on this issue especially after the evolution of COVID and post COVID era, so it may be acceptable for us as physicians to pay a little attention to that issue if we were evaluating any inflammatory musculoskeletal condition.[18] The findings of Increased IgM level in 26 patients with PAS call attention about role of viral infection as a causative factor. In a literature review, pro-inflammatory cytokines that induce by viruses may cause tendon pain and impair physiological responses of tenocytes, influencing matrix remodeling and degenerative progress in tendinopathy.[28] Although seven of them already have OA which may contributes to the presence of PAS which may be biased on estimating it rather it is not a rule to find an elevated IgM in patients having PAS with OA, so it is reasonable to consider it in the check process.

The findings of 17% of patients with PAS had history of recent steroid knee intra-articular injection, most of them within first 1-2 weeks after injection, was very interesting and we think that it was not been mentioned before, and although almost all of them having KOA which could be the main factor in PAS occurrence but it looks like that an aggravating factors may contributes to this. After a long period of restricted motion duo to the knee pain, with rapid knee pain relief, patients regain motion, so an abrupt physical activity may cause unusual mechanical load on pes anserinus tendon; because of limited or cautious motion before injection, a biomechanical knee factors, like hidden knee instability would be apparent after rapid pain relief as the patients start motion leading to PAS occurrence.[29] These findings may indicate that such individuals should get the proper rehabilitation in order to prevent this kind of occurrence.

History of surgical intervention around the knee has been found in 13% of patients with PAS, most of them were underwent TKA which has been reported and the incidence was found to be 5.6%[30], a need for appropriate rehabilitation regime can yield favorable outcomes. Although rare, PAS has been reported in pediatrics as a cause of knee pain but with no actual data about incidence or prevalence.[31]

CONCLUSION

Because the contributing factors for PAS, and in order to ensure adequate treatment on the understanding front, it is important to further assessment of underlying factors like age, sex, presence of osteoarthritis and body mass index with paying more attention to the role of viral event, effect of rapid of pain relief of knee osteoarthritis and surgeries in & around the knee as a causative factors of Pes anserine syndrome for better and adequate therapy and prevention of recurrence.

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Original Article

A Study of Blood Velocity and Blood Pressure in Kidney Disease Patients on Regular Dialysis

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ABSTRACT

Objective: Assessment of the changes in blood velocity and blood pressure for patients with chronic kidney diseases undergoing hemodialysis.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Al-Hussein and Al-Nasiriyah Teaching Hospitals, Iraq from 1st July 2023 to 30th November 2023.

Methods: Ninety patients were effects of hemodialysis on blood velocity and blood pressure was (aged 21-70 years) selected using convenient sampling methods were enrolled. Blood pressure was measured using a sphygmomanometer, and blood flow velocity was assessed using Doppler ultrasonography before and after hemodialysis.

Results: Significant alterations in blood velocity and blood pressure were observed pre and post hemodialysis.

Conclusion: The dramatic changes in blood velocity during dialysis. Monitoring for low blood pressure may help to adjust the dialysis schedule, such as electrolyte levels and hemofiltration rates, to reduce complications.

Key Words: Hemodialysis, Blood pressure, Blood velocity

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INTRODUCTION

Chronic kidney disease is a common health problem where kidney replacement therapy becomes needed for treating end-stage kidney failure (ESRF). Hemodialysis is a widely used treatment; however, it often causes problems, with low blood pressure caused by dialysis (dialysis-induced hypotension) being one of the most serious. Dialysis-induced hypotension, which happens in 20-30% of hdemodialysis patients, usually appears during or toward the end of a session.[1-3] When it happens, it needs careful watching, because severe episodes can lead to issues like heart disease, stroke, and gut damage.[4,5] In these cases, dialysis may need to be stopped, which makes it less effective.[6]

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The main cause of dialysis-induced hypotension is lower blood volume caused by too much fluid removal and slower refilling of plasma into the blood vessels.[7] Other things that add to the problem include weak narrowing of blood vessels, existing heart problems[8], or less common causes like bleeding, severe infection, or air bubbles in the blood. The body's natural responses to dialysis-induced hypotension include a drop in vein capacity, an increase in artery tightness, and stronger heart pumping.

Compared to hemodialysis, peritoneal dialysis has a lower chance of causing low blood pressure because of the way it removes fluid. dialysis-induced hypotension can show up suddenly as a drop in the top blood pressure number (systolic) below 90 mmHg, or it can happen repeatedly over time (chronic episodes). Blood velocity, which means how fast blood moves through the vessels is affects by things like blood pressure, blood volume, and how stretchy the artery walls. Doppler ultrasound works well to measure blood flow speed, and it helps show changes caused by hemodialysis.[9]

Even though some researchers disagree that there is a direct link between relative blood volume (RBV) and blood pressure changes during hemodialysis[10-12], studies show clear changes in brain artery speed after dialysis.[13] There is not much research on how hemodialysis affects blood volume and blood pressure levels in kidney failure patients, so more studies are needed in this area.

METHODS

This cross-sectional study was conducted at Al-Hussein and Al-Nasiriyah Teaching Hospitals, Iraq from 1st July 2023 to 30th November 2023 vide letter No. MEC-2001/Approval/JSDJNS dated June 21, 2023. A total of 90 CKD patients (50 men and 40 women) who were having HD on a regular basis were enrolled. The patients were split into five age groups as 21-30 years: 7 patients (3 men, 4 women), 31-40 years: 18 patients (10 men, 8 women), 41-50 years: 42 patients (22 men, 20 women), 51-60 years: 14 patients (11 men, 3 women) and 61-70 years: 9 patients (4 men, 5 women). Those patients who had chronic kidney disease and were on hemodialysis, with no past episodes of sudden kidney failure or diabetes were included. Patients had too much body fluid, fistulas in the cubital fossa (inner elbow area), or any other major health problems not related to chronic kidney disease were excluded.

Blood pressure was recorded using a regular mercury blood pressure device before the dialysis session and (4 hours) after it ended. The readings followed the Korotkoff sounds method to make sure they were correct.

Blood velocity was measured using Siemens Acuson X300 Doppler ultrasound device (Germany) at the same time points before and after dialysis.

All measurements were made under normal conditions in the hospital's dialysis unit. Patients were watched closely for signs of low blood pressure caused by dialysis (dialysis-induced hypotension), which was defined as a drop in the top blood pressure number (systolic) below 90 mmHg or symptoms of low blood pressure during hemodialysis. The data was analyzed to look at changes in blood pressure and blood velocity before and after hemodialysis. Statistical significance was determined using a two-tailed paired t-test, with a p-value at 0.05 considered statistically meaningful.

RESULTS

The study found a clear increase in blood velocity after hemodialysis in most age groups. On the other hand, blood pressure showed a clear drop, especially in groups 4 and 5 (P<0.0001). Low blood pressure (hypotension) was seen in 27.7% of patients, mostly in the older age groups (Tables 1-2, Fig. 1).

Table No. 1: Blood pressure in relation to age and sex pre and post dialysis

Age (years)	No.	Before dialysis Mean BP (mmHg)	After dialysis Mean BP (mmHg)	Male:Female
21-30	7	92.4	83.1	0.75:1
31-40	18	97.1	97.2	1.2:1
41-50	42	100.6	93.1	1.1:1
51-60	14	106.1	96.1	3.66:1
61-70	9	104.8	100.8	0.8:1
Total	90	100.4±7.42	94.7±8.13	

Table No. 2: Blood velocity in relation to age and sex pre and post dialysis

Age (years)	No.	Before dialysis Mean BV (cm/sec)	After dialysis Mean BV (cm/sec)	Male:Female
21-30	7	45.6	51.5	0.75:1
31-40	18	42.5	53.7	1.2:1
41-50	42	43.8	55.7	1.1:1
51-60	14	51.2	58.2	3.66:1
61-70	9	48.6	55.9	0.8:1
Total	90	48.76±6.84	56.48±6.12	

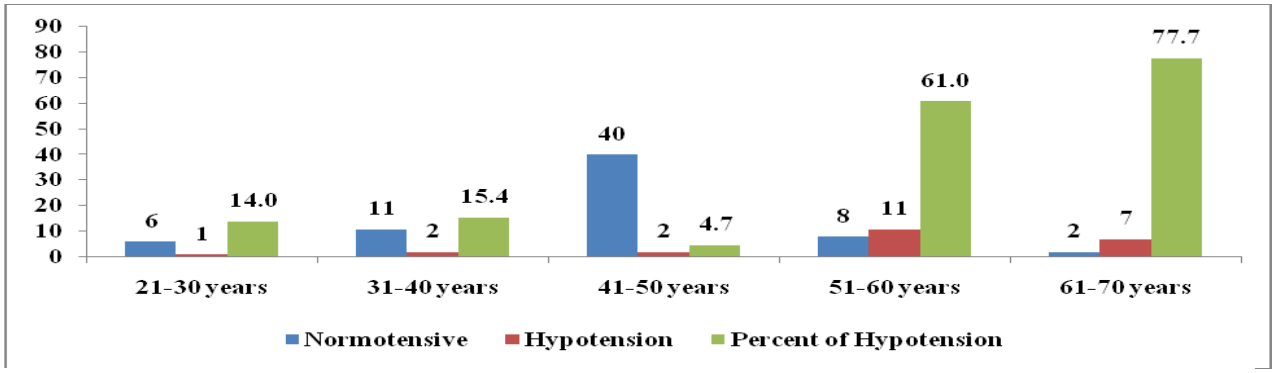

Figure No. 1: Distribution of dialysis induced hypotension according to age

DISCUSSION

The link between age, gender, and the development and worsening of chronic kidney disease has been studied a lot. Women generally have a lower risk of developing end-stage kidney disease (ESRD) during their childbearing years, likely because of the protective effects of estrogen. However, this trend flips after menopause, where women may face a higher rate of ESRD compared to men. This finding agrees with reports from the Japanese Society for Dialysis Therapy, which found lower ESRD rates in women than in men.[14] Many factors add to this gender difference, including genetics, environmental factors, lifestyle differences, and hormone effects.[15-17]

The current study showed that most ESRD patients belong to middle-aged and older groups. This result makes sense, given the natural drop-in kidney filtration rate that comes with aging kidneys. Supporting this, the National Health and Nutrition Examination Survey (NHANES) 1999–2004 indicated that about one-third of people aged 70 or older have poor kidney function.[18]

This study also showed clear differences in blood pressure before and after hemodialysis ($P < 0.0001$), with a large number of patients experiencing low blood pressure caused by dialysis (dialysis-induced hypotension). The causes of dialysis-induced hypotension are many and include lower blood volume, shifts in fluid thickness (osmolality), changes in electrolyte balance, and poor blood vessel tone and nerve responses. These factors are often made worse in patients who already have heart problems.[19-21] Also, the study found a clear increase in arm artery blood flow velocity after dialysis. This finding highlights the usefulness of BV as a sign of how well an arteriovenous fistula is working, with low flow rates often indicating that the fistula may need medical attention.[22,23]

CONCLUSION

Low blood pressure (hypotension) during hemodialysis is a common and potentially serious complication in ESRD patients. Keeping a close watch on blood pressure during dialysis sessions is necessary to lower risks. Noticing when low blood pressure occurs during the session can help guide changes to the dialysis settings, such as adjusting electrolyte levels and the speed of fluid removal. The study also shows that men are more likely to develop chronic kidney disease, which highlights the need for regular check-ups for high-risk men, especially those with diabetes or high blood pressure. Using prevention plans that are tailored to gender-based and age-based risk factors may improve patient outcomes.

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Original Article

Histological Diagnostic Study of Breast Cancer in Maysan Governorate: A Comparative Analysis between Male and Female Patients

Yasser Al-Yasin

ABSTRACT

Objective: To characterize the histopathological spectrum of breast cancer and to provide the comparisons by sex where possible.

Study Design: Descriptive histopathology study

Place and Duration of Study: This study was conducted at the Oncology Department, Al-Sadr Teaching Hospital (Maysan) from 1st January 2026 to 31st March 2026.

Methods: 100 breast tumor tissue specimens (97 females and 3 males) obtained from the tissues were fixed in 10% formalin and processed using routine paraffin embedding and Hematoxylin–Eosin staining were selected. Slides evaluated by light microscopy (10^X, 40^X, 100^X). Recorded features included tumor architecture and cytology (e.g., nuclear pleomorphism, hyperchromasia, prominent nucleoli, multinucleation), stromal changes, tumor-infiltrating lymphocytes, and vascular/lymphovascular involvement.

Results: Invasive ductal carcinoma of no special type predominated. Common microscopic findings included cohesive malignant epithelial clusters with marked nuclear atypia and dense chromatin; frequent tumor-infiltrating lymphocytes; and evidence of intravascular/lymphovascular tumor cells in a subset of cases. Additional observations comprised stromal reactions and occasional multinucleation with prominent nucleoli. These features collectively indicate aggressive biological potential and risk of dissemination in part of the cohort.

Conclusion: Invasive ductal carcinoma of no special type predominated, with frequent lymphovascular invasion and marked nuclear atypia, underscoring the need for earlier detection, stronger pathology services, and a baseline for receptor/molecular subtyping studies.

Key Words: Cancer, Breast cancer, Carcinoma, Diagnostic, Histology

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INTRODUCTION

A group of diseases referred to as breast cancer is distinguished by uncontrolled cellular replication within breast tissue, typically presenting as a mass. Most lesions are believed to arise from the lobules or the lactiferous ducts. It is widely recognized as the most prevalent cancer in women and the primary contributor to cancer mortality among females.[1] The most common diagnostic type of cancer in the world was the breast cancer.

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According to GLOBOCAN 2020 estimates, 2.3 million new breast cancers were diagnosed worldwide in 2020.A 47% increase in cases of new cancers worldwide is expected between 2020 and 2040.[2] It has also revealed that one in 11 women will develop breast cancer.[3] Among females in Western regions, breast cancer represents the leading form of cancer, with lifetime risk close to one in ten. In the US, the projected lifetime incidence of invasive breast cancer is about 12%, or roughly one woman in eight. High-income countries have achieved the greatest gains in prognosis, mainly through a combination of earlier detection programs and the routine use of adjuvant therapy conversely, middle-income and poor countries are being ravaged by breast cancer.[4] In Iraq, the number of cases of this type of breast cancer increased after the year 2000 from (52.00/100,000) to the year 2019 (91.66/100,000). Optimal breast cancer management is contingent on accessible, high-quality prognostic and predictive factors from clinical and pathological assessment, which steer decision-making and therapy selection.[5] Among people with early-stage breast cancer, treatment selection is individualized, and risk

stratification primarily considers nodal status, tumor diameter, and pathological (histologic) grade.

Among Iraqi women, mortality has been led by breast cancer, which constituted about one-third of all cancer cases documented nationally in 2024.[6] Breast cancer encompasses diverse entities that differ in histology, biology, clinical presentation, behavior, and treatment response. Most microarray work has centered on invasive ductal carcinoma, no special type.[7]

This study purpose to describe the major histological changes observed in breast cancer tissues diagnosed at Al-Sadr Teaching Hospital, Maysan and to compare the frequency and pattern of key microscopic features such as lymphoid cell infiltration, intravascular tumor cells, nuclear atypia between female and male patients.

METHODS

This descriptive histopathology study was conducted at Oncology Department, Al-Sadr Teaching Hospital (Maysan) from 1st January 2026 to 31st March 2026 vide letter No. 314152/QM/Approval/JSDJNEHU dated December 20, 2025. One hundred breast tumor tissue specimens (97 females and 3 males) obtained from the tissues were fixed in 10% formalin and processed using routine paraffin embedding and Hematoxylin–Eosin staining were selected. A histological examination was conducted on it and after confirming the appearance of the pathological signs of the injury site, a tissue biopsy was taken from it, the tissue sections were prepared and a series of consecutive operations were performed.

The samples placed in 10% formalin solution for 24 hours, then the samples were washed with running water for several times to get rid of formalin. Then the samples were passed by an ascending series of ethyl alcohol concentration (70%, 80%, 90%, 100%) for a period of two hours for each concentration. For tissue thinning, samples were placed with solutions of a mixture of absolute alcohol with xylene in volume ratios (1:1-1:3) for one hour for each mixture and then put in pure xylene for half an hour. Then the samples were embedded in wax, then the samples were drunk by placing them in molten paraffin wax at a temperature of (58-60). It was placed inside special square-shaped molds and left the molds at room temperature and then cooled and kept in the refrigerator to freeze, then the sections obtained by using a manual microtome with a thickness of (3-5) microns. These sections were placed in a 50° water bath, then transferred onto clean glass slides coated with Meyer's albumin and placed on a Hot Plate for 5 minutes at the temperature of room for 24 hours. Then the samples were passed with descending concentrations of alcohols (100%, 90%, 80%, 70%), then the sections were stained by placing them in Haematoxylin eosin dye for 30 seconds, after which the slides were dried and placed in xylol. The glass slides were photographed by Micros Estuarine microscope under magnification (100x-40x-10x) respectively.

RESULTS

Most types of breast cancer observed in the study samples which have been examined were invasive (metastatic) ductal carcinoma with a percentage of 100%, Other types were found but with a small percentage. The presence of cancerous and lymphatic cells in breast tissue is evidence. The lymph nodes have been invaded by cancer cells near the breast tissue, and the observance of lymphoid cells on histological examination, is an indication of a danger to the patient's life (Fig. 1).

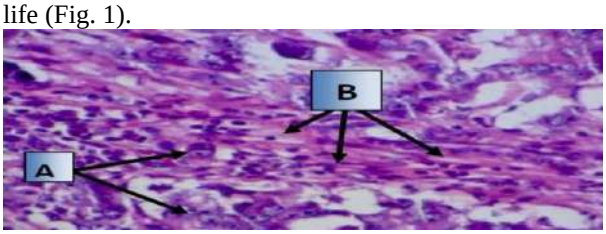

Figure No. 1: A cross section of human (female) breast tissue Cancer cells (A) Malignant cells, Lymphocytes (B) (40x) H&E

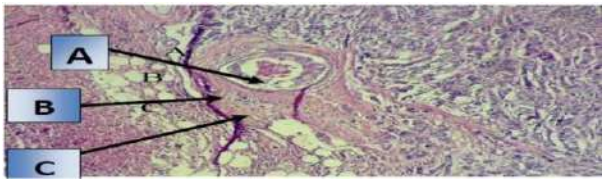

Figure No. 2: A cross section of human female breast tissue showing: (A): cancer cells, (B) RBC red blood cells (C) Malignant cell, blood vessel (10X) (H & E)

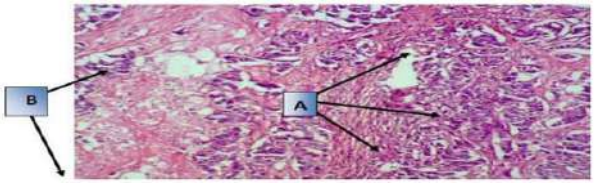

Figure No. 3: A cross-section of human (female) breast tissue with metastatic ductal carcinoma shows: Combined cancer cells (A) Fatty cells, (B) (H & E) (10 X)

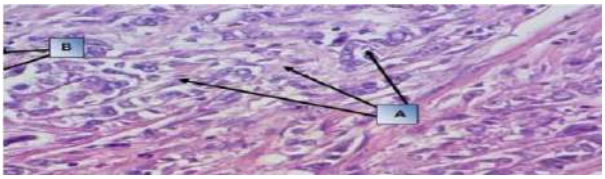

Figure No. 4: A cross section of human breast tissue (female) with metastatic ductal carcinoma (A) Nucleus (H&E) (40x) (B) Hyperplastic tumor cells

It can also be observed that the spread of cancer cells within the blood vessel is an evidence of the ability of the cancer cells to grow and spread, which Metastasis the other part of the body that is close to the breast tissue through the bloodstream, and this process is known as diffusion (Fig. 2).

It was also noted that the cancer cells were grouped together in separate places from each other, separated by cells of connective tissue and fat cells could be observed under the microscope in white(Fig. 3).

It was observed in the current study that the cancer cells in the affected breast tissue are very clearly scattered and excessive, and the nucleus is clear and can be seen easily and the nuclear to nucleus ratio is large and clear and the nuclear is prominent, and the chromatin is very dense (Figs. 4-5).

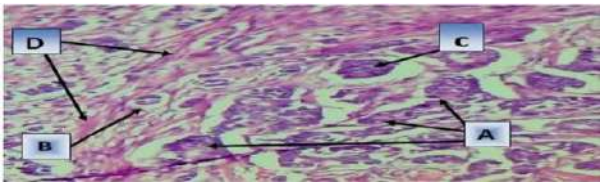

Figure No. 5: A cross section of human breast tissue (female) with invasive (metastatic) ductal carcinoma. (A) illustrates B Tumor cells, dense chromatin, C, nucleoli), stroma D, (H & E) (40 X)

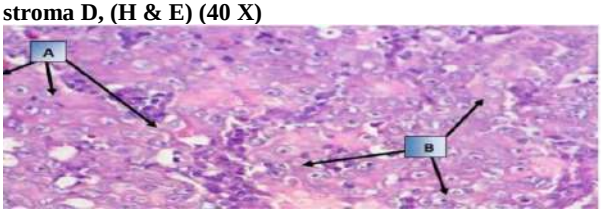

Figure No. 6: A cross section of the breast tissue of a human (female) with metastatic ductal carcinoma Multiple nuclei (B), cancer cells (A) (H & E) (10 X)

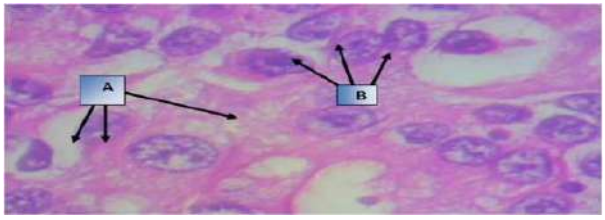

Figure No. 7: A cross section of human breast tissue (female) with metastatic ductal carcinoma Dense chromatin (A) (H&E) (100x), (B) shows poly nuclear intra nuclear

The present study results have shown that the carcinoma cells are scattered in the breast tissue and formed in the form of scattered assemblies that can be distinguished clearly. The nuclei are prominent, and as we note that some cells contain multiple nuclei and are scattered in the breast tissue affected by invasive ductal carcinoma (Fig. 6). It was also noted that the nuclei are multiple in the breast tissue affected by invasive ductal carcinoma and we note that the nucleus is large in size and very dense chromatin and contains multiple nuclei that can be seen clearly under the power of magnification(100x) (Fig. 7).

DISCUSSION

This study showed a similarity in the type of breast cancer that affects both women and men, as there was a similarity in the pattern of the cancerous tissue, which was of the invasive ductal carcinoma type. Histological examination of patient samples revealed the absence of other types of breast cancer (invasive lobular carcinoma, ductal carcinoma in situ and lobular carcinoma in situ), which is consistent with what was stated by Al-Khayat et al[8], 97% of breast cancer cases were ductal invasive and 3% were lobular invasive when histological examinations were conducted on patient samples in Najaf Governorate. This aligns with the findings of Mayada[9], who, in her study, found that ductal breast cancer was the most prevalent type among women, 89.5%, while invasive lobular carcinoma represented 5.9% of the samples while the rest includes other types (invasive lobular carcinoma, ductal carcinoma in situ, and lobular carcinoma in situ). Diagnostics of breast cancer depend on the structure of the cancerous cell, which can be varied and have more types. However, due to the location of this cell in the breast ducts, this type of cancer is called ductal breast cancer to help diagnose and differentiate it. This type is considered the most common and because ducts in breast tissue are the most responsive place to the action of female sex hormones, the cell membrane in the ducts contains receptors for hormones, especially estrogen, which is responsible for their development. The tissue sections were examined after staining with hematoxylin-eosin to observe the histological changes in the sample and to diagnose the type of disease. Since it is one of the reliable methods It can also be chosen as the best method for diagnosing tissue tumors.[10] This can be demonstrated by examining significant changes in the structure and composition of the tissue and its parts on the basis of histological examination of samples taken from breast tissue and observation of changes, the type of tumor can be classified, tumors are of various types, ranging from low-grade tumors showing the least possible multiple forms and high-grade tumors showing polymorphous tumors.[11] Invasive ductal carcinoma can be distinguished on the basis of distinct microscopic characteristics, including ductal carcinoma in situ or the nuclei appear in an irregular arrangement and vary in size and shape, and can be distinguished by the hyperpigmentation of hematoxylin-eosin and the protrusion of the nuclei. That is why this type of tumor was diagnosed by observing the characteristics of this type during histological examination of samples, and this agrees with the researcher.[12] It was also in the diagnosis of invasive ductal carcinoma in the current study that there are most changes in the structure and shape of the tissue, including that the malignant cells in the tissue can be clearly observed through the irregular shape of the cells, the nuclei are prominent and the nucleus is large in size, the chromatin is very dense. This is in agreement with Koss and Melamed[13], reported that mammary gland cells that affected by ductal cancer are

Because of its large size, it can be easily distinguished. Peripheral cytoplasmic blebs and protrusion appear in the peripheral cytoplasm. They also noted during the examination of tissue samples that the nucleus was so large that it appeared swollen. As it was observed through the microscopic examination of the Slice samples in this study in the breast tissue affected by breast cancer, the cancer cells are spread in the tissue and spread into the blood vessels, is an indication of the possibility of spreading to other parts of the body. This is consistent with what was stated by Hunter et al[14], showed that the process of spreading cancer cells. The diffusion process, which occurs through specific steps, is a complex process and includes the migration of cancer cells through the blood vessels in the blood stream and migrates to other parts of the body. Also, this result are identical with Mahdi et al[15], pointed out that the histological changes were evident when examining the samples under a microscope, revealing that the chromatin was dense, and therefore the cells had it has the potential to infect other parts of the tissue with its different layers, whether epithelial or connective, that surround the cancerous tissue, it was also pointed out that the connective tissue cells are scattered on a base of polymorphous cells, which are abnormal in shape and size that cannot be distinguished easily. As it was shown during the histological examination of the samples in this study cancer cells appear close together, but in many places and separated, each group from the other. This is in agreement with Rabban et al[16], which reported that breast cancer tissue, that in most cases when cancer develops, its cells clump together in a ball-like shape and have multiple nuclei. The cells may be close together or far apart, a characteristic not observed in normal tissues and, consequently, in normal cells. It was observed during the current study of breast tissue affected by invasive ductal breast cancer that the cancer cells are excessively dispersed and far from each other and the chromatin is dense , this is consistent with the results of Koss and Melamed[13], who indicated during his study that breast tissue with invasive ductal carcinoma has dense chromatin and large cells appear in clusters and scattered and their characteristic is very large nuclei, this distinguishes it from diffuse lobular carcinoma, in which the cells appear very small and are single, and the cytoplasm is mucous. The pathological significance of these tissue changes is unknown, but it can be used during surgical operations, to distinguish normal tissue from the affected tissue, and thus helps the surgeon to get rid of the diseased tissue and get rid of the disease.[16]

CONCLUSION

This Maysan-based series is characterized chiefly by invasive ductal carcinoma of no special type with recurrent adverse histological features, including lymphovascular involvement and pronounced nuclear atypia. The findings reinforce the need for early detection and robust pathology services in the region and provide a baseline for future studies integrating receptor status and molecular subtyping to refine prognostication and therapy selection.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Yasser Al-Yasin
Drafting or Revising Critically:	Yasser Al-Yasin
Final Approval of version:	The above author
Agreement to accountable for all aspects of work:	The above author

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

Hospital Work Environment and Nursing Performance: Insight from Mosul, Iraq

Atheer Abd Ahmed

ABSTRACT

Objective: To examine the relationship between the hospital work environment and nursing performance and to identify the key environmental factors associated with variations in nurses' effectiveness and productivity.
Study Design: Cross-sectional study
Place and Duration of Study: This study was conducted at the Department of Nursing Clinical Sciences, University of Mosul, College of Nursing, Mosul, Iraq from 13th October 2024 to 4th May 2025.
Methods: This cross-sectional study was conducted at in Mosul city, the Governorate of Nineveh, Iraq, in four large hospitals namely the Al-Salam Teaching Hospital, Ibn-Sena Teaching Hospital, Ibn Al-Atheer Teaching Hospital, and Mosul General Hospital from 13th October 2024 to 4th May 2025 among 250 nurses selected using a convenience sampling technique.
Results: More than 75% of nurses agreed or strongly agreed that they perform their duties efficiently, emphasize quality of care, and are willing to work overtime. Nursing performance demonstrated a positive correlation with all dimensions of the work environment, with the highest correlation observed for the overall work environment scale (r=0.660). Additionally, training (r=0.497), incentives (r=0.449), and technological empowerment (r=0.468) were identified as significant predictors of performance.
Conclusion: The significant influence of the work environment on nursing performance. While training and technological empowerment appear to be adequately supported, improvements in incentives and nurses' involvement in decision-making are necessary to enhance job satisfaction and overall performance.
Key Words: Work Environment, Nurses, Performance

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INTRODUCTION

The hospital work environment is a key determinant of nursing performance, nurse wellbeing, and healthcare quality. Nurses, as the largest group of healthcare providers, perform complex roles that include clinical care, decision-making, coordination, and patient support. A supportive work environment enhances efficiency and job satisfaction, whereas poor conditions contribute to burnout and reduced care quality.[1]

The work environment includes structural, organizational, and psychosocial factors such as staffing levels, leadership, workload, teamwork, and resource availability. These elements significantly influence nurses' professional experience and performance. Evidence shows that unfavorable environments are linked to job dissatisfaction and turnover, while positive environments improve both nurse outcomes and patient care.[2]

Nursing performance is a multidimensional aspect that includes clinical competence, standard compliance, patient satisfaction, and teamwork, psychological aspects such as stress and involvement.[3] The studies continuously prove that the sufficient staffing, favorable leadership, and professional autonomy are linked to the improved performance, and the workload and insufficient resources have adverse consequences.[4] Also, training, technological empowerment, incentives, and decision-making are also some of the key factors that are predictive of nursing performance especially within the Middle Eastern context in healthcare.[5] The work conditions in hospitals should be improved to increase the performance of nurses and improve the quality of healthcare. Specific leadership, resource, and staff assistance are essential, particularly where the resources are limited, like in Mosul, Iraq.[6]

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METHODS

This cross-sectional study was conducted in Mosul city, the Governorate of Nineveh, Iraq, in four large hospitals namely the Al-Salam Teaching Hospital, Ibn-Sena Teaching Hospital, Ibn Al-Atheer Teaching Hospital, and Mosul General Hospital from 1st November 2024 to 4th May 2025 vide letter No. 3434/QM/Approval/EFEF3 dated 22nd October 2024 among 250 nurses selected using a convenience sampling technique who were actively involved in direct patient care were eligible to be enrolled. Such hospitals offer full-fledged medical care and have a high number of nursing personnel. The questionnaire is based on the instrument employed by Althobaiti et al[7] in their study The Impact of the Work Environment on the Performance of Nurses in the Saudi Healthcare Sector. Some small changes were also done to fit it in the context and goals of the present study. This tool was divided into three parts; sociodemographic factors (20 items), work environment (25 items that included training, incentives, technological empowerment, work conditions, and decision-monitoring), and nursing performance (15 items). The ratings were done on a five-point Likert scale with results of higher scores reporting a more positive perception. The content and face validity were determined by the review of the experts, a panel of ten specialists, and the reliability was determined by Cronbachs alpha after pilot test that was done on a sample of 25 nurses. The data was analyzed with SPSS-26. Pearson correlation coefficient was used to test the relationship with statistical significance of $p \leq 0.05$.

RESULTS

The mean age was 26.89±5.95 years with a mean experience of 3.40±4.94 years, indicating a relatively young and less-experienced workforce. The average number of training courses was 2.31±2.37. Females slightly predominated (52.4%). Most participants had institute-level education (47.6%), followed by bachelor's degree holders (41.6%). The majority were employed at Al-Salam Teaching Hospital (53.2%). Regarding work units, the highest proportion worked in the emergency department (28.8%), followed by intensive care (14.4%) and neurology units (14.8%) [Table 1].

