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Business Manager: Nayyar Zia Ch.

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Times University, Multan.
Mobile No. 0312-9233333 Email: drmabbas786@gmail.com

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Editorial**Arthritis – A Global Burden****Prof. Dr. Azhar Masud Bhatti**

Editor-in-Chief

Introduction

Arthritis is derived from the Greek term “disease of the joints.” It is defined as an acute or chronic joint inflammation that often co-exists with pain and structural damage.¹ Arthritis is not synonymous with arthralgia, which refers to pain localized to a joint, regardless of the origin of the pain (which may or may not be due to joint inflammation).

Arthritis is a frequent illness that affects your joints. Inflammation and discomfort may result, making it challenging to move or maintain activity. Inflammation and injury to the joints, surrounding tissues, and other connective tissues are symptoms of more than 100 illnesses collectively referred to as arthritis.

The tendons and ligaments around the joint, however, may also be impacted by inflammation. A person's ability to carry out daily chores may be hampered by the symptoms, which may appear gradually or unexpectedly.

Types of Arthritis

There are over a hundred different types of arthritis. Arthritis may generally be divided into the following categories:

Degenerative or Mechanical Arthritis:

Degenerative or Mechanical Arthritis primarily entail harm to the cartilage that surrounds the ends of the bones. The supple, slippery cartilage's primary function is to facilitate easy gliding and motion in the joints. This kind of arthritis causes the cartilage to weaken and roughen.

The body starts remodelling the bone to restore stability to make up for cartilage loss and changes in joint function. Osteophytes, which are unwanted bone growths, may form as a result. The joint may develop a misalignment. This ailment is generally referred to as osteoarthritis. Osteoarthritis may also develop as a result of joint injuries, such as a fracture, or joint inflammation.

Inflammatory Arthritis:

A typical aspect of the body's healing process is inflammation. As a preventative measure against germs and viruses or as a reaction to wounds like burns, it frequently occurs. On the other hand, patients who have inflammatory arthritis experience inflammation that is not immediately obvious.

Damaged inflammation that does not naturally develop in response to injury or illness defines inflammatory arthritis. The damage caused by this sort of inflammation, which results in discomfort, stiffness, and swelling, is counterproductive and harmful to the afflicted joints.

Multiple joints may be affected by inflammatory arthritis, and the inflammation can harm both the bone

under the skin and the joint's surface which also rheumatoid arthritis causes. Following are some examples of inflammatory arthritis:

- ? Rheumatoid arthritis
- ? Ankylosing spondylitis and psoriatic arthritis.

Childhood Arthritis

Numerous forms of arthritis may be mentioned here. The most typical kind of arthritis is juvenile idiopathic arthritis (JIA), also known as juvenile rheumatoid arthritis (JRA). There is no treatment for childhood arthritis, which can permanently damage joints. Remission, on the other hand, is conceivable and occurs when the illness is dormant. Immune system issues might be at blame.

Chronic Connective Tissue Disease (CTD)

Supporting, uniting, or dividing other bodily tissues and organs are the functions of connective tissues. Among them are cartilage, tendons, and ligaments. Inflammation and joint discomfort are symptoms of CTD. In addition to the skin, muscles, lungs, and kidneys, inflammation may also develop in other tissues, such as the lungs and muscles. CTD examples include

- ? Lupus, or SLE,
- ? Systemic sclerosis, also known as scleroderma
- ? dermatomyositis
- ? Sjogren's

Infectious Arthritis

Inflammation in joints can occasionally be brought on by bacteria, viruses, or fungi. Joint-infecting microbes include:

- ? Shigella and salmonella, which are transmitted through tainted or contaminated food
- ? Sexually transmitted illnesses including gonorrhoea and chlamydia (STDs)
- ? Hepatitis C, a blood-to-blood infection that can be contracted via receiving blood transfusions or using shared needles,

Antibiotics or other antimicrobial drugs might be prescribed by a doctor to treat a joint infection. On the other hand, if the infection has continued for a while, arthritis may occasionally turn chronic and the damage to the joints may be irreparable.

Metabolic Arthritis

When the body breaks down purine-containing compounds, urate is produced as a chemical. Human cells and several dietary sources contain purines. The majority of uric acid dissolves in the blood and is carried to the kidneys. Urine is produced thereafter, and it leaves the body. Some people have high amounts of uric acid because either their bodies naturally make

more than they require, or because their bodies cannot remove the uric acid rapidly enough.

Some individuals have a buildup of uric acid that results in the formation of needle-like crystals in the joint, which can cause rapid spikes in their level of acute joint pain or a gout attack. If the amounts of uric acid are not lowered, gout can either develop into a chronic condition or occur in episodes.

The big toe and hands are typical joints that are affected, along with a few other smaller joints. Typically, it has an impact on the extremities. According to one idea, uric acid crystals grow in joints that are colder and further from the body's core heat.

Septic Arthritis

An infection, either bacterial or fungal, can cause septic arthritis, an inflammation of the joints. Hip and knee joints are frequently impacted. It normally affects 2–6 people out of 100,000. A joint may become infected with a microbe directly through an injury or surgery, or it may become infected when bacteria or other disease-causing germs travel to a joint through the blood.

Most cases of acute septic arthritis are brought on by bacteria like *Streptococcus*, *Staphylococcus*, or *Neisseria gonorrhoeae*. Chronic septic arthritis is brought on by microbes like *Candida albicans* and *Mycobacterium tuberculosis*. Similar to acute septic arthritis, this is less frequent. The likelihood of getting septic arthritis is increased by the following conditions:

- ? Joint injury or illness currently present
- ? Inserts for artificial joints
- ? Infected with microorganisms somewhere else in the body
- ? Bacterial presence in the blood
- ? Chronic sickness or illness (such as diabetes, RA, and sickle cell disease)
- ? Drug usage by injection or intravenous (IV)
- ? Medicines that lower immune function
- ? Recently injured joint
- ? Recent arthroscopy or other surgery on a joint
- ? Disorders that reduce immunity, such as HIV
- ? Diabetes
- ? Older age

Common Symptoms of Arthritis

General symptoms include:

- ? Joint pain
- ? Limited ability to move the affected joint
- ? Redness
- ? Stiffness
- ? Swelling
- ? Warmth

Symptoms of Arthritis according to Types

Two of the most common osteoarthritis (OA) and rheumatoid arthritis (RA).

The different types of arthritis have the same general symptoms, like joint pain and stiffness, but the affected joints and other symptoms differ.

Osteoarthritis

OA is a disease that usually affects the hands, hips, and knees. Similar to other types of arthritis, OA symptoms include:

- ? Instability when walking
- ? Loss of movement
- ? Pain
- ? Stiffness

Symptoms are usually worse in the morning or upon standing up after sitting for a while. The pain usually improves within 30 minutes of movement.

Some people with OA may develop cysts (fluid-filled pockets) behind the knee. Swelling in the knee typically triggers the formation of cysts.

Rheumatoid Arthritis

RA is an autoimmune disorder, meaning the immune system attacks healthy cells. It can cause bone erosion and cartilage changes.²

These changes can lead to joint stiffness that lasts longer than 30 minutes and pain while moving and at rest. Symptoms often develop in the same joint on both sides of the body.

RA can also cause symptoms like:

- ? Fever
- ? Joints that are tender and warm to the touch
- ? Loss of appetite
- ? Nodules (round, hardened lumps) that may limit the range of motion and push your joints out of alignment
- ? Swelling, usually in your wrist, hands, and feet
- ? Tiredness

RA can also affect other organs, including the eyes, blood, and nerves, if it is untreated. It may cause scarring on the lungs that makes it hard to breathe.

Psoriatic Arthritis

Psoriatic arthritis (PsA) is an inflammatory disease that affects your joints and skin. It mainly affects the joints in your hands, wrists, and feet, and can also affect the elbows, spine, and other joints. You may have swelling and discomfort in these areas.³

PsA also causes changes to your skin, similar to psoriasis. You may have raised red, dry, and itchy areas of skin called plaques. They usually develop on the elbows or knees. PsA can also affect your nails.⁵²

PsA is a complex disease that causes widespread symptoms, such as:

- ? Changes to your bowel movements
- ? Depression or anxiety
- ? Difficulty sleeping
- ? Eye swelling
- ? Fatigue
- ? Hypertension (high blood pressure)

Ankylosing Spondylitis

Ankylosing spondylitis (AS) is an inflammatory disease that primarily affects the spine. It can also impact large joints, such as your shoulders and knees, and the joints in your hands and feet.⁴

Symptoms of AS may include:⁵

- ? Anxiety or depression
- ? Decreased mobility
- ? Hunched spine, which can make it hard to breathe
- ? Pain or stiffness in the affected areas, especially in the morning
- ? Trouble sleeping

In rare cases, AS may cause swollen fingers. Some people may develop osteoporosis (weak and brittle bones) in the spine.