Table No. 1: Demographic characteristics of the participants (n=250)

Variable	No.	%
Gender		
Male	119	47.6
Female	131	52.4
Education level		
Nursing preparatory	18	7.2
Institute	119	47.6
Bachelor	104	41.6
Master	9	3.9
Hospital name		
Al-Salam	133	53.2
Ibn Senna	81	32.4
Mosul General	20	8.0
Ibn Al-Atheer	16	6.4
Hospital unit		
Emergency	72	28.8
Surgical	23	9.2
Medical	32	12.8
Paediatric	34	13.6
Intensive care unit	36	14.4
Physiotherapy	7	2.8
Insulation	9	3.6
Neurology	37	14.8

Table No. 2: Distribution of nurse performance measure (N = 250)

Item	Strongly Disagree	Disagree	Neutral	Agree	Strongly Agree
I strive to provide healthcare services with the highest efficiency, productivity, and quality	1.8%	4.5%	11.7%	40.5%	41.4%
I perform my duties at the hospital according to the highest international quality standards	-	8.1%	11.7%	45.9%	34.2%
I perform my duties at the hospital according to national quality standards	-	9%	12.6%	46.8%	31.5%
I ensure the quality of medical services and patient satisfaction	-	4.5%	16.2%	46.8%	32.4%
I am willing to work outside regular hours if necessary	-	4.5%	22.5%	40.5%	32.4%
I have sufficient experience to resolve problems at work	0.9	6.3%	18%	43.2%	31.5%
I provide guidance and answer patients' questions	0.9%	4.5%	10.8%	46.8%	36.9%
I have the ability and willingness to assume responsibility	0.9%	3.6%	15.3%	39.6%	40.5%
I communicate effectively with patients and staff	0.9%	5.4%	12.6%	43.2%	37.8%

I follow hospital rules and policies	-	4.5%	17.1%	39.6%	38.7%
I receive training on modern medical technologies	-	8.1%	12.6%	38.7%	40.5%
I complete tasks on time with high productivity	1.8%	4.5%	11.7%	40.5%	41.4%
I pursue personal development and improve my skills	-	8.1%	11.7%	45.9%	34.2%
Incentives increase my motivation and productivity	-	9%	12.6%	46.8%	31.5%
Productivity evaluation helps determine incentives	-	4.5%	16.2%	46.8%	32.4%

Table No. 3: Description of work environment scale scoring

Variable	Category	No.	%
First Dimension: Training	Very weak	-	-
	Weak	-	-
	Moderate	27	10.8
	Strong	147	58.8
	Very strong	76	30.4
Second Dimension: Incentives	Very weak	9	3.6
	Weak	52	20.8
	Moderate	61	24.4
	Strong	86	34.4
	Very strong	42	16.8
Third Dimension: Technical Empowerment	Weak	20	8.0
	Moderate	65	26.0
	Strong	131	52.4
	Very strong	34	13.6
Fourth Dimension: Nature and Conditions of Work	Very weak	2	0.8
	Weak	32	12.8
	Moderate	65	26.0
	Strong	101	40.4
	Very strong	50	20.0
Fifth Dimension: Participation in Decision-Making	Weak	36	14.4
	Moderate	65	26.0
	Strong	104	41.6
	Very strong	45	18.0

Table 4: Pearson correlation matrix between nurses' performance and work environment variables (N = 250)

Variable	Nurses' perfor-mance	Training	Incentives	Tech. Empower-ment	Partici-pation	Nature & Conditions	Work Environment
Nurses' Performance Scale	1						
Training Score	.497**	1					
Incentives	.449**	375**	1				
Technological Empowerment	.468**	.549**	.393**	1			
Participation in Decision Making	.465**	.437**	.401**	.556**	1		
Nature & Conditions of Work	.478**	.385**	.363**	.583**	.625**	1	
Work Environment Scale	.660**	.674**	.692**	.727**	.767**	.765**	1

The self-reported performance of the nurses, based on the 15 items, which indicates that most nurses feel that they are trying to give high quality care, conform to the policies and standards within the hospital, have positive communication skills, and are focused on professional development, also shows that the overall performance perceptions are positive. A high level of nursing performance, with most participants selecting "agree" or "strongly agree" across all items were indicated. Nurses reported strong commitment to quality care, task completion, communication, and professional responsibility. High agreement was also observed regarding adherence to standards, training, and personal development. Nonetheless, there was also a certain N amount of neutral answers concerning the workload, experience, and incentive systems. The results in general are good with some areas of improvement required (Table 2).

The greatest proportion of nurses had positive views about the work environment, especially training, technical empowerment and work conditions where most of them were rated strong. The involvement in decision-making was moderate to high. But incentives were rated comparatively low in nature. In general, the results reveal that the working environment is rather positive and that incentives need improvement in some cases (Table 3, Figs. 1-2).

The performance of nurses showed significant positive correlations with each one of the work environment dimensions, with the highest correlation being noted with the overall work environment scale (r =.660, p ≤ 0.01) [Table 4]

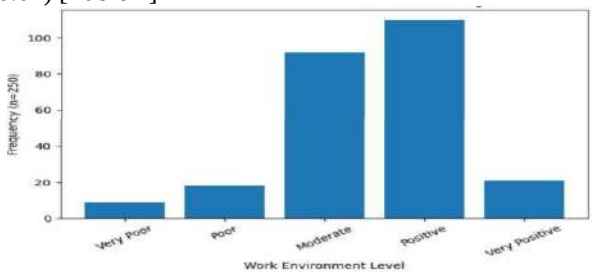

Figure No. 1: Work environment scale

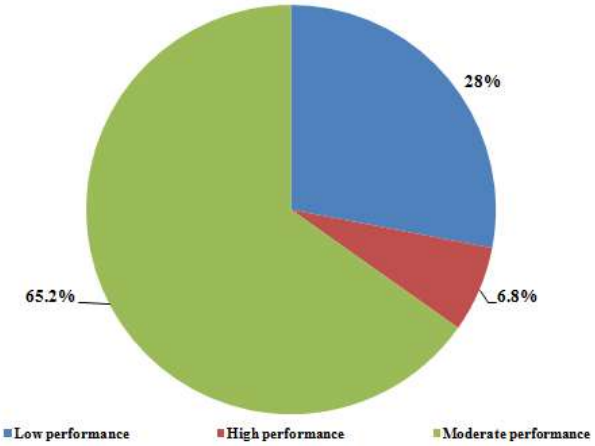

Figure No. 2: Nurses' performance scale

DISCUSSION

The current study revealed an overall positive hospital workplace and moderate high nursing performance among respondents. In particular, 44.1% of the nurses noted the positive working environment, and 36.9% noted the moderate one. Performance wise, most of the nurses showed moderate performance (65%), with the only 7% reporting high performance. These results can be used to conclude that despite the relatively favorable working conditions, these conditions do not immediately result in high performance rates, so some improvements are necessary. It also indicated that there were positive, significant relationships between nursing performance and all the work environment dimensions with the highest correlation coefficient to the overall work environment scale (r =.660, p ≤ 0.01). This has been in line with past researchers that have insisted on the direct effects of working environment on nursing performance and patient outcomes.[8,9] Research have indicated that positive working conditions that are typified by sufficient staffing, leadership, and collaboration contribute positively to the productivity of nurses and burnout.[10,11]

Regarding specific dimensions, training was associated positively with performance (r = .497) and this evidence confirms the results of previous studies in which continuous education and professional development were deemed the key elements of clinical competence and efficiency.[12,13] Similarly, performance was positively correlated with technological empowerment (r =.468), as was identified in the research that emphasizes the role of access to modern equipment and digital systems in enhancing healthcare delivery and decision-making.[14,15]

There was also a significant relationship between performance with participation in decision-making (r =.465). This observation has been reinforced by past studies that reveal that giving nurses authority to participate in the decision making process of an organization increases job satisfaction, independence and responsibility, which in turn boosts performance.[16,17] In addition, the nature and conditions of work (r =.478) were positively associated with performance and this is in line with the literature that reports that workplace under safe and well-organized and resource-sufficient conditions reduces stress and enhances productivity.[18]

Conversely, incentives had a comparatively low correlation with performance (r =.449) and the descriptive outcomes revealed that a significant percentage of nurses held incentives as being weak or moderate. It is also consistent with the previous studies in the low-resource context, in which inadequate financial and non-financial rewards have been found to impede motivation and the ability to boost performance.[19,20]

The high interrelationships that were found between the work environment dimensions especially between involvement in decision-making and nature of work conditions (r =.625) further affirm the holistic nature of organizational determinants to nursing performance. The same trends have been documented in past research and it has been noted that when one is improved in the working environment, the rest of the dimensions are most likely to be positively influenced.[21]

Overall, the current results confirm the available evidence that a favorable working environment in the hospital is a crucial factor of nursing performance. Nevertheless, under the overall positive situation, the situation with moderate performance levels is the most common, which proves the necessity of special actions, especially the improvement of incentive systems and the number of nurses who are involved in decision-making. These results, in particular, are applicable to the situation in the city of Mosul, Iraq, where the challenge of healthcare resources and workforce persists, and the significance of organizational changes to streamline the work of nurse professionals and healthcare delivery is especially high.

CONCLUSION

The hospital work environment significantly influences nursing performance. Despite generally positive conditions, performance remained mostly moderate. Strong associations were found between performance and all work environment dimensions, particularly the overall environment. Improving incentives and involvement in decision-making is essential to enhance nursing performance and healthcare quality.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Atheer Abd Ahmed
Drafting or Revising Critically:	Atheer Abd Ahmed
Final Approval of version:	The above author
Agreement to accountable for all aspects of work:	The above author

Conflict of Interest: The study has no conflict of interest to declare by any author.

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Original Article

A Comparative Study of Diagnostic Accuracy in Soft- and Hard-Tissue Lesions: Integration of Ultrasound and Conventional Radiography in Oral Radiology

Sarmad M. Hamozi, Ameer Yousif and Abdulsahib S. Jubran

ABSTRACT

Objective: To ascertain whether the integration of ultrasound imaging with conventional radiography enhances the detection and characterisation of oral and maxillofacial lesions in comparison to each modality utilised independently.

Study Design: Prospective cohort study

Place and Duration of Study: This study was conducted at the Oral & Maxillofacial Radiology Clinic at Central Hospital, Iraq from 1st May 2025 31st October 2025.

Methods: 80 patients with diverse oral lesions received standard intraoral and/or panoramic radiographs, succeeded by intraoral or extraoral ultrasound examinations utilising a high-frequency (≥10 MHz) linear probe. Histopathology, surgical results, or clinical follow-up constituted the reference standard. We calculated diagnostic metrics like sensitivity, specificity, accuracy, positive predictive value, and negative predictive value for radiography alone, ultrasound alone, and the combination of the two.

Results: Ultrasound was better at diagnosing soft-tissue lesions than radiography (sensitivity 92%, specificity 85% vs. 68% and 78% for radiography). The combined method increased the overall accuracy for hard-tissue lesions from 78% (radiography alone) to 85%.

Conclusion: Ultrasound is a useful addition to standard radiography in oral radiology. Combining both methods increases diagnostic confidence, especially for soft tissue lesions, and decreases the need for ionising radiation.

Key Words: Oral radiology, Ultrasound, Radiography, Diagnostic accuracy, Periapical lesions, Salivary gland pathology

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INTRODUCTION

Imaging plays a central role in oral diagnosis and treatment planning. Traditional modalities such as intraoral radiographs, panoramic images, and cone-beam computed tomography (CBCT) provide structural (hard-tissue) detail but have limitations, particularly when evaluating soft tissues or lesions without significant bone change. Likewise, they bring to light patients to ionizing rays, which is a trouble specifically for constant imaging or for weak inhabitants (e.g. children, pregnant women).[1]

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Ultrasound imagination (US), a non-ionizing, real-time imaging apparatus, has been extensively commissioned in medical diagnostics (abdomen, thyroid, vessels). In latest years, developments in high frequency, reduced probes have sanctioned the expansion of ultrasound into dental and maxillofacial fields. Researchers have discovered intraoral and extraoral ultrasound requests for salivary glands, mucosal lesions, lymph nodes, and even periapical lesions.[2] Ultrasound can perceive between cystic and solid lesions, recognize vascular stream via Doppler modes, and measure soft-tissue depth with good correspondence to histology or CBCT and adoption in routine oral radiology stays restricted.[3] Regardless of the guarantee of ultrasound, there is limited confirmation evaluating its performing directly versus established radiography or combination in a fitted clinical study. Many preceding pieces are examining articles, case reports, or small model studies. The diagnostic yield, particularly in mixed lesion types (soft + hard), remains underexplored.[4] In soft-tissue lesions, ultrasound will outperform conventional radiography in sensitivity and specificity. In hard-tissue lesions, combining ultrasound with radiography will yield significantly higher diagnostic accuracy than

radiography alone. Increased diagnostic confidence and fewer ambiguous cases will result from the adjunctive use of ultrasound.[5] In oral radiology practice, if the combined imaging approach proves to be better, it may minimise radiation exposure, improve patient management, and eliminate the need for repeated or advanced imaging (such as CT). Additionally, it might encourage the use of ultrasound and dental radiology training.[2,5] In contrast to using radiography or ultrasound alone, this study attempts to determine whether combining ultrasound with traditional radiography techniques enhances diagnostic accuracy in oral radiology, particularly across soft-tissue and hard-tissue lesions.

METHODS

This is a comparative prospective diagnostic accuracy study was conducted at Oral & Maxillofacial Radiology Clinic at Central Hospital, Iraq from 1st May 2025 31st October 2025 vide letter No. 123r/QM/Approval/ almebpq dated April 2, 2025. Completed the course of 12 months, affected role were showing oral or maxillofacial scratches, counting clinically supposed mucosal crowds, salivary gland ailments, periapical radiolucency, and lymph bulge expansion. Adult (≥18 years), scratches manageable to both radiographic imaging and ultrasound, approval to undertake imaging and, if shown, biopsy or surgical proof were included. Lesions totally hidden following dense bone exclusive of acoustic view, contraindications to surgery, poor support were excluded. Eighty patients with diverse oral lesions received standard intraoral and/or panoramic radiographs, succeeded by intraoral or extraoral ultrasound examinations utilising a high-frequency (≥10 MHz) linear probe

Radiography (CR) of normal intraoral periapical radiographs or panoramic imagery (or both) are regarded per lesson. Radiographs are understood by two blinded oral radiologists, who classify lesions (e.g. cystic vs solid, radiolucent/radiopaque, periapical laceration vs non) as in Figure 1.

High-frequency lined probe (e.g. 10–18 MHz), with B-mode and Doppler ultrasound qualifications. For intraoral lesions, use mini "hockey-stick" or miniature intraoral probe some place appropriate; for extraoral advance, percutaneous scanning is done. Experienced sonographer directed in oral imaging. Gray scale lesion presence (hyperechoic, hypoechoic, mixed), borders (well-defined, irregular), vascular configuration (using Doppler), sizes (length, width, depth) as in Figure 2.

A consensus reading combining information from radiographic and ultrasound images, considering both modalities to make a final diagnosis were combined interpretation. Lesions biopsied or surgically removed, histological diagnosis is the gold standard. For benign or non-surgical lesions, a follow-up period (e.g. 6–12 months) with stability or resolution justifies diagnosis. In ambiguous cases, diagnosis is resolved by panel consensus.

For each lesion and imaging modality (radiography alone, US alone, combined), compute (True positives (TP), true negatives (TN), false positives (FP), false negatives (FN). Compare the three modalities using McNemar's test (for paired categorical data) or equivalent to test for statistically significant differences in sensitivity and specificity.

RESULTS

McNemar's test comparing radiography alone vs combined in soft-tissue lesions: $p = 0.012$. McNemar's test comparing radiography alone vs combined in hard-tissue lesions: $p = 0.023$.

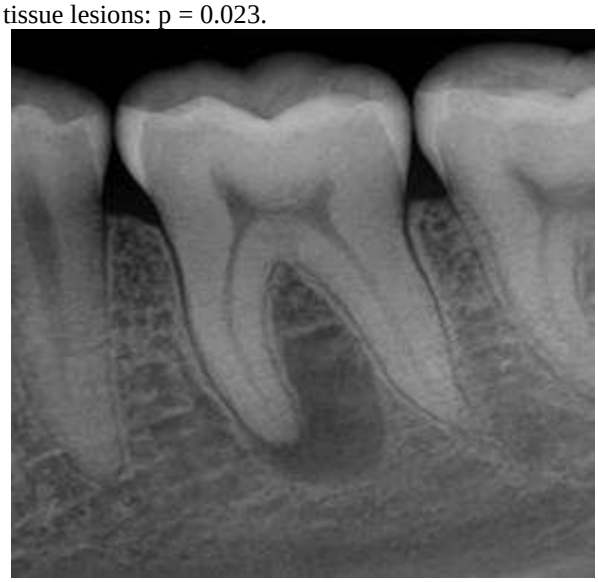

Figure No. 1: Example of periapical radiograph of mandibular premolar with radiolucency

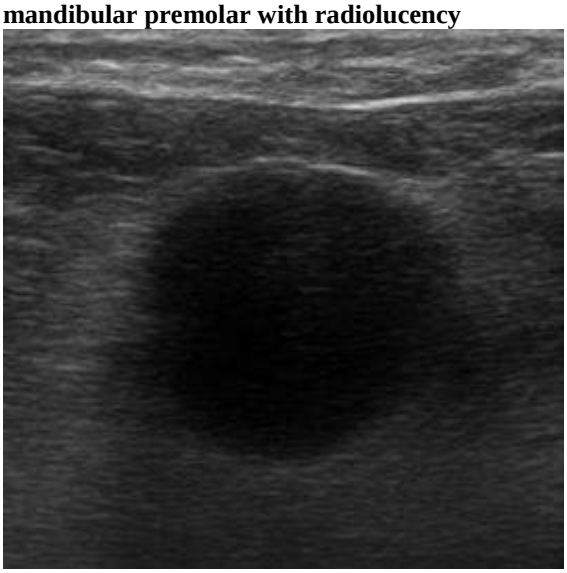

Figure No. 2: Corresponding ultrasound B-mode image of the same lesion, showing a hypoechoic region with defined margins

ROC AUC values: Radiography alone (soft-tissue): 0.78, Ultrasound alone (soft-tissue): 0.91, Combined (soft-tissue): 0.95, Radiography alone (hard-tissue): 0.80, Ultrasound alone (hardtissue): 0.68, Combined (hard-tissue): 0.88. Compute Receiver Operating Characteristic (ROC) curves and Area Under Curve (AUC) for each modality or combined method (Tables 1-3, Fig. 3).

Table No. 1: Participant demographics (n=80)

Variable	Value
Age (years)	45.2±12.8
Gender	
Male	42 (52.5%)
Female	38 (47.5%)
Lesion types	
Soft-tissue	35 (43.7%)
Hard-tissue (periapical)	30 (37.5%)
Salivary gland/lymph nodes	15 (18.8%)

Table No. 2: Diagnostic performance metrics

Lesion type/Modality	Sensitivity	Specificity	Accuracy	Positive predictive value	Negative predictive value
Soft-tissue radiography alone	68%	78%	73%	70%	76%
Soft-tissue Ultrasound alone	92%	85%	88%	88%	90%
Soft-tissue Combined (CR + US)	95%	90%	93%	92%	94%
Hard-tissue Radiography alone	80%	75%	78%	82%	72%
Hard-tissueUltrasound alone	65%	70%	68%	69%	66%
Hard-tissue Combined (CR + US)	88%	82%	85%	87%	83%

Table No. 3: Cross-tabulation of imaging diagnoses versus reference standard for combined modality

Imaging diagnosis (combined)	Histopathology + Followup positive	Histopathology + Followup negative	Total
Positive diagnosis	50	5	55
Negative diagnosis	3	22	25
Total	53	27	80

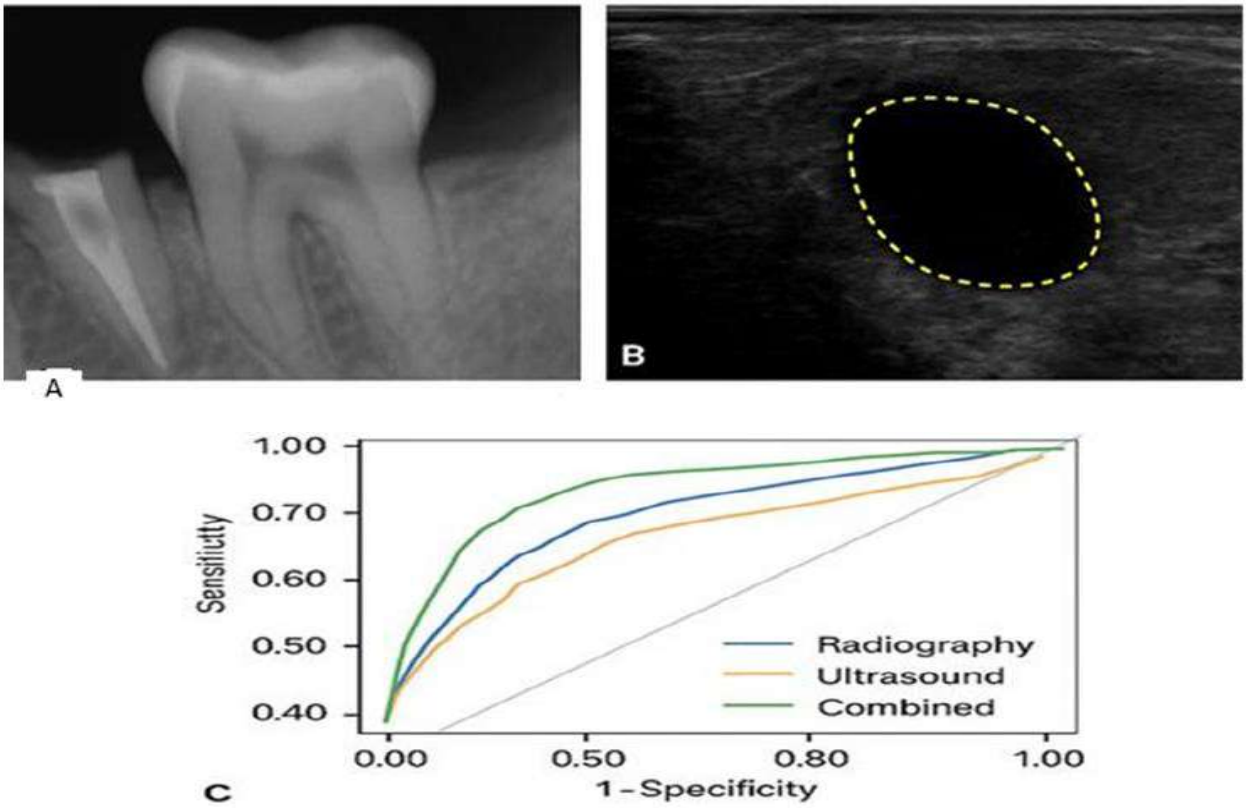

Figure No. 3: Receiver operating characteristic curves and area under curve

DISCUSSION

In this study, ultrasound demonstrated excellent diagnostic performance in identifying soft-tissue lesions (mucosal lesions, salivary gland nodules, lymph nodes) compared with conventional radiography. Sensitivity reached 92% and specificity 85%. When combined with radiographic images, overall accuracy increased to 93%. This supports the idea that ultrasound is a useful addition to radiography, especially when looking at soft tissues.[6-8]

These results are consistent with previous reviews highlighting the ability of ultrasound to image soft tissues, differentiate cystic from solid masses, and apply Doppler to assess vascularity.[9,10]

For osseous lesions like periapical pathology, radiography was fairly accurate (78% in our example), but ultrasound alone was not as accurate (68%). But when both methods were used together, the accuracy went up to 85%. This indicates that ultrasound alone is inadequate in these instances; however, it is beneficial when combined, potentially providing supplementary information regarding tissue components at the lesion periphery or surrounding oedema.[11] Other studies indicate that ultrasound can distinguish abscesses from granulomas based on acoustic voids and echogenic patterns.[12,13]

Results of McNemar's test revealed that the performance difference between conventional radiography and the combined approach was statistically significant ($p < 0.05$). Furthermore, ROC curve analysis showed that the AUC of the combined modality was greater than either modality alone, indicating that it is the superior diagnostic strategy.[14].

Strengths, the comparative and prospective design with a reference standard (histopathology/follow-up) adds credibility, use of a standardized protocol for imaging and interpretation[15] and comprehensive statistical analysis (sensitivity, specificity, AUC). Limitations, the sample size is exemplary but may not be sufficient to generalize results to rare conditions.[16,17] Heavy reliance on the ultrasound operator; performance may vary with clinician expertise. Some deep or intraosseous lesions behind dense bone may not be visible on ultrasound due to acoustic shadowing and possible selection bias toward cases more accessible to ultrasound imaging. High-frequency probes are expensive and not widely available in general dental practice.[18]

Ultrasound ought to be incorporated into oral radiology clinics as a supplementary instrument, especially for soft-tissue cases or for the differential diagnosis of masses. Radiologists and dentists ought to receive training in the utilisation of oral and maxillofacial ultrasound techniques.[6,19] It is recommended to develop specialised high-frequency probes for intraoral and gingival use to surmount osseous barriers and constricted anatomical spaces. More research is needed on a wider range of samples, such as those from different sites, depths, and complicated cases.[20,21] Subsequent research ought to investigate longitudinal applications (temporal monitoring) to assess treatment outcomes or patient follow-up, including recovery post-abscess drainage or endodontic therapy.

CONCLUSION

Using the ultrasound imaging with regular X-rays greatly improves the accuracy of oral radiology diagnoses. Ultrasound is great for looking at soft tissue lesions on its own, but it doesn't do as well with hard tissue lesions. But using both methods together gives you better accuracy, sensitivity, and specificity than just using radiography and support the use of ultrasound as an extra tool in oral radiology workflows.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Sarmad M. Hamozi, Ameer Yousif
Drafting or Revising Critically:	Sarmad M. Hamozi, Abdulsahib S. Jubran
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Prevalence and Determinants of Family Violence Exposure among University Students

Marwa Karim Jabr[1], Inaam Abdulkareem Abas[2], Ragad Saleh Mirdan[3] and Haidar Hassan Hussain[4]

ABSTRACT

Objective: To provide evidence-based information to support nursing practice, public health interventions, and policy development to reduce family violence and improve student well-being.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the College of Nursing, University of Al-Essra, Iraq from 15th January 2026 to 31st March 2026.

Methods: Convenience sampling was used to find participants. The WHOQOL-BREF questionnaire and a validated violence scale were used to gather data in order to achieve the goals of the study.

Results: An overall moderate mean prevalence of family violence exposure among the students (1.83±0.930), though a significant proportion of participants reported experiencing high levels of abuse. Age and social status were found to be significantly associated with a student's exposure to family violence. Conversely, academic year and financial status did not demonstrate a statistically significant relationship with violence exposure.

Conclusion: Baseline of family violence across the broader student population may skew lower, the significant subset of students experiencing moderate to high levels of household abuse is a major concern. The identification of age and social status as key determinants highlights the urgent need for targeted, sociodemographically tailored interventions and preventive strategies to protect and support vulnerable young adults.

Key Words: Violence, University student, Quality of life

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INTRODUCTION

Violence is the deliberate application of physical force or power, whether threatened or actual, against oneself, another individual, or a group. This behavior may lead to physical injury, psychological damage, developmental issues, or deprivation.[1] Physical, psychological, emotional, sexual, and verbal manifestations comprise the multifaceted and intricate phenomenon of violence.[2] It affects individuals across the lifespan and represents a major public health issue with significant social, economic, and healthcare consequences.[3]

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Family violence is a distinct type of interpersonal violence that transpires within the home and encompasses violent actions by parents, caretakers, or other relatives.[4] Family violence includes physical punishment, emotional abuse, psychological neglect, sexual abuse, and verbal aggression.[5] Exposure to family violence during childhood and adolescence is associated with long-term health consequences and can negatively influence academic performance, mental health, and social functioning among students.[6]

From a public health and nursing perspective, family violence is a critical determinant of health.[7] Nurses and healthcare professionals frequently encounter victims of family violence in clinical and community settings, often without disclosure of abuse.[8] Family violence contributes to physical injuries, chronic health problems, mental disorders, and increased healthcare utilization. Students exposed to violence at home may present with psychosomatic complaints, emotional distress, and maladaptive coping behaviours.[9] In the Middle East, including Iraq, family structures are strongly influenced by cultural norms, traditional gender roles, and patriarchal values.[10] The sociocultural factors may contribute to the normalization of violence within families and discourage victims from seeking help. Limited awareness, stigma, and insufficient

reporting mechanisms further complicate the identification and management of family violence.[11]

Exposure to familial violence is linked to several detrimental psychological and behavioral consequences, such as anxiety, depression, post-traumatic stress disorder, diminished self-esteem, aggression, substance addiction, and suicidal tendencies. Students exposed to violence may experience impaired cognitive functioning, reduced academic achievement, and difficulties in peer relationships.[12] Several theoretical frameworks explain the occurrence and transmission of violence within families. Social learning theory posits that individuals develop violent tendencies by observing and imitating family members.[13] Attachment theory proposes that early relationships with caregivers shape emotional regulation and interpersonal behaviors, with insecure attachment increasing vulnerability to violence.[14]

Cultural beliefs, gender norms, and socialization practices play a significant role in shaping attitudes toward violence and acceptable disciplinary practices within families.[15] In traditional societies, strict gender roles and hierarchical family structures may reinforce tolerance of violence and reduce reporting.[16] Despite increasing research on dating violence, cyber violence, and workplace violence, studies focusing on family violence among student populations remain limited, particularly in Iraq and the Middle East.[17] Existing research has often focused on adult populations or specific types of violence, with limited comprehensive assessment of family violence exposure among students.[18] There is a need for empirical data to inform policy development, nursing education, and public health strategies aimed at preventing violence and supporting affected students.

The purpose of this study is to assess the prevalence, types, and determinants of family violence among students and to examine demographic, social, and psychological factors associated with exposure to family violence.

METHODS

This cross-sectional study was conducted at College of Nursing, University of Al-Essra, Iraq from 15th January 2026 to 31st March 2026 letter No. 127 dated January 5, 2026. The universities were chosen because of their key characteristics, including the availability of a sufficient sample, accessibility, cost, student collaboration, appropriate administrative facilities, and time-saving advantages. Fifty university students were enrolled undergraduate and postgraduate students. A convenience sampling method used to recruit participants. The university student's undergraduate or graduate, be at least eighteen years old, give informed consent to take part in the research and have witnessed or experienced physical, mental, or psychological family violence at some point in their lives were included. The student are not currently enrolled as students at the university., age under 18 years of age and do not provide informed consent were excluded. The data was collected from the respondents. and divided into three sections.

Part 1: This section describes the study participants' demographics, including factors like age, household, income level, marital status, and academic standing.

Part 2: Physical health, psychological health, social relationships, and environment are the four key areas measured by the 26 items that make up the WHOQOL-BREF, a condensed version of the WHOQOL-100. Two generic items that assess general health satisfaction and overall quality of life are also included in the measure. Depending on the type of question, each item is assessed on a 5-point Likert scale, with response possibilities ranging from 1 (very poor/very dissatisfied/not at all) to 5 (very good/very satisfied/extremely). Better perceived quality of life is indicated by higher scores. Daily living activities, reliance on medical care, energy and exhaustion, mobility, pain and discomfort, sleep and rest, and job capacity are all included in the physical health area. Positive emotions, thinking, learning, memory, focus, self-esteem, body image, and negative emotions are all evaluated in the psychological domain. Social support and interpersonal relationships are assessed in the social relationships area. Financial resources, safety and security, access to health and social services, the home environment, chances to learn new knowledge and skills, engagement in recreational activities, the physical environment, and transportation are all included in the environmental domain. Scoring of the WHOQOL-BREF is performed by calculating the mean of items within each domain and transforming the scores linearly to a 0–100 scale, if required, to allow comparison across domains.

Part3: Violence scale: The scale consists of 28 items covering multiple dimensions of violence, including physical violence (e.g, being physically beaten), psychological and emotional violence (e.g, belittling opinions, making the student feel worthless), social violence (e.g, isolation from society, restriction of movement), economic violence (e.g, refusal of personal allowance, considering educational expenses a burden), and educational violence (e.g, forcing a specific major, threatening to prevent continuation of studies). Responses are rated on a four-point Likert scale (Always, Often, Rarely, Never), allowing participants to indicate the frequency of their experiences. Higher scores indicate greater exposure to violence. Some items are positively worded (being listened to, receiving appropriate care) and require reverse scoring to ensure accurate interpretation of total scores. The scale demonstrates acceptable psychometric properties in terms of internal consistency and content validity, making it suitable for assessing the prevalence and

severity of family-directed violence among female university students in academic research settings.

The data was analyzed through SPSS-26. To investigate relationships between family violence and demographic and psychosocial variables, inferential statistics such as chi-square tests, t-tests, and logistic regression analysis will be employed. The threshold for statistical significance will be set at $p < 0.05$.