Gout

Gout is a form of arthritis caused by the formation of uric acid crystals inside the joint. Alcohol, meat, seafood, and other foods rich in the chemical compound purine can trigger gout flares.

The most commonly affected joint is the big toe. The rest of your foot, ankle, and leg can also develop symptoms. You may have intense pain and swelling in these areas.

Some people may develop a tophus over the affected joint. This hardened deposit under the skin typically appears on the fingers or around the ears.

Etiology

The etiology of arthritis varies with the type of arthritis. In osteoarthritis, the major contributory factors include advancing age, female sex, joint trauma, and obesity. Some genetic factors have been described such as mutations in genes encoding types II, IV, V, and VI collagens.^{6,7}

Rheumatoid arthritis (RA), on the other hand, is an autoimmune systemic inflammatory disorder.

In Gout, prolonged hyperuricemia leads to uric acid deposition in joints, which then leads to joint inflammation. There are several genetic mutations that can cause hyperuricemia, although this accounts for less than 10% of gout. The majority of patients with gout are under-excretors i.e. they are not able to get rid of all the uric acid that is produced in them as a result of endogenous or exogenous purine metabolism. Male sex, advancing age, chronic kidney disease, alcoholism, and certain drugs such as the diuretics are additional risk factors for hyperuricemia and gout.

Septic arthritis is acute arthritis that is rare in the general population, but patients with pre-existing risk factors such as immunodeficiency, advancing age, diabetes mellitus, prosthetic joints, rheumatoid arthritis, and intravenous drug abuse are at a higher risk.

Arthritis can frequently be seen in patients with other autoimmune diseases and is one of the most common clinical features in patients with systemic lupus erythematosus (SLE). Other diseases frequently associated with arthritis include inflammatory bowel disease, psoriasis, celiac disease, Sjogren syndrome, systemic sclerosis, dermatomyositis, mixed connective tissue disease (MCTD), etc.

Pathophysiology

Osteoarthritis is characterized by a degenerative cascade of progressive cartilage loss which leads to bone damage. Characteristic findings include subchondral cysts, osteophytes, and subchondral plate thickening. Interleukin-6, monokines, interferon-induced protein-10, and macrophage chemotactic protein induce proteolytic enzymes such as matrix metalloproteinases, serine proteases, and cysteine proteinases and result in the degradation of joint collagen.⁸ Calcification of the surrounding articular cartilage reduces the thickness of and eventually destroys the cartilaginous matrix. Old age also is associated with a decrement in chondrocyte function, enhancing susceptibility to osteoarthritic degeneration.

Symptoms of rheumatoid arthritis are typically more severe than those of osteoarthritis. Rheumatoid arthritis is a systemic and chronic inflammatory state caused by an autoimmune response to an environmental trigger.

Septic arthritis is typically an inflammatory response to a monobacterial infection. Bacterial entry into the synovial fluid triggers a release of cytokines, chemokines, and proteases that degrade cartilage and trigger hyperplasia of the synovial membrane. Toxins produced by bacteria play an additional destructive role within the joint space itself.

Epidemiology / Prevalence of Arthritis

According to WHO,

- ? In 2019, about 528 million people worldwide were living with osteoarthritis; an increase of 113% since 1990.
- ? About 73% of people living with osteoarthritis are older than 55 years, and 60% are female.
- ? With a prevalence of 365 million, the knee is the most frequently affected joint, followed by the hip and the hand.
- ? 344 million people living with osteoarthritis experience severity levels (moderate or severe) that could benefit from rehabilitation.
- ? With ageing populations and increasing rates of obesity and injury, the prevalence of osteoarthritis is expected to continue to increase globally.

Prevalence of Osteoarthritis in Pakistan rose from 2.85 million in 1990 to 8.49 million in 2021, with a 17.9% increase in age-standardized cases, disproportionately affecting women and urban areas. The prevalence of knee osteoarthritis contributes to over 61% of new cases, with rates significantly higher in women and in some studies showing a 18.13% overall prevalence with higher rates in rural regions (70.11%).

Over one-third of the American population has arthritis on imaging, and this number is bound to increase with the mean population age,⁹ of the arthritides, osteoarthritis is most prevalent.

Between 19% and 30% of adults over the age of 45 years have knee osteoarthritis, 27% have osteoarthritis of the hand, and 27% have osteoarthritis of the hip. It is estimated that 40% of men and 47% of women will develop osteoarthritis in their lifetime, with the incidence increasing to 60% if they have a body mass index greater than 30.13.

Gout is the most common inflammatory arthritis in the United States, affecting more than 8 million individuals in the United States with a prevalence of 3.9%,¹⁰ with a prevalence of more than 9% in individuals over 60 years of age.

Rheumatoid arthritis is found in approximately 1% of Caucasians, with females being affected more frequently than males (lifetime risk of 3.6% in women vs. 1.7% in men).¹¹

Septic arthritis is typically caused by bacterial seeding of an already arthritic joint via the hematogenous spread, most often from skin or urinary tract infection. Septic arthritis has a prevalence of 0.01% in the general population and 0.7% in patients with rheumatoid arthritis.

Evaluation

History and physical examination plays a crucial role in the evaluation of arthritis and determining the type of arthritis, and differentiating symptoms from non-articular etiologies.

Usual symptoms of arthritis are pain, swelling, loss of function, stiffness, deformity, weakness, and instability. They may also be accompanied by fatigue, sleep disturbance, emotional lability and symptoms of the underlying systemic illness.

Physical examination is the most important tool in assessing arthritis and arthralgias. Inflammatory arthritis is associated with tenderness, swelling, effusion, erythema and warmth.

The next step shall be assessing the arthritis onset, the number of joints involved, symmetry, distribution, and pattern.

Laboratory and radiographic evaluation can assist in the diagnosis and grading of the severity of an arthritic condition.

Inflammatory arthritides are associated with an elevation in markers of inflammation (ESR and CRP). Anemia of chronic disease is common. Leukocytosis can be seen in septic arthritis as well as gout, pseudogout and Adult-onset Still disease, while leukopenia and thrombocytopenia can be seen in RA and SLE-associated arthritis. Serum uric acid may be elevated in patients with gout, although this shall not be the sole diagnostic criterion. Serologies such as rheumatoid factor, anti-citrullinated peptide antibodies, Anti-Nuclear antibodies, and more specific autoantibodies shall be performed when appropriately indicated to assist diagnosis.¹²

Plain radiographs shall be the initial imaging modality. Joint space narrowing, osteophytes and effusion are common findings in osteoarthritis.

If radiographs are non-diagnostic, further imaging can be considered. MRI is a very helpful tool and can assist in evaluating the presence or absence of synovitis, erosions, sacroiliitis with a much higher sensitivity than X-rays.

The synovial fluid examination is one of the most important tests especially for the initial diagnosis of arthritis.

A synovial biopsy is rarely performed but can be considered especially in cases of monoarthritis where other modalities have failed to provide a diagnosis.

Treatment / Management

The goals of arthritis symptoms and treatment include managing pain, reducing joint deterioration, and enhancing or maintaining function and quality of life.

Medication

The kind of arthritis will determine the medication. Typical medications include

Analgesics: They ease suffering. They do not, however, affect inflammation.

Anti-inflammatory medications that are not steroidal: These lessen discomfort as well as inflammation. Some NSAIDs are offered as patches, gels, or lotions that can be administered directly to the affected joints.

Counterirritants: The compound that gives hot peppers their fiery flavour, capsaicin, is included in several lotions and ointments. These can regulate pain signals from the joint and minimise discomfort when applied to the skin over an uncomfortable joint.

Antirheumatic medications that treat disease: The immune system's onslaught on the joints is slowed or stopped with DMARDs, which are used to treat RA.

Biologics: These medications have undergone genetic engineering and are designed to target different protein molecules involved in the immune response.

Corticosteroids: Inflammation is reduced and the immune system is suppressed by prednisone and cortisone.

Natural Solutions

People with arthritis can improve their general health and lessen the intensity of their symptoms by eating a healthy, balanced diet, getting enough exercise.

Natural Solutions are:

Diet: Consuming certain foods may assist to lessen inflammation. These meals provide several nutrients that are beneficial for joint health and can reduce joint inflammation.

- ? Fatty Fish
- ? Seeds and nuts
- ? Veggies and fruits
- ? Beans
- ? Olive oil

Polyunsaturated fatty acids, Berries, Cherries, Wholegrains, Vitamin D, E, Vit. B12 and Folate

Physical activity and treatment: Physical therapy is frequently advised by medical professionals to help

arthritis sufferers overcome certain difficulties and lessen movement restrictions. The following types of physical treatment might be suggested:

Physical therapy: Exercises that are customised to the illness and each person's demands are occasionally paired with pain-relieving therapies like cold or hot packs and massage.

Occupational therapy: Useful advice on managing daily duties, selecting specialised aids and equipment, preventing joints from additional injury, and controlling tiredness

Additionally, even though those who have arthritis may temporarily feel more pain when they start exercising, regular exercise can successfully lessen long-term symptoms.