RESULTS

The mean age was 21.88±2.30. Also, half of the students were in the 4th stage of university, 40% were single, and the majority (40%) of them have great financial status (Table 1). The level of family violence among students was at low level with a total mean score of 1.83±0.93. The results indicates that students had high level of family violence among student' for the items 6. 17, 20 and 23 (Tables 2-3).

There is a significant relationship between the level of family violence and social status (p=0.081). However, there is no significant relationship between levels of family violence among students and other socio-demographical characteristics (Table 4).

Table No. 1: Sociodemographic characteristics of participated students (N=50)

Sociodemographic characteristics	No.	%	Mean±SD
Age (years)			21.88±2.30
Academic Year			
Second Stage	9	18.0	3.52±0.90
Third Stage	11	22.0	
Fourth Stage	25	50.0	
Fifth Stage	5	10.0	
Social Status			
Single	40	80.0	1.20±0.40
Married	10	20.0	
Divorced	-	-	
Financial Status			
Enough	40	80.0	1.20±0.40
Somehow Enough	10	20.0	
Not Enough	-	-	

Table No. 2: Level of family violence against university students

Rarely	Little	Most of the time	Always	Mean±SD	Level of Family Violence
46 (92%)	3 (6%)	1 (2%)	-	1.10±0.363	Low
9 (18%)	10 (20%)	13 (26%)	18 (36%)	2.80±1.12	Moderate
36 (72%)	7 (14%)	3 (6%)	4 (8%)	1.50±0.93	Low
36 (72%)	7 (14%)	3 (6%)	4 (8%)	1.50±0.931	low
39 (78%)	7(14%)	2 (4%)	2 (4%)	1.34±0.745	Low
8 (16%)	6 (12%)	12 (24%)	24 (48%)	3.04±1.124	High
31 (62%)	13 (26%)	1 (2%)	5 (10%)	1.60±0.947	Low
40 (80%)	6 (12%)	1 (2%)	3 (6%)	1.34±0.798	Low
11 (22%)	4 (8%)	10 (20%)	25 (50%)	2.98±1.220	Moderate
37 (74%)	7 (14%)	2 (4%)	4(8%)	1.46±0.908	Low
43 (86%)	5 (10%)	-	2 (4%)	1.22±0.648	Low
36 (72%)	8 (16%)	4 (8%)	2 (4%)	1.44±0.812	Low
34 (68%)	10 (20%)	4 (8%)	2 (4%)	1.48±0.814	Low
17 (34%)	9 (18%)	12 (24%)	12 (24%)	2.38±1.193	Moderate
34 (68%)	7 (14%)	4 (8%)	5 (10%)	1.60±1.010	Low
33 (66%)	10 (20%)	3 (6%)	4 (8%)	1.56±0.929	Low
4 (8%)	4 (8%)	7 (14%)	35 (70%)	3.46±0.952	High
41 (82%)	4 (8%)	3 (6%)	2 (4%)	1.32±0.767	Low
38 (76%)	5 (10%)	4 (8%)	3 (6%)	1.44±0.884	Low
9 (18%)	5 (10%)	9 (18%)	27 (54%)	3.08±1.175	High
44 (88%)	3 (6%)	-	3 (6%)	1.24±0.743	Low
35 (70%)	7 (14%)	2 (4%)	6 (12%)	1.58±1.031	Low
11 (22%)	4 (8%)	1 (2%)	34 (68%)	3.16±1.283	High
40 (80%)	5 (10%)	3 (6%)	2 (4%)	1.34±0.772	Low
35 (70%)	6 (12%)	3 (6%)	6 (12%)	1.60±1.049	Low
36 (72%)	2 (4%)	7 (14%)	5 (10%)	1.62±1.066	Low
35 (70%)	9 (18%)	3 (6%)	3 (6%)	1.48±0.862	Low
31 (62%)	10 (20%)	5 (10%)	4 (8%)	1.64±0.963	Low
Total Mean				**1.83±0.930**	**Low**

Level of Family Violence = Low: 1.1.99, Moderate: 2-2.99, High: 3-4

Table No. 3: The mean of family violence among students

Level of Family Violence against University Students	No.	%	Mean±SD
Moderate level of family violence	40	80.0	2.20±0.40
High level of family violence	10	20.0	

Table No. 4: The relationship between Students' socio-demographic characteristics and their level of family violence

Students Characteristics	No.	%	Value	df	P value
Academic Year					
Second Stage	9	18.0	52.203	60	.753
Third Stage	11	22.0			
Fourth Stage	25	50.0			
Fifth Stage	5	10.0			
Social Status					
Single	40	80.0	29.340	20	.081*
Married	10	20.0			
Divorced	-	-			
Financial Status					
Enough	40	80.0	17.361	20	.629
Somehow Enough	10	20.0			
Not Enough	-	-			

*P value≤ 0.001

DISCUSSION

The results of the present study showed that the mean age of students was 21.88±2.309 years, indicating that most participants were young adults. Half of the students were in the fourth academic year, which may reflect higher participation among senior students who are more available and aware of research activities. The majority of students were single (80%) and reported having sufficient financial status (80%). These findings are consistent with Noori et al[11], where most participants were unmarried young adults with moderate to good financial status. Another study by Kolanati et al[6] found that majority were mean ages of 20.11 years in their second year in college. Another study reported by Haj-Yahia & de Zoysa[19] showed most students were with low financial status in their third year of college. Zhang et al[20] also reported that the majority of the young adolescents in their finale high school year and their involvement in school bullying and violence. Another study consistent with our findings is conducted by Adelman et al[21] which reported that majority of females were aged in their twenties and are survivors of violence.

This study reported level of family violence among students was low, with a total mean score of 1.83±0.930. Most items showed low exposure to family violence, indicating that the majority of students rarely experienced violent behaviors within their families. However, several items 6, 17, 20, and 23 demonstrated high levels of violence. The overall violence levels were low but specific forms of psychological or physical violence were reported at higher frequencies among young adults by Alotaibi & Mukred.[8] Aksoy et al[22] also reported different findings from our research which showed increased level of violence suffered by nursing students during their clinical training. Le et al[14] reported the experience of domestic violence among university students which was higher among Vietnamese university student owing to the environment and cultural beliefs. However the study conducted by Oydemir & Alan-Dikmen[16] reported that most female student in the university suffer a higher proportionate of violence and cyber victimization's and effecting the happiness levels and resilience among those females. The study conducted in Turkey by Küçük et al[23] reported an assessment of perceptions of students nurses for obstetric violence which showed that the study low level of perception against violence and thereby nictitating the need for increasing awareness on those populations. Carter et al[15] reported that among individuals who are exposed to domestic violence the majority had a higher level of violence reported during the study. However our findings differ from those of Zhu et al[24], which showed a higher level of violence among the study with fewer individual with low level of family violence. Gershoff & Cuartas[25] reported the specific forms of violence and psychological stressors remain prevalent among a subgroup of young adults. Variations in prevalence rates across studies may be attributed to differences in cultural context, measurement tools, and academic and social pressures experienced by students. Noori et al[11]

revealed that overall level of family violence among university students was low, although some students reported moderate to high levels for specific items. This may be explained by the generally positive attitudes of students toward rejecting family violence. The university students often demonstrate a positive attitude against domestic violence because they recognize its negative consequences on family stability and social well-being.[5]

The study found no significant relationship between academic year and financial status with the level of family violence ($p>0.05$). However, age and social status showed significant relationships with family violence ($p\leq0.001$). Older students and those with different marital statuses (single or married) may experience different family dynamics, which could influence exposure to violence. These findings are consistent with Zhang et al[20] suggesting that age and marital status can affect family relationships and conflict patterns. Adelman et al[21] suggested that level of violence is affected by social status of the students as well as their age. Consistent our findings with Lin et al[26] that the socialization of school children was related to their level of family violent owing to their academic failure. This finding is consistent with previous research by Barbon et al[27], which has shown that family dynamics, socioeconomic conditions, and interpersonal relationships play a crucial role in influencing exposure to violence and psychological distress among young people. Family conflicts and financial difficulties have been identified as major contributors to adverse family environments and student vulnerability.[21]

CONCLUSION

Overall level of family violence among university students was low, a significant proportion experienced moderate to high levels. Age and social status were significantly associated with family violence, while academic year and financial status were not.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Marwa Karim Jabr, Inaam Abdulkareem Abas
Drafting or Revising Critically:	Ragad Saleh Mirdan, Haidar Hassan Hussain
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Histomorphometrical Analysis of the Umbilical Cord and Placenta in Human Fetuses with Macrosomia

Lina A. Salih

ABSTRACT

Objective: To evaluate the histomorphometrical changes in the umbilical cords and placenta associated with excessive fetal growth.

Study Design: Comparative cross-sectional study

Place and Duration of Study: This study was conducted at the College Science, University of Baghdad, Baghdad, Iraq from 1st September 2025 to 28th February 2026.

Methods: A total of 160 Iraqi pregnant women at 3rd trimester of pregnancy with their neonates under vaginal or caesarean delivery were enrolled.

Results: No significant differences (P≥0.05) observed in maternal age between groups, the mean maternal age with normal fetus weight was 24.21±20.5 years, women carrying macrosomic fetus was 25.11±18.5 years. The pregnant with macrosomic fetus showed significantly (p≤0.01) shorter gestational age and higher maternal and neonatal weights 32.10±1.2, 94±3.2 kg, 4.8±2.5 kg than control group 36.1±1.5, 80±10.5 kg, 2.5±0.4 kg respectively. The macroscopic examination showed significant differences in placental and umbilical cords between groups(P≤ 0.05) the placental weight and length were lower in the macrosomic infants (319.5±10.03g, 16.43±1.04 cm) while in the non-macrosomic infants (509.17±11.42 g,19.15±2.05 cm)while umbilical cords length and diameter were significantlyincreased (72±0.06, 55±3.05 cm) compared to control 3.44±2.15, 1.82±0.06cm) .The morphometric analysis demonstrated reduced placenta surface area 190±20.5cm, diameter 15.33±10.5cm^2, and the placental thickness 1.32±1.5 cm compared to the non-macrosomic infants 210.2±18.5 cm, 18.3±1.4 cm^2, 1.72±1.2 cm respectively. The placental villiin macrosomic infants appeared increased surface area and villous diameter (1.38 ± 0.1 mm2,, 0.14 ± 0.02mm) while blood vessel diameter was reduced in the macrosomic infants 0.03 ± 0.02 mm.

Conclusion: Placental morphometrical index is associated with fetal macrosomia and understanding gestational complications.

Key Words: Macrosomia, Histomorphometrical, Fetal growth, Placenta

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INTRODUCTION

Fetal macrosomia is a major obstetric problem commonly defined as birth weight 4,000-4,500 g or more, regardless of the gestational age.[1] It's associated with increased maternal and fetal complications during pregnancy and delivery.[2] Several factors are involved in fetal overweight like maternal diabetes, pre-gestational diabetes, maternal overweight, many births, the advanced age of the mother, in addition to genetic factors.[3]

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Increased glucose to the placenta stimulates fetal insulin, adipose tissue deposition and faster growth of the fetus.[4]

The placenta is a main factor in regulating fetal development, the changes in the size of the placenta, and weight may cause structural immaturation of some chorionic villi and abnormal circulation in placenta.[5] The structural changes in umbilical cord effect on blood flow.[6] These histological changes are clinical important for understand of the mechanisms of foetal development, and may provide better chances to develop more effective strategies in managing pregnancy.[7]

METHODS

This comparative cross-sectional study was conducted at College Science, University of Baghdad, Baghdad, Iraq from 1st September 2025 to 28th February 2026 vide letter No. 2111B/BU/Approval/JSDJNEHU Dated August 25, 2025. A total of 160 Iraqi pregnant women at 3rd trimester of pregnancy with their neonates under vaginal or caesarean delivery, they divided into two

groups; group1 the mothers who had macrosomic infants, (fetuses with weight ≥4000 g) group 2 the mothers delivered fetus with birth weight (<4 kg). The mothers who had twins or previous abortion, any genetic or autoimmune diseases, and pregnancy age ≤37 weeks of gestation were excluded. Fifty placentae with membranes and umbilical cord were collected within 1 h after delivery. Fresh tissue samples were placed in 10% buffered neutral formalin solution until time of histological procedure.[8] Hematoxylin and Eosin (H&E) was used.[9] All sections selected located close to the midline of the blocks, used about 10-20 sections(5-6µm. thick). Digital pictures of the serial histological sections were measured by using the software programs 2015 Motic Image Plus version 2.0.

RESULTS

Table 1 indicated no significant alterations (P≥0.05) in the maternal age between groups, the maternal age in the pregnant women with normal fetus weight was 24.21±20.5 years, while mother with macrosomic fetus was 25.11±18.5 years. The gestational age, was short significantly (P≤0.01), (32.10±1.2 w) compared to the control group (36.1±1.5 w), maternal weight in the pregnant women with macrosomic fetus was increase highly significant (P≤0.01) (94±3.2 kg) compared to other group (80±10.5 kg) the weight of the neonates in the macrosomic group was increase significantly (P≤0.05) (4.8±2.5 kg) compared to control (2.5±0.4 kg)

The histological examination of the placenta showed in figures 1,2, immature placental villus with few blood vessels and visible deposition of fibrin in villus , the histological sections appeared crowding of the villi with reduced intervillous space while in the non-macrosomic placenta the histological texture appeared normal mature villi with obvious blood vessels without fibrosis. In the figure 3, the sections showed normal appearance of differentiated mature villus containing blood vessels, cytotrophoblasts, cyncytiotrophoblast and few syncytial knot, while the macrosomic villus showed less development and with peri-villous edema, with fibrosis and increased syncytial knotting.

The histological examination of the umbilical cords showed in figure 4, normal appearance of umbilical with normal section in artery a layer of normal texture. Wharton's jelly with normal distribution of mesenchymal cells (A&B), at 100x, the Wharton's jelly in the macrosomia distinguished with much fat droplet deposition when compared to the non-macrosomia (C&D)

The median placental weight was 319.5±10.03gm in the macrosomic infants, while in the non-macrosomic infants 509.17±11.42 gm considered significant statistically (P≤0.05), the length of the placenta showed significant differences (P≤0.05) between the studied groups; the length of placental was shorter in the macrosomic infants compared to the non-macrosomic infants 16.43±1.04, 19.15±2.05 cm (Table 2). The gross measurements of the umbilical cords proved highly significant differences (P≤0.01) between the two groups; the umbilical cords length was increased in the macrosomic fetus compared to the non-macrosomic infants 72±0.06, 55±3.05 cm respectively, the umbilical cords diameter was increased in the macrosomic infants 3.44±2.15 cm compared to the non-macrosomic 1.82±0.06 cm.

The placental morphometric results appeared decreased statistically ; the surface area of the placenta was 190±20.5cm, diameter of the placenta was 15.33±10.5cm^2, and the placental thickness was 1.32±1.5 cm compared to the non-macrosomic infants (210.2±18.5 cm, 18.3±1.4 cm^2, 1.72±1.2 cm) respectively (Table 3).

The placental villus surface area and diameter had higher measurements significantly (P≤0.01) in the macrosomic infants (1.38±0.1 mm^2, 0.14±0.02mm) compared to the non-macrosomic infants (0.58±0.5 mm^2, 0.07±0.09 mm) respectively. The blood vessel diameter results appeared low significant measurements in the macrosomic infants compared to the non-macrosomic infants (0.03±0.02, 0.05±0.16) mm respectively (Table 4).

Table No. 1: Parameters of maternal and neonates

Parameters	Non-macrosomic infants (n=80)	Macrosomic fetus (n=80)	P-value
Maternal age (years)	24.21±20.5	25.11±18.5	0.0610 NS
Gestational age (weight)	36.1±1.5	32.10±1.2	0.0001**
Maternal weight (kg)	80±10.5	94±3.2	0.0180*
Neonatal weight (kg)	2.5±0.4	4.8±2.5	0.01*

*significant (P≤0.05), **highly significant (P≤0.01) NS = non- significant P≥0.05

Table No. 2: The mean differences of macroscopic gross of placenta in the studied groups

Variable	Non-macrosomic infants (n=80)	Macrosomic fetus (n=80)	P-value
Placental weight (g)	509.17±11.42	319.5±10.03	0.03*
Placental length (cm)	19.15±2.05	16.43±1.04	0.01*
Umbilical cords length (cm)	55±3.05	72±0.06	0.001**
Umbilical cords diameter (cm)	1.82±0.06	3.44±2.15	0.001**

*Ssignificant (P≤0.05) **Highly significant (P≤0.01)

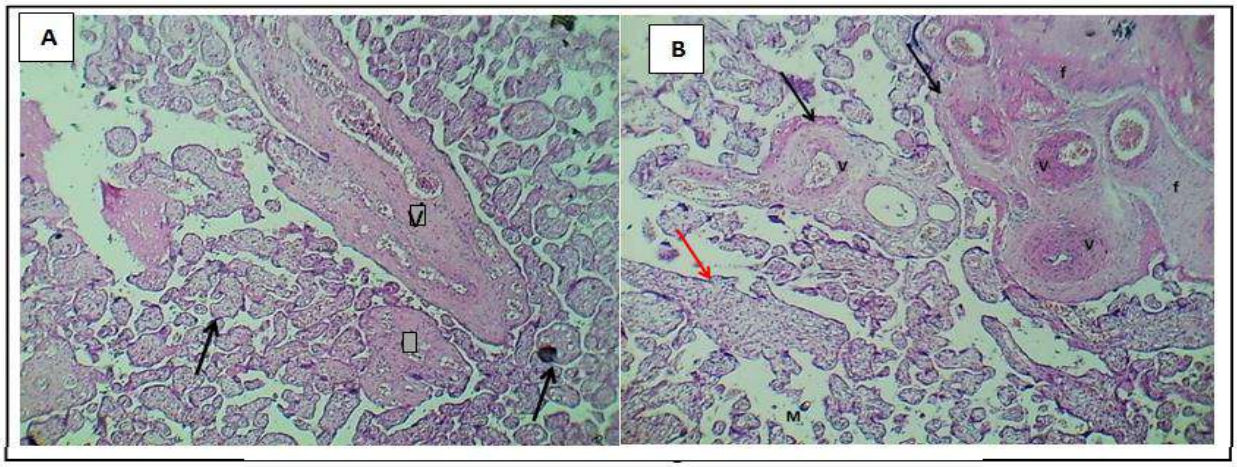

Figure No. 1: CS of normal placenta, normal appearance of differentiated stem villus (Black arrows) containing blood vessels (v) surrounded by progressive fibrosing (f) & differentiated mature intermediate villus (Red arrows) maternal blood space (m). A:40x.B:100x

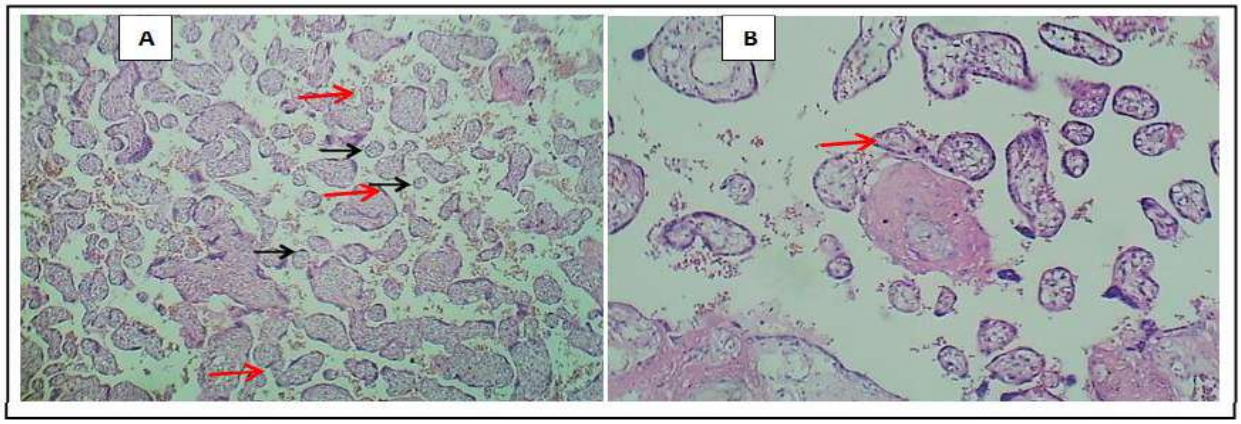

Figure No. 2: CS of section of macrosomic placenta show hypoplasia of immature villus (black arrows) with few blood vessels, atrophy of stem villus some peri-villous edema (red arrows) A:40x. B:100x

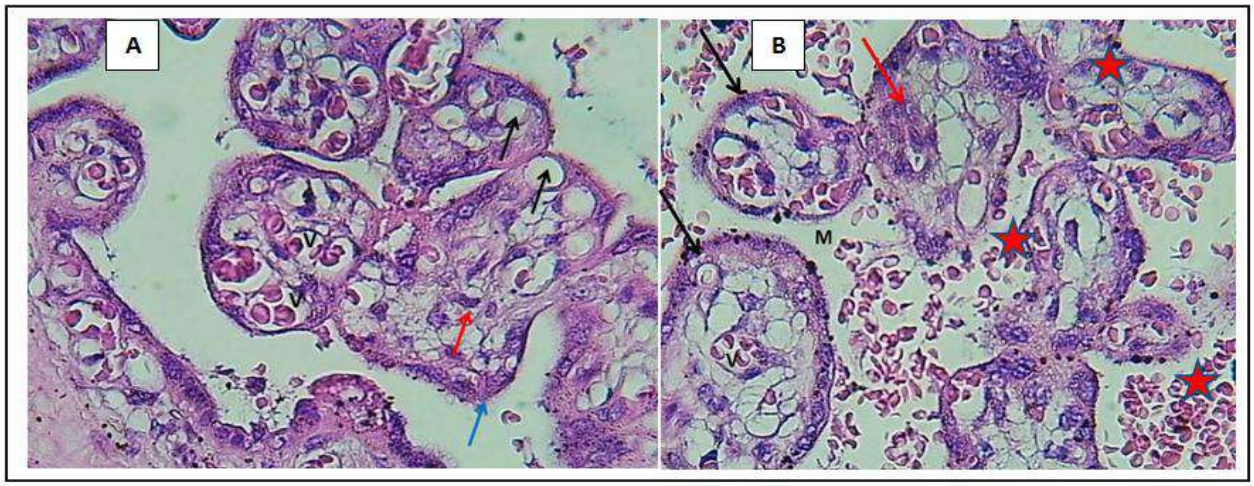

Figure No. 3: CS of section of macrosomic placenta shows A: normal appearance of differentiated maturevillus containing blood vessels (v) cytotrophoblasts (red arrow) & cyncytiotrophoblast (blue arrow). B: macrosomic mature villus with several syncytial knot(red star)H&E.400x

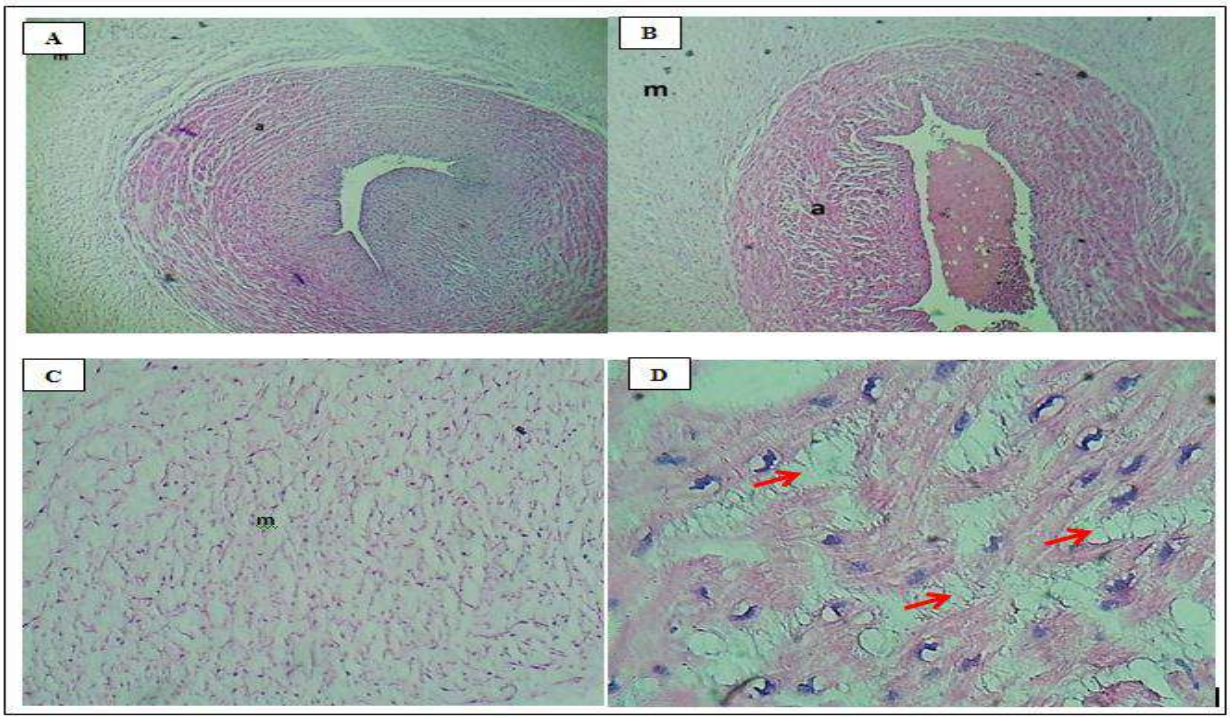

Figure No. 4: CS in the umbilical cords, A&B normal appearance of umbilical artery (a) & layer of Wharton's jelly (m). H&E 40x. C: normal texture of Wharton's jelly with mesenchymal cells, D: shows fat droplet deposition. (red arrows) H&E.100x A, C: non-macrosomia B, D: macrosomia

Table No. 3: Placental morphometric parameters

Variable	Non-macrosomic infants (n=80)	Macrosomic fetus (n=80)	P-value
Placental Surface area (cm)	210.2±18.5	190±20.5	0.0001**
Placental diameter (cm2)	18.3±1.4	15.33±10.5	0.0001**
Placental thickness (cm)	1.72±1.2	1.32±1.5	0.0200*

*Significant (P≤0.05) **Highly significant (P≤0.01)

Table No. 4: Placental villus histomorphometrical parameters

Type of villus	Non-macrosomic infants (n=80)	Macrosomic fetus (n=80)	P-value
Villus surface area (mm^2)	0.58±0.5	1.38±0.1	0.0001**
Villus diameter (mm)	0.07±0.09	0.14±0.02	0.0001**
Blood vessel diameter (mm)	0.05±0.16	0.03±0.02	0.0001**

**Highly significant (P≤0.01)

DISCUSSION

Macrosomia is one of the risk results of the maternal complications lead sometimes to fetal death during delivery or cause many metabolic syndromes during life.[10] The maternal age did not have direct effect, because the range of the ages wasn't much different, according to the random selection of subjects, as previous studies proved that maternal age is not a primary factor in the risk of macrosomia.[11]

Many previous studies proved direct correlation of increased maternal weight with development of fetal overgrowth in the early pregnancy and later incidence of macrosomia[12], this agree with the present study showed the increased maternal weight involved in the macrosomic group. Maternal obesity frequently leads to macrosomia by various mechanisms, such as increased body fat levels, then cause insulin resistance later , this can occur even in women without diabetes, leading to elevated pass of glucose to fetus, placental lipases break down triglycerides in the maternal bloodstream, facilitating the transfer of excess free fatty acids to the developing fetus.[13] The study by Sweeting et al[9] showed that the risk of fetal macrosomia is more closely associated with maternal obesity than gestational diabetes alone

The availability and quantifiably of umbilical cord and placenta make them organs for expecting birth weight in a short time.[14] Some results find a strong relation between placental growth in the second trimester and birth weight.[15] The weight and length of the placenta in

macrosomic infants appeared lower than the normal infants' weight significantly; this explained the effect of the insufficient development of placenta meaning a decrease in placental index (i.e. weight and length). These results might be showing the rate of the fetal growth unequal to placental growth. The placental index is influenced by various factors, including the nutritional status of the mother, her metabolic activity, and the presence of some diseases like, gestational hypertension or gestational diabetic.[16]

These previous findings documented the abnormal syncytial knots, on the surface of terminal villi in the placenta, potentially indicating significant stress on the placenta, such as oxidative stress or hypoxia this explains the placental insufficiency.[17]

The mass of the umbilical cord depends on the amount and content of the Wharton's jelly present which surround the cords; Wharton's jelly, a mucous connective tissue rich in proteoglycans, give physical protection and stability.[18] The connection between thickness of the umbilical cord and neonate's weight.[19] The length and diameter of the umbilical cord in macrosomic fetuses were greater than in the non-macrosomic group, supporting numerous earlier studies.[20]

Previous studies suggest that irregularities in placental shape frequently serve as a compensatory mechanism to meet the heightened metabolic demands linked to macrosomia.[21] Redman et al[22] verified high weight, thickness, and diameter of placenta in macrosomic fetuses, supporting findings maternal complications stimulates placental hypertrophy. This growth is realized as an adaptation manner to get the higher nutritional and oxygen stresses of the overgrowth of the fetus.

A small sized placenta in a macrosomic pregnancy often indicates that the placenta is functioning under high stress to support a large fetus, resulting in a low fetal-to-placental weight ratio cause the fetus to grow large, but the placenta itself does not grow proportionally or may even experience structural, inefficient, or fibrotic changes, leading to decreased transport efficiency.[23]

The data of the current study has been proven surface area and diameter of the placental villus increased macrosomia. The average surface area of the placenta in mothers with diabetes is larger than that the control group, the placenta exhibits a significantly higher amount of parenchymal and villous tissues, which results in an increase in tissue mass rather than surface area measurements.[24]

Carrasco-Wong et al[25] examined the harmonic thickness of the villous membrane was found in the macrosomic group compared to the controls. The fall in the specific diffusing capacity of the villous membrane may donate to the fetal hypoxia and increased chance of Stillbirths.[26]

The volume of blood flow in the umbilical vessels shows a positive correlation with fetal weight and growth, and birth weight, it has been previously noted that resistance to blood flow in the uterine and umbilical arteries can result in a decreased volume of blood reaching the fetus in pregnancies complicated by fetal macrosomia.[27] Breaks and erosion in the endothelial layer lining of the umbilical arteries, leading to increased permeability and bleeding and leakage of plasma proteins into the interstitial spaces of Wharton's jelly.[28]

CONCLUSION

The maternal gestational complications may contribute in the overgrowth of the fetus; macrosomia, this leads to increased risk of cases during delivery; shoulder dystocia, birth injuries or many long-term complications later in life. Therefore the quantitative assessment obtained from this article involved in the histological, morphometric investigation about placenta and umbilical cords may add better understand the relationship between placental index and its influence on maternal and neonatal outcome.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Lina A. Salih
Drafting or Revising Critically:	Lina A. Salih
Final Approval of version:	The above author
Agreement to accountable for all aspects of work:	The above author

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Original Article

Effect of an In Instructional Program on Mothers Knowledge Regarding Prevention of Uterine Prolapse

Mothers Knowledge Regarding Prevention of Uterine Prolapse

Fatima Kareem Naeem[1] and Wafaa Ahmed Ameen[2]

ABSTRACT

Objective: To assess effect of the program on mothers' knowledge of uterine prolapse preventive measures and determine the relationship between knowledge of and specific obstetrical and demographic factors.
Study Design: A quasi-experimental study
Place and Duration of Study: This study was conducted at the Bint Al-Huda Teaching Hospital, Iraq from 1st October 2024 to 31st March 2025.
Methods: 70 mothers who were enrolled. The demographic and reproductive information, as well as areas of knowledge related to prolapse were recorded. This was implemented through structured instructional sessions, followed by a post-test.
Results: Level of knowledge was weak before implementing the program in all areas, while they improved significantly after the intervention, as the overall scores increased from a weak level to a good level of knowledge. A association also found between occupation, family history of prolapse and the level of knowledge, while most other demographic and obstetrical characteristics did not show any significant relationships only previous pelvic surgery.
Conclusions: Health instructional programs can increase mothers' awareness and knowledge of uterine prolapse prevention.