Surgery

There may be a need for various surgical procedures on the damaged joints depending on the type of arthritis. Depending on the severity of a person's symptoms, and if previous therapies have been effective, it could vary. There are several arthritic surgery alternatives

Types of Surgery

- ? Synovectomy
- ? Complete replacement of joints
- ? Osteotomy
- ? Synovial fusion

Prevention

Arthritis patients may avoid the following:

Sugary treats
 Refined carbohydrate
 Food and drinks that are highly processed
 Drinks with added sugars
 Purines
 Salty foods
 Red meat
 Alcohol
 Fats and fried foods
 Avoid smoking

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Detection of Escherichia Coli Strains among Bacteriuria of Diabetic and Non-Diabetic patients, With Their Antibiotic Resistant and Hematuria Containing Enterotoxin (Sea) Gene

Zainab S. Baqer and Munaff J. Abd Al-Abbas

ABSTRACT

Objective: Detection of Escherichia coli Strains among bacteriuria of diabetic and non-diabetic patients

Study Design: Descriptive (cross-sectional) study

Place and Duration of Study: This study was conducted at the Department of Biology, College of Science, University of Basrah, Basrah, Iraq from 2nd March 2024 to 3rd April 2025.

Methods: Out of 42 Gram-positive and Gram-negative bacterial isolates from diabetic and non-diabetic patients, across 26 antibiotics, 89 pattern results were observed versus 83. Three Escherichia coli isolates that shared identical biochemical profiles and antibiotic resistance patterns were found to be genetically different strains using random amplified polymorphic DNA – polymerase chain reaction.

Results: The 22 bacteria isolated from diabetic patients showed that 17 (77%) had the Seagene, with 17 (100%) hematuria samples, compared to 13 (65%) with the Sea gene, with 8 (61%) hematuria among 20 bacteriuria samples from non-diabetic patients.

Conclusion: The bacteriuria from diabetic patients exhibited high resistance for Ticarcillin, Piperacillin and Ciprofloxacin antibiotics revealing a significant difference from that bacteriuria of non-diabetics' patients. There is a relationship between the presence of enterotoxin and hematuria.

Key Words: Urinary tract infection, diabetes, Sea gene, Hematuria, Antibiotic resistance

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INTRODUCTION

Urinary tract infections (UTIs) are more frequent and severe in diabetic patients due to impaired immunity, poor glycemic control, and bladder dysfunction. E.coli is the predominant pathogen, thriving in glucose-rich urine and causing recurrent infections, particularly in females.¹ Other uropathogens, including Klebsiella, Proteus, and Pseudomonas, are also common and often exhibit increased antimicrobial resistance.²

Automated identification and antimicrobial susceptibility testing using the VITEK 2 Compact system enables rapid and accurate detection through metabolic analysis with Gram-specific AST cards.³

Department of Biology, College of Science, University of Basrah, Basrah, Iraq.

Correspondence: Zainba S. Baqer, Department of Biology, College of Science, University of Basrah, Basrah, Iraq.
Contact No: +9647755886756
Email: zainabsadeq97@gmail.com

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UTIs in diabetic patients pose a clinical challenge because common pathogens such as E. coli and Klebsiella pneumoniae frequently show resistance to widely used antibiotics, including third-generation cephalosporins and fluoroquinolones. Compared with non-diabetics, diabetic patients harbor more diverse microbial flora, including Proteus, Pseudomonas, and Enterococcus species, driven by glycosuria, immune dysfunction, and repeated antibiotic exposure.⁴ Random Amplified Polymorphic DNA analysis is widely used for strain differentiation, epidemiological tracing, and susceptibility pattern discrimination, enabling detection of genetic variation without prior genomic knowledge.⁵ In addition, toxin production—particularly exotoxins and enterotoxins - plays a key role in bacteriuria pathogenesis in diabetic patients by damaging host tissues and disrupting immune responses. Common uropathogens, including E. coli and Enterobacter spp, may harbor genes such as the Seagene, encoding staphylococcal enterotoxins. PCR-based detection of these toxin genes provides valuable diagnostic and epidemiological insights.⁶

METHODS

This descriptive (cross-sectional) study was conducted at College of Science, University of Basrah from 2nd March 2024 to 3rd April 2025 vide letter. 3/6/95 dated 5th October 2022. Forty-two bacteriuria isolates as Gram-positive and Gram-negative were identified by 16S rRNA gene sequencing. The data were analyzed for comparing among isolates from diabetic and non-diabetic patients enabling the detection of biochemical pattern and specific antibiotic resistance trends in each group.

Three *E. coli* isolates (No. 26, 38 and 42) that showed the identical biochemical patterns and antibiotic resistance were further examined to understand their genetic relationship. RAPD technique was used. The primers, PCR reagents and conditions for amplification followed the method described by Zare et al.⁷ The RAPD-PCR reaction was prepared in a total volume of 25 µl consisting of 12 µl Go Taq green master mix (Promega, USA), 4 µl DNA template, 2 µl RAPD primer (Bioneer, Korea) and 7 µl nuclease-free water (Bioneer, Korea). The PCR program included the following thermal cycling conditions: an initial denaturation at 94°C for 5 minutes (1 cycle), followed by 35 cycles of denaturation at 94°C for 1 minute, annealing at 42°C for 1 minute and extension at 72°C for 2 minutes. A final extension was performed at 72°C for 5 minutes (1 cycle). The primer used for RAPD was 5'-AGAGGGCACA-3' (Macrogen, Southkorea). Detection of RAPD products using agarose gel electrophoresis was performed using 2% agarose in 100 ml of TBE buffer (Bioneer, Korea), with the addition of 0.5 µl of ethidium bromide (Biobasic, Canada). A 100 bp DNA ladder (Promega, USA) was used as a molecular marker to detect the banding patterns of *E. coli* strains under UV illumination using a transilluminator (Wisd, Korea). The distances between the RAPD bands of all isolates were calculated based on the DNA ladder using Microsoft Word. The data were then analyzed using the Unweighted Pair Group Method with Arithmetic Mean (UPGMA) to construct a dendrogram representing the genetic relationships among isolates.⁸

RESULTS

The isolates were further categorized into resistant (R) and sensitive (S). The Antibiotic resistance in Gr-ve bacteria showed the ability of 50 isolates resistant to 14 different antibiotics while 118 isolates were sensitive to them in diabetics group, while 64 versus 118 in non-diabetics, respectively, with significant differences ($P \leq 0.05$). In Gr+ve bacteria 39 isolates were resistant to 12 different antibiotics versus 93 sensitive in diabetic, while in non-diabetic, 53 versus 19 respectively, with significant differences ($P \leq 0.05$). Generally, the study found that both Gr+ve and Gr-ve

bacterial isolates from diabetic showed resistance in 89 isolates to 26 different types of antibiotics versus 211 isolates were sensitive.

Table No. 1: The antibiotic susceptibility of different bacterial species in diabetic and non-diabetic cases

Type of bacteria	Antibiotic	Diabetic		Non-diabetic	
		S	R	S	R
Gram negative bacteria (n=25)					
Escherichia coli (n=8)	TIC	1	11	-	13
Escherichia fergusonii (n=4)	TIC/CLA	8	4	10	3
Klebsiella pneumoniae (n=4)	PIP	2	10	-	13
Citrobacter (n=1)	PIP/TAZ	10	2	10	3
Enterobacter hormaechei (n=2)	CAZ	6	6	8	5
Enterobacter bugandensis(n=1)	FEP	11	1	11	2
Raoultella ornithinelytica (n=2)	IPM	11	1	13	-
	MEM	11	1	13	-
Pluralibacterge	AMK	12	-	13	-
Enterobacter cloacae (n=1)	GEN	10	2	8	5
	TOB	10	2	8	5
	CIP	9	3	6	7
	COL	8	4	13	-
	SXT	9	3	5	8
Total (24)		118*	50	118	64
Gram positive bacteria (n=17)					
Pseudomonas fragi (n=1)	BenzPen	5	6	2	4
Staphylococcus aureus (n=2)	OXA	6	5	2	4
Staphylococcus hominis (n=3)	MOX	8	3	5	1
Bacillus safensis (n=2)	ERY	8	3	4	2
	CLI	10	1	6	0
Bacillus velezensis (n=1)	LNZ	9	2	5	1
Coryne-bacterium aurimucosum (n=2)	TEC	9	2	5	1
Kocuria Rhizophila (n=1)	VAN	9	2	5	1
Staphylococcus saprophyticus	TET	7	4	5	1
Staphylococcus epidermidis (n=1)	TGC	9	2	5	1
Lachnospiraceae bacterium (n=1)	FUS	4	7	4	2
Candidatus Erwinia (n=1)**	RIF	9	2	5	1
Total (10)		93*	39	53*	19
Total (42)		211*	89	171*	83

* $P \leq 0.05$

***Candidatus Erwinia* was recorded as Gr+ve of antibiotic susceptibility test only

Table No. 2: Comparison of biochemical test for E. coli isolates

Test	No. Escherichia coli isolates							
	Healthy					Diabetics		
	6	15	26	33	38	41	42	51
ADO	-	-	-	-	-	+	-	-
IARL	-	-	-	-	-	-	-	-
dCEL	-	-	-	+	-	+	-	-
BGAL	+	-	+	-	+	+	+	+
H ₂ S	-	-	-	-	-	-	-	-
AGLU	-	-	-	-	-	-	-	-
BGLU	-	-	-	+	-	+	-	-
dMAL	+	-	+	-	+	+	+	+
dMAN	+	-	+	+	+	+	+	+
dMNE	+	-	+	+	+	+	+	+
BXYL	-	-	-	-	-	-	-	-
LIP	-	-	-	-	-	-	-	-
PLE	-	-	-	-	-	+	-	-
URE	-	-	-	-	-	-	-	-
dSOR	-	-	+	+	+	+	+	+
SAC	+	-	+	+	+	+	+	+
dTAG	-	-	-	-	-	-	-	-
dTRE	+	-	+	+	+	+	+	+
MNT	-	-	-	-	-	-	-	-
ILATK	+	+	-	-	-	+	-	+
AGAL	+	-	+	-	+	+	+	+
Total	8 (38%)	1 (4.7%)	8 (38%)	7 (33.3%)	8 (38%)	13(61.9%)	8 (38%)	9(42.8%)

Table No. 3: Distance matrix for bacterial strains (26, 38 and 42) based on RAPD analysis

Strains	26	42	38	1C*
26	-	138.448	102.711	0.000
42		-	103.450	138.448
38			-	102.711
1*				-

*Out group

Table No. 4: Frequency of Sea gene among different bacterial species

Bacteria species	Total	Diabetics (n = 22)			Non-diabetics (n=20)		
		No.	Sea	Haematuria	No.	Sea	Haematuria
Escherichia coli	8	3	3 (100%)	3 (100%)	5	3 (60%)	2 (40%)
Klebsiella pneumoniae	4	2	1 (50%)	2 (100%)	2	1 (50%)	-
Escherichia fergusonii	4	2	2 (100%)	2 (100%)	2	2 (100%)	1 (50%)
Staphylococcus hominis	3	1	1 (100%)	1 (100%)	2	1 (50%)	2 (100%)
Enterobacter hormaechei	2	1	1 (100%)	-	1	1 (100%)	1 (100%)
Raoultella ornithinolytica	2	1	1 (100%)	-	1	-	-
Corynebacterium aurimucosum	2	-	-	-	2	2 (100%)	1 (50%)
Bacillus safensis	2	2	1 (50%)	1 (50%)	-	-	-
Staphylococcus aureus	2	1	1 (50%)	1 (100%)	1	-	-
Kocuria rhizophila	1	1	1 (100%)	-	0	-	-
Bacillus velezensis	1	-	-	-	1	1 (100%)	1 (100%)
Enterobacter cloacae	1	-	-	-	1	1 (100%)	-
Mammaliococcus vitulinus	1	1	1 (100%)	1 (100%)	-	-	-
Candidatus Erwinia	1	-	-	-	1	-	-
Enterobacter bugandensis	1	-	-	1 (100%)	1	1 (100%)	1 (100%)
Staphylococcus saprophyticus	1	1	-	1 (100%)	-	-	-
Lachnospiraceae bacterium	1	1	-	1 (100%)	-	-	-
Staphylococcus epidermidis	1	1	-	1 (100%)	-	-	-
Citrobacter amalonaticus	1	1	1 (100%)	1 (100%)	-	-	-
Micrococcus luteus	1	1	1 (100%)	1 (100%)	-	-	-
Pluralibacter gergoviae	1	1	1 (100%)	1 (100%)	-	-	-
Pseudomonas fragi	1	1	1 (100%)	-	-	-	-
Total	42	22	17 (77%)	17 (100%)*	20	13 (65%)	8 (61%)*

*P≤0.05

In contrast, non-diabetic showed 83 versus 171 respectively, with significant differences ($P \leq 0.05$) [Table 1].

Table 2 showed the results of biochemical production for all 8 *Escherichia coli* isolates, it was observed that only three isolates (No.26,38 and 42) showed consistent patterns across all biochemical production, these isolates were selected to test by RAPD analysis for further explore their genetic similarities to detect the strains level (Figs. 1,2, Table 3). By added an outgroup data (1C) to the profile sharing in the phylogenetic tree distance, the tree showed all the 3 isolates were from different strains.

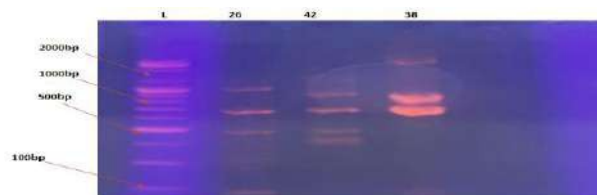


Figure No. 1: Agarose gel electrophoresis (2%) showing RAPD pattern of *Escherichia coli* Lane L: 100 bp Marker, Lane 26, 42 and 38: RAPD gene bands of *Escherichia coli*

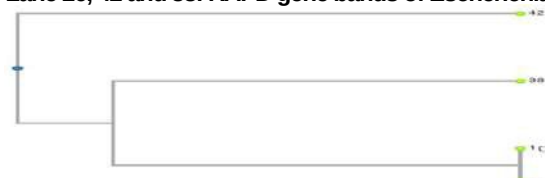


Figure No. 2: Dendrogram of 3 bacterial strains (26, 38 and 42) constructed by a set of RAPD bands using the Unweighted Pair Group Method with Arithmetic Mean (UPGMA) algorithm. Boots trap values after 100 repetitions were indicated. Strain 26 and the out group (1C) were identical with a branch length of strain 26. No strains were identical with other

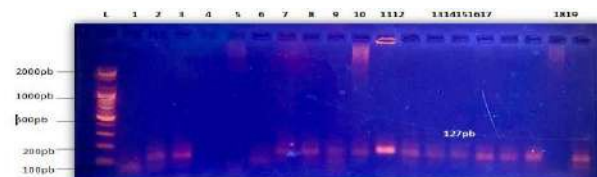


Figure No. 3: Agarose gel electrophoresis (2%) showing amplified Sea gene (127 bp)



Figure No. 4: Urine sample A shows visible hematuria with presence of blood in the urine, while sample B appears clear and free of any visible blood representing a normal urine sample.

The results of the Sea gene analysis showed its presence in 17 (77%) bacteriuria isolates out of 22 from

diabetic and 13 (65%) isolates of 20 from non-diabetic cases with no significant differences ($P \leq 0.05$) [Fig. 3, Table 4]. Hematuria was observed in all the 17 isolates (100%) possessing the Sea gene from diabetic patients, suggesting an association between the presence of this gene and urinary tract damage in this group. In contrast, hematuria was present in only 8 (61%) of 13 (65%) of Sae positive in non-diabetic patients. There is a distinct difference between the two groups of patients in hematuria ($P \leq 0.05$) [Fig. 4].

DISCUSSION

Gram-positive and Gram-negative bacteria isolated from glucose-rich urine showed higher antibiotic sensitivity than resistance regardless of diabetic status, indicating that sugar fermentation alone does not explain antimicrobial response patterns. Gram-negative isolates such as *Escherichia coli* and *Klebsiella pneumoniae* demonstrated increased susceptibility, consistent with evidence that glucose enhances metabolic activity and vulnerability to antimicrobials.⁹ This may result from altered transporter expression, stress-response pathways, and oxidative stress under fermentable glucose conditions. Similarly, Gram-positive isolates including *Enterococcus faecalis* and *Planomicrobium* showed elevated sensitivity, supporting previous findings of notable susceptibility patterns.¹⁰ These observations indicate that antimicrobial responsiveness is not solely determined by cell wall structure but by interactions among metabolic pathways, host immunity, and antimicrobial exposure.¹¹

Glucose-rich environments may enhance antibiotic uptake or modify resistance mechanisms¹², and may reduce biofilm-related virulence gene expression, as observed in *Pseudomonas aeruginosa*.¹³ Overall, antibiotic responsiveness in UTI pathogens is multifactorial and influenced by metabolic stress, environmental composition, and antimicrobial pressure.¹⁴ Although *E. coli* isolates (26, 38, and 42) shared biochemical and antimicrobial profiles, RAPD-PCR revealed distinct banding patterns, confirming genetic diversity. This demonstrates that biochemical similarity does not necessarily reflect genetic identity under diverse selective pressures.¹⁰ Elevated urinary glucose, particularly in isolate 42 from a diabetic patient, may contribute to oxidative stress and increased mutation rates, promoting genomic variability and rearrangements.¹⁵ Such environmental stressors and selective pressures can generate minor but significant genetic divergence among strains.¹