Key Words: Effect, Knowledge, Prevention, Uterine prolapse

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INTRODUCTION

When the supporting ligaments and muscles that keep the uterus in its proper place become too weak, the uterus may prolapsed.[1] According to reports, the prevalence of UP is approximately 9% worldwide. However, estimates range greatly (3.4-56.4%) and are close to 20% in w- and middle-income nations. According to symptoms, the prevalence is 3-6%, and according to vaginal examinations, it can reach 50%.[2] The cause of uterine prolapse is likely to be multi factorial; attributable to a combination of risk factors, varying from patient to patient. The most reliable risk factors for prolapse are vaginal childbirth, young age at first childbirth, frequent childbirths, insufficient rest and nutrition during the prenatal and postnatal periods, aging, and rising body mass index.[3]

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METHODS

A quasi-experimental study was carried out at Bint Al-Huda Teaching Hospital, Iraq from 1st October 2024 to 31st March 2025 vide letter No. 3434/QM/Approval/EFEF3 dated September 15, 2024 and 70 mothers who were enrolled. Inclusion criteria are who are married and become pregnant. Unmarried women and refused to cooperate were excluded. Sociodemographic tool and obstetrical variables were noted. The semi-structured questionnaire has 31 multiple choice questions on knowledge. Tool validated by list of experts the split-half approach was used to test the tool's dependability on seven moms, and the results showed that it was dependable (r=0.81). The 45-minute program on UP prevention was done. The data was entered and analyzed through SPSS-25. To determine the relationship between particular variables and knowledge scores, analysis of variance (ANOVA) was employed.

RESULTS

Almost half of the sample were between the ages of 31 and 40, one-third have completed a secondary school, more than half was unemployed, three-quarters were married, rather than two-third of mothers reside in urban, rather than two-thirds reside in a nuclear family and nearly half reported having an income that was sufficient to some extent (Table 1).

Nearly half of the participants (48.6%) were married between the ages of 21–25 years. More than half of the women, all of whom were sampled (65.7%), had their first pregnancy between the ages of 20-25 years, over three-quarters of the participants (71.4%) had a one- to two-year interval between their first and second pregnancies, more than half of the participants (58.6%) delivered in hospitals, 65.7%) had a vaginal delivery of history, one-third of the participants (31.4%) had only one child, whereas more than one-third but less than one-half (40%) had between two and five children, and approximately one-quarter (28.6%) had more than five children and less than one-fifth of participants (17.1%) had a history of pelvic surgery, while more than three-quarters, 82.9% reported no such history (Tables 2-3).

Table No. 1: Distribution according to sociodemographics (n=70)

Variable	No.	%
Age (years)		
<20	6	8.6
20-30	13	18.6
31-40	51	72.9
Educational level		
Read and write	10	14.3
Primary graduate	15	21.4
Secondary graduate	24	34.3
Diploma or college or above	21	30
Occupation		
Employed	30	42.94
Unemployed	40	57.1
Social status		
Married	52	74.3
Widow	12	17.1
Divorced	6	8.6
Family type		
Nuclear	50	71.4
Extended	20	28.6
Residence		
Urban	47	67.1
Rural	23	32.9
Economic status		
Sufficient	21	30.0
Sufficient to some extent	25	35.7
Insufficient	24	34.3
Uterine prolapse history		
Yes	23	32.9
No	47	67.1

Table 4 demonstrates that the level of knowledge following the implementation of the program and their overall knowledge following the intervention were not impacted by the socio-demographic ($p>0.05$ for all).

There is a statistically association between occupation, family history and knowledge after the program, as women with a family history showed a higher level of knowledge (Table 5). Table 6 showed the knowledge after implementing program was not related to any of their obstetric characteristics. There is no association between knowledge of mothers after the training program and the place or type of birth while there are highly association with previous pelvic surgeries [$p>0.05$] (Table 7).

Table No. 2: Distribution of sample by obstetric history

Variable	No.	%
Age of marriage		
<20	18	25.7
21-25	34	48.6
26-30	15	21.4
31-40	3	4.3
Age of first pregnancy		
<20	4	5.7
20-25	46	65.7
26-30	17	24.3
31-40	3	4.3
Period between 1st and 2nd pregnancy		
Less than a year	8	11.4
One year - two years	50	71.4
Three years or more	12	17.1
Place of delivery		
House	29	41.4
Hospital	41	58.6
Type of delivery		
Cesarean section	24	34.3
Normal vaginal delivery	46	65.7
Number of child		
1	22	31.4
2-5	28	40
<5	20	28.6
Previous pelvic surgery		
Yes	12	17.1
No	58	82.9

Table No. 3: Mean differences between the overall assessment of the knowledge

Questions		Pre-test				Post-test				T value	P value
		No.	%	Mean±SD	Ass.	No.	%	Mean±SD	Ass.		
General information	Poor	55	78.6	1.60±0.40	Incorrect	12	17.1	2.31±0.36	Uncertain	-11.451	0.000
	Good	15	21.4			58	82.9				
Cause & Risk factors	Poor	63	90	1.51±0.31	Incorrect	8	11.4	2.33±0.35	Correct	-13.725	0.000
	Good	7	10			62	88.6				
Symptoms	Poor	60	85.7	1.53±0.35	Incorrect	8	11.4	2.31±0.36	Uncertain	-	0.000

	Good	10	14.3			62	88.6			13.913	
Complications	Poor	40	57.1	1.66±0.61	Incorrect	13	18.6	2.27±0.58	Uncertain	-5.650	0.000
	Good	30	42.9			57	81.4				
Prevention	Poor	59	84.3	1.62±0.38	Incorrect	15	21.4	2.16±0.46	Uncertain	-7.708	0.000
	Good	11	15.7			55	78.6				
Management & treatment	Poor	38	54.3	1.70±0.63	Incorrect	11	15.7	2.43±0.64	Correct	-7.172	0.000
	Good	32	45.7			59	84.3				
Over all mean score	Poor	66	94.3	1.58±0.19	Incorrect	7	10.0	2.26±0.18	Uncertain	-21.049	0.000
	Good	4	5.7			63	90.0				

Table No. 4: Mean differences between the overall assessment knowledge demographic data

Variable		Square	df.	Mean square	F value	P value
Age	Between Groups	0.054	2	0.027	0.601	0.551 N.S
	Within Groups	3.003	67	0.045		
Education	Between Groups	0.077	3	0.026	0.566	0.639 N.S
	Within Groups	2.980	66	0.045		
Marital status	Between Groups	0.013	2	0.007	0.143	0.867 N.S
	Within Groups	3.044	67	0.045		
Income	Between Groups	0.003	2	.001	0.030	0.970 N.S
	Within Groups	3.054	67	.046		

Table No. 5: Mean differences between the overall assessment of the knowledge according to their some demographic data

Variables	Group	Mean	Sd.	T value	P value
Occupation	Employed	2.3143	0.18796	2.604	0.011
	Unemployed	2.2023	0.16349		
Family type	Nuclear	2.2624	0.19630	0.276	0.784
	Extended	2.2760	0.15843		
Residence	Urban	2.2545	0.18323	0.761	0.449
	Rural	2.2904	0.19108		
Family history	Yes	2.3314	0.15574	2.571	0.012
	No	2.2202	0.19227		

Table No. 6: Mean differences between the overall assessment of knowledge according to their obstetrical data

Variables		Square	Df.	Mean square	F value	P value
First marriage	Between Groups	0.276	3	0.092	2.182	0.098
	Within Groups	2.781	66	0.042		
First pregnancy	Between Groups	0.260	3	0.087	2.045	0.116 N
	Within Groups	2.797	66	0.042		
Period between first & second pregnancy	Between Groups	0.040	2	.020	0.447	0.641
	Within Groups	3.017	67	.045		
Number of children	Between Groups	0.107	2	0.054	1.215	0.303
	Within Groups	2.950	67	0.044		

Table No. 7: Mean differences between the overall assessment of knowledge at according to obstetrical data

Variables	Group	Mean	Sd.	T value	P value
Place of delivery	House	2.3069	0.18270	1.559	0.124 N.S
	Hospital	2.2376	0.18380		
Type of delivery	C/S	2.2542	0.18870	0.393	0.696 N.S
	NVD	2.2726	0.18519		
Previous pelvic surgery	Yes	2.4258	0.14951	3.541	0.001 H.S
	No	2.2333	0.17537		

DISCUSSION

In the present study, fewer than half of the participants fell into the age group (31-40) years, with corresponding mean study groups. Near to one-third of participants have completed a secondary school, more than half of mothers was unemployed, reveals more than two-third of participants reside in urban areas, three-quarters of the sample were married women. Rather than two-thirds of the samples live in nuclear family and income was sufficient to some extent, one-third of the participants reported having a history of uterine prolapse. The study congruent with Elsayed et al[4], who found that a total 300 participants 36.5% of the mothers were more than 30 years of age. Shrestha et al[5] also reported 51.7% of the 110 sample had finished secondary school. EidAbd El-hamid et al[6] at Benha University Hospital supports this finding. They found that out of 60 women, most were housewives.

The result is consistent with Sansthan[7] which found that all 60 women in the sample were married. This finding contradicts a study by Nathan et al[8] which found that 67.5% from sample lived in rural areas. This high percentage draws attention to the participants' preponderance of urban dwellers, which may indicate the impact of urban environments on health awareness and knowledge in comparison to those who live in rural areas. Mohammed et al[9] also supports this finding. Of the 90 sample, the majority of responders (72.7%) came from nuclear families. A household's health education dynamics, family roles, and health awareness levels may all be impacted by this pattern.

This result in line with study conducted by Maharjan et al.[10] One-third of the ninety participants in their study were classified as having a somewhat adequate income.

The current study's findings showed that over half of the women had their first pregnancy between the ages of 20 and 25, and over half of the mothers were married between the ages of 21 and 25, over three-quarters of the participants (71.4%) had a one- to two-year interval between their first and second pregnancies, slightly more than half of the participants delivered in hospitals, more than two-thirds of the total sample and clearly exceeding half had a of vaginal delivery history, about one-third of the participants had only one child and approximately one-quarter had more than five children. About half of the participants were married between the ages of 21 and 25, depending on the study's findings about the obstetrical features, relation to previous pelvic surgery the study showed that less than one-fifth of mothers (17.1%) had a history of previous pelvic surgery (Table 2). The preventive strategies have been demonstrated to be effective in reducing the risk of prolapse, study conducted by Mohamed & Ezz El Din[9] improved knowledge, and prevented any cases of uterine prolapse in the intervention group. Lucente et al[11], advanced age at first delivery is linked to morphological and functional reductions in pelvic floor structures, including pelvic muscle dysfunction, levatorani abnormalities, and genital hiatus ballooning. This relatively short interval may contribute to inadequate pelvic floor healing, posing a greater risk for uterine prolapse, as supported by existing literature on optimal birth spacing conducted by Wassihun et al.[12] Badacho et al[2] reported that women who delivered their first child at home had 3.33 times higher odds of developing UP compared to those who delivered in health institutions. Recent research indicates that women who give birth vaginally have a four to eleven times higher chance of having POP than women who have never given birth vaginally.[13] This aligns with previous studies emphasizing that family planning, birth spacing, and limiting parity are key preventive strategies for POP.[5] These findings suggest that most participants in the current study had an advantage in terms of prolapse prevention, as they were not exposed to surgical trauma to the pelvic floor. This is consistent with earlier research highlighting the increased risk of developing POP associated with a history of pelvic surgery. POP can be brought on by gynecological procedures such radical pelvic organ resection, pelvic mass removal, and total hysterectomy, which can harm the muscles, ligaments, and connective tissue that support the pelvic floor.[14]

Table 3 shows knowledge was weak before the program, as the averages ranged between (1.5876), while after the program (2.266). The T-test showed highly differences between the pre-post-measurements, indicating the effectiveness of the program in improving knowledge. (66 out of 70) moved from a poor level to a good level after the intervention, which reflects the clear impact of program in enhancing awareness. These findings are consistent with Muñiz et al[15] who report improvement in knowledge, with an increase in total PIKQ scores and prolapse-specific knowledge, with effects sustained after four weeks. These findings are line with Mohammed et al[9] who found knowledge improved statistically after the intervention. highlighting that most participants initially had inadequate knowledge.

The results of tables 4-5 showed that the demographic characteristics of mother's, such as age, educational level, marital status, and economic status, did not have a significant effect on the knowledge after implementing program and their overall knowledge after the intervention ($p > 0.05$), While there is association with occupation and history of UP. This indicates that the program was effective across all subgroups. These finding are consistent with study conducted by Rashad et al[3], reported that married women who were illiterate, housewives aged 36–50 years, and women with limited household income had inadequate knowledge of pelvic organ prolapse. The results align with Ameen & Kheleel[16], which

discovered a correlation between lack of POP proficiency and advanced age, high education, and moderate family income. These traits can be important indicators of mother's knowledge in our underdeveloped countries, but even in wealthy, highly educated countries, there is a lack of awareness about POP because it is a neglected topic in maternity care.

Knowledge after the implementation of the program was unrelated to any of their obstetric characteristics, as all differences were not statistically significant ($p>0.05$). [Table 6] This finding suggests that all mothers, regardless of their reproductive experience, benefit similarly from instructional intervention in terms of knowledge gains. These results are consistent with Kara[17] dealt with the concept of "healthy reading" was the factor that most influenced the well-being of pregnant women, while social or obstetric factors had no significant impact. Rawat[18] also found no relationship between knowledge score and other reproductive variables, such as age in year at first delivery, number of children, and last delivery mode, which were not significant at the (0.05) significance level.

There is no relationship between knowledge and the place or type of birth ($p>0.05$) only previous pelvic surgery (Table 7). This finding supports by study conducted by Muñiz et al[15] who reported lack of knowledge about disorders of pelvic floor is widespread between pregnant mothers, and that educational programs represent the most prominent factor in raising awareness.

CONCLUSION

Post-test understanding of prevention strategies had significantly improved. Women's understanding of uterine prolapse was inadequate, with the great majority lacking any knowledge at all. There were no statistically significant correlations found between most obstetric and demographic variables and mother's knowledge.

Recommendations

1. Implementing a campaign to educate expectant moms about uterine prolapse and how to avoid it.
2. Putting in place an educational program to raise maternity nurses' knowledge preventative strategies.
3. The curriculum for basic nursing education should change to include pelvic organ prolapse guidelines that provide sufficient information.

Author's Contribution:

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Original Article

Serum Kisspeptinin Iraqi Men with Beta-Thalassemia Major: A Cross-Sectional Study

Bushra Mussad Kadim and Ekhlas Abdallah Hassan

ABSTRACT

Objective: To evaluate serum concentrations of kisspeptin in Iraqi men diagnosed with beta-thalassemia major and to identify factors that may influence circulating kisspeptin levels

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the National Centre for Thalassemia Patients in Baqubah, Iraq from 1st September 2024 to 30th June 2025.

Methods: Eighty individuals with beta-thalassemia major and 40 healthy controls were included. The parameters measured included kisspeptin, luteinizing hormone, follicle-stimulating hormone, total testosterone, fasting blood glucose as well as hematological assessments and oxidative stress markers (malondialdehyde and ischemia-modified albumin).

R**esults:** Men with hypogonadism due to beta-thalassemia major exhibited significantly higher kisspeptin levels compared to controls (P=0.001). Conversely, levels of testosterone, luteinizing hormone and follicle-stimulating hormone were notably lower in the beta-thalassemia major group than in the control group. Within the patient group, we observed negative correlations between kisspeptin levels and luteinizing hormone and testosterone (P<0.05). Additionally, positive correlations were found for kisspeptin versus inhibin B (r=0.782, P=0.001) and kisspeptin versus ferritin (r=0.286, P=0.010). Lower levels of luteinizing hormone (OR=2.95, P=0.0319), testosterone (OR=0.86, P=0.04) and increasing age (OR=0.927, P=0.014) were associated with elevated kisspeptin levels among Iraqi males with beta-thalassemia major.

Conclusion: Elevated kisspeptin with suppressed luteinizing hormone and testosterone in male thalassemia patients is a hallmark of complex hypothalamic-gonadal-pituitary axis disruption due to iron overload.

Key Words: Kisspeptin, Hypogonadism, Beta-thalassemia, Testosterone

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INTRODUCTION

Kisspeptin, a reproductive neuropeptide, has emerged as a crucial regulator of mammalian reproduction, primarily due to its role as an upstream modulator of gonadotropin-releasing hormone (GnRH) secretion.[1] The release of GnRH from GnRH neurons into the hypophyseal portal circulation prompts the stimulation of pituitary gonadotrophs, leading to the secretion of gonadotropins, specifically luteinizing hormone (LH) and follicle-stimulating hormone (FSH).

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In males, LH stimulates Leydig cells to produce testosterone, while FSH acts on Sertoli cells to promote spermatogenesis.[2] The first investigation into kisspeptin administration in humans was conducted in 2005 using kisspeptin-54. Healthy male volunteers demonstrated dose-dependent increases in circulating LH following a 90-minute infusion (0.25–12 pmol/kg/min). Although there were increases in FSH and testosterone levels, these changes were not dose-dependent.[3] The stimulatory effect of kisspeptin on LH release is significantly more pronounced than that on FSH concerning increases above baseline levels.[4]

The relationship between serum kisspeptin levels and primary hypogonadism is an important factor in understanding male patients with beta thalassemia major. Hypogonadism is the most common endocrine complication, affecting 70-80% of patients with thalassemia major. This condition is likely caused by hypertransfusion therapy, leading to iron accumulation in the gonads, pituitary gland, or both. However, hypogonadotropic hypogonadism (HH), resulting from iron deposition in the pituitary gonadotropes, is more frequently observed. Kisspeptin serves as a potent stimulant of GnRH neurons, suggesting its involvement in the etiology of HH.[5-7]

The purpose was to evaluate kisspeptin concentrations in Iraqi men with beta thalassemia major, examining their relationship with testosterone levels, LH, FSH and identifying other clinical factors that may influence kisspeptin levels.

METHODS

This cross-sectional study was conducted at National Centre for Thalassemia Patients in Baqubah, Iraq from 1st September 2024 to 30th June 2025 vide letter No. 3434/QM/Approval/JSDJNEHU dated 15th August 2024 and eighty patients with beta-thalassemia major were enrolled. Hypogonadism was diagnosed based on low levels of LH, FSH, free and total testosterone, along with patient history and physical examination findings that were consistent with the condition. The patient history included the onset of hypogonadism, marital status, presence of children, libido, and the adequacy of erection and ejaculation. Patients were evaluated using the Tanner classification.[8] The study group comprised newly diagnosed hypogonadism patients, who demonstrated onychoid features and were classified within Tanner stages 1-2. Transfusion-dependent patients with β-thalassemia major from various Iraqi populations, aged between 15 and 42 years, none of whom had undergone splenectomy or exhibited any obvious clinical infections, such as hepatitis were included. The data was collected their name, age, diagnosis, age at the onset of symptoms, splenectomy status, and any chronic illnesses. 5 ml of blood was drawn from all patients and controls. The blood samples were divided into two portions: 3 ml in tubes containing K3-EDTA and 2 ml in plain tubes with a gel separator. The tubes were then centrifuged at 300 rpm for five minutes to isolate the serum, which was subsequently transferred to another tube and stored at -20°C.

The determination of serum kisspeptin was conducted using an ELISA kit supplied by CUSABIO, China. Serum kisspeptin concentration was estimated through the sandwich technique of the ELISA method. The microplate being pre-coated with a specific antibody against kisspeptin and standards were introduced into the wells, allowing binding to occur when kisspeptin was present in the samples through the immobilized antibody. Following a washing process to eliminate any unbound enzyme reagents, horseradish peroxidase was introduced. After another washing step, the substrate solution was added to develop the end product color. The intensity of the color was measured after the color development was halted. Serum levels of T3, T4, TSH, FSH, LH, and testosterone were assessed using a Vidas kit provided by BioMeriux – France. The hormones were estimated through the Enzyme-Linked Fluorescent Assay (ELFA) method. The principle of the Vidas assay is based on a competitive immunoassay utilizing ELFA techniques. During the testing process, Solid Phase Receptors (SPR) served as the solid phase, alongside a device for pipetting. All steps of the assay were performed immediately using the VIDAS measuring device. The sample was introduced into wells containing hormone antigens labeled with alkaline phosphatase, which acts as the conjugate. The conjugated enzyme catalyzes the hydrolysis of this substrate, yielding a fluorescent product, 4-methyl-umbelliferone, which is measured at a wavelength of 450 nm. VIDAS automatically computes the results based on the calibration curve. Malondialdehyde was evaluated using the thiobarbituric acid reactive substance (TBARS) assay and ischemia-modified albumin levels were measured through the albumin cobalt binding (ACB) test. Serum glucose was determined using an enzymatic colorimetric method with a kit provided by Bio System, Spain. Serum urea levels were assessed through an enzymatic colorimetric reaction utilizing the Biomaghreb kit. Serum creatinine was measured using a kinetic test that does not require deproteinization, employing a kit from Biomaghreb-Maghreb, in conjunction with Spinreact, Spain. With a comprehensive menu of diagnostic tests and a high capacity for samples and reagents, the ARCHITECT c4000 is user-friendly and features advanced sample management capabilities, including a three-dimensional robotic sample handler.

The statistical analysis was using SPSS-24 The Student's t-test was employed to compare the diabetic and non-diabetic subjects. Spearman's product-moment correlation coefficient (rho) analysis was utilized. Additionally, multivariate analysis was performed to determine the independent contributions of various factors to the variance in kisspeptin.

RESULTS

The levels of iron, ferritin, glucose, urea, platelet count, ALT, AST, ALK, direct bilirubin, total serum bilirubin (TSB), TSH, Kisspeptin, IMA, and MDA were significantly higher ($P<0.05$) in BTM patients compared to the control group. In contrast, BMI, creatinine, Hb, HCT, T3, T4, FSH, LH, testosterone and inhibin-B levels were notably lower among the BTM patients compared to their controls (Table 1).

In the patient group, significant negative correlations were identified between kisspeptin and LH, testosterone, ALT, AST, UIBC, urea, creatinine, T4, and TSH ($P<0.05$). Additionally, a positive correlation was observed between serum kisspeptin and INH-b ($r=0.782$, $P=0.001$), as well as between serum kisspeptin and ferritin ($r=0.286$, $P = 0.010$) within the beta-thalassemia major patient cohort (Table 2).

The analysis identified age (OR=0.927, P=0.014), LH (OR=2.95, P=0.0319), and testosterone (OR=0.86, P=0.04) as independent variables correlated with the development of low kisspeptin levels in patients with beta-thalassemia major (Table 3).

Table No. 1: Clinical and biochemical measurements of study participants

Characteristic	Patients (n=80)	Control (n=40)	P value
Age (years)	21.88±4.95	23.60±5.22	0.207
BMI (kg/m2)	19.69±3.68	24.96±2.54	0.001
Iron (µg\dl)	230.99±6.23	117.63±5.17	0.001
Ferritin (ng\ml)	1725.89±59.67	127.86±8.27	0.001
Glucose (mg/dl)	93.08±16.91	79.46±8.56	0.031
Urea (mg/dl)	28.49±4.76	22.67±4.68	0.001
Creatinine (mg/dl)	0.48±0.16	0.78±0.16	0.001
Hb	7.09±1.06	15.29±1.12	0.001
HCT	21.22±3.52	45.49±3.11	0.001
Platelet	487.5±57.2	265.8±42.4	0.001
TIBC (µg\dl)	284.08±10.35	295.90±7.05	0.501
UIBC (µg\dl)	99.28±7.76	178.10±6.00	0.001
ALT (U\L)	32.6±3.2	22.2±1.1	0.048
AST (U\L)	40.85±3.24	23.77±1.29	0.002
ALK (U\L)	164.56±10.7	97.86±4.53	0.001
Direct bilirubin (mmol\l)	0.97±0.05	0.26±0.02	0.001
TSB (mmol\l)	2.72±0.15	0.82±0.03	0.001
T3 (ng\mL)	0.71±0.18	1.82±0.43	0.001
T4 (ng\mL)	13.21±4.32	38.1±35.38	0.001
TSH (ng\mL)	0.68±0.13	0.23±0.05	0.001
FSH (ng\mL)	3.52±0.71	6.59±0.79	0.001
LH (ng\mL)	1.08±0.20	2.68±0.49	0.001
Testosterone (ng\mL)	2.19±0.36	4.77±0.97	0.001
Kisspeptin (pg/ml)	259.87±34.3	77.72±11.4	0.001
IMA (ng\mL)	5004.5±360.3	2191.6±254.3	0.001
Inhibin-b (INH-b) pg/mL	66.44±12.6	153.84±17.5	0.001
MDA (ng\mL)	394.14±45.8	198.8±30.9	0.001

P-value < 0.05 is statistically significant

Table No. 2: Associations between several correlates and the hypothalamic-pituitary-gonadal axis

Characteristic	Kisspeptin		LH		FSH		Testosterone	
	r	P	r	P	r	P	r	P
Kisspeptin	1							
LH	-0.279	0.012*	1					
FSH	0.174	0.123	0.895	0.001*	1			
Testosterone	-0.232	0.038*	0.771	0.001*	0.739	0.001*	1	
IMA	-0.126	0.267	-0.254	0.023*	-0.323	0.004*	-0.204	0.068
INH-b	0.782	0.001*	0.018	0.876	0.084	0.461	-0.083	0.462
MDA	-0.063	0.587	0.081	0.477	0.104	0.358	-0.131	0.446
ALT	-0.226	0.043*	0.063	0.576	0.110	0.331	-0.128	0.256
AST	-0.235	0.036*	0.114	0.315	0.134	0.238	-0.148	0.191
ALK	-0.081	0.477	0.194	0.084	0.286	0.010*	-0.211	0.060
TIBC	-0.206	0.066	0.082	0.469	0.035	0.760	0.016	0.890
UIBC	-0.307	0.006*	-0.176	0.118	-0.114	0.316	-0.054	0.633
Ferritin	0.286	0.010*	0.111	0.329	0.111	0.326	-0.041	0.718
Iron	-0.004	0.972	-0.660	0.001*	-0.599	0.001*	-0.651	0.001*
Hb	0.117	0.303	-0.295	0.008*	-0.263	0.018*	-0.107	0.334
HCT	0.034	0.767	-0.214	0.057	-0.210	0.062	-0.098	0.385
Platelet	0.008	0.944	0.057	0.618	0.093	0.410	0.011	0.924
Urea	-0.279	0.012*	-0.192	0.089	-0.079	0.487	-0.098	0.389
Creatinine	-0.232	0.038*	-0.157	0.163	-0.118	0.298	-0.151	0.182
T3	0.174	0.123	-0.083	0.465	-0.127	0.261	0.012	0.915
T4	-0.279	0.012*	-0.074	0.517	-0.113	0.318	-0.013	0.909
TSH	-0.232	0.038*	-0.113	0.320	0.100	0.376	-0.038	0.735

r = Correlation coefficient P* = <0.05 is significant

Table No. 3: Risk assessment of serum kisspeptin

Risk factors	OR	95% CI	P
Age	0.927	0.46-1.83	0.014
LH	2.95	0.02-33.8	0.0319
FSH	0.403	0.04-3.87	0.416
Testosterone	0.86	0.39-1.57	0.04*
BMI	0.459	0.08-2.36	0. 341

*Significance at $P < 0.05$

DISCUSSION

The kisspeptin concentrations were elevated in men with beta thalassemia major (BTM), while levels of FSH, LH, and testosterone were significantly lower compared to the control group in the present study. This aligns with the study of Öztin et al[9], who examined 30 male patients with hypogonadotropic hypogonadism (HH) over the age of 30 and found significantly higher kisspeptin levels in this patient group, coupled with notably lower averages of FSH, LH, and testosterone. Similarly, De Sanctis et al[10] studied 11 adult men with thalassemia major, ranging in age from 26 to 54 years (34.3±8.8 years), compared to 12 age- and sex-matched patients with thalassemia major who exhibited normal pubertal development as a control group. Al-Zuhairy et al[11] also conducted research on 50 children with β-thalassemia major, aged 11 to 16 years, against a control group of 50 age- and sex-matched healthy adolescents. The results indicated that male patients had significantly lower serum levels of FSH, LH, testosterone, and estradiol compared to controls, suggesting an altered function of the hypothalamic cells that secrete luteinizing hormone-releasing hormone (LHRH).[12]

rashid

In transfusion-dependent thalassemia (TDT), chronic blood transfusions result in iron overload within the pituitary and hypothalamus, this accumulation of iron catalyzes the production of reactive oxygen species (ROS), which can damage gonadotropes and GnRH neurons, disrupting the pulsatility of GnRH. Approximately 50% of men with TDT develop hypogonadotropic hypogonadism (HH), characterized by impaired secretion of GnRH and gonadotropins, leading to low testosterone levels and compromised spermatogenesis. Ali et al[21] have shown significantly elevated serum kisspeptin levels in thalassemic men with HH, which were inversely correlated with testosterone and gonadotropin levels. Clark et al[14] also elevated kisspeptin may act as a biomarker for disruption of the hypothalamic-pituitary-gonadal (HPG) axis. According to Skorupskaite et al[15], the rise in kisspeptin levels is likely attributable to reduced testosterone feedback, resulting in unopposed kisspeptin secretion that cannot effectively stimulate GnRH due to the damage occurring downstream.

Our study's association reveals significant dysregulation within the hypothalamic-pituitary-gonadal (HPG) axis, marked by distinct correlations among kisspeptin, gonadotropins, testosterone, and various metabolic and hematological parameters. We found a strong positive correlation between kisspeptin and inhibin, suggesting that kisspeptin may play a compensatory role in regulating Sertoli cell function, potentially offsetting impaired spermatogenesis associated with thalassemia.[16,17] Additionally, there were notable inverse correlations with LH (r=−0.279, p=0.012) and testosterone (r=−0.232, p=0.038), indicating disrupted feedback mechanisms, likely caused by chronic iron overload that suppresses hypothalamic kisspeptin release.[18] We also observed negative correlations with ALT (r=−0.226, p=0.043), AST (r=−0.235, p=0.036), and TSH (r=−0.232, p=0.038), emphasizing the multisystem involvement in the suppression of the HPG axis. These findings highlight the multifactorial disruption of the HPG axis in thalassemia, driven by factors such as iron overload, hepatic dysfunction, and anemia. Kisspeptin's dual role-stimulating inhibin B while inversely correlating with LH and testosterone-positions it as a potential biomarker for gonadal health.[11,15] While iron chelation and hormonal replacement remain critical, targeted therapies involving kisspeptin merit further investigation.[19]

This study indicated a potential interplay between kisspeptin regulation and gonadal function, LH and Testosterone levels, along with an age-dependent effect .This triad (↑Kisspeptin, ↓LH, ↓Testosterone) suggests a combination of primary and central hypogonadism due to iron overload, which is a hallmark complication of transfusion-dependent thalassemia. There are three primary mechanisms involved: First, iron deposition directly damages Leydig cells in the testes, impairing testosterone synthesis. Srisukh et al[20] documented the presence of iron deposition and fibrosis in Leydig cells, which was directly correlated with the severity of hypogonadism. The consequence of this is that low testosterone results in reduced negative feedback to both the hypothalamus and the pituitary gland. Second, iron accumulation occurs in the pituitary gland, particularly affecting gonadotrophs-cells responsible for producing LH and FSH. Bozdağ et al[21] demonstrated that MRI hypointensity in the pituitary, indicative of iron deposition, correlates with low LH/FSH levels in thalassemic males. Consequently, despite low testosterone levels (which would normally stimulate LH release through diminished negative feedback), the damaged pituitary gland fails to adequately respond by increasing LH secretion. This result in secondary (hypogonadotropic) hypogonadism superimposed upon primary failure. There is a compensatory increase in Kisspeptin (↑Kisspeptin). Kisspeptin neurons in the hypothalamus exhibit relative resistance to iron toxicity when compared to GnRH neurons or pituitary gonadotrophs. The hypothalamus senses the chronically low testosterone levels resulting from the combined

testicular and pituitary failure. Yeo et al[22] suggested that kisspeptin neurons integrate metabolic and endocrine signals, driving GnRH release in response to low sex steroid levels. However, this compensatory mechanism fails in the long term due to damage to the pituitary gonadotropins and their inability to respond effectively to GnRH. Furthermore, the GnRH cells themselves may be partially damaged by chronic iron exposure or inflammation. Also Oxidative stresslead to chronic diseases.[23]

CONCLUSION

Elevated kisspeptin levels have been observed in Iraqi males diagnosed with beta thalassemia major. Additionally, lower concentrations of LH and testosterone, along with older age, serve as independent predictors of increased kisspeptin levels in men. The importance of kisspeptin in the regulation of the gonadal-pituitary axis and may inform the management of hypogonadism in men.