Hematuria was more frequent in diabetic patients and was strongly associated with uropathogens such as *E. coli* and *Klebsiella pneumoniae*, likely due to glucose-enhanced bacterial growth and tissue damage leading to bleeding within the urinary tract.⁴ Visible hematuria was observed in these infections, while other cases

were detectable only by urine tests. Hematuria in diabetics was also associated with *Staphylococcus aureus*, *S. saprophyticus*, and *S. epidermidis*, which produce hemolysins capable of lysing erythrocytes and irritating urinary tissues.¹⁶ *Enterobacter hormaechei* was isolated from both patient groups, suggesting roles for host immune responses or bacterial genetic factors in tissue damage across different hosts. Conversely, glycosuria in diabetics may sometimes reduce tissue destruction and hematuria occurrence.¹⁷

The detection of *Enterobacter bugandensis*, a recently described pathogen, supports its role in urothelial adhesion and vascular permeability leading to hematuria. *Staphylococcus hominis*, detected in both groups, likely causes only mild irritation due to its lower virulence. The absence of significant differences between groups suggests that host immunity and bacterial behavior influence clinical severity.¹⁸ These findings highlight the importance of identifying hematuria-associated uropathogens, particularly in diabetic patients.¹⁹ Enterotoxin genes, particularly the *Seagene*, play a major role in UTI pathogenicity. The *Seagene* encodes staphylococcal enterotoxin A, a potent toxin capable of epithelial damage, necrosis, and inflammation.⁶ In this study, the *Seagene* was detected in most isolates, except *Candidatus Erwinia*, *Staphylococcus saprophyticus*, *Lachnospiraceae* bacterium, and *Staphylococcus epidermidis*, consistent with variability in enterotoxin gene distribution. The presence of hematuria in several samples correlated with *Seagene* detection, suggesting toxin-mediated mucosal damage.²⁰

CONCLUSION

The bacteriuria from diabetic patients exhibited high resistance for Ticarcillin, Piperacillin and Ciprofloxacin antibiotics revealing a significant difference from that bacteriuria of non-diabetics' patients. All the predominant *E. coli* were of different strains depending on genetical analysis. Importantly, the present of *Seagene* reveals to play a role in hematuria samples.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Zainab S. Baqer, Munaff J. Abd Al-Abbas
Drafting or Revising Critically:	Zainab S. Baqer, Munaff J. Abd Al-Abbas
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Physiology of Smart Nanoparticles for Anti-Cancer Drug Delivery

Smart
Nanoparticles
for Anti-
cancer Drug
Delivery

Shaymaa J. Mohammed¹, Adel J. Hussein², Sanaryh Mohammed Al-awad¹,
H.N.K. AL-Salman³, Falah Hassan Shari¹ and Hussein H. Hussein⁴

ABSTRACT

Objective: To study the drug loading and release under physiological and acidic conditions and their response to MCF-7 breast cancer cells and HEK293 cells.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Almaaqal University College of Dentistry, Basrah, Iraq from 10th May 2025 to 30th September 2025.

Methods: This experimental study made smart nanoparticles that can respond to pH changes. The conjugating folic acid targeting ligands to poly (lactic-co-glycolic acid) or PLGA and DOX or doxorubicin as the anticancer drug were used. The characterization of nanoparticles used DLS, TEM and XPS. The drugs load up and how they release that drug in physiological conditions and acidic conditions. The MCF-7 breast cancer cells and HEK293 normal cells were used for an in vitro cytotoxicity followed by cellular uptake.

Results: The synthesised smart nanoparticles display a uniform spherical morphology with mean diameter of 147.3 ± 8.2 nm and zeta potential of -18.6 ± 2.1 mV. The efficiency of loading of drugs was investigated. $78.4 \pm 3.7\%$ of drug loading efficiency was found. Further, pH-responsive release behavior was investigated which resulted in 23.1% drug release (pH 7.4) and it was 89.7% at 5.0 over 72 hours. Compared with free DOX ($IC_{50} = 11.7 \pm 1.2$ mM), the smart nanoparticles showed 4.2 times higher cytotoxicity against MCF-7 cells ($IC_{50} = 2.8 \pm 0.3$ mM). After 24 hours, the drug that we got through SNPs accumulated inside the cell 3.8 times more than the free drug. Selectivity index was 5.6 times higher in cancer cells than in normal cells.

Conclusion: A successfully developed and characterized pH-response smart folate-conjugated doxorubicin nanoparticles for targeted delivery to cancer cells. Smart nanoparticles exhibited the best physicochemical properties, uniform size distribution, a high drug loading efficiency, and excellent colloidal stability.

Key Words: Smart nanoparticles, Targeted drug delivery, Cancer therapy, pH-responsive, Folic acid, Doxorubicin

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INTRODUCTION

Cancer is one of the most important health problems worldwide. Around 19.3 million new cancer cases and 10.0 million cancer deaths occurred in 2020.¹ While cancer treatments have improved, normal chemotherapy still has major limitations, including low specificity,

rapid clearance in the body, and side effects that affect the quality of life of patients.² Smart drug delivery systems based on Nanotechnology are revolutionary solutions to overcome challenges like Solubility, Distribution, and Toxicity. Smart nanoparticles (SNPs) are a particularly promising class of nanocarriers that respond to biological stimuli such as pH, temperature, enzymes, or redox condition in the tumour microenvironment or similar.³ The solid tumor phenomena of enhanced permeability and retention (EPR) effect, and low extracellular pH (6.5-7.0), allow for selective accumulation and release of drugs.⁴

Researchers are very interested in pH-responsive nanoparticles because the pH of normal physiology (7.4) and a tumour microenvironment are very different. This variation in pH can be used to allow selective drug release at the target site while remaining stable during circulation in the system.⁵ It is possible to enhance cellular uptake by using active targeting involving conjugation of specific ligands like folic acid which cause receptor-mediated endocytosis; this is especially true in the case of cancer cells which overexpress folate receptors.⁶

¹. Almaaqal University College of Dentistry, Basrah, Iraq

². Department of Anatomy & Histology, University of Basrah, Iraq

³. Department of Pharmaceutical Chemistry, College of Pharmacy, University of Basrah, Iraq

⁴. Department of Chemistry, College of Science, University of Basrah, Basrah, Iraq

Correspondence: H.N.K. AL-Salman, Pharmaceutical Chemistry Department, College of Pharmacy, University of Basrah, Iraq.

Contact No: 009647702683703

Email: hsennaserh@yahoo.com

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Poly (lactic-co-glycolic acid) (PLGA) is a biodegradable polymer matrix which is extensively used for the formulation of nanoparticles because of its excellent biocompatibility and controlled degradation kinetics. PLGA is FDA-approved and has copolymer commercial availability.⁷ PLGA-derived systems with pH-sensitive linkages and targeting moieties can produce complex drug delivery systems with enhanced therapeutic indices.⁸

METHODS

This experimental study was conducted at Almuqall University College of Dentistry, Basrah, Iraq from 10th May 2025 to 30th September 2025 vide letter No. 239 dated 4th May 2025. Poly (lactic-co-glycolic acid) (PLGA, 50:50, MW 30,000-60,000 Da), folic acid, doxorubicin hydrochloride, NN'-dicyclohexylcarbodiimide (DCC), N-hydroxysuccinimide (NHS), and polyvinyl alcohol (PVA) were purchased from Sigma-Aldrich (St. Louis, MO, USA). Dulbecco's Modified Eagle Medium (DMEM), fetal bovine serum (FBS), and antibiotic-antimycotic solution were obtained from Gibco (Thermo Fisher Scientific, Waltham MA, USA). MCF-7 human breast adenocarcinoma cells and HEK293 human embryonic kidney cells were acquired from American Type Culture Collection (ATCC, Manassas, VA, USA). All other reagents were of analytical grade and used without further purification.

Folic acid conjugation to PLGA was performed using carbodiimide chemistry. Briefly, folic acid (100 mg) was dissolved in dimethyl sulfoxide (DMSO, 10 mL) and activated with DCC (103 mg) and NHS (57 mg) for 4 hours at room temperature under nitrogen atmosphere. PLGA (1 g) was dissolved in dichloromethane (DCM, 20 mL), and the activated folic acid solution was added drop-wise under continuous stirring. The reaction was allowed to proceed for 24 hours at room temperature in darkness. The product was precipitated using cold diethyl ether, filtered, and dried under vacuum. The conjugation efficiency was confirmed by ¹H NMR spectroscopy and UV-vis spectrophotometry.

DOX-loaded smart nanoparticles were prepared using a modified emulsion-solvent evaporation technique. FA-PLGA (100 mg) and DOX (10 mg) were dissolved in DCM (5 mL) and emulsified with aqueous PVA solution (1% w/v, 20 mL) using a high-speed homogenizer (Ultra-Turrax T25, IKA, Germany) at 15,000 rpm for 3 minutes. The resulting emulsion was stirred at 500 rpm for 4 hours at room temperature to allow solvent evaporation. Nanoparticles were collected by centrifugation (15,000 rpm, 30 minutes, 4°C), washed three times with distilled water, and lyophilized for 48 hours.

Particle size, polydispersity index (PDI), and zeta potential were measured using dynamic light scattering

(Zetasizer Nano ZS, Malvern Instruments, UK) at 25°C. Morphological analysis was performed using transmission electron microscopy (TEM, JEOL JEM-2100F, Japan) with negative staining using phosphotungstic acid (2% w/v). Surface chemical composition was analyzed by X-ray photoelectron spectroscopy (XPS, Thermo Fisher K-Alpha, USA).

Drug loading content and encapsulation efficiency were determined by dissolving lyophilized nanoparticles in DMSO and measuring DOX concentration using UV-vis spectrophotometry at 485 nm. Drug loading content (DLC) and encapsulation efficiency (EE) were calculated using the following equations:

$$\text{DLC (\%)} = (\text{Weight of drug in nanoparticles} / \text{weight of nanoparticles}) \times 100$$

$$\text{EE (\%)} = (\text{Weight of drug in nanoparticles} / \text{initial weight of drug}) \times 100$$

pH-responsive drug release was evaluated using dialysis method. DOX-loaded SNPs (equivalent to 2 mg DOX) were suspended in phosphate-buffered saline (PBS) at pH 7.4 and acetate buffer at pH 5.0, placed in dialysis bags (MWCO 12-14 kDa), and immersed in release medium (50 mL) maintained at 37°C with gentle agitation (100 rpm). At predetermined time intervals, samples were withdrawn and replaced with fresh medium. DOX concentration was determined spectrophotometrically and cumulative release profiles were constructed.

MCF-7 and HEK293 cells were cultured in DMEM supplemented with 10% FBS and 1% antibiotic-antimycotic solution at 37°C in a humidified atmosphere with 5% CO₂. Cells were subcultured when confluence reached 80-90% using trypsin-EDTA solution.

Cell viability was assessed using MTT assay. Cells were seeded in 96-well plates (1×10⁴ cells/well) and incubated overnight. Various concentrations of free DOX and DOX-loaded SNPs (0.1-100 μM DOX equivalent) were added and incubated for 48 hours. MTT solution (5 mg/mL, 20 μL) was added to each well and incubated for 4 hours. Formazan crystals were solubilized with DMSO, and absorbance was measured at 570 nm using a microplate reader. IC₅₀ values were calculated using non-linear regression analysis.

Cellular uptake was evaluated using fluorescence microscopy and flow cytometry. MCF-7 cells were treated with free DOX or DOX-loaded SNPs (10 μM DOX equivalent) for various time periods (1, 4, 12, and 24 hours). For microscopy, cells were fixed with 4% paraformaldehyde, nuclei were stained with DAPI, and DOX fluorescence was observed using confocal laser scanning microscopy. For quantitative analysis, cells were harvested, washed with PBS, and analyzed by flow cytometry measuring DOX fluorescence intensity. Statistical significance was determined using Student's t-test or one-way ANOVA followed by Tukey's post-

hoc test. P-values less than 0.05 were considered statistically significant.

RESULTS

Successful conjugation of folic acid to PLGA was confirmed by ^1H NMR spectroscopy and UV-vis analysis. The conjugation efficiency was determined to be $12.3 \pm 1.8\%$ based on spectrophotometric analysis at 363 nm. XPS analysis revealed the presence of nitrogen peaks characteristic of folic acid, confirming successful surface modification. Smart nanoparticles loaded with DOX were prepared. Their physicochemical properties were measured (Table 1). According to TEM examination, morphology was spherical and uniform, exhibiting a smooth surface (Fig. 1). The size distribution of the nanoparticles obtained from the simplest method, alongside its PDI shows acceptable batch-to-batch reproducibility.

The smart nanoparticles had a distinct releasing behaviour according to pH. Under physiological conditions (pH 7.4) the drug release was minimal. Only $23.1 \pm 2.8\%$ cumulative release was observed over 72 hours indicating good stability in system circulation. On the other hand, under acidic conditions mimicking the tumor microenvironment (pH 5.0), the drug was released $89.7 \pm 4.2\%$ cumulatively within the same time ($p < 0.001$) (Table 2, Fig. 2)

Cytotoxicity studies shows that DOX-loaded smart nanoparticles are much more effective than free DOX against MCF-7 breast cancer cells. The IC_{50} of the SNPs is $2.8 \pm 0.3 \mu\text{M}$, which is 4.2 times more potent than free DOX ($\text{IC}_{50} = 11.7 \pm 1.2 \mu\text{M}$, $p < 0.001$). Significantly, the SNPs had a lower toxicity on normal HEK293 cells (IC_{50} of $15.7 \pm 2.1 \mu\text{M}$) compared with MCF-7 cells, giving a selectivity index of 5.6 (Table 3). Quantitative cellular uptake analysis showed that time-dependent accumulation of DOX in MCF-7 cells is more in case of SNP formulation as compared to free drug. Following a 24-hour incubation, the intracellular fluorescence intensity of DOX-loaded SNPs increased 3.8-fold compared with free DOX ($p < 0.001$), indicating that interaction facilitated receptor-mediated endocytosis targeting (Table 4, Figs. 3-4)

Figure 5 showed the mechanism of folic acid-targeted smart nanoparticle drug delivery showing (1) passive

targeting via EPR effect, (2) active targeting through folate receptor binding, (3) receptor-mediated endocytosis, (4) pH-triggered drug release in acidic endosomes/lysosomes, and (5) nuclear localization of released DOX.

Table No. 1: Physicochemical characterization of DOX-loaded smart nanoparticles

Parameter	Mean $\pm$ SD
Particle size (nm)	147.3 $\pm$ 8.2
Polydispersity index	0.18 $\pm$ 0.03
Zeta potential (mV)	-18.6 $\pm$ 2.1
Drug loading content (%)	7.3 $\pm$ 0.4
Encapsulation efficiency (%)	78.4 $\pm$ 3.7

Table No. 2: pH-responsive drug release kinetics from smart nanoparticles

Time (h)	pH 7.4 (% Release)	pH 5.0 (% Release)	Release ratio (pH 5.0/7.4)
2	3.2 $\pm$ 0.5	18.7 $\pm$ 2.1	5.8
6	7.1 $\pm$ 1.2	34.2 $\pm$ 3.4	4.8
12	11.5 $\pm$ 1.8	52.6 $\pm$ 4.1	4.6
24	16.3 $\pm$ 2.3	71.4 $\pm$ 3.8	4.4
48	19.8 $\pm$ 2.6	83.2 $\pm$ 4.5	4.2
72	23.1 $\pm$ 2.8	89.7 $\pm$ 4.2	3.9

Table No. 3: In vitro cytotoxicity of free DOX and DOX loaded smart nanoparticles

Formulation	MCF-7 IC_{50} (μM)	HEK293 IC_{50} (μM)	Selectivity Index	Enhancement Factor
Blank SNPs	>100	>100	-	-

*** $p < 0.001$ compared to free DOX

Table No. 4: Quantitative cellular uptake analysis by flow cytometry

Time (h)	Free DOX (Mean fluorescence intensity)	DOX-SNPs (Mean fluorescence intensity)	Uptake Enhancement Ratio
1	125 $\pm$ 18	198 $\pm$ 24*	1.6
4	287 $\pm$ 32	524 $\pm$ 41**	1.8
12	456 $\pm$ 48	1,342 $\pm$ 97***	2.9
24	623 $\pm$ 56	2,367 $\pm$ 156***	3.8

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ compared to free DOX

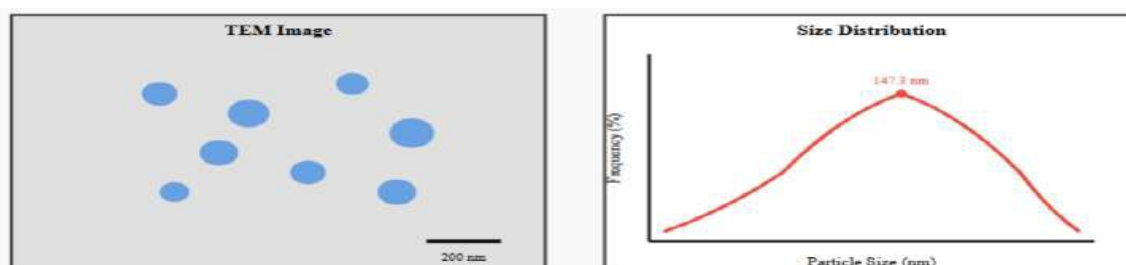


Figure No. 1: (A) Transmission electron microscopy images of DOX-loaded smart nanoparticles showing uniform spherical morphology (B) Dynamic light scattering size distribution histogram. Scale bar = 200 nm