Author's Contribution:

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Drafting or Revising Critically:	Bushra Mussad Kadim, Ekhlas Abdallah Hassan
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Association of Oxidative Stress, Inflammatory Markers and Lipid Profile with Chronic Obstructive Pulmonary Disease in Al-Muthanna Governorate, Iraq

Ali Adil Ajeel

ABSTRACT

Objective: To evaluate the association and correlation between oxidative stress markers, inflammatory indicators, and lipid profiles in patients diagnosed with Chronic Obstructive Pulmonary Disease.

Study Design: Case-control study

Place and Duration of Study: This study was conducted at the Specialized Private Laboratories in Al-Muthanna Governorate, Iraq between 15th January 2025 to 15th July 2025.

Methods: Two hundred participants were enrolled, including 100 patients and 100 apparently healthy control subjects. The diagnosis of chronic obstructive pulmonary disease was confirmed by specialist physicians.

Results: The significant increase in oxidative stress and inflammatory markers, including malondialdehyde, high-sensitivity C-reactive protein, tumor necrosis factor-α in the patient group compared with controls. A significant decrease was observed in albumin and zinc levels whereas no significant differences were found in magnesium. Triglyceride levels were significantly elevated, while high density lipoprotein levels were significantly reduced. However, total cholesterol showed no significant difference between the studied groups.

Conclusion: Oxidative stress, inflammation, and metabolic changes in the patient group are clearly related. Reduced albumin and zinc levels point to a weakened antioxidant defense system, whereas elevated malondialdehyde, high-sensitivity C-reactive protein and tumor necrosis factor-α levels show increased oxidative and inflammatory activity.

Key Words: Chronic obstructive pulmonary disease (COPD), Oxidative stress, Inflammatory markers, Trace elements

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INTRODUCTION

A serious worldwide health issue, chronic obstructive pulmonary disease (COPD) is mainly brought on by exposure to harmful particles or gases and is defined by ongoing respiratory symptoms and restricted airflow. COPD has long been acknowledged as a major global cause of morbidity and mortality, and its prevalence has been rising in recent decades as a result of smoking, environmental pollution, aging populations, and occupational exposures.[1-3]

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Globally, 391.8 million persons between the ages of 30 and 79 were predicted to have COPD in 2019, with the majority (nearly 80%) residing in low- and middle-income countries (LMICs), indicating notable regional inequalities.[4] The Americas and the Western Pacific region have the highest prevalence rates, with men often showing higher prevalence than women, while estimates show that female prevalence will rise more quickly until 2050.[5] Despite some decreases in age-standardized death rates and disability-adjusted life years (DALYs) as a result of better healthcare and tobacco control initiatives, COPD continues to be a major cause of death, accounting for over 3 million deaths yearly and ranking sixth globally overall and fourth among those aged 50-74.[6] Continued efforts focusing on smoking cessation, reducing air pollution, occupational hazard control, and improved diagnosis and management are critical to addressing the growing global burden of COPD, especially in under-resourced regions.[7]

The widespread, progressive lung condition known as COPD is characterized by a continuous restriction in airflow and respiratory symptoms include persistent coughing and dyspnea. Although cigarette smoking is the main cause of COPD, exposure to indoor and

outdoor air pollution, occupational hazards, genetic predisposition, respiratory illnesses in childhood, and low socioeconomic status are all important risk factors.[2,8] Chronic inflammation, oxidative stress, airway remodeling, and accelerated lung aging are all part of the pathogenesis of emphysema and irreversible airway blockage.[9] The primary goal of treatment is to manage symptoms with inhaled long-acting bronchodilators and corticosteroids for some individuals; nevertheless, quitting smoking is still the only intervention that has been shown to reduce the course of the condition.[10] Respiratory infections, environmental exposures, previous exacerbations, and comorbidities that aggravate lung function decline and prognosis are risk factors for exacerbations.[11] To enhance quality of life and lower morbidity, comprehensive care also entails lifestyle modifications, pulmonary rehabilitation, and management of cardiovascular risk factors.[12]

An imbalance between oxidant (pro-oxidant) and antioxidant systems that favors oxidants and results in disrupted redox signaling or molecular damage is known as oxidative stress.[13] More precisely, oxidative stress is a reflection of the following: Overproduction of ROS and RNS in comparison to antioxidant defenses, including hydrogen peroxide ($H2O_2$), superoxide ($O2•^-$), peroxyl radicals, hydroxyl radical (•OH), peroxynitrite ($ONOO^-$), and nitric oxide (NO•).[14,15] A change in cellular redox couples that affect the oxidation state of lipids, proteins, and nucleic acids, such as GSH/GSSG, thiol/disulfide pairs, and $NADPH/NADP^+$.[16,17]

METHODS

This case–control study was carried out in specialized private laboratories in Al-Muthanna Governorate, Iraq between 15th January 2025 to 15th July 2025 vide letter No. 132/QM/Approval/KDJEGVVD Dated Jan 2, 2025. A total of 200 participants were enrolled in this study, including 100 patients and 100 apparently healthy control subjects. The diagnosis of chronic obstructive pulmonary disease (COPD) was confirmed by specialist physicians. Blood samples were collected from all participants after obtaining informed consent and in collaboration with the hospital laboratory staff.

The patient group consisted of 100 individuals diagnosed with COPD, including 50 males and 50 females, aged between 40 and 70 years. The control group included 100 apparently healthy subjects (50 males and 50 females) within the same age range (40–70 years), with no history of respiratory or chronic systemic diseases. Approximately 5 mL of venous blood was collected from each participant and transferred into plain tubes. The samples were allowed to clot at room temperature and subsequently centrifuged at (3000 rpm, 10 min) to obtain serum. The separated serum was stored at -20°C until further analysis of the studied biochemical markers when not analyzed immediately.

All studied biomarkers were determined according to previously described methods in the referenced literature. Serum MDA levels were measured using a commercial enzyme-linked immunosorbent assay (ELISA) kit (Sunlong, China). hs-CRP was determined according to the method described in reference. TNF-α was measured using a sandwich enzyme-linked immunosorbent assay (ELISA) kit. Serum Alb was determined by the Bromocresol Green method using a commercial kit (Biolabo, France). Elemental concentrations in serum samples were measured using the flame atomic absorption spectrophotometric method. Serum TG were determined according to the Fossati and Prencipe method. Total cholesrol by the enzymatic method[23], and HDL-C according to the method described in reference. Microsoft Excel 2021 was used for statistical analysis. A two-way analysis of variance (two-way ANOVA) was used to assess differences between the groups under study. A statistically significant was considered P-value ≤0.05.

RESULTS

The results showed a significant increase in oxidative stress and inflammatory markers, including MDA, hs-CRP, TNF-α in the patient group compared with controls (P≤0.05). A significant decrease was observed in Alb and Zn levels, whereas no significant differences were found in Mg. Triglyceride levels were significantly elevated, while HDL levels were significantly reduced. However, TC showed no significant difference between the studied groups. With respect to gender differences, females exhibited significantly higher levels of hs-CRP, HDL, and TG, along with significantly (P≤0.05) lower levels of Alb and Zn compared with males (Tables 1-3).

Table No. 1: Inflammatory, oxidative stress and mineral parameters in COPD patients versus healthy controls (n=200)

Group	MDA(µmol/L)	Alb (g/dL)	hs-CRP(mg/L)	TNF-α (pg/mL)	Zinc Znµmol/L	Mgmmol/L
Control	1.60 ±0.27	4.48±0.26	1.84±0.53	3.65±0.43	15.98±1.84	0.79±0.15
COPD	4.47 ±0.31	3.46±0.21	5.84 ±0.63	7.38±1.23	10.33±1.99	0.79±0.12
LSD	0.27	0.18	0.69	0.52	0.28	0.27

Table No. 2: Serum lipid profile in COPD patients versus healthy controls (n=200)

Groups	TC (mg/dL)	TG (mg/dL)	HDL-c (mg/dL)
Control	187.20±28.46	121.56±22.13	55.69±4.83
COPD	187.81±29.32	172.62±27.25	37.06±3.06
LSD	11.92	10.88	5.67

Table No. 3: Serum parameters according to sex in control and COPD groups

Concentration	Gender	Control	COPD	LSD
	Male	n= 50	n= 50	
	Female	n= 50	n= 50	
MDA (µmol/L)	Male	1.67±0.56b	4.13±0.62a	0.35
	Female	1.54±0.62b	4.82±0.71a	0.34
	LSD	0.42	0.67	
Alb (g/dL)	Male	4.73±0.41a*	3.61±0.25b*	0.36
	Female	4.24±0.46a	3.32±0.22b	0.32
	LSD	0.45	0.43	
hs-CRP (mg/L)	Male	1.63 ±0.65b	5.27 ±0.71a	0.61
	Female	2.06 ±0.72b*	6.42±0.84a*	0.81
	LSD	0.64	0.87	
TNF-α (pg/mL)	Male	3.48±0.64b	7.64±0.63a	0.81
	Female	3.81±0.71b	7.12±0.36a	0.73
	LSD	0.61	0.65	
Zinc (µmol/L)	Male	16.35±1.68a*	11.27±2.31b*	0.25
	Female	15.61±1.44a	9.39±1.43b	0.36
	LSD	0.23	0.24	
Magnesium (mmol/L)	Male	0.88±0.09a	0.77±0.08a	0.24
	Female	0.69±0.07a	0.81±0.06a	0.22
	LSD	0.26	0.28	
TC (mg/dL)	Male	187.57±32.67a	188.27±35.74a	9.38
	Female	186.83±37.34a	187.36±26.32a	10.47
	LSD	11.34	12.03	
TG (mg/dL)	Male	120.81±30.21b	171.25±34.32a	8.03
	Female	122.32±32.11b*	173.98±35.91a*	9.17
	LSD	4.34	5.18	
HDL-C (mg/dL)	Male	54.73±4.31a	35.38±4.33b	3.15
	Female	56.64±5.78a*	38.73±4.68b*	4.63
	LSD	2.64	3.82	

DISCUSSION

The current results showed that patients had significantly higher levels of oxidative stress and inflammatory markers, such as MDA, hs-CRP, and TNF-α, than the control group. The elevated MDA level is indicative of increased lipid peroxidation brought on by an overabundance of reactive oxygen species (ROS). This suggests that the pathophysiology of the illness is significantly influenced by oxidative damage to cellular membranes. Additionally, the higher levels of TNF-α and hs-CRP indicate the existence of a persistent inflammatory state, which may exacerbate oxidative stress by activating immune cells through cytokines and producing ROS.

The notable decrease in albumin and zinc levels in relation to trace elements and serum proteins may be linked to elevated oxidative burden and inflammatory processes.[16] By binding metal ions and scavenging free radicals, albumin functions as a crucial antioxidant protein in plasma; as a result, a decrease in albumin may lower the blood's overall antioxidant capacity. Similarly, the structure and operation of several antioxidant enzymes, including superoxide dismutase (SOD), depend on zinc, an essential trace metal. Reduced zinc levels can worsen oxidative stress and weaken the antioxidant defense system. Magnesium levels, on the other hand, did not significantly change between the groups, indicating that under the settings under investigation, magnesium homeostasis may be mostly maintained or less impacted.[14]

The presence of metabolic disorders is further supported by the changes in the patient group's lipid profile. Impaired lipid metabolism and elevated cardiovascular risk may be the cause of the notable rise in triglyceride levels and fall in HDL cholesterol. HDL

is well-known for its anti-inflammatory and antioxidant qualities as well as its beneficial function in reverse cholesterol transfer.[12] Consequently, oxidative stress and inflammatory reactions may be made worse by low HDL levels. However, the lack of a discernible shift in total cholesterol would suggest that the metabolic disruption mostly impacts the metabolism of triglycerides rather than total cholesterol.

The current investigation also showed gender-related disparities. Compared to males, females had considerably lower albumin and zinc concentrations and considerably higher levels of hs-CRP, HDL, and TG. Hormonal effects, variances in the distribution of body fat, and gender-specific differences in inflammatory and metabolic responses could all be responsible for these discrepancies. The observed biochemical differences may be attributed to hormonal variables, especially estrogen, which may have an impact on inflammatory marker expression and lipid metabolism.[6]

Evidence showing oxidative and inflammatory processes are closely related and enhanced in different disease states is consistent with the observed rise in oxidative stress markers in patients, such as MDA, hs-CRP, and TNF-α. While unchanged magnesium (Mg) levels show specific trace element changes, declining albumin (Alb) and zinc (Zn) levels point to a decline in antioxidant defenses because both are involved in reducing oxidative damage.[18,19] Reduced HDL cholesterol and elevated triglycerides (TG) indicate a dysregulated lipid profile that is frequently linked to inflammation and an increased risk of cardiovascular disease.[20,21] Martínez de Toda et al[22] Research demonstrating sex-specific changes in oxidative stress and inflammatory responses, potentially affected by hormonal and metabolic variables, is consistent with gender differences showing higher hs-CRP, HDL, and TG but lower Alb and Zn in females compared to males. Despite certain protective lipid profiles, females frequently show higher levels of oxidative stress and inflammatory markers, which may contribute to differences in disease susceptibility or progression between the sexes.[18]

CONCLUSION

Oxidative stress, inflammation, and metabolic changes in the patient group are clearly related. Reduced albumin and zinc levels point to a weakened antioxidant defense system, whereas elevated malondialdehyde (MDA), high-sensitivity C-reactive protein (hs-CRP) and tumor necrosis factor-α (TNF- α) levels show increased oxidative and inflammatory activity. Dyslipidemia which is typified by elevated triglycerides and decreased HDL may exacerbate the course of the illness and its complications. The possible involvement of oxidative stress and trace element imbalance in the disease's underlying biochemical pathways and may offer helpful markers for tracking the state of the illness and developing treatment plans.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Ali Adil Ajeel
Drafting or Revising Critically:	Ali Adil Ajeel
Final Approval of version:	The above author
Agreement to accountable for all aspects of work:	The above author

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Original Article

Evaluation of the Effectiveness and Outcome of Platelet Rich Plasma (PRP) Intratesticular Local Injection in Infertile Men with Asthenospermia: A Prospective Case Control Study

Ahmed Ali Obaid, Ahmed Abdul Ameer Alwan and Shiren Ali AlHamzawi

ABSTRACT

Objective: To assess and evaluate the effectiveness of intratesticular local injection of platelet rich plasma in patient with history of infertility had asthenospermia diagnosed by seminal fluid analysis.

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the Infertility Clinic, Urology Department, Aldiwaniyah Teaching Hospital Iraq from 15th March 2024 to 31st December 2025.

Methods: Two hundred patients with history of infertility their age 25-40 years had asthenospermia confirmed by seminal fluid analysis at where enrolled. Seminal fluid analysis and hormonal evaluation were done in all patients before platelet rich plasma injection and at one, three and six months post injection, the local intratesticular platelet rich plasma were done under sterile condition in all patients. There are two types of outcomes were observed, the primary outcome was sperm motility improvement and the secondary outcomes were the changes that observed in sperm count and morphology and the safety profile of the procedures.

Results: Sperm motility show a significant improvement following platelet rich plasma injection progressive motility increased from 16.3%±4.1 at baseline to 38.9%±4.5 at 6 months ($p<0.001$), while total motility improved from 27.5%±7.2 to 48.7%±8.1 ($p<0.001$). Sperm count increased from 19.5±7.3 to 30.2±6.4 million/ml, and normal morphology improved from 4.6%±1.3 to 6.8%±1.9 ($p<0.001$). Generally, 80% of participates showed significant improvement. The process was safe, and mild temporary complications like scrotal pain 15%, swelling 7.5% and hematoma 2.5%.

Conclusion: Intratesticular platelet rich plasma injection, can be consider as a safe and promising minimally invasive therapy for improving sperm motility and overall semen parameters in men with asthenospermia.

Key Words: Asthenospermia, Platelet rich plasma, Male infertility, Intratesticular injection

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INTRODUCTION

Approximately 40–50% of cases of male infertility are due to male factor which include abnormality in sperm parameters which include (count, morphology and motility) which is inability of sperm to fertilized ova. oxidative stress, mitochondrial dysfunction, hormonal imbalance, and structural abnormalities of the sperm flagellum can lead to low sperm motility that may occur alone or as part of OAT syndrome.[1]

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There are many methods of medical treatment for male infertility which include modification in lifestyle, antioxidant measures, hormonal treatments, and assisted reproductive technologies (ART) such as intracytoplasmic sperm injection (ICSI). These techniques mainly bypass the underlying pathology rather than recovering normal spermatogenesis or function of sperm. Consequently, gold therapeutic strategies designed at improve spermatogenesis and improving quality of sperm directly at the level of testicular has attracted increasing scientific interest.[2]

Platelet rich plasma is intratesticular injection therapy, which include the direct injection of platelet rich plasma into the testicular tissue for stimulation of spermatogenesis and promote semen parameters. PRP injection has a direct action on germ cell, seminiferous tubules and Sertoli cells and leading to local microenvironment that's is necessary for production and maturation of the sperm. Previous studies have showing that PRP intratesticular injection led to modification in the function of Sertoli cell, supporting

the role of this technique of the treatment of male reproductive disorder.[3]

Because of high concentration of cytokines, growth factor and regenerative substances that found in the platelet-rich plasma (PRP), it considers as is one of the most important widely studied biological therapeutic approaches. Vascular endothelial growth factor (VEGF), transforming growth factor-β (TGF-β), platelet-derived growth factor (PDGF) had a major role in reducing decreasing oxidative stress, and enhancing healing of tissue, and promoting the spermatogenesis process within the testes.[4]

Direct injection of PRP into the testis had been demonstrated by initial clinical studies to improve spermatogenesis and positively affected the hormonal balance in men with compromised testicular function, these finding demonstrate the potential role of this type of therapy as an important therapeutic method for the disorder associated with impairment of process of spermatogenesis. However, further randomized control studies are needed to show the true clinical value of this type of treatment. Nevertheless, intratesticular injection has recently attracted growing interest as a potential method for restoring testicular function and enhancing sperm motility in men affected by asthenospermia.[5]

METHODS

This prospective study was carried out at Infertility Clinic, Urology Department, Aldiwaniyah Teaching Hospital Iraq from 15th March 2024 to March 31st December 2025 vide letter No. .MF/B-26 Dated March 7, 2024. Two hundred infertile patients with asthenospermia identified by seminal fluid analysis were enrolled. All patients age 1.25-40 years old, one year history of infertility, two seminal fluid analysis revealed asthenospermia at 2-7 days interval and signed written informed consent were included. Those patients with azoospermia or severe oligospermia, obstructive causes of infertility, varicocele needs surgical correction, pyospermia on SFA, past history of testicular tumor, undescended testicle or previous testicular surgery and chronic Endocrine disease that affects fertility, like diabetes mellitus, thyroid disorder, or hypogonadism were excluded.

The patients were evaluated and assessed by Thurow history taking, physical examination, laboratory evaluation which include SFA after 3-5 days of abstinence and at least two sample of seminal fluid collected before intervention and assessed for volume of ejaculate, count, morphology, vitality and motility including progressive and total motility. Also, FSH, LH, testosterone and prolactin level were checked in all patients. Radiological evaluation in form of scrotal ultrasound was performed in all patients to exclude varicocele or testicular abnormalities. After the evaluation and under strict sterile environment all patients received PRP intratesticular injections by placing the patients in supine position ,preparation and sterilization of the scrotal skin by bovidine iodine antiseptic solution and applying local anesthesia before PRP injunction by using a fine needle sterile syringe directly and carefully into the both testes and all patients were kept under observations for short time to identify any complications that might be occurred postoperatively. After PRP intratesticular injection of both testes all patients arranged for follow up to assessed the amount of improvement in sperm motility and detection of any complications related to the procedure and the assessment including clinical assessment for edema, infection or another adversing events and also seminal fluid analysis that performed one, three, and six months postoperatively by comparing the seminal fluid parameters pre and post treatment.

There are two types of outcomes, the primary outcome and the secondary outcome, the primary outcome of the study is to assess the improvement in the sperm motility in seminal fluid analysis after PRP intratesticular injection. The secondary outcome was observation the changes that occurred in sperm count and morphology and volume of ejaculate and hormonal changes after treatment and the complications related to the procedure. The data was entered and analyzed through SPSS-25. The paired t-test was used. A $p<0.05$ was considered statistically significant.

RESULTS

The mean age of the patients was 32.9±6.74years, and the range of age was 25-40 years. The average period of infertility was 2.8±1.5 years. Those patients with history of primary infertility were 140 (70%) while those with history of secondary infertility were 60 (30%). 40% of the participants in this study were smokers and the other 60% of the participants were non-smokers (Table 1). Low sperm motility asthenospermia in seminal fluid analysis before intratesticular injunction of PRP. The mean semen volume was 2.6±0.6 ml. The mean sperm count was 19.5±7.3 million/ml. The progressively motile sperm mean was 16.3±4.1%, while the mean of total motility was 27.5±7.2 %. The mean percentage of normal morphology shaped was 4.6±1.3% (Table 2).

Changes post PRP injection, sperm motility revealed a marked improvement post PRP intratesticular injection. Regarding the progressive motility the mean was increased from 16.3±4.1%at baseline to 28.8±6.9 % after one month, 33.8±7.1% after three months, and 38.9±4.5% after six months, this increase in progressive motility was a statistically significant in comparison to the baseline initial levels ($p<0.001$). The mean of total sperm motility also increased from the initial baseline level before treatment that was 27.5±7.2% to 35.2±5.8% at one month, 42.9±6.1% at three months, and 48.7±8.1% at six months, this rising in values was also statistically significant ($p<0.001$). Also, the other semen parameters revealed gradual improvement through the period of follow up. The mean sperm count

increase from 19.5±7.3 million/ml before injunction to 24.8±5.6 million/ml after one month, 27.1±8.1 million/ml after three months, and 30.2±6.4 million/ml after six months, which was statistically significantly increase ($p<0.001$). Moreover, the mean percentage of morphology of spermatozoa in the seminal fluid analysis was also enhance and became better through the follow up period of study increasing from 4.6±1.3% prior to PRP injunction reaching to 5.3±22% at one month, 6.1±21% at three months, and 6.8±19% at six months, this rising in values was also statistically significant ($p<0.001$) [Table 3].

A significant percentage of studied participants (80%, n=160) showed a significant increase in progressive sperm motility, nevertheless 40 (20%, n=40) showed little or no improvement following treatment. PRP intratesticular injunction show excellent safety and well tolerated by all patients. Very mild transient scrotal pain and mild scrotal swelling had been recorded occurred in 30 15% and 7.5% respectively. Very mild and small scrotal hematoma occurred in 5 (2.5%). No other severe complications like infection or atrophy of the testis had been recorded (Table 4). Intratesticular injection significantly improved sperm motility in men diagnosed with asthenospermia. Both progressive and total motility increased gradually during follow-up, with the greatest improvement recorded at six months post-treatment. Significant improvements were also noted in sperm concentration and morphology. Overall, the treatment was safe and associated mainly with mild, temporary complications.

Table No. 1: Demographic and clinical characteristic of patients (n=200)

Variable	Value
Age (years)	32.9±6.74
Infertility duration (years)	2.8±1.5
Primary infertility	140(70%)
Secondary infertility	60 (30%)
Smokers	80 (40%)
Non-smokers	120 (60%)

Table No. 2: Seminal fluid analysis baseline characteristic

Variable	Value
Semen volume (ml)	2.6±0.6
Sperm count (million/ml)	19.5±7.3
Progressively motile sperm (%)	16.3±4.1
Total motility (%	27.5±7.2
Normal morphology shaped (%)	4.6±1.3

Table No. 3: Semen changes post PRP injection

Variable	Changes post PRP injection			P value
	1 month	3 months	6 months	
Progressive motility (%)	28.8±6.9	33.8±7.1	38.9±4.5	< 0.001
Total sperm motility (%)	35.2±5.8	42.9±6.1	48.7±8.1	< 0.001
Sperm count (million/ml)	24.8±5.6	27.1±8.1	30.2±6.4	< 0.001
Morphology (%)	5.3±22	6.1±21	6.8±19	< 0.001

Table No. 4: Complications following intratesticular injection

Complication	%
Scrotal pain	15.0
Scrotal swelling	7.5
Scrotal hematoma	2.5
Infection	-
Testicular atrophy	-

DISCUSSION

Male infertility considered as a general global health problem accounting about 40-50% of infertility cases among couples worldwide and this mostly related to genetic, environmental and social factors like smoking and obesity and this necessary to raising the awareness and early diagnosis of this problem and provide several therapeutic measures with low cost to overcome this big social problem.[6,7]

The spermatogenesis is a complex physiological process that required approximately 64-74 days within the seminiferous tubules and many divisions and differentiation stages to produce a mature spermatozoon capable for motility and fertilization and can affected by the therapeutic measures at this period.[8]

Local intratesticular injunction of PRP had been stimulate the testicular tissues to produce spermatozoa and increasing the levels of testosterone through direct and close interactions with Sertoli cells, Leydig cells and germinal epithelial layers with minimal adverse systemic effects.[9,10]

The oxidative stress is one of the main reasons of male infertility and this result from the imbalance between the free radicals and reactive oxygen species and this imbalance led to damage of the wall of the spermatozoa and fragmentation of DNA and decreasing of the count and motility which lead to the inability of spermatozoa to fertilized the ova.[11]

In this study, the direct intratesticular local injection of PRP not restricted only to improve sperm motility but also it led to a noticeable improvement in the sperm count and morphology through the period of follow up and this give a great opportunity for treatment of male infertility cases.

Intratesticular injunction of PRP can be considered as a promising technology in regeneration of the testicular tissues because it contains several biological growth

factors like Platelet derived growth factor (PDGF), transforming growth factor B (TGFB) and vascular endothelial growth factor (VEGF), these factors leading to enhancement of testicular tissues repair and improving local testicular blood flow and promoting spermatogenesis.[12,13]

The results of this study refer to there is a great improvement in seminal fluid analysis parameters after PRP intratesticular injection and this results clearly consistent with many of previous clinical and investigational studies for evaluation of regenerative therapeutic approaches in treatment of male infertility.[14,15]

In this study, platelet rich plasma intratesticular injunction is a highly safe procedure with little complications in form of mild scrotal pain, mild scrotal swelling and mild local scrotal hematoma these complications were transient well tolerated by all patients and managed conservatively and resolved within short period of time, these results consisting with most of the earlier reports that demonstrate that PRP local intratesticular injunction was a safe procedure if done under sterile environment. There were encouraging but still there were many limitations for this study, first of them is the absence of the control group to make a clear and definitive conclusions for assessment and evaluation of the effectiveness this technique in management of male infertility, the other limitation was the short period of follow-up that restrict the evaluation of long term outcomes of reproduction like pregnancy, still birth and miscarriage rates.

CONCLUSION

Platelet rich plasma intratesticular injection therapy may lead to significant improvement in seminal fluid analysis parameters including asthenospermia and it can be considered as a safe and promising minimally invasive technique for management of male infertility cases.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Ahmed Ali Obaid, Ahmed Abdul Ameer Alwan
Drafting or Revising Critically:	Ahmed Ali Obaid, Shiren Ali AlHamzawi
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Cognitive Impairment and Brain Oxygenation in Chronic Obstructive Pulmonary Disease

Abdulsattar Hussein Abdullah, Mohamed Ghalib Zakari and Bassam Taha Saleh

ABSTRACT

Objective: To explore the potential connection between cognitive deficiency and cerebral oxygenation in chronic obstructive pulmonary disease sufferers and to examine potential links with their prevalent inflammatory, oxidative, and vascular markers levels.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Tikrit Teaching Hospital, Iraq from 1st January to 31st December 2025.

Methods: This cross-sectional study was conducted at the Tikrit Teaching Hospital, Iraq from 1st January to 31st December 2025 on a sample of 200 chronic obstructive pulmonary disease participants and 100 healthy volunteers between the ages of 35-75 years. The chronic obstructive pulmonary disease group will include sociodemographic information and clinical characteristics and some standard respiratory signs as forced expiratory volume in 1, forced vital capacity, SpO_2, and arterial blood gas, among other data. Cerebral oxygen saturation was measured by near-infrared spectroscopy, and cognitive function was assessed by the Montreal Cognitive Assessment test.

Results: Chronic obstructive pulmonary disease patients had significantly lower mean rSO_2 levels at 59.8±5.3%, and worse Montreal cognitive assessment scores at 22.4±3.1 compared to the control group at 68.4±4.7% and 27.1±1.9, correspondingly. Inflammatory and oxidative markers C-reactive protein, interleukin-6, tumor necrosis factor-α, elevated malondialdehyde were elevated in chronic obstructive pulmonary disease patients, and total antioxidant capacity and brain-derived neurotrophic factor were reduced, all $p<0.001$. There was a strong positive correlation between Montreal cognitive assessment scores and rSO_2 at 0.68, SpO_2 at 0.62, brain-derived neurotrophic factor at 0.58, and negative with partial carbon monoxide pressure at -0.47 and C-reactive protein at -0.51.

Conclusion: Since the neuromuscular oxygenation of chronic obstructive pulmonary disease is correlated with markedly diminished cerebral oxygenation and systemic hypoxemia and various indicators of inflammation and oxidative stress are increased while those of neurotrophic factors reduced, neuromuscular oxygenation and its markers should be included for the measurement to enable early identification and treatment for these conditions.

Keywords: Chronic obstructive pulmonary disease, Cerebral oxygenation, Cognitive impairment, Hypoxemia, Brain-derived neurotrophic factor

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INTRODUCTION

Chronic Obstructive Pulmonary Disease is characterized by persistent airflow limitation and chronic inflammatory responses in the airways and lungs. It develops over the years primarily due to injury caused by harmful particles or gases, such as cigarette smoke.[1]

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COPD is a major global health problem and prevalence is rising. It is the third leading cause of death and the seventh leading cause of disability worldwide.[2] As part of its extrapulmonary sequel, cognitive deficiency is probably one of COPD's most underestimated but practically relevant aftermaths – the one that has the most disastrous impact on the quality of life, which, in turn, influences adherence to treatment and irreversibly worsens the overall outcome.[3]

The pathophysiological links between COPD and cognitive decline are varied and complex. The most discussed causes of the damaging effects of severe cases of COPD are represented by chronic hypoxemia and hypercapnia Since COPD patients have severe COPD, the concentration of these gases in the body could directly affect the results.[4] These two mechanisms affect the central nervous system directly, causing changes in cerebral perfusion, metabolic

activity of neurons, and intensified white matter damage.[5]

The human brain's tissues need constant access to oxygen due to its strong dependence on oxidative activity to effectively produce ATP.[6] Hypoxia consequently limits oxygen delivery and causes a decrease in the oxygen pressure in neuroglial tissues. Mitochondrial energy production, or oxidative phosphorylation, turns down; more energy released through glycolysis is insufficient and inefficient to maintain cellular functions.[7]

Apart from hypoxia, systemic inflammation and oxidative stress are big actors in how COPD is related to memory and cognition decreases. COPD is noticed by permanent systemic inflammation, with high blood level of pro-inflammatory cytokines such as interleukin-6, guerilla necrosis factor-alpha, and C-reactive protein.[8] Oxidative stress, which occurs when there are too many revolutions oxygen form and not enough antioxidants, furthermore facilitates cell loss in the lungs and brain.[9] The oxidative-inflammatory succession then damages neurovascular coupling, deteriorates synaptic plasticity, and speeds up cognitive decrease.[10]

Vascular dysfunction could be another explanation for COPD patients' poor mentation. Due to damaged endothelium, stiff arteries, and more atherosclerosis, this can worsen hypoxia of the brain as a result of cerebrovascular insufficiency secondary to bronchus COPD patients.[11] These data support the emerging concept that COPD is unable to be regarded as mere pulmonary pathology but rather should be considered a neurologically threatening multisystem disorder.[12] The main purpose of this study was to evaluate the relationship between cognitive impairment and cerebral oxygenation in the COPD patient cohort and explore concomitant effects of systemic inflammation, oxidative stress, and neurotrophic factors.

METHODS

This cross-sectional observational survey was carried out in Tikrit Teaching Hospital, Iraq from 1st January to 31st December 2025 vide letter No. MEC-24054/Approval/JSDJNEHU date 15th December 2024. A total of 300 people, males and females, from 35 to 75 years were enrolled. Thus, the subjects were divided into two groups: 200 COPD patients who were diagnosed according to the GOLD criterion and 100 in apparently healthy people, age- and sex-matched, who served as controls. Subjects with a history of cerebrovascular disease, head injury, chronic anemia, hepatic or renal failure, psychiatric diseases, and quitting smoking within the last six months were excluded. Sociodemographic data that included age, sex, level of education, place of work, or income were collected using structured interviews. To all the COPD patients, the medical history, duration of disease, number of exacerbations per year, and the names of drugs were also evaluated. Also, everyone's height, weight, and the body mass index were measured.

We used standardized spirometry to test lung function with the measurement of FEV1, FVC, and their ratio FEV1/FVC. A pulse oximeter checked the resting oxygen saturation; an ABG test was done to reveal PaO2, PaCO2, pH, and HCO3 − levels.

Cerebral oxygenation was monitored using near-infrared spectroscopy. Near-infrared spectroscopy is a non-invasive optical technique for measuring regional cerebral oxygen saturation. The target was the anoxic zone of the frontal cortex. To examine the quality and accuracy of the data used in our investigation, rSO_2 measurement was taken three times for each participant and averaged.

The Montreal Cognitive Assessment test assessed cognitive ability in various aspects, including memory, visuospatial abilities, attention, executive functions, language, and orientation. The MMSE score is less than 26 points, suggesting that an individual may be cognitive impaired. All assessments were conducted by independent and informed researchers to minimize bias risk and maintain evaluation uniformity.

We assess different blood biomarkers to investigate the potential paths of hypoxia that could result in cognition impairment. The majority of them are the inflammatory markers such as C-reactive protein, ICAM-1, IL-1β, IL-6, and TNF-α. In addition, we check serum lactate, malondialdehyde, total antioxidant capacity, and brain-derived neurotrophic factor.

SPSS software version 23 was utilized for all statistical analyses. Pearson's or Spearman's correlation coefficients were used to look at the links between cognitive scores and physiological parameters. A p-value of less than 0.05 was deemed statistically significant.

RESULTS

The COPD patients had a longer history of smoking and more comorbidities, such as high blood pressure and diabetes (Table 1). The pulmonary function indicators exhibited significant decreases in COPD patients relative to controls (Table 2). The average FEV_1 and FEV_1/FVC ratio were significantly lower in the COPD group ($p<0.001$). Cerebral oxygenation, evaluated through near-infrared spectroscopy, was markedly diminished in COPD patients relative to controls. The cognitive domains most impacted were attention, executive function, and delayed recall. About 63% of patients with COPD fulfil the criteria for mild cognitive impairment (MoCA <26), while only 14% of controls did (Table 3).

As shown in Table 4, inflammatory and oxidative stress markers were much higher in COPD patients than in controls. Table 5 showed that carotid intima-media thickness (CIMT) was significantly elevated in the

COPD cohort, indicating subclinical atherosclerosis and a potential vascular role in cognitive decline. Using Pearson's test for correlation analysis Table 6, we discovered strong correlations between cognitive performance MoCA scores and oxygenation parameters. MoCA correlated positively with SpO_2 (Fig. 1) and cerebral oxygen saturation rSO_2 (Fig. 2), and negatively with PaO_2 and CRP (Fig. 3).

Table No. 1: Demographic and clinical characteristics of the study participants

Variable	COPD Group (n=200)	Control Group (n=100)	p-value
Age (years)	58.9 ± 8.7	58.1 ± 9.3	0.52
Male/Female	126/74	61/39	0.94
BMI (kg/m^2)	28.7 ± 3.9	26.3 ± 3.4	0.001
Smoking history (%)	85%	42%	<0.001
Hypertension (%)	49%	23%	<0.001
Diabetes mellitus (%)	38%	17%	0.002

Table No. 2: Pulmonary function and arterial blood gas analysis

Parameter	COPD Group (n=200)	Control Group (n=100)	p-value
FEV_1 (% predicted)	51.4±12.8	92.7±8.5	<0.001
FVC (% predicted)	74.3±10.1	95.8±6.9	<0.001
FEV_1/FVC ratio	0.54±0.08	0.79±0.05	<0.001
SpO_2 (%)	89.6±4.2	96.1±1.7	<0.001
PaO_2 (mmHg)	61.2±7.9	86.5±6.3	<0.001
$PaCO_2$ (mmHg)	47.6±5.8	38.9±4.1	<0.001
pH	7.36±0.05	7.42±0.03	<0.001
HCO_3^- (mmol/L)	28.4±3.7	24.1±2.8	<0.001

Table No. 3: Cerebral oxygenationcognitive and function assessment in COPD and control groups

Variable	COPD Group (n=200)	Control Group (n=100)	p-value
rSO_2 (%)	59.8±5.3	68.4±4.7	<0.001
Total MoCA Score	22.4±3.1	27.1±1.9	<0.001
Cognitive impairment (%)	63%	14%	<0.001

Table No. 4: Inflammatory and oxidative biomarkers in study groups

Parameter	COPD Group (n=200)	Control Group (n=100)	p-value
CRP (mg/L)	8.6±2.9	3.1±1.4	<0.001
IL-6 (pg/mL)	12.7±4.5	5.9±2.1	<0.001
TNF-α (pg/mL)	9.8±3.4	4.3±1.7	<0.001
Lactate (mmol/L)	2.8±0.6	1.6±0.4	<0.001
MDA (µmol/L)	4.9±1.3	2.2±0.9	<0.001
TAC (mmol Trolox eq./L)	0.87±0.19	1.43±0.22	<0.001
BDNF (ng/mL)	12.5±3.8	18.9±4.6	<0.001

Table No. 5: Cardiovascular parameters in copd and control groups

Parameter	COPD Group (n=200)	Control Group (n=100)	p-value
Heart rate (bpm)	86.2±10.4	78.7±8.3	<0.001
Systolic BP (mmHg)	136.4±14.8	130.2±13.5	0.04
Diastolic BP (mmHg)	84.1±9.3	82.5±8.8	0.21
CIMT (mm)	0.89±0.13	0.68±0.09	<0.001

Table No. 6: Correlations between cognitive function and physiological/biochemical parameters

Variable	r-value	p-value
SpO_2 (%)	0.62	<0.001
rSO_2 (%)	0.68	<0.001
PaO_2 (mmHg)	0.55	<0.001
$PaCO_2$ (mmHg)	–0.47	<0.001
CRP (mg/L)	–0.51	<0.001
IL-6 (pg/mL)	–0.44	<0.001
MDA (µmol/L)	–0.49	<0.001
BDNF (ng/mL)	0.58	<0.001

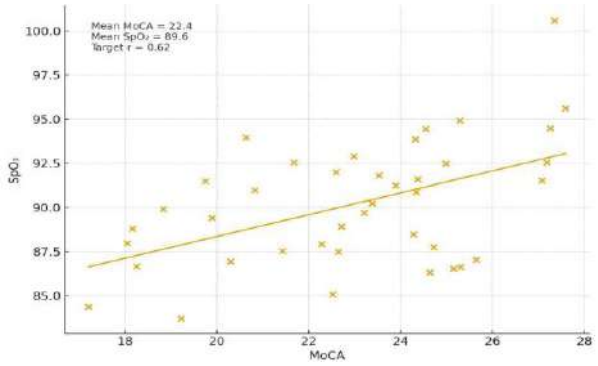

Figure No. 1: Correlations between MoCA and SpO_2

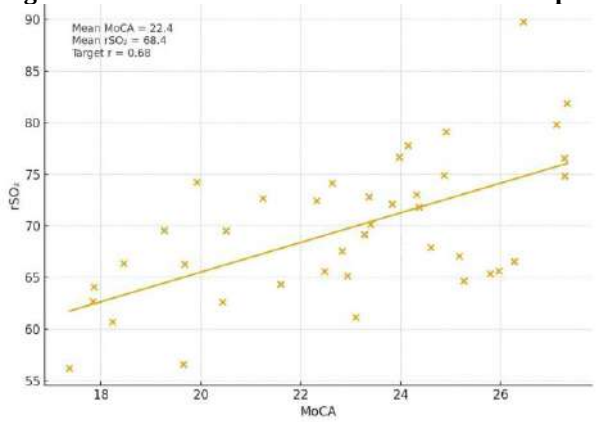

Figure No. 2: Correlations between MoCA and rSO_2

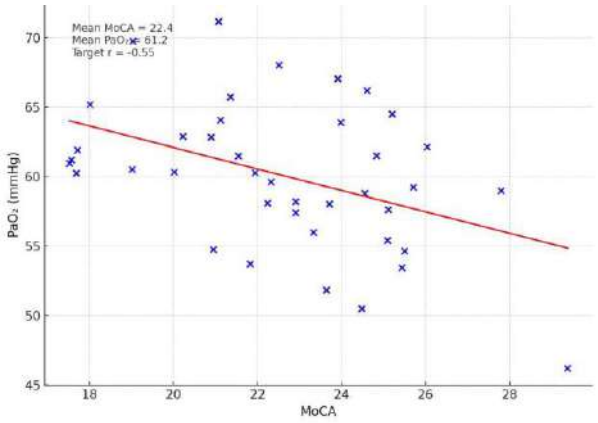

Figure No. 3: Correlations between MoCA and PaO_2

DISCUSSION

This study showed a strong connection between cognitive impairment assessed by Montreal Cognitive Assessment and reduced cerebral oxygenation in COPD patients. Considering the fact that the study has suggested the major role of COPD as a risk factor for cognitive decline, it supported our results. In a recent study involving 1,202 patients with COPD, the odds ratio for cognitive impairment was 2.42 compared to controls, while low baseline oxygen saturation of ≤88% raised the odds ratio to 5.45.[13]

Our results add another building block to the current pathophysiological model of cerebral-type manifestation of cognitive dysfunction by measuring the concentration of cerebral oxygenation by NIRS and correlating it with systemic inflammatory, oxidative, and neurotrophic biomarkers. From a mechanistic perspective, chronic hypoxia and hypercapnia, often seen in COPD, could induce perfusion and oxygen delivery dysfunction in the brain, rendering neurons functionally deficient and more vulnerable in excess network activity. The structural neuroimaging literature has shown gray matter atrophy in frontal and limbic areas in COPD patients with low pulmonary function.[14-16] In our sample, the point correlation coefficient between the MoCA and rSO_2 accounted for 0.68, highlighting cerebral hypoxia's pathophysiological significance. Further, arterial oxygen saturation SpO_2 correlated with cognitive functioning at r=0.62, indicating the link between a systemic and cerebral level.

Inflammatory pathways and oxidative stress were similarly compelling. In this study, COPD patients had higher CRP, IL-6 and TNF-α in COPD patients, which were inversely correlated with cognitive scores. This is consistent with a prior meta-analysis showing associations between inflammatory markers such as IL-6 and TNF-α and age-related cognitive decline.[17,18] The hypocarbia group similarly had abnormal oxidation stress markers, with higher MDA and lower TAC levels. Other COPD studies have found increased MDA levels and the activity of anti-oxidant enzymes such as superoxide dismutase, peroxides overpowered, and catalase to be independent of lung function.[19-21]

Hence, we hypothesize that ventilation and triad even activity led to hypoxia, inflammation, oxidative stress, as well as neurotropic support e.g, lower BDNF levels result in worse cognitive performance. Neurotrophic BDNF was lower in COPD patients, and there was a positive line correlation with MoCA scores r=0.58. The majority of the literature on BDNF has focused on neurodegenerative diseases and mood disorders. However, there is evidence of low serum BDNF levels in mild cognitive impairment MCI in general aging patterns.[22-25] It is believed that reduced serum BDNF in COPD may be due to lower central plasticity or repairing capacity in the setting of extended systemic stress.

Our multiple regression model in which rSO_2, SpO_2, $PaCO_2$, and BDNF all emerged as independent predictors of cognitive performance further substantiates the multi-factorial etiology of cognitive deterioration with our patients, the fact that cerebral oxygenation remained the strongest single predictor of cognitive performance irrespective of controlling for age, education, and disease severity suggests its importance. From a clinical perspective, evaluation of cognitive status and monitoring of cerebral oxygenation may play a role in early pre-emption. However, some limitations are also worth noting. The cross-sectional

nature of our design prohibits any causative conclusions, and it is likely that our findings might be reversed in terms of time directionality.

CONCLUSION

COPD patients frequently exhibit cognitive impairment, a condition closely related to the decline in cerebral oxygenation, hypoxemia, and increased pneumological dysfunction. Specifically, the diminished rSO_2, revealed in our study, proved to be the most powerful independent predictor of worse MoCA scoring, adjusting for the covariates. COPD-related neuropsychological alterations are likely to be attributed to chronic hypoxemia, CO_2 retention, systemic inflammation, free oxygen radicals, and the deficient activity of neurotrophic factors, such as BDNF. Examination of the cerebral oxygenation status can be used to identify the patients at risk of the cognitive deterioration and the necessity for the screening of the cognitive status of the COPD population.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Abdulsattar Hussein Abdullah, Mohamed Ghalib Zakari
Drafting or Revising Critically:	Abdulsattar Hussein Abdullah, Bassam Taha Saleh
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

A Novel Combination of Melittin and Palbociclib for Esophageal Cancer: In Vitro Evidence of Synergy and Mechanistic Insights

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ABSTRACT

Objective: To measured the possible synergistic effect of melittin in combination with palbociclib against KYSE-30 esophageal squamous cell carcinoma cells.
Study Design: A inivtro study.
Place and Duration of Study: This study was conducted at the College of Medicine, University of Babylon, Iraq from 1st June 2025 to 30th November 2025.
Methods: KYSE-30 and HEK normal cells were treated with melittin (0.15625-20 µg/mL) and palbociclib (0.625-80 µg/mL) and then KYSE-30 were treated with combination of these two substances. Using the MTT test, we calculated the cell viability. The cyclin-D1, Nrf2 and IL-6 concentrations using enzyme-linked immunosorbent assay. Cell migration was assessed by wound healing assay.
Results: Melittin (5-10 µg/mL) significantly reduced KYSE-30 viability ($p < 0.05$) but only affected HEK cells at 20 µg/mL ($p<0.001$). Palbociclib (20-80 µg/mL) reduced KYSE-30 viability with an IC_{50} of 22 µg/mL. Palbociclib alone significantly increased cyclin-D1 ($P<0.001$), while the combination of melittin (10 µg/mL) + palbociclib (22 µg/mL) significantly decreased cyclin-D1 ($P=0.048$). Palbociclib (11 µg/mL) increased Nrf2 ($P=0.029$), but the combination decreased Nrf2 ($P<0.05$).When compared to palbociclib alone, the combination approach produced greater suppression of IL-6 levels ($P=0.016$, $P=0.004$) and inhibited cell migration with wound expansion at higher doses.
Conclusion: In KYSE-30 cells, the combination treatment with melittin (10 µg/mL) and palbociclib (22 µg/mL) produced a pharmacodynamic potentiation on cell viability, regulation of cell cycle, antioxidant response, inflammation, and migration, suggesting the need for additional in vivo studies.
Key Words: Esophageal squamous cell carcinoma, Melittin, Palbociclib, Combination therapy, Cyclin-D1

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INTRODUCTION

Esophageal cancer represents one of the most lethal and aggressive tumor types worldwide.[1,4] Its ranking among cancers globally is eleventh, and among cancer mortality, it ranks seventh.[4,5] It has two histological types: esophageal squamous cell carcinoma (ESCC) and adenocarcinoma (EAC).[1,4] ESCC is most common in East and Middle Asia, especially in developing countries, linked to smoking and diet.[4,6] EAC is common in Western countries, linked to GERD and Barrett's esophagus.[2,4] ESCC represents 85% of esophageal cancers.[4] Its rapid progression and late diagnosis make it difficult to treat.[7,8]

In spite of a strong biological rationale for targeting the Cyclin D-CDK4/6-RB pathway in ESCC, no CDK4/6 inhibitor is currently approved for this disease.[4,9] Palbociclib, a selective CDK4/6 inhibitor, induces arrest of cell cycle at G1 phase but produces primarily a cytostatic effect rather than direct cancer cell death.[9,10] The mechanisms help ESCC cells survive treatment. These mechanisms develop quickly and activation of the PI3K/AKT/mTOR pathway. They also include ERBB/RTK signaling. Cancer cells can change their metabolism. They can use autophagy. They also avoid being recognized by the body's immune system.[11,12] Thus, treatment with palbociclib alone does not work for ESCC patients. This necessitates proper combination therapies that inhibit cell cycle progress and avoid other survival mechanisms.[9,13] Melittin is a natural compound that comes from bee venom. It works as an anticancer agent through cell membrane disruption.[14,15]

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This, however, requires large amounts of melittin that have toxic effects on normal cells. Palbociclib arrests ESCC cell growth. This arrest may sensitize cells to melittin.[16] Thus, a low-dose melittin combination with palbociclib may be effective and less toxic.

METHODS

This inivtro study was conducted at College of Medicine, University of Babylon, Iraq from 1st June 2025 to 30th November 2025 vide letter No. 152/QM/Approval/KDJEGVVD dated May 17, 2025. We obtained KYSE-30 esophageal cancer cells and HEK normal cells from the Tissue Culture Laboratory at the College of Medicine, University of Babylon. These cell lines were propagated in RPMI-1640 medium (Gibco, UK) fortified with 10% fetal bovine serum (FBS, Gibco, UK), 1% penicillin/streptomycin, and 50 µg/mL gentamicin (Ajanta, India), and incubated at 37°C under 5% CO_2 atmosphere. In distilled water Melittin (Shyuanye, China) was dissolved to prepare a stock solution of 1 mg/mL. Palbociclib (Bidepharm, China) was dissolved in dimethyl sulfoxide (DMSO, Roth, Germany) to produce a stock solution of 1 mg/mL. Working concentrations were prepared by dilution in culture medium immediately before each experiment.

Phosphate-buffered saline (PBS) was prepared by dissolving one tablet (Gibco, UK) in deionized distilled water and sterilized by autoclaving at 120°C for 20 minutes. Trypsin-EDTA solution was prepared by dissolving trypsin-EDTA powder (Gibco, UK) in deionized distilled water, adjusting the pH to 7.2, and sterilizing by serial filtration through 0.45 µm and 0.22 µm filters (Biofil, China). MTT solution (5 mg/mL) was prepared by dissolve MTT powder (Roth, Germany) in PBS, sterilized using a 0.22 µm filter (Biofil, China), and stored in a light-protected bottle at 4°C.

Cell viability was assessed using the MTT assay. A total of $2\times10_4$ cells were placed into each well of 96-well plates and allowed to attach overnight at 37°C. Following drug treatment, MTT working solution (0.5 mg/mL) was introduced and plates were incubated for an additional 4 hours at 37°C.[19,20] The culture medium was subsequently removed, and 100 µL of DMSO was added to solubilize the formazan precipitate. Optical density was determined at 570 nm with a microplate reader (Human, Germany). Cell viability was calculated using the formula:

Cell viability (%) = (Abs sample - Abs blank) / (Abs control - Abs blank) × 100

Melittin was tested on KYSE-30 cells at concentrations of 0.3125, 0.625, 1.25, 2.5, 5, and 10 µg/mL for 24 hours. On HEK normal cells, melittin was tested at concentrations of 0.15625, 0.3125, 0.625, 1.25, 2.5, 5, 10, and 20 µg/mL for 24 hours. Palbociclib was tested on both KYSE-30 and HEK cells at concentrations of 0.625, 1.25, 2.5, 5, 10, 20, 40, and 80 µg/mL for 48 hours.

The IC_{50} was calculated by generating a standard curve of cell inhibition percentage versus log drug concentration using Microsoft Excel. The concentration equivalent to 50% inhibition was calculated from the dose-response curve.

We tested the combination on KYSE-30 cells. The treatment lasted 48 hours. We used a fixed dose of palbociclib (22 µg/mL). We added different doses of melittin. These were 0.625, 1.25, 2.5, 5, 10, and 20 µg/mL. Then we measured cell survival. We did this using the MTT test.[19,20]

Following 48 hours of incubation, the cell culture supernatant was harvested for the determination of IL-6 levels. In case of intracellular markers such as Cyclin-D1 and Nrf2, cells were lysed using RIPA buffer. ELISA sandwich assays for all markers were conducted according to the manufacturer's guidelines using kits from Sunlong (China). The absorbance reading was carried out at 450 nm wavelength using a Human ELISA reader from Germany.

Cell culture of KYSE-30 cells was performed on 48-well plates (Biofil, China) till they became 90-100% confluent. At this point, a scratch line was created in all wells using sterile tips of a 200 µL pipette. The cell monolayers were gently washed with PBS to create clear areas, as per standardized procedures.[22,23] Next, we added drugs to the wells. Some wells got melittin (2.5 or 5 µg/mL). Some got palbociclib (2.5 or 5 µg/mL). Some got both (2.5+2.5, 2.5+5, or 5+5 µg/mL). We mixed all drugs in serum-free medium. We also had control wells. One control had no drugs. Another had only the vehicle. The pictures of the scratches at 0, 24, and 48 hours were taken. We used an inverted microscope from T.C Meiji Tech (Japan). We measured cell movement using Image J software.

We conducted all experiments in triplicate and expressed the data as mean ± standard deviation (SD). Using Sigma Plot, we performed one-way ANOVA with Holm-Sidak correction (MTT assay) or Tukey's post-hoc test (scratch assay) to determine statistical significance. We considered $p\leq0.05$ to be statistically significant.

RESULTS

Melittin treatment inhibited the growth of KYSE-30 and HEK cells in a concentration-dependent manner. Melittin at 5 and 10 µg/mL significantly reduced KYSE-30 cell viability compared to control ($p<0.001$). Concentrations of 0.3125-2.5 µg/mL showed no significant effect ($p>0.05$) [Fig. 1A]. Melittin significantly reduced HEK cell viability only at the highest concentration tested (20 µg/mL) ($p<0.001$). No significant effect was observed at 0.15625-10 µg/mL ($p>0.05$) [Fig. 1B].

Palbociclib at 20, 40, and 80 µg/mL significantly reduced KYSE-30 viability ($p<0.001$). Lower concentrations (0.625-10 µg/mL) had no effect. The IC_{50} was calculated to be 22 µg/mL [Fig. 2A]. Palbociclib at 20, 40, and 80 µg/mL also significantly reduced HEK viability ($p<0.05$), while concentrations of 2.5-10 µg/mL showed no significant effect ($p > 0.05$) [Fig. 2B].

Fixed palbociclib (22 µg/mL) combined with melittin (0.625-20 µg/mL) significantly reduced KYSE-30 viability at all concentrations compared to control ($P<0.05$). Compared to palbociclib alone, combinations with melittin at 5, 10, and 20 µg/mL showed significantly greater cytotoxicity ($P<0.001$). Lower melittin doses (0.625, 1.25, and 2.5 µg/mL) did not significantly differ from palbociclib alone ($P>0.05$) [Fig. 3]/

Palbociclib at 11 µg/mL did not significantly alter Cyclin-D1 levels in KYSE-30 cells compared to control (Dunn's method, $P>0.05$) while Palbociclib at 22 µg/mL significantly increase Cyclin-D1 level. A non-significant reduction was observed at 11 µg/mL (2.0 vs. 2.6 pg/mL) (Fig. 4A). Melittin at 11 µg/mL and 22 µg/mL did not significantly alter Cyclin-D1 levels (Dunn's method, $P>0.05$) (Fig. 4B). In comparison to Palbociclib, the combination of melittin 10, 12.5 and 20 µg/mL + palbociclib 22 µg/mL significantly decreased Cyclin-D1 levels the combination of (melittin 2.5 µg/mL with palbociclib) did not show significant changes ($P > 0.05$) (Fig. 4C).

Palbociclib at 11 µg/mL significantly increased Nrf2 levels compared to control ($P = 0.028$). Palbociclib at 22 µg/mL did not significantly alter Nrf2 levels ($P=0.127$) (Fig. 5A). Melittin significantly reduced Nrf2 levels at both 6.25 µg/mL ($P=0.024$) and 12.5 µg/mL ($P=0.013$) compared to control (Fig. 5B). The combination of melittin 10 and 12.5 µg/mL + palbociclib 22 µg/mL significantly decreased Nrf2 levels compared to control ($P<0.05$). Other combinations (melittin 12.5, and 20 µg/mL with palbociclib) and palbociclib alone did not show significant changes ($P > 0.05$) while the combination 2.5 µg/mL melittin and 22 palbociclib is significantly increase Nrf2 level ($P=0.016$) (Fig. 5C)

Melittin at 6.25 and 12.5 µg/mL did not significantly alter IL-6 levels ($P=0.257$) [Fig. 6A]. Palbociclib also at 11 and 22 µg/mL did not alter IL-6 levels ($P=0.089$) (Fig. 6B). Palbociclib alone (22 µg/mL) did not significantly alter IL-6 levels compared to control ($P=0.080$). However, the combinations of melittin 10 and 12 µg/mL + palbociclib 22 µg/mL ($P = 0.016$) and melittin 12.5 µg/mL + palbociclib 22 µg/ml ($P=0.004$) significantly decreased IL-6 levels compared to palbociclib alone. No significant differences were observed compared to the control group (Fig. 6C).

The wound healing assay was accomplished to estimate cell migration. The control group achieved complete wound closure at 48 hours (from 330 pixels at 0 h to 0 pixels at 48 h), confirming normal cell migration. Treatment with palbociclib alone at 2.5 and 5 µg/mL significantly inhibited cell migration, with wound areas remaining high at 48 hours (324 pixels for both concentrations), corresponding to wound closure percentages of 3.8% and 1.8%, respectively. The combination of melittin 2.5 µg/mL + palbociclib 2.5 µg/mL showed similar inhibition (1.4% closure), with no significant difference compared to palbociclib alone. However, the combinations meliin 2.5 µg/mL + palbociclib 5 µg/mL and melittin 5 µg/mL + palbociclib 5 µg/mL resulted in wound expansion, with closure percentages of -2.7% and -3.2%, respectively, indicating a cytotoxic effect at higher combination doses (Table 1).

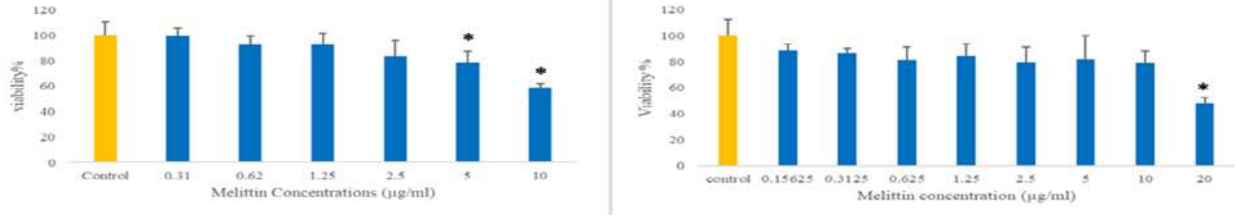

Figure No. 1A: Effect of palbociclib on KYSE-30 and HEK cell viability after 48h exposure

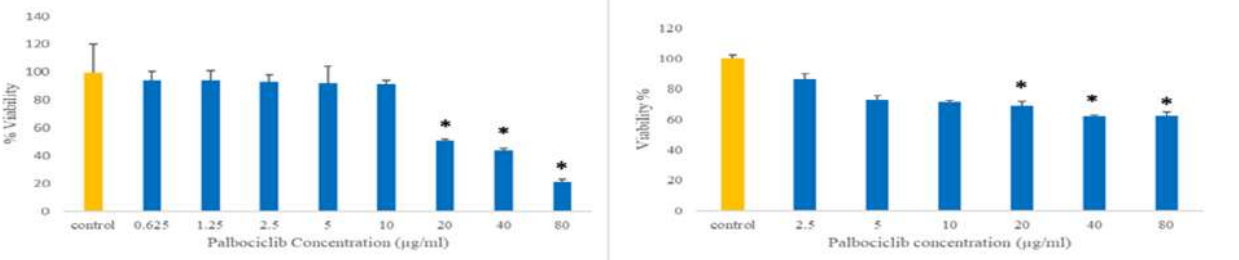

Figure No. 2B: Effect of palbociclib on KYSE-30 and HEK cell viability after 48h exposure

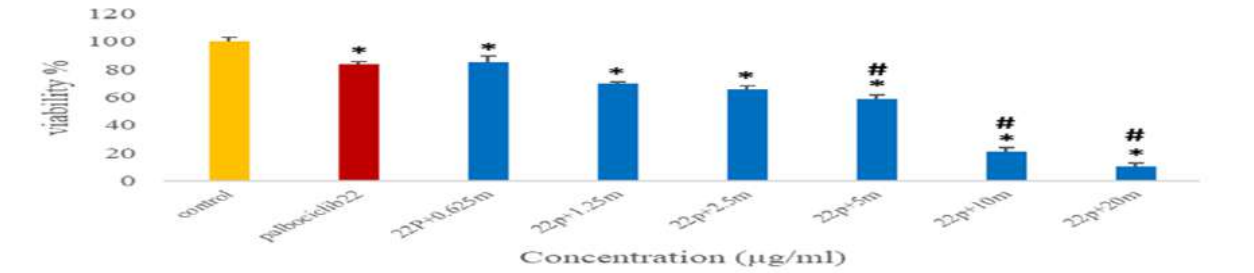

Figure No. 3C: Combination effect of fixed palbociclib (22 µg/mL) with varying melittin concentrations on KYSE-30 cell viability after 48h exposure

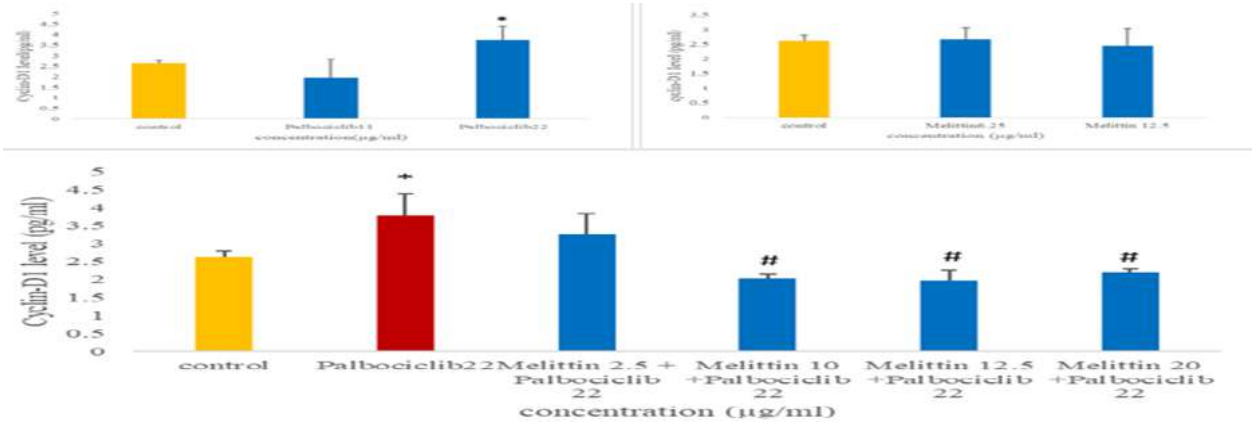

Figure No. 4A: Effect of palbociclib (11 and 22 µg/mL) on Cyclin-D1 level. Fig. 4B: Effect of melittin (11 and 22 µg/mL) on Cyclin-D1 level (Dunn's method). Fig. 4C: Effect of melittin and palbociclib combination on Cyclin-D1 level. Palbociclib (22 µg/mL) was used alone or in combination with melittin (2.5, 10, 12.5, and 20 µg/mL)

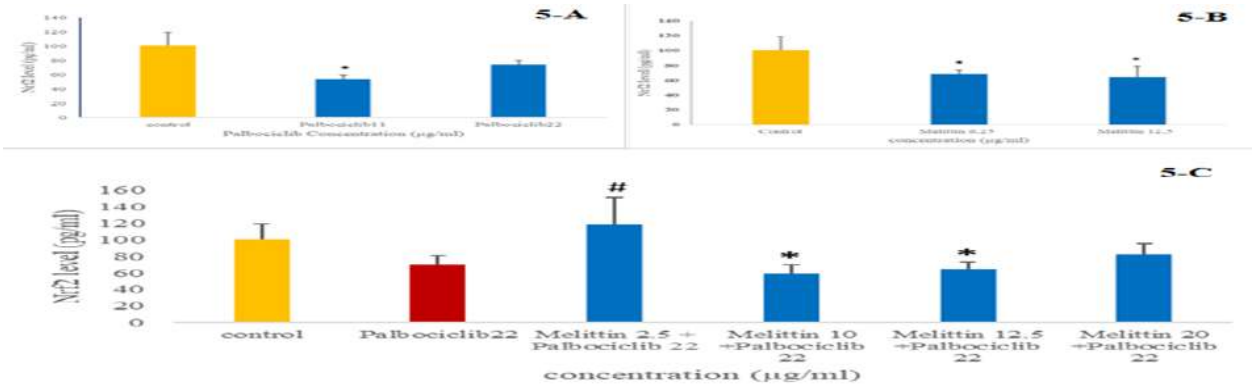

Figure No. 5A: Effect of palbociclib (11 and 22 µg/mL) on Nrf2 level. Fig. 5B: Effect of melittin (6.25 and 12.5 µg/mL) on Nrf2 level. Fig. 5C: Effect of melittin and palbociclib combination on Nrf2 level. Palbociclib (22 µg/mL) was used alone or in combination with melittin (2.5, 10, 12.5, and 20 µg/mL).