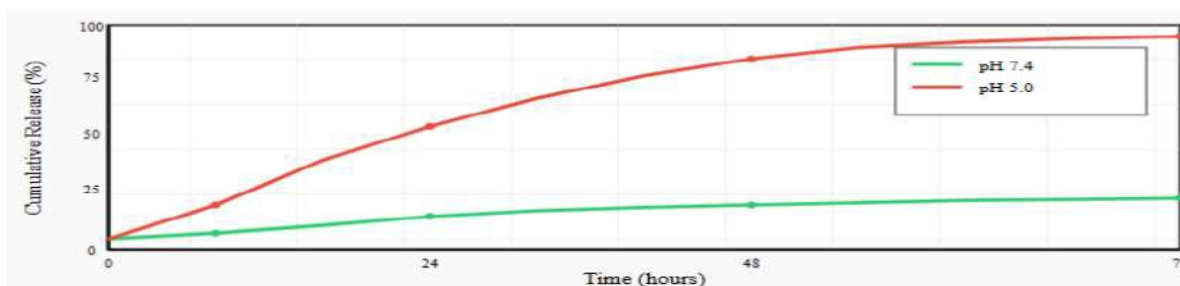


Figure No. 2: Cumulative drug release profiles of DOX-loaded smart nanoparticles at pH 7.4 (physiological) and pH 5.0 (tumor microenvironment) over 72 hours. *** $p < 0.001$

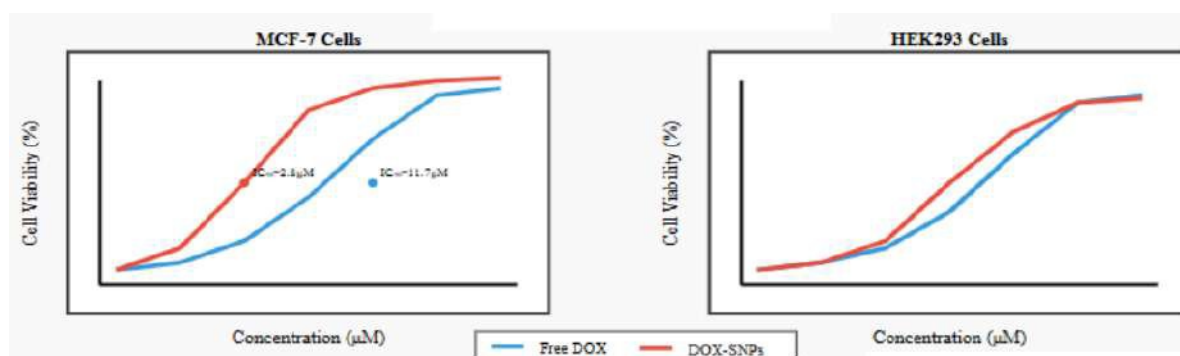


Figure No. 3: Dose-response cytotoxicity curves of free DOX and DOX-loaded smart nanoparticles in (A) MCF-7 cancer cells and (B) HEK293 normal cells after 48-hour treatment

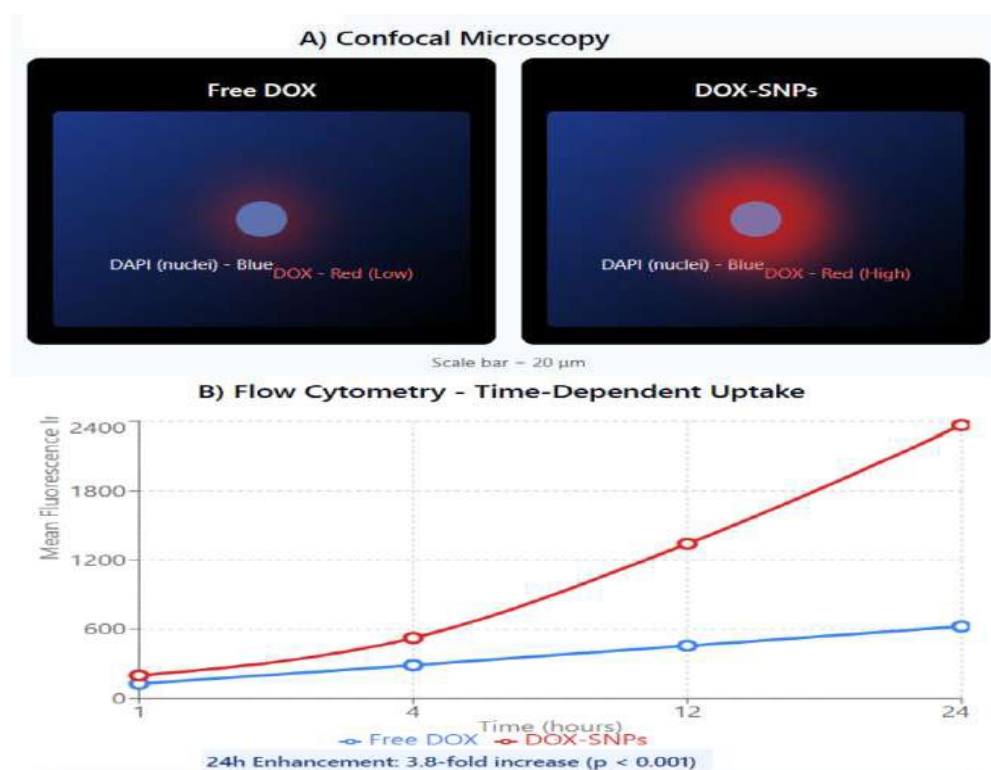


Figure No. 4 (A) Confocal laser scanning microscopy images showing DOX uptake (red fluorescence) in MCF-7 cells treated with free DOX or DOX-SNPs for 24 hours. Cell nuclei are stained with DAPI (blue). (B) Flow cytometry analysis of time-dependent cellular uptake. Scale bar = 20 μm

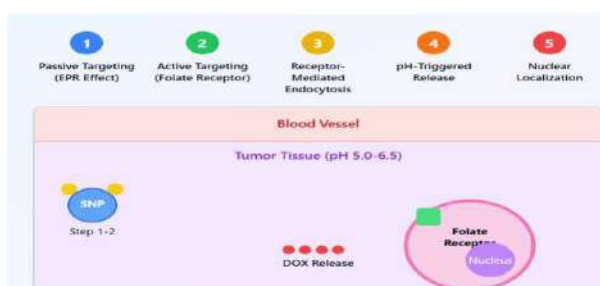


Figure No. 5: Proposed mechanism of folic acid-targeted smart nanoparticle drug delivery showing (1) passive targeting via EPR effect, (2) active targeting through folate receptor binding, (3) 12 receptor-mediated endocytosis, (4) pH-triggered drug release in acidic endosomes/lysosomes, and (5) nuclear localization of released DOX.

DISCUSSION

The development of smart nanoparticle systems for anticancer drug delivery represents a significant advancement in precision medicine approaches to cancer therapy. The results demonstrate that pH-responsive folic acid-conjugated PLGA nanoparticles can effectively enhance the therapeutic index of doxorubicin through improved targeting specificity, controlled drug release, and enhanced cellular uptake mechanisms. The physicochemical characterisation of our SNPs highlighted their suitability for intravenous drug delivery. The measured particle size of 147.3 ± 8.2 nm indicates that our formulation has ideal characteristics for tumor accumulation via the enhanced permeability and retention (EPR) effect, while avoiding rapid renal clearance and RES uptake.⁹ The surface charge value (zeta potential) of the delivery system (-18.6 ± 2.1 mV) was slightly negative which provides enough colloidal stability of the formulation and lowers non-specific protein adsorption and cell interactions to a maximum extent for providing longer systemic circulation as reported.¹⁰

Through a modified emulsion-solvent evaporation technique, a high encapsulation efficiency of $78.4 \pm 3.7\%$ was achieved, which is comparable to earlier reports and a lesser drug cost. The presence of drug loading content $7.3 \pm 0.4\%$ ensures that sufficient dosage is loaded while its stability and release characteristics are kept intact.^{6,11-12}

Our smart nanoparticles showed new pH-responsive release behaviour. At pH 5.0, the amount of drug released was 3.9 times greater than that at pH 7.4 after 72 hours. This pH-dependent behavior can be utilized for selective drug release in the acidic tumor microenvironment. Release of the mechanism is thought to be due to increased polymer chain mobility as well as hydrolytic degradation of the pH-labile linkages under acidic conditions. The low release of this drug at pH 7.4 (23.1% for 72 hours) indicates high stability in the systemic circulation which should minimize the off-target toxicity.

The increased potency of DOX-loaded SNPs over free drug, with cytotoxicity enhanced by 4.2-fold, may result from multiple synergistic mechanisms. The folate-based targeting ligand allows receptor-mediated endocytosis in folate receptor overexpressing cancer cells to enhance cellular uptake^{4,13}, based on our flow cytometry results. There was a direct evidence for enhanced drug delivery efficiency as there was a 3.8 fold increase of intracellular drug accumulation after 24 hrs.^{3,14,15}

The selectivity index of 5.6 for SNPs and 1.2 for free DOX suggests a greater therapeutic window for SNPs. The reason for this selectivity advantage is due to differential folate receptor expression, where many cancer cell types express 10-100 fold higher receptor compared to normal tissues.^{16,17}

CONCLUSION

A successfully developed and characterized pH-response smart folate-conjugated doxorubicin nanoparticles for targeted delivery to cancer cells. SNPs exhibited the best physicochemical properties, uniform size distribution, a high drug loading efficiency, and excellent colloidal stability. The pH-responsive release feature displayed a release of the drug in acidic microenvironments and stability at physiological pH making it a good option for effective tumor-targeted drug delivery. These more potent anti-cancer effects (4.2 times lower IC_{50} against MCF-7 breast cancer cells), together with higher selectivity (5.6 times a selectivity index over normal cells) suggests therapeutic efficacy of this smart delivery system. The effective active target delivery of drug was proved as 3.8 times increase in uptake by the cells.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Shaymaa J. Mohammed, Adel J. Hussein, Sanaryh Mohammed Al-awad
Drafting or Revising Critically:	H.N.K. AL-Salman, Falah Hassan Shari, Hussein H. Hussein
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.

Source of Funding: None

Ethical Approval: No. 239 Dated 04.05.2025

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Comparative Study Between Menopause and Productive Younger Age Group Women as Regard Oral Cavity Health

Menopause and Productive
Younger age Group as
Regard Oral Cavity Health

Nafi. A. Alani¹, Sabreen S. Abed¹, Saad G. Hussein and Mortadha S. Abed²

ABSTRACT

Objective: To compare the parameter above regarding dental caries, vitamin D₃ deficiency, and periodontal health between the two groups (menopause and productive age).

Study Design: Comparative study

Place and Duration of Study: This study was conducted at the Dental Department, Al Hikma University College, Baghdad Iraq 1st October 2024 to 31st March 2025.

Methods: The samples were selected by a systematic random sample who attended collecting laboratory estrogen level of 30 cases. They were divided in two groups; 15 cases in each group randomly after referring them to the laboratory clinics to measure estrogen levels in both groups.

Results: The productive age group have lower occurrence of dental carries and significant ($P < 0.05$) difference of menopause women with production age group. There is a relationship between productive younger age and menopause women as dental caries occurrence. Vitamin D₃ is lower in productive age group women while represents 2 cases in menopause women show decrease in vitamin D₃ in eight cases. Both age groups in younger and menopause women are statistically significant with vitamin D₃. The oral cavity health problems increased in menopause women in comparison with productive age. Statistically the difference was significant ($P < 0.05$).

Conclusion: There were great differences between the two groups regarding dental caries, vitamin D₃ and periodontal health.

Key Words: Vitamin D₃, Menopause women, Productive younger age, Estrogen, dental caries

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INTRODUCTION

Estrogen level is a vital factor hormone in women especially in menopause and the productive age because this estrogen hormone plays fluctuate level during menstrual cycle in the productive age group (from 25 to 45 pg/mL) while during menopause women the level of estrogen is significantly fall to less than 25 pg/mL. Once the woman reaches into full menopause age the estrogen level is significantly decrease and stay at low level in this transitional period. However, a decrease level of estrogen in menopause women will give her negative impact on teeth and the oral mucous membrane. During menopause period the women will feel suddenly irregular menstrual cycle and maybe cessation of menstrual period.

¹. Al Hikma University College, Baghdad Iraq

². Osol AL-Eim University College, Baghdad Iraq

Correspondence: Nafi. A. Alani, Al Hikma University College, Baghdad Iraq.

Contact No: +9647822383713

Email: nafi.aziz@hinc.edu.iq

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This condition affects the epithelial tissue of vagina that is similar to oral cavity.¹ The productive age group and menopause women represent the receptor of estrogen that found out in the salivary glands and buccal cavity.²⁻⁴

METHODS

This comparative study was carried out at Dental Department, Al Hikma University College, Baghdad Iraq from 1st October 2024 to 31st March 2025 vide letter No. 43egr/QM/Approval/Jhd734 dated 1st September 2024. The study deal with 30 women half of them are in menopause cases and the other half are productive younger age group. Through checking clinic in the dental department through choosing 15 cases in each group randomly after referring them to the laboratory clinics to measure estrogen levels in both groups. The research was as comparison between different cases of oral cavity and dental caries in menopause and younger women. All the data were collected from patients who attend the dental department for checking. The data was entered and analyzed through SPSS-25.

RESULTS

The productive age group have lower occurrence of Dental carries, which show difference of menopause

women with production age group P-value is $P < 0.05$, at significant level of 95% (Table 1). There is relationship between productive younger age and menopause women as regard dental caries occurrence (Fig. 1).

Table No. 1: The relationship between age groups and dental caries

Age	Dental caries		Chi square	P value
	Ladies No.	2 nd		
45-55	15	12	0.731	0.69
22-26	15	7		

$P < 0.05$ (Significant)

Table No. 2: Vitamin D₃ level is decreased in menopause women

Vitamin D ₃	No.	D ₃ deficiency	P. value
Menopause age decreased	15	8 (5.3%)	0.0001
Productive age decreased	15	3 (2%)	

Table No. 3: Relationship of age groups and periodontitis for menopause women in comparison with age group

Age group	Periodontitis		P value
	+ve	-ve	
45-50	11	2	0.97
22-26	6	-	
51-55	14	1	
22-26	5	-	
56 ⁺	10	1	
>26	8	-	

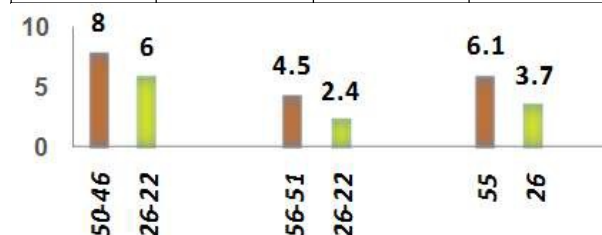


Figure No. 1: Relationship between productive younger age and menopause women

Vitamin D₃ is lower in productive age group women while represents 2 cases in menopause women show decrease in vitamin D₃ in eight cases. Thus statistically shows highly significant ($P < 0.0001$) difference (Table 2). Both age groups in younger and menopause women are statistically significant as regard vitamin D₃ ($P < 0.0001$) [Fig. 2].

Table 3 showed oral cavity health problems increased in menopause women in comparison with productive age. Statistically the difference was significant ($P < 0.05$). Figure 3 showed increase number of periodontitis in age 50-55 years old in comparison with productive age group 22-26.

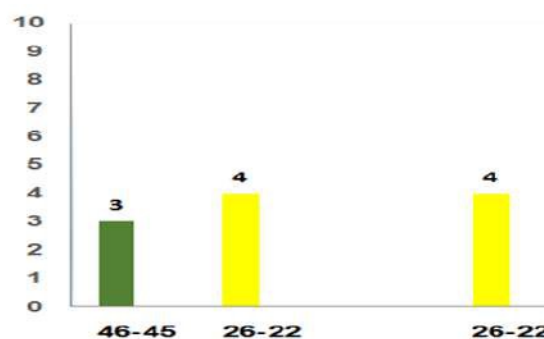


Figure No. 2: Comparison of younger age and menopause women

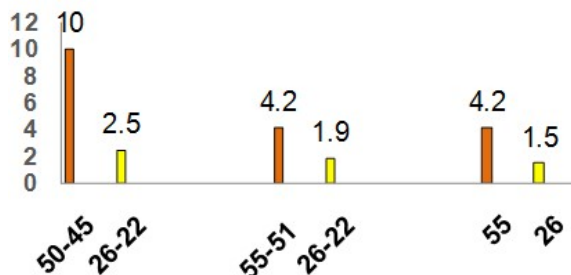


Figure No. 3: Number of periodontitis in age groups

DISCUSSION

It is found that productive age in comparison with menopause women as regard oral cavity health problems, as follow due to low level of estrogen. There are more dental caries in menopause women in comparison with productive age due to the fact that estrogen level is satisfactory and normal, while in menopause women the estrogen levels is low or absent, that lead to dryness of the mouth due to decrease secretion of saliva in comparison with productive younger age group, the result is significant (Tables 1-3). The hormonal fluctuation in younger age group throughout the puberty, pregnancy and delivery period as well in menopause women, these physiological situation and major variation in estrogen and progesterone levels and their effect on oral health. This study is consistent with fluctuation between hormonal levels in both study and their periodontal health status.⁵⁻⁹

In the present study, vitamin D₃ is the same in both menopause and younger productive age group, which is statistically not significant ($P > 0.05$). However vitamin D₃ is not significant between menopause and productive age group and P value is not significant ($P > 0.05$). Meanwhile periodontitis is more prevalent in menopause women, rather than productive age group due to hypo-estrogenism in menopause women which give significant differences $P < 0.05$. More over dental caries are more prevalent in menopause women in comparison with productive age group due to estrogen levels difference in both group which is significant difference ($P < 0.05$).¹⁰⁻¹³

Increased parathyroid hormones can cause decrease the calcium and phosphate in the bone. The