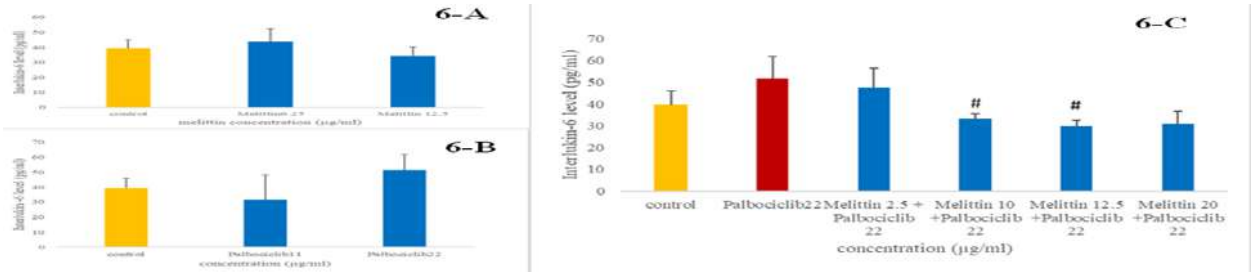

Figure No. 6A: Effect of melittin (6.25 and 12.5 µg/mL) on IL-6 level. Fig. 6B: Effect of palbociclib (11 and 22 µg/mL) on IL-6 level. Fig. 6C: Effect of melittin and palbociclib combination on IL-6 level. Palbociclib (22 µg/mL) was used alone or in combination with melittin (2.5, 10, 12.5, and 20 µg/mL)

Table No. 1: Wound closure over time measured in pixels

Groups	Wound with			% Closure at 48 h
	0 h	24 h	48 h	
Control	330	155.33	-	100%
Palbociclib 2.5 µg/mL	336.66	326	324	3.8%
Palbociclib 5 µg/mL	330	303.33	324	1.8%
Melittin 2.5 + Palbociclib 2.5	335.33	333.66	330.66	1.4%
Melittin 2.5 + Palbociclib 5	332.33	333.66	341.33	-2.7%
Melittin 5 + Palbociclib 5	333.33	340.66	344	-3.2%

DISCUSSION

Esophageal squamous cell carcinoma (ESCC) is one of the most aggressive malignancies with limited treatment choices and poor prognosis.[1,4] Although palbociclib, a selective CDK4/6 inhibitor, has shown efficacy in breast cancer, its monotherapy in ESCC has been largely ineffective due to intrinsic and acquired resistance mechanisms.[10,12] Melittin has the capacity to kill cancer cells through membrane damage and apoptosis.[14,15] Nevertheless, it can be used only be active at very high doses that might affect normal cells as well.[16]

The MTT assay demonstrated that melittin significantly reduced KYSE-30 cell viability at concentrations of 5 and 10 µg/mL after 24 hours, while showing toxicity to normal HEK cells only at the highest concentration tested (20 µg/mL). This selective cytotoxicity is consistent with previous reports indicating that melittin preferentially targets cancer cells due to their altered membrane composition and higher negative charge.[14,15] Zhu et al[15] previously demonstrated that melittin inhibited ESCC cell growth in a time- and dose-dependent manner with IC_{50} values of 1.88 µM for ECA109 and 1.64 µM for TE13 cells, and also showed that melittin enhanced radiation sensitivity in ESCC through induction of apoptosis.

Palbociclib significantly reduced KYSE-30 viability at concentrations of 20-80 µg/mL after 48 hours, with an IC_{50} of 22 µg/mL. However, palbociclib also reduced HEK normal cell viability at similar concentrations (20-80 µg/mL), indicating that palbociclib lacks selective toxicity between cancer and normal cells. the results obtained correspond to the mode of action of CDK4/6 inhibitors. CDK4/6 inhibitors block cell proliferation; however, they do not cause cell death directly. This effect is called cytostatic effect.[9,10]

The cells were treated with a fixed concentration of palbociclib (22 µg/mL) and various concentrations of melittin (0.625 to 20 µg/mL). The effect of all combinations on KYSE-30 cell viability was found to be significantly lower than the effect observed in the control group ($p<0.001$). Particularly, the combined treatment was effective in low concentrations of melittin that did not show any activity in monotherapy. In such a case, the combined effect of palbociclib and melittin is likely to be synergistic. It is possible that one mechanism of the synergy is the increased sensitivity of cancer cells after their cycle arrest by palbociclib, which enhances the ability of melittin to damage the membranes.

Cyclin-D1 serves as a regulatory protein and governs the G1-to-S phase transition during the cell cycle. ESCC cells typically show elevated expression of this protein. Our study revealed that palbociclib alone at 22 µg/mL caused an unexpected rise in Cyclin-D1 levels. This observation runs counter to the known action of CDK4/6 inhibitors, which usually reduce Cyclin-D1 via a feedback mechanism involving Rb and FOXM1.[9] This increase most likely reflects a compensatory adaptive response. Cancer cells boost Cyclin-D1 production to survive drug-induced pressure. Similar resistance patterns have been reported in other cancer models.[11]

In contrast, melittin by itself did not change Cyclin-D1 levels. This suggests that melittin's killing effect does not depend on cell cycle disruption. Earlier work supports this view, showing that melittin triggers ESCC cell death through Bcl-2 family protein modulation, not through cell cycle blockade.[15]

When combined, melittin (10, 12.5, and 20 µg/mL) with palbociclib (22 µg/mL) gave a different picture. The combination markedly lowered Cyclin-D1 expression. Hence, melittin corrected the palbociclib-driven increase, thereby countering a key resistance pathway.[9,13] It was absent at the smallest melittin concentration (2.5 µg/mL). This finding emphasizes that an ideal drug ratio is essential for synergy.[16]

Nrf2 is a transcription factor that regulates the antioxidant defense machinery of the cell. Many cancers including ESCC maintain high Nrf2 activity to avoid oxidative damage from chemotherapy. The important rise of Nrf2 levels with palbociclib at 11 µg/mL. Palbociclib effects are reduced by cancer cells activating antioxidant pathways. Such adaptive responses are known well to power drug resistance. Similar findings have been observed in previous studies of CDK4/6 inhibitors.[9,12] At the higher dose (22 µg/mL), palbociclib did not change Nrf2 and the injury was so severe that no effective defense could be made.

Melittin alone gave a reverse effect. It significantly decreased ($P=0.024$) Nrf2 level at 6.25 µg/mL and 12.5 µg/mL. This is in agreement with earlier studies showing that melittin disrupts membrane structure and

induces oxidative stress.[14,15] This behavior of melittin might avoid the usual resistance mechanisms.[17,18]

When given together, melittin (10 and 12.5 µg/mL) plus palbociclib (22 µg/mL) significantly lowered Nrf2 levels ($P<0.05$). Similar to Cyclin-D1, melittin reversed palbociclib induced Nrf2 upregulation. Not all combinations did this however. In contrast, melittin (2.5 µg/mL) plus palbociclib (22 µg/mL) increased the level of Nrf2. The result indicates the importance of the melittin dose. Since the findings are consistent across the use of two different molecular markers (Cyclin-D1 and Nrf2), they provide solid evidence that the synergistic action is indeed present. In light of Nrf2 induction being one of the factors leading to drug resistance, the ability of melittin to inhibit it can help overcome resistance to palbociclib.[13,16]

IL-6 is a pro-inflammatory cytokine. It promotes tumor development and metastasis and contributes to treatment resistance. These functions have been well-documented in ESCC and other malignancies. Melittin alone at 6.25 and 12.5 µg/mL did not cause any significant change in IL-6 levels. Also, palbociclib alone at 11 and 22 µg/mL had no effect on IL-6 levels. However, the combined therapy induced definitive effect, 10 µg/mL melittin with 22 µg/mL palbociclib has decrease the level of IL-6 ($P=0.016$), 12.5 µg/mL melittin with 22 µg/mL palbociclib has decrease the level of IL-6. High IL-6 levels are associated with worse outcomes and greater drug resistance in ESCC patients. Thus, lowering IL-6 is therapeutically useful. Beyond its direct cancer-killing activity, melittin may also act as an anti-inflammatory agent. Its ability to reduce IL-6 levels could enhance patient survival. Additionally, the melittin-palbociclib combination might decrease tumor-driven inflammation.

In the untreated control group, cells closed the gap entirely within 48 hours (100% closure). This reflects the typical migratory behavior of cancer cells. Palbociclib given alone strongly suppressed cell movement. At 2.5 µg/mL, the wound closure rate was just 3.8%. At 5 µg/mL, it was only 1.8%. These results show that palbociclib effectively blocks ESCC cell motility and cell migration represents a crucial step in the metastatic process.

The combination of melittin (2.5 µg/ml) and palbociclib (2.5 µg/ml) generated the same results, with a wound closure rate of 1.4%. This difference was not statistically significant compared to the use of palbociclib alone. The higher combined doses produced a different effect. The use of melittin (at a concentration of 2.5 µg/ml) with palbociclib (at a concentration of 5 µg/ml) resulted in a 2.7% decrease in wound healing. Using the same concentration also resulted in a 3.2% decrease. These negative ratios indicate that the wound is widening, not healing. That is, the size of the wound has increased over time. This is strong evidence of a cytotoxic effect. The combination not only prevented the movement of cells, but also killed them, causing the wound area to increase. The results strongly support the synergistic toxic effect of the combination of melittin and palbociclib.

CONCLUSION

The pharmacodynamic potentiation of melittin (10 µg/mL) in combination with palbociclib (22 µg/mL) on KYSE-30 esophageal cancer cells. The combination decreased cell viability, decreased Cyclin-D1 levels, suppressed the Nrf2 antioxidant defense, decreased IL-6 levels and blocked cell migration. These results suggest that melittin may block two major resistance mechanisms to palbociclib: cyclin-D1 feedback upregulation and Nrf2 activation. This combination could be a promising new treatment for esophageal squamous cell carcinoma (ESCC). However, these results need to be supported by further animal studies before clinical application.

Author's Contribution:

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Original Article

The Vascular Endothelial Growth Factor, Microalbuminuria, and β2-Microglobulin as Angiogenic and Renal Dysfunction Indicators in Patients with Diabetic Foot Ulcer

Hind Chassab Karam[1], Haider Kamil Zaidan[2] and Walaa Salih Hassan[2]

ABSTRACT

Objective: To evaluate the serum vascular endothelial growth factor, microalbuminuria, and beta-2 microglobulin as concurrent markers of angiogenic impairment and renal injury.

Study Design: A cross-sectional study.

Place and Duration of Study: This study was conducted at the University of Babylon, Iraq from 1st November 2025 to 31st March 2026.

Methods: Ninety participants, 50 patients with confirmed diabetic foot ulcer, 20 diabetics without identifiable complications (positive control), and 20 healthy volunteers (negative control) were enrolled.

Results: Fasting blood sugar, glycated hemoglobin, vascular endothelial growth factor, microalbuminuria, and beta-2 microglobulin were significantly elevated in diabetic foot ulcer patients relative to both control groups ($P \leq 0.01$). A meaningful positive correlation was identified between serum vascular endothelial growth factor and microalbuminuria ($r=0.284$, $P=0.045$), pointing to a shared microvascular pathological process.

Conclusion: The routine and combined measurement of serum vascular endothelial growth factor, microalbuminuria, and beta-2 microglobulin is recommended as part of standard clinical monitoring for diabetic foot ulcer patients, providing clinicians the opportunity to intervene before complications become irreversible.

Key Words: Diabetic foot ulcer, Vascular endothelial growth factor, Beta 2-microglobulin, Microalbuminuria, Diabetic nephropathy, Angiogenesis

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INTRODUCTION

Diabetes mellitus (DM) continues its global expansion, placing mounting pressure on health systems at every income level.[1] When blood glucose remains poorly controlled over years, a cascade of tissue-damaging events unfolds - touching the heart, kidneys, eyes, and peripheral nerves alike.[2] For populations in lower-income settings, where screening and treatment remain out of reach for many, the resulting morbidity and economic loss are especially severe.[3]

Among the complications that clinicians dread most is the diabetic foot ulcer (DFU). It is the leading cause of non-traumatic lower limb amputation worldwide, and once established, it tends to recur – demanding prolonged wound care and repeated hospitalizations.[4] DFUs do not arise from a single cause; rather, they reflect the convergence of peripheral neuropathy, compromised vasculature, and defective immune defense, all driven by the chronic metabolic disturbance of diabetes.

Angiogenesis occupies a central position in DFU pathogenesis. Vascular endothelial growth factor (VEGF) is the principal mediator of new blood vessel formation, regulating endothelial cell migration and proliferation. In diabetic foot tissue, sustained hyperglycemia renders endothelial cells dysfunctional and markedly reduces local VEGF output, leaving wounds without the neovascularization needed for healing. A key molecular explanation lies in the disruption of the HIF-1/VEGF signaling axis: chronic high glucose blunts the hypoxic induction of pro-angiogenic factors, leaving the wound microenvironment in circulatory inadequacy.[5] Therapeutically, exogenous VEGF administration accelerates wound closure in DFU patients[6], while VEGF-A specifically drives early re-vascularization and re-epithelialization at wound margins.[7]

Diabetic foot ulcer rarely exists without concurrent renal involvement. Both conditions share a common root in chronic hyperglycemia-induced microvascular

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injury, which affects glomerular capillaries much as it affects peripheral vessels. Microalbuminuria - the earliest detectable sign of glomerular damage - is recognized as an independent cardiovascular risk indicator in diabetes and has been widely reported among Iraqi T2DM patients. A troubling limitation, however, is that kidney structure can deteriorate silently before albumin spills into the urine; roughly one-third of patients already show declining renal function before microalbuminuria becomes measurable, motivating the search for earlier complementary markers.[8]

Beta 2-microglobulin (β2-MG) fills part of this gap. This small protein associated with MHC class I antigens, passes freely through the glomerular filter and is reabsorbed almost entirely in the proximal tubule under normal conditions. When filtration slows or tubular cells are injured, serum β2-MG rises and crucially, this rise can precede detectable microalbuminuria, offering a window for earlier intervention in diabetic kidney disease.[9] The serum β2-MG as a stronger predictor of kidney failure requiring replacement therapy than conventional markers such as creatinine.[10] Measuring VEGF, microalbuminuria, and β2-MG together in DFU patients therefore captures the dual vascular-renal burden of this complication and may yield clinically actionable information before structural damage becomes irreversible.

METHODS

This cross-sectional study was conducted at University of Babylon, Iraq from 1st November 2025 to 31st March 2026 vide letter No. 11488/QM/Approval/JSDJNEHU dated October 28, 2025. Ninety participants were recruited and assigned to one of three groups: (1) 50 individuals with confirmed type 2 DM who had an active diabetic foot ulcer at enrollment, (2) 20 diabetic patients without identifiable complications (positive control), and (3) 20 apparently healthy individuals serving as negative controls. For every participant, demographic and clinical data including age, sex, and duration of diabetes were recorded in a standardized manner.[11]

Peripheral venous blood was drawn under aseptic conditions after a 12-hour fast, then centrifuged at 3000 rpm for 10 minutes; serum was stored at −80°C until analysis.[12] Fasting blood glucose was measured by the glucose oxidase method and HbA1c by high-performance liquid chromatography. Serum concentrations of microalbuminuria, β2-MG, and VEGF were quantified using commercially available ELISA kits per manufacturer specifications.[13]

All computations were performed using SPSS-26.0. One-way ANOVA compared group means, followed by pairwise testing via the LSD post hoc procedure. Pearson's correlation coefficient and simple linear regression examined relationships between continuous variables.[14] Statistical significance was defined as $P<0.05$.

RESULTS

There was significant ($P<0.05$) differences between age, depth of ulcer, side of ulcer and recurrence rate and no significant ($P>0.05$) differences between age and duration of diabetes (Table 1).

Table No. 1: Distribution of sample study according to gender, age, diabetic duration, depth of ulcer, side of ulcer and recurrence rate in patients group

Factor/Variables		No. n=50	%	P-value
Gender	Male	26	52.0	0.7773 NS
	Female	24	48.0	
Age (year)	< 50	10	20.0	0.0149*
	50 - 60	26	52.0	
	> 60	14	28.0	
Diabetic duration (years)	< 5	10	20.0	0.1323 NS
	5 – 10	20	40.0	
	> 10	20	40.0	
Depth of ulcer	Superficial	31	62.0	0.000**
	Deep	14	28.0	
	Deep with bone	5	10.0	
Side of ulcer	One foot	43	86.0	0.0001**
	Both feet	7	14.0	
Recurrence rate	Once	31	62.0	0.0001**
	Twice	6	12.0	
	2 - 3 times	11	22.0	
	> 3 times	2	4.0	

*P≤0.05 **P≤0.01, NS = Non-Significant

Table 2: Comparison between groups in FBS, HbA1c, Microalbuminuria, B2 Microglobulin and VEGF

Parameters	Patients with DFU	Patients without DFU	Negative control	L.S.D.	P-value
FBS (mg/dl)	247.02±5.23 a	194.20±10.77 b	108.60±1.16 c	48.219**	0.0001
HbA1c (%)	8.57±0.26 a	7.84±0.19 a	5.09±0.07 b	0.7794**	0.0001
Microalbuminuria (mg/L)	71.83±9.95 a	45.17±2.92 b	10.83±0.80 c	27.974**	0.0002
B2 Microglobulin (mg/L)	16.83±0.28 a	8.46±1.72 b	5.50±0.81 c	2.397**	0.0001
VEGF (Pg/ml)	320.56 ±10.97 a	246.92 ±9.24 b	154.61 ±6.98 c	35.116**	0.0001

Means with different letters in the same column differ significantly. **P≤0.01

There was significant (P<0.05) differences in FBS, HbAIc, microalbuminuria, B2 microglobulin and VEGF between patients with diabetic foot and patients without diabetic foot (Table 2).

There was correlation between vascular endothelial growth factor, fasting blood sugar, glycated hemoglobin, Microalbuminuria and beta 2 Microglobulin in patients group (Table 3, Figs.1-2).

Table 3: Correlation between VEGF, FBS, HbA1c, Microalbuminuria and B2 Microglobulin in patients group

Parameters	FBS	HbA1c	Microalbuminuria	B2 MG	VEGF
FBS	—	p=0.0001** r=0.574	p=0.808 NS r=0.035	p=0.756 NS r=-0.045	p=0.212 NS r=-0.179
HbA1c	—	—	p=0.882 NS r=0.022	p=0.492 NS r=0.100	p=0.529 NS r=-0.091
Microalbuminuria	—	—	—	p=0.216 NS r=0.178	p=0.046* r=0.284
B2 Microglobulin	—	—	—	—	p=0.598 NS r=0.076
VEGF	—	—	—	—	—

*P≤0.05, **P≤0.01, NS: Non-significant

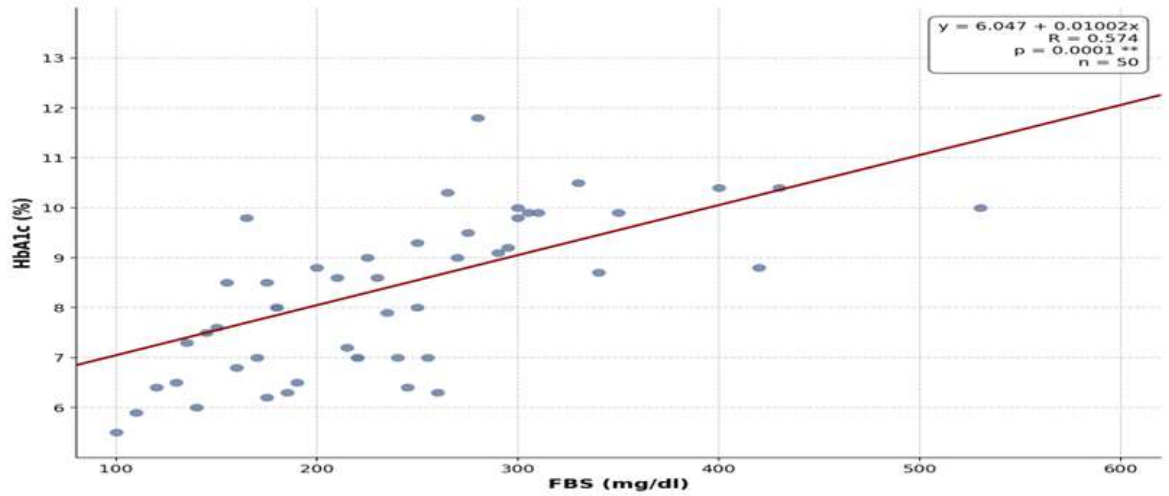

Figure No. 1: Positive linear regression between FBS (mg/dl) and HbA1c (%) in diabetic foot ulcer patients

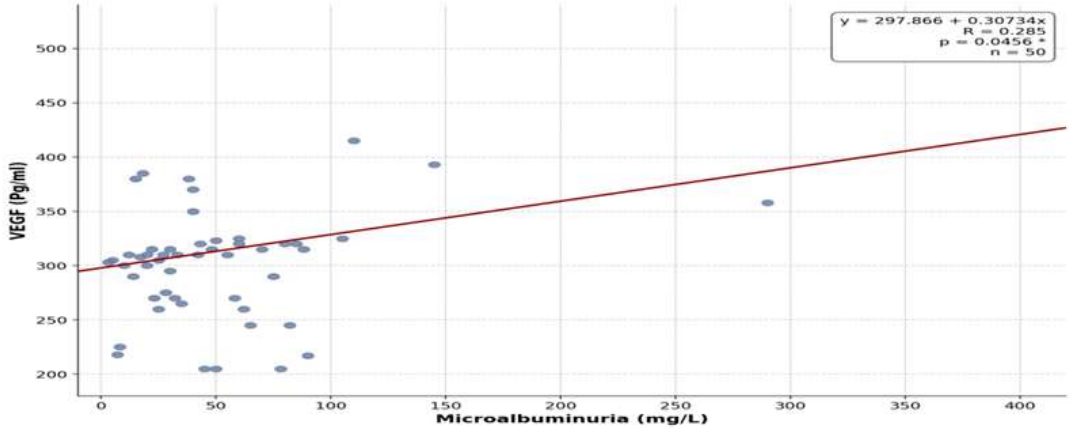

Figure No. 2: Weak positive linear regression between VEGF (pg/ml) and microalbuminuria (mg/L) in diabetic foot ulcer patients

DISCUSSION

The glycemic picture that emerged was unambiguous. FBS averaged 247.02±15.23 mg/dl in DFU patients - well above the 194.20±10.77 mg/dl in uncomplicated diabetics and far beyond the 108.60 ± 1.16 mg/dl in healthy controls (P=0.0001). HbA1c followed the same hierarchy: 8.57±0.26%, 7.84±0.19%, and 5.09±0.07%,

respectively (P=0.0001). HbA1c values were statistically comparable between the two diabetic groups, suggesting that chronic glycemic burden is a shared feature across T2DM rather than exclusive to those with ulcers. What the DFU group does exhibit is a compounding effect: poor long-term control simultaneously intensifies local ischemia and suppresses immune responses, creating conditions that actively prevent tissue repair.[4]

At the molecular level, persistent hyperglycemia restrains HIF-1 transcriptional activity, which in turn dampens VEGF expression in wound tissue and locks the local vasculature in a state of inadequacy.[5] Population data reinforce what the bench science predicts: HbA1c values above 8% are independently linked to both microvascular and macrovascular complications, including peripheral neuropathy and foot ulceration[1], and are directly associated with reduced wound-tissue VEGF output and poorer DFU prognosis.[15] A pooled analysis spanning more than 141 million participants from 1108 studies confirmed that chronic fasting hyperglycemia and elevated HbA1c consistently drive organ damage across diverse populations worldwide.[2]

Microalbuminuria rose in a clear stepwise pattern - from 10.83±0.80 mg/L in healthy controls, to 45.17±2.92 mg/L in uncomplicated diabetics, and peaking at 71.83±9.95 mg/L in DFU patients (P=0.0002). This gradient is not coincidental. Glomerular capillaries, like peripheral vessels, are vulnerable to the hemodynamic and oxidative stress of sustained hyperglycemia; as that damage accumulates, albumin leaks through the filtration barrier in progressively greater amounts. The finding therefore tracks a deepening of renal microvascular injury that parallels the overall severity of diabetic complications.

As the earliest detectable marker of diabetic nephropathy and an independent cardiovascular risk predictor[8], microalbuminuria holds a well-established clinical role - yet its limitations deserve acknowledgment. Around one-third of patients experience declining renal function before any albumin becomes detectable in the urine, meaning reliance on this marker alone will miss a meaningful share of early cases.[8] In the context of DFU, chronic hyperglycemia and microvascular disease are the shared soil from which both the ulcer and nephropathy grow, and microalbuminuria has been validated as a useful surrogate for the total vascular burden these patients carry.[4] Without treatment, up to 80-85% of insulin-dependent patients who develop microalbuminuria progress to advanced nephropathy within roughly a decade[13], and rising global microalbuminuria rates track closely with the spread of diabetic nephropathy in regions of poor glycemic control.[3]

The β2-MG findings were striking. DFU patients showed serum levels of 16.83±0.28 mg/L more than double the 8.46±1.72 mg/L in uncomplicated diabetics and nearly three times the 5.50±0.81 mg/L in healthy controls (P=0.0001). This sharp, complication-severity-dependent elevation points directly to progressive disruption of both glomerular filtration and proximal tubular re-absorption. Because β2-MG is ordinarily cleared with high efficiency at the tubule, rising serum concentrations sensitively reflect injury at that segment before conventional renal markers shift.

This early-detection advantage is increasingly recognized. Tubular damage in diabetic nephropathy frequently precedes glomerular deterioration, and β2-MG's sensitivity to proximal tubule dysfunction makes it a more timely indicator than albumin-based tests for some patients.[9] Serum β2-MG has also been shown to outperform standard markers including creatinine and albumin in predicting end-stage kidney disease requiring replacement therapy in biopsy-confirmed diabetic nephropathy.[10] A large prospective cohort study further established β2-MG as an independent predictor of ESRD and all-cause mortality in high-risk diabetic populations.[16] The markedly higher β2-MG concentrations in DFU patients compared to uncomplicated diabetics suggest that active ulceration is associated with accelerated renal tubular decline and reinforce the case for including this biomarker in routine DFU follow-up.[17]

Mean serum VEGF followed a consistent upward trajectory: 154.61±6.98 pg/ml in healthy controls, 246.92±9.24 pg/ml in uncomplicated diabetics, and 320.56±10.97 pg/ml in DFU patients (P=0.0001). At first glance, the highest VEGF in the sickest group might seem paradoxical if VEGF drives angiogenesis, why are DFU wounds failing to heal? The answer lies in the distinction between systemic compensatory upregulation and local functional impairment. Circulating VEGF rises as the body attempts to counteract peripheral ischemia, but the endothelial machinery in a chronically hyperglycemic environment is too damaged to respond effectively.[18]

Locally, endothelial dysfunction under persistent high glucose substantially reduces VEGF synthesis within wound tissue, leaving neovascularization deficient precisely where it is needed (Huang et al., 2025). The HIF-1/VEGF pathway—normally activated by tissue hypoxia cannot mount an adequate response when hyperglycemia disrupts HIF-1α activity, reducing downstream pro-angiogenic signaling and worsening local oxygen deprivation.[5] Compounding this, activation of the polyol, protein kinase C, hexosamine, and AGE pathways generates reactive oxygen species, promotes chronic inflammation, and further suppresses HIF-1α, collectively stalling angiogenesis and tissue repair.[19] Elevated AGEs together with TNF-α also stimulate secretion of soluble VEGFR-1, which sequesters free VEGF as a decoy receptor, stripping it of biological activity at the wound site.[20]

Despite these barriers, therapeutic strategies targeting VEGF retain real promise. Exogenous VEGF delivery promotes wound closure through vasodilation, basement membrane proteolysis, and coordinated endothelial migration and proliferation.[6] VEGF-A appears especially important in initiating the earliest angiogenic steps and epithelial re-growth at wound margins, while VEGF-C contributes a complementary role by promoting lymphangiogenesis during granulation tissue formation.[15] Altogether, the VEGF profile in this cohort underscores why restoring its local bioactivity remains a priority research target for improving DFU outcomes.[4]

CONCLUSION

Patients with diabetic foot ulcers demonstrated significantly elevated serum concentrations of serum vascular endothelial growth factor, microalbuminuria, and beta-2 microglobulin compared to both diabetic and healthy control groups - evidence of concurrent angiogenic dysregulation and progressive renal impairment occurring side by side. The significant positive correlation between serum vascular endothelial growth factor and microalbuminuria suggests these two processes share an underlying microvascular mechanism rather than developing independently. Combined with glycemic indices, this biomarker triad offers a broader and more clinically meaningful evaluation of the systemic impact of diabetes. The routine and combined measurement of serum vascular endothelial growth factor, microalbuminuria, and beta-2 microglobulin is recommended as part of standard clinical monitoring for diabetic foot ulcer patients, providing clinicians the opportunity to intervene before complications become irreversible.

Author's Contribution:

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Original Article

Self-Management of Hypertensive Patients in Accordance with Their Knowledge

Hasanain Mahmood Abdoul Ameer

ABSTRACT

Objective: To evaluate hypertensive patients' knowledge about hypertension, evaluate self-management behaviors; and then investigate the relationship between knowledge and self-management.
Study Design: A descriptive cross-sectional study
Place and Duration of Study: This study was conducted at the Al Diwaniyah City, located in Diwaniyah Governorate, Iraq from 16th October 2025 to 1st March 2026.
Methods: 165 hypertensive patients were enrolled.
Results: Most patients had a high level of knowledge of hypertension, as 81.8% of patients had good knowledge. Smoking, alcohol consumption, dietary control, exercise and follow-up visits were especially relevant to the patient, but complication concerns and abnormal blood pressure values were still present. Self-management was relatively fair in general and 77.0% exhibited moderate self-care practices. Knowledge resulted in a highly significant relationship with self-management.
Conclusion: Better knowledge was associated with better self-management. Enhancing patient education, counseling and behavioral support could enhance daily self-care and blood pressure control.

Key Words: Hypertension, Self-management, Patient knowledge, Self-care behavior, Blood pressure control

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INTRODUCTION

Hypertension continues to be a serious chronic health issue and involves a long-term approach of both pharmacological treatment and ongoing lifestyle modification. All of the studies we reviewed demonstrated that self-management is at the heart of the treatment of hypertension, as patients need to engage in many daily decisions around the use of medications, as well as diet, exercise, blood pressure monitoring, and other routine health checks.[1,2] Qualitative and quantitative studies contribute to the evidence on self-management in hypertensive patients across different aspects including medication adherence, low-salt and healthy dietary practices, physical activity, blood pressure monitoring, abstaining from smoking, and follow-up with health services.[3-5] Most patients have poor conduct in executing these behaviors. The medication, diet, physical activity, and blood pressure monitoring are nonaligned, such could lead to inadequate control of blood pressure, leading to complications.[4-6]

The availability and awareness of hypertension are often called attention to as a driving force for the ability of patients to control their condition. Patients who have established how hypertension is defined, the need for lifelong treatment, lifestyle modification, and regular monitoring will be more likely to engage in appropriate self-care behaviours.[6,7] An association exists between poor knowledge and misconceptions about treatment, medication utilization, poor diet control, sedentary lifestyle, and infrequent blood pressure checks.[4,8] Further information through education and self-management support to patients could help achieve such improvement, and it has been reported that enhanced patient's knowledge can lead to improved treatment adherence, self-care, and blood pressure control.[1,7] This may indicate that knowledge should not only be considered as a cognitive state but also as a practical foundation for improved clinical control of hypertensive disease.

Martin et al[6] found a positive correlation between knowledge and hypertension self-management practice, while Gusty et al[4] reported that knowledge was significantly related to adherence in weight management and physical activity. Rikmasari et al[2] identified disease knowledge as the strongest factor associated with better self-management, and Asmoro et al[8] showed that better knowledge in hypertension self-management was linked to more normal blood pressure

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values. Although these findings emphasize the importance of knowledge in shaping self-management, assessment of this relationship remains important in different clinical and cultural settings. Therefore, the present study aims to assess the level of knowledge about hypertension among hypertensive patients attending selected public health clinics in Al-Diwaniyah City, evaluate their self-management behaviors related to medication adherence, diet, physical activity, blood pressure monitoring, and follow-up care, and examine the relationship between patients' knowledge of hypertension and their self-management practices.

METHODS

This descriptive cross-sectional study was conducted at Al Diwaniyah City, located in Diwaniyah Governorate, Iraq from 16th October 2025 to 1st March 2026 vide letter No. 3434/QM/Approval/JSDJNEHU dated 1st October 2025. The study was comprised of four public health care clinics, namely Al-Intifada Public Clinic, Al-Furat Public Clinic, Al-Talia Public Clinic, and Al-Iskan Al-Qadeem Public Clinic. A total of 165 hypertensive patients were enrolled. Participants came from four public clinics in Al-Diwaniyah City: 65 patients were selected from Al-Intifada Public Clinic, 28 patients were selected from Al-Furat Public Clinic, 34 patients were selected from Al-Talia Public Clinic, and 38 patients were selected from Al-Iskan Al-Qadeem Public Clinic. Sample size was determined with the Neuman formula. The data was entered and analyzed through SPSS-25.

RESULTS

The patients had an overall high level of knowledge regarding hypertension with a general mean of 2.61±0.649. The highest knowledge scores were found in items related to lifestyle risk factors and healthy behaviors, particularly the harmful effect of smoking on hypertension (98.8%, mean=2.98±0.174),

Table No. 1: Response of patient knowledge regarding hypertension (n=165)

Item	I know		I uncertain		I don't know		Mean±SD	Assessment
	No.	%	No.	%	No.	%		
Hypertension is a serious condition that can lead to complications	93	56.4	6	3.6	66	40.0	2.16±0.97	Moderate
An individual with hypertension should go for check-ups regularly	141	85.5	2	1.2	22	13.3	2.72±0.68	High
It is important for a patient with hypertension to have a reliable means of blood pressure monitoring between visits to their health care provider	111	67.3	14	8.5	40	24.2	2.43±0.85	High
A blood pressure level of above 130/90 is considered abnormal	69	41.8	27	16.4	69	41.8	2.0±0.91	Moderate
A blood pressure level of less than 120/80 is considered to be normal	112	67.9	14	8.5	39	23.6	2.44±0.85	High
Smoking cigarettes has a negative effect on persons with hypertension.	163	98.8	1	0.6	1	0.6	2.98±0.17	High
Drinking alcohol has a negative effect on persons with hypertension.	157	95.2	3	1.8	5	3.0	2.98±0.17	High
Increased physical exercise actually decreases the blood pressure of a person with hypertension.	142	86.1	5	3.0	18	10.9	2.92±0.36	High
A diet which contains fruits and vegetables is good for a person with hypertension.	155	93.9	6	3.6	4	2.4	2.75±0.63	High
A diet consisting of low-fat milk and whole wheat bread is good for a person with hypertension.	149	90.3	5	3.0	11	6.7	2.92±0.35	High
Corned beef and salted meat is harmful for a person with hypertension.	151	91.5	0	0.0	14	8.5	2.84±0.52	High
A meal rich in green bananas, baked chicken and beans is good for a person with hypertension.	102	61.8	16	9.7	47	28.5	2.83±0.55	Moderate
Overall mean±SD							2.61±0.64	High

the harmful effect of alcohol (95.2%, mean=2.92±0.366), the benefit of fruits and vegetables (93.9%, mean=2.92±0.356), and the harmful effect of corned beef and salted meat (91.5%, mean=2.83±0.559). A high proportion of respondents also knew that hypertensive patients should attend regular check-ups (85.5%, mean=2.72±0.686), that physical exercise can reduce blood pressure (86.1%, mean=2.75±0.638), and that low-fat milk and whole wheat bread are good dietary choices (90.3%, mean=2.84±0.521). In contrast, only moderate knowledge was observed in some important clinical areas. Just 56.4% knew that hypertension is a serious condition that can lead to complications (2.16±0.971), while knowledge of diagnostic blood pressure thresholds was limited, as only 41.8% identified that blood pressure above 130/90 mmHg is abnormal and an equal proportion (41.8%) did not know this item (2.00±0.917). Knowledge was also moderate regarding specific healthy meal composition, with 61.8% recognizing that a meal rich in green bananas, baked chicken, and beans is appropriate for patients with hypertension (2.33±0.893) [Table 1].

Table 2 demonstrates that the general knowledge of hypertension among the patient population was mainly favorable. There were 135 (81.8%) had good knowledge scores in the range of 29–36; 27 (16.4%) had fair knowledge scores in the range of 21–28; only 3 (1.8%) had low knowledge scores in the range of 12–20. There was a large average knowledge score of 30.89 with a standard deviation of 3.59, which is a high level of knowledge of hypertension in respondents. This indicates that most patients understood hypertension, its management, and self-care behaviors are important to consider, while a smaller percentage of participants did not seem to know enough and might need more health education. The current finding that knowledge among the hypertensive patients was generally good is consistent with many previous studies which demonstrate that patient knowledge is an important cornerstone of hypertension self-management.

Table No. 2: Overall patient knowledge regarding hypertension

Level	No.	%	Mean	St. deviation
Low level 12-20	3	1.8	30.89	3.59
Fair knowledge 21-28	27	16.4		
Good knowledge 29-36	135	81.8		

Most respondents had fair self-care behavior, with 127 respondents (77.0%) falling in this category. Meanwhile, 35 respondents (21.2%) had good self-care behavior and only 3 respondents (1.8%) had poor self-care behavior. The overall mean self-care score was 42.59 with a standard deviation of 5.85, indicating that, on average, respondents were in the fair category (Table 3).

Table 3: Overall sample response regarding self-care behavior

Level	Score Range	No.	%	Mean	St. deviation
Poor level	20–33.33	3	1.8	42.59	5.85
Fair level	33.34–46.66	127	77.0		
Good level	46.67–60	35	21.2		

DISCUSSION

This study suggested that the knowledge of behavioral and dietary risk factors was higher compared to the clinical severity and diagnostic information regarding hypertension. The knowledge level being generally high indicates that most patients understand basic hypertension management concepts, especially those of smoking cessation, reduction of alcohol consumption, exercise, healthy diet, and ongoing follow-up. This trend is not different from previous studies which have found that a knowledge of disease is an important factor in the improvement of self-efficacy and self-management of hypertensive patients.[2] The relatively high levels of knowledge found in lifestyle-related items can be consistent with a focus on non-pharmacological management in health education at primary care level. Other studies have demonstrated that better knowledge may help to advance treatment adherence and self-management as well as blood pressure control in the study setting, coupled with supportive health care provision.[7] Knowing also significantly supports blood pressure outcomes as well since enhanced knowledge was associated with improvements in blood pressure control.[8] However, significant gaps are also seen in the current table, especially with the characterization of hypertension as a serious condition and abnormal blood pressure measurement. Such weaknesses are significant because poorly defined information on the degree of disease and target blood pressure can reduce patients' ability to faithfully monitor their condition and respond appropriately to indications.

The moderate knowledge in some domains also indicates that knowledge itself does not necessarily guarantee appropriate self-management conduct. This supported this interpretation in past studies reporting that even though patients might have learned enough knowledge, having self-care behavior is not always linked to knowledge, which can be influenced by other factors such as motivation, self-efficacy, employment status, age, and social support.[2,9] The same qualitative evidence revealed self-management practices among

hypertensive patients, which are limited not only by knowledge but are shaped and facilitated as well by daily barriers like fatigue, medication side effects, long treatment duration, and the availability of resources (family and health-worker support).[3] Safitri et al[5] reported likewise that most hypertensive patients showed only a moderate degree of self-management capability, indicating room for improving patients' awareness even when there is awareness. There also existed evidence from Nepal at the community level where less than half of adults had good knowledge about hypertension, and it was evident that awareness-raising activities and education programs needed to be implemented.[10-12] Therefore, the current study imply that educational interventions for hypertensive patients should move beyond general advice and place greater focus on clinical understanding, including blood pressure thresholds, complications, and practical dietary planning, while also reinforcing motivation, self-efficacy, and social support to improve long-term self-management outcomes.

Martin et al[6] stated that most hypertensive patients had good knowledge, and higher knowledge was positively correlated with self-management practices (r=0.320, p=0.000), thus indicating better-informed patients are more likely to undertake appropriate self-care. Similarly, Satyal et al[13] reported that 57.5% of patients had adequate knowledge and that knowledge was related to improved self-care practice (r=0.209, p=0.002). The relatively higher proportion of good knowledge (81.8%) in the current study may reflect differences in setting, patient exposure to health information, or access to health services. This finding is even greater than the one provided by Basnet et al[10] where only 44.4% of adults had good knowledge of hypertension, which indicates the variation in knowledge across different populations and contexts. In addition, Rikmasari et al[2] found that knowledge on disease was one of the most important predictors of self-efficacy and self-management, while better self-management was related to controlled blood pressure and improved health-related quality of life. This is in accordance with the knowledge that knowledge not only facilitates greater understanding, but also indirectly influences better clinical outcomes through increased confidence and healthier day-to-day living. Nevertheless, this is not a consistent relationship, as Sari et al[9] reported that 53.9% of the patients had sufficient knowledge and 53% had a satisfying level of self-care; however, the relationship between the knowledge and self-care was not significant (p=0.099, r=0.155). This might highlight that what individuals know alone may not be enough, and that other influences, like motivation, social support, and self-efficacy can augment knowledge.

This interpretation is strengthened by Asmoro et al[8], who found that both knowledge and motivation were significantly related to blood pressure control, and by Kurt and Gurdogan[7], who demonstrated that self-management support improved knowledge, treatment adherence, self-care, and blood pressure outcomes. Therefore, while the high level of knowledge found in this study is encouraging, ongoing education and supportive interventions remain necessary to translate knowledge into sustained self-management behaviors among hypertensive patients.

In the present study self-management among hypertensive patients in this study was generally adequate but not yet optimal, because the majority had not reached the good category of self-care behavior. The predominance of fair self-care behavior suggests that most hypertensive patients were able to perform some components of self-management, but their practices may not have been sufficiently consistent to achieve a good level (Table 3). This pattern is in line with Safitri et al[5], who found that 85% of hypertensive patients had sufficient self-management, with weaknesses particularly in self-integration, self-regulation, and blood pressure monitoring. The present findings may also reflect the important role of knowledge in shaping self-management behavior, as several of the attached studies showed that better knowledge was associated with better self-care or self-management. Martin et al[6] reported a positive correlation between knowledge and hypertension self-management practice, while Gusty et al[4] found that knowledge was significantly related to adherence in weight management and physical activity. Similarly, Rikmasari et al[2] identified disease knowledge as the strongest factor associated with both self-efficacy and self-management and showed that patients with better self-management were more likely to have controlled blood pressure and better health-related quality of life. In addition, self-efficacy and motivation appear to strengthen self-management performance. Hadibrata et al[14] and 15 found a significant positive relationship between self-efficacy and self-care management, while Asmoro et al[8] showed that higher knowledge and motivation were significantly associated with better blood pressure outcomes. Supportive interventions also seem important, because Kurt and Gurdogan[7] demonstrated that self-management support significantly improved knowledge, treatment adherence, self-care management, and blood pressure control. Qualitative evidence from Nurarifah and Damayanti[3] further suggests that diet, physical activity, medication adherence, blood pressure checks, smoking behavior, and social support are key dimensions influencing hypertension self-management. Therefore, the high proportion of respondents in the fair category in this study may indicate that patients possess a basic level of self-care ability, but still require stronger education, motivation, self-efficacy enhancement, and family or health-worker support to improve their self-

management to a good level and ultimately achieve better blood pressure control.[1]

CONCLUSION

The hypertensive patients can only improve outcomes when there is greater education on hypertension, which must go both hand in hand with education about complications and blood pressure thresholds, and the provision of ongoing information and continuous counselling, motivation, behavioral support and follow-up. Strengthening these areas could assist patients to translate knowledge into routine practice for better daily lifestyle for achieving better blood pressure control and decreased risk of adverse events.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Hasanain Mahmood Abdoul Ameer
Drafting or Revising Critically:	Hasanain Mahmood Abdoul Ameer
Final Approval of version:	The above author
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Narrative Review

Artificial Intelligence-Powered Tools and Clinical Decision Support Systems for Prosthodontic Treatments

Muhammad Faheemuddin

ABSTRACT

Objective: To provide a narrative overview of the applications, performance, and limitations of artificial intelligence (AI) diagnostic tools and clinical decision support systems (CDSS) in prosthodontics, spanning diagnosis, treatment planning, prosthesis design, and prognosis.

Place and Duration of Study: This study was conducted at the Department of Prosthodontics and Implantology, College of Dentistry, King Faisal University, Al-Ahsa, Saudi Arabia, from September 2025 to March 2026.

Methods: A narrative review of the literature was conducted, synthesising evidence from published systematic reviews, scoping reviews, diagnostic-accuracy studies, and clinical reports. PubMed, Scopus, Web of Science, Google Scholar, and Semantic Scholar were searched for English-language articles published between 2021 and 2026 using combinations of the terms "artificial intelligence," "machine learning," "deep learning," "convolutional neural network," "clinical decision support system," "prosthodontics," "fixed/removable prosthodontics," "dental implant," "maxillofacial prosthesis," "tooth shade," "occlusion," and "digital smile design." The review followed the Introduction-Methods-Results-Discussion structure commonly used for narrative reviews.

Results: AI diagnostic tools demonstrated high accuracy in image-based recognition tasks relevant to prosthodontics, including implant-system identification on radiographs and classification of partially edentulous arches, while performance in objective shade matching, margin detection, and multivariable prognosis was more modest. AI-assisted methodologies in treatment planning and prosthesis design have demonstrated clinically promising accuracy and significant workflow efficiencies. However, it is noteworthy that the majority of evidence supporting these findings originates from retrospective or simulation-based studies. CDSS, including case-based and rule-based systems, improved the consistency and evidence-basis of clinical decision-making, but real-world adoption, maturity, and clinician uptake remained limited. Persistent barriers included a lack of prospective validation, limited data standardisation, limited model interpretability, and ethical and regulatory concerns.

Conclusion: AI diagnostic tools and CDSS show considerable potential to enhance diagnostic precision, treatment planning, and prosthesis design in prosthodontics. However, current evidence is largely early-stage, and prospective clinical validation, transparent models, and clear regulatory frameworks are required before routine clinical adoption. AI is best positioned as an adjunct that supports, rather than replaces, the prosthodontist.

Key Words: Artificial intelligence; Deep learning; Prosthodontics; Clinical decision support systems; Digital dentistry; Prosthesis design

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INTRODUCTION

Prosthodontics is the dental discipline concerned with the replacement of lost intraoral and extraoral structures. It also includes the restoration of partially or completely destroyed anatomical structures. This is achieved predominantly through prostheses, appliances, and restorations fabricated indirectly in the dental laboratory. This indirect, laboratory-based pathway distinguishes prosthodontics from restorative dentistry, in which restorations are fabricated directly at the chairside. The prosthodontic scope therefore includes fixed tooth- and implant-supported crowns and bridges, dental implants, removable complete and partial dentures, and maxillofacial prostheses. To deliver these predictably, the prosthodontist must diagnose and monitor tooth wear, occlusion, occlusal vertical dimension, facial esthetics, masticatory loading, and the broad range of patient-related factors that influence the design and longevity of a prosthesis.

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Artificial intelligence (AI) refers to computational systems that perform tasks ordinarily requiring human intelligence. Within AI, machine learning (ML) enables systems to learn statistical patterns from data, while deep learning (DL) particularly convolutional neural networks (CNNs) has proven exceptionally capable in analysing images such as radiographs and intraoral scans [1,3]. Over the past two decades, AI has expanded across all dental specialities, with the majority of applications image-based and focused on diagnosis and decision support [1,2,3]. Prosthodontics is especially amenable to AI because its modern workflows are increasingly digital and generate large volumes of image and three-dimensional data well suited to pattern-recognition models [2,4].

Two converging applications are reshaping the field: AI diagnostic tools, which interpret clinical and imaging data, and clinical decision support systems (CDSS), which provide clinicians with evidence-based recommendations at the point of care. This narrative review summarises the current applications and performance of AI diagnostic tools and CDSS across the prosthodontic workflow, and considers the principal challenges and future directions

METHODS

A narrative review was undertaken to allow a broad synthesis across heterogeneous study designs. PubMed, Scopus, Web of Science, Google Scholar, and Semantic Scholar were searched for English-language articles published between 2021 and 2026. Search terms combined AI-related vocabulary ("artificial intelligence," "machine learning," "deep learning," "convolutional neural network," "clinical decision support system") with prosthodontic vocabulary ("prosthodontics," "fixed prosthodontics," "removable prosthodontics," "dental implant," "maxillofacial prosthesis," "tooth shade," "occlusion," "occlusal vertical dimension," "digital smile design") using the Boolean operators AND and OR. Systematic reviews, scoping reviews, diagnostic-accuracy studies, and representative clinical and technique reports relevant to prosthodontic diagnosis, treatment planning, prosthesis design, prognosis, and decision support were prioritised. Articles concerning AI applications outside prosthodontics, or lacking a description of the AI model or its performance, were not emphasised.

AI Diagnostic Tools in Prosthodontics

Digital diagnosis and data capture

AI increasingly supports the diagnostic phase that precedes prosthetic treatment. Intraoral scanning and digital records can be analysed by AI to classify clinical situations and recognise anatomy. A CNN trained on intraoral occlusal images classified seven distinct maxillary prosthodontic scenarios, including dentate, partially edentulous, edentulous, and various maxillectomy presentations, with test accuracies of 0.90 to 0.95 and area-under-the-curve values of 0.98 to 1.00, as a first step toward an automated diagnosis and prosthesis-design system [13]. In implant prosthodontics, a deep-learning object-detection model identified implant brands on periapical radiographs with very high precision and recall and outperformed clinicians across experience levels, although the authors noted the absence of external validation as a key limitation [12]. Scoping evidence confirms that AI and other digital applications are being applied chiefly to diagnostics and treatment planning, with virtual treatment simulation among the most frequent diagnostic uses [9].

Occlusion, occlusal vertical dimension, and tooth wear

Accurate assessment of static and dynamic occlusion is central to prosthodontic diagnosis. Digital occlusion technologies, intraoral scanners, optical jaw-tracking systems incorporating AI algorithms, and computerised occlusal-analysis devices, now allow virtual articulation and analysis of occlusal contacts and mandibular motion, providing powerful diagnostic and design tools, though their accuracy for capturing static and dynamic occlusion requires further validation [10].

Tooth shade selection and facial esthetics

Objective shade determination and esthetic analysis are long-standing prosthodontic challenges. A systematic review found intraoral scanners highly repeatable for shade matching and superior to visual selection, while still recommending visual verification of results [11]. AI-driven digital smile design (DSD) has advanced rapidly: a scoping review reported that AI-generated smile designs did not differ significantly from manually created designs in esthetic perception, with three-dimensional designs more accurate than two-dimensional ones [19], and a systematic review and meta-analysis found AI-based DSD improved esthetic outcomes and yielded a pooled satisfaction prevalence of around 58%, albeit with moderate risk of bias [20].

AI in Treatment Planning, Prosthesis Design and Prognosis

Fixed and implant-supported treatment planning

AI has been applied extensively to implant planning. A systematic review with meta-analysis reported pooled accuracies of approximately 96% in the mandible and 83% in the maxilla for AI identification of edentulous areas and bone measurements on cone-beam computed tomography, while emphasising the need for further well-conducted studies [15]. A scoping review of AI in fixed tooth- and implant-supported prosthodontics found high accuracies (90–99.5%) for implant site detection and bone assessment, with prognostic models achieving over 90% accuracy in predicting implant

survival, but cautioned that most evidence remained early-stage and simulation-based [7].

Prosthesis design

AI is being used to automate and accelerate the design of indirect prostheses. A feasibility study using a generative adversarial network designed biomimetic single-molar restorations matched to natural teeth, demonstrating proof of concept while indicating that accuracy required further optimisation [16]. For removable prosthodontics, a CNN classified partially edentulous arches with accuracies of 99.5% (maxilla) and 99.7% (mandible) as the foundation of a removable partial denture (RPD) design system [17]. Systematic and narrative reviews confirm AI applications across automated restoration design, margin-line detection (accuracy approximately 90.6–97.4%), casting optimisation, prediction of facial changes in removable-prosthesis patients, and RPD design [6,14], and contemporary digital-workflow reviews report promising AI performance in shade selection, automated tooth-anatomy design, and removable-prosthesis design [8]. In maxillofacial prosthodontics, a case-based reasoning system predicted definitive obturator designs for maxillectomy patients, with confidence scores correlating strongly with clinician-judged correct designs and a high precision among the most similar retrieved cases.[18]

Prognosis and longevity

Beyond design, AI is being explored to predict prosthesis and implant outcomes. Reported prognostic models show promising but moderate performance, constrained by limited datasets and biological variability [7,8], consistent with the broader observation that long-term outcome prediction remains less mature than image-recognition tasks [5].

CLINICAL DECISION SUPPORT SYSTEMS (CDSS) IN PROSTHODONTICS

Clinical decision support systems are platforms that provide clinicians with patient-specific, evidence-based recommendations at the point of care, increasingly powered by AI [21,22]. Several prosthodontic applications already function as decision-support tools: case-based reasoning for obturator design [18] and rule-based and CNN-driven expert systems for RPD design and education effectively encode expert knowledge to guide treatment planning [6,17].

Evidence from medicine and dentistry indicates that AI-driven CDSS can improve diagnostic accuracy, optimise treatment selection, and reduce errors by delivering individualised recommendations [21]. A dental example demonstrated that integrating an electronic health record–based CDSS markedly increased appropriate clinical actions in routine practice [24]. Nevertheless, the maturity and real-world adoption of CDSS remain limited: a systematic review found that most CDSS rely on rule-based logic and rarely progress beyond an early maturity level, with the decision "choice" and "implementation" phases underrepresented [23], while reviews of CDSS more broadly highlight persistent challenges of data privacy, system integration, and clinician acceptance [22].

CHALLENGES, LIMITATIONS, AND ETHICAL CONSIDERATIONS

Despite strong technical performance, several barriers limit clinical translation. Most prosthodontic AI evidence derives from retrospective, simulation-based, or tightly controlled studies, and umbrella-level appraisal has found that many supporting systematic reviews are of low or critically low methodological quality, underscoring the scarcity of prospective validation [5]. Data limitations constrain model generalisability, and the "black-box" nature of deep-learning models challenges clinician trust and accountability. Ethical and regulatory concerns regarding bias, patient-data privacy, and liability remain unresolved and are recognised as critical to responsible adoption [25]. Workflow misalignment and limited clinician uptake further slow integration into daily prosthodontic practice [22,23].

FUTURE DIRECTIONS

The field is moving toward multimodal data integration, combining imaging with clinical and laboratory data, and toward generative, AI-assisted prosthesis design and individualised, prediction-based treatment planning [4,8]. Priorities for the coming years include the development of explainable and interpretable models, prospective clinical trials in diverse populations, robust regulatory frameworks addressing bias and privacy, and seamless point-of-care decision support embedded within existing digital workflows.

CONCLUSION

AI diagnostic tools and clinical decision support systems are increasingly capable across the prosthodontic workflow, delivering high accuracy in image-based diagnosis and recognition, clinically promising performance in implant planning and prosthesis design, and meaningful gains in efficiency and consistency of decision-making. However, performance in objective shade matching and long-term prognosis is more modest, and the overall evidence base is still maturing, with limited prospective validation and unresolved ethical, regulatory, and integration challenges. At present, AI is best regarded as a complementary adjunct that augments the prosthodontist's diagnostic and decision-making capacity rather than a substitute for clinical judgement, with its full potential contingent on rigorous validation and responsible implementation.

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Case Report

Cultural Beliefs Delaying Treatment of Temporal Lobe Epilepsy with Psychosis: A Case Report

Cultural Beliefs and Delayed Epilepsy Care

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ABSTRACT

Epilepsy is a chronic neurological disorder frequently associated with psychiatric comorbidity and substantial social stigma, particularly in low- and middle-income countries. Cultural interpretations of seizures as supernatural or spiritual phenomena may influence how patients and families understand the illness and may delay engagement with medical care. This report describes a patient with temporal lobe epilepsy whose treatment was significantly delayed because her family attributed the seizures to spiritual causes. A 30-year-old woman presented to a psychiatric outpatient clinic with behavioral changes including mood instability, suspiciousness, hallucinations, and progressive social withdrawal. Her first seizure occurred thirteen years earlier following eclampsia, and recurrent seizures continued without consistent neurological treatment. For many years the family sought help from a religious healer who performed spiritual rituals, as they believed the episodes were caused by spirit possession. During this period the patient experienced progressive seizures, cognitive decline, and the emergence of psychotic symptoms. Neuroimaging revealed bilateral mesial temporal sclerosis and electroencephalography demonstrated epileptogenic activity in the temporal regions. The patient received antipsychotic medication together with psychotherapy and psychoeducation directed toward both the patient and her family. This case illustrates how cultural beliefs surrounding epilepsy may contribute to prolonged delays in treatment and may allow neurological and psychiatric complications to develop. Clinicians working in culturally diverse settings should approach such beliefs with cultural sensitivity and dialogue rather than judgment, as respectful engagement with families may facilitate earlier acceptance of medical care and improve long term outcomes.

Key Words: Epilepsy; Temporal Lobe Epilepsy; Psychotic Disorders; Cultural Beliefs

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INTRODUCTION

Epilepsy is one of the most common neurological disorders worldwide and affects approximately fifty million people. A large proportion of these individuals live in low- and middle-income countries where access to neurological care remains limited.[1,2] In these settings the epilepsy treatment gap, defined as the proportion of people with epilepsy who require treatment but do not receive appropriate care, remains a major public health concern.[1,2] Untreated epilepsy is associated with increased risk of injury, cognitive impairment, psychiatric disorders, and reduced quality of life.[3]

In addition to structural barriers within healthcare systems, sociocultural factors play a major role in shaping how epilepsy is understood and managed. In many communities, seizures are interpreted through spiritual or supernatural frameworks and may be attributed to spirit possession, curses, or other non-medical causes. Such interpretations often lead families to seek help from religious or traditional healers before consulting medical professionals. While these practices reflect deeply rooted cultural values, reliance on them as the primary form of treatment may delay diagnosis and medical management.[4,5]

Psychiatric complications are common in individuals with epilepsy, particularly in patients with long standing or poorly controlled seizures. Psychosis associated with epilepsy has been reported in several clinical forms and may significantly impair social and occupational functioning.[6] The present case describes a patient with temporal lobe epilepsy whose treatment was delayed for more than a decade due to cultural interpretations of her illness, ultimately resulting in the development of psychotic symptoms. The case

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highlights the importance of culturally sensitive communication in bridging the gap between traditional beliefs and evidence based medical care.

Case Presentation: A 30-year-old woman was referred to the psychiatric outpatient clinic by a neurologist because of progressive behavioral changes and suspected psychotic symptoms. She had experienced recurrent seizures for approximately thirteen years. Her first seizure occurred in 2011 following an episode of eclampsia that required admission to an intensive care unit for twenty-eight days because of decreased consciousness. After discharge her level of consciousness gradually improved, although she remained confused and socially withdrawn.

In the years following this initial event the patient continued to experience recurrent seizures with varying clinical presentations. Some episodes involved sudden loss of consciousness accompanied by limb rigidity, while others were characterized by agitation, abnormal movements, and incoherent speech. Episodes could last from several minutes to approximately thirty minutes and were often triggered by emotional stress. The most recent seizure occurred one week before presentation and involved rigidity of the head and extremities followed by transient loss of consciousness. The patient had no recollection of the episode afterward.

Soon after the onset of seizures the patient's family attributed the condition to spiritual causes. The family believed that the patient had been affected by supernatural forces and repeatedly sought help from a religious healer who performed a spiritual healing ritual (incantation) and provided blessed water for treatment. The healer suggested that the patient had been used as a sacrificial offering in a ritual associated with wealth seeking practices. Because of this belief the family relocated their home several times in an attempt to escape spiritual influence. During this period the patient did not receive consistent neurological care.

Over time the patient began to develop significant behavioral and emotional changes. During the year before psychiatric evaluation, she experienced persistent sadness, irritability, and episodes of anger directed toward family members. She became socially withdrawn and spent most of her time alone in her room. She also reported suspiciousness toward others and frequently accused people of intending to harm her. Hallucinations were present, including visual experiences of an unfamiliar male figure and auditory perceptions of a voice commenting on her actions.

The patient also demonstrated cognitive impairment. She reported difficulty remembering recent events and often forgot daily activities. This impairment contributed to poor adherence to medication and increased distrust toward family members who attempted to assist with treatment. During clinical interview she appeared confused at times and required repeated questions to maintain focus. Her mood fluctuated rapidly between sadness and irritability. Clinical events over the course of illness are summarized in Table 1.

Magnetic resonance imaging with contrast revealed bilateral mesial temporal sclerosis. Electroencephalography demonstrated intermittent slow activity in the left temporo occipital region as well as sharp waves in the right temporal and left anterior temporal regions, findings consistent with epileptogenic activity. Psychiatric examination revealed labile affect, paranoid delusions, hallucinations, impaired volition, and significant decline in social and occupational functioning.

The patient was treated with haloperidol 0.5 mg twice daily to address psychotic symptoms. In addition to pharmacological treatment, supportive psychotherapy and psychoeducation were provided to both the patient and her family. Educational sessions focused on improving understanding of epilepsy, addressing beliefs regarding supernatural causation, and encouraging adherence to medical treatment.

DISCUSSION

Psychiatric comorbidities are common in individuals with epilepsy and may significantly influence prognosis and quality of life. Mood disorders and anxiety disorders are among the most frequently reported conditions, although psychotic disorders can also occur. Psychosis associated with epilepsy may appear in several forms, including postictal psychosis, interictal psychosis, or psychotic disorder related to structural brain abnormalities. The risk of psychosis appears to increase in patients with long standing epilepsy and temporal lobe involvement.[2,6]

In the present case the patient developed psychotic symptoms including hallucinations, paranoid delusions, and behavioral disturbances after many years of poorly controlled seizures. Neuroimaging findings of bilateral mesial temporal sclerosis further support the association between temporal lobe pathology and psychiatric manifestations. Early recognition and treatment of epilepsy may reduce the likelihood of such complications.

Cultural beliefs surrounding epilepsy can strongly influence health seeking behavior. In several societies seizures are interpreted as manifestations of supernatural forces or spirit possession. Such interpretations may encourage families to seek help from traditional healers rather than medical professionals. While traditional healing practices can provide emotional and spiritual support within communities, exclusive reliance on these approaches may delay diagnosis and treatment.[4,5] Studies from different regions of Indonesia have documented persistent stigma toward epilepsy. Individuals with epilepsy may face discrimination in education, employment, and marriage. Families sometimes

conceal the diagnosis because of fear of social exclusion. These social pressures may reinforce cultural interpretations of seizures and discourage early medical evaluation.[7,8]

The present case illustrates how such beliefs can lead to prolonged treatment delays. For more than a decade the patient's seizures were primarily managed through spiritual rituals rather than neurological care. During this time seizures continued and psychiatric symptoms gradually emerged. The eventual referral to medical services occurred only after the frequency of seizures increased and behavioral changes became difficult for the family to manage.

Improving epilepsy care in culturally diverse settings requires approaches that acknowledge local beliefs while promoting evidence-based treatment. Culturally sensitive communication is an essential component of this process. Healthcare providers should engage patients and families with empathy, avoid dismissing traditional beliefs, and provide clear explanations regarding the biological mechanisms of epilepsy. Collaboration with community leaders and religious figures may also facilitate acceptance of medical treatment.[4,5]

CONCLUSION

This case demonstrates how cultural interpretations of epilepsy as a supernatural phenomenon may delay medical treatment and contribute to the development of psychiatric complications. In communities where epilepsy is strongly associated with spiritual beliefs, culturally sensitive communication and family education are essential for improving treatment adherence and reducing stigma. Early engagement with both patients and families may help bridge the gap between traditional beliefs and modern medical care, ultimately improving outcomes for individuals living with epilepsy.

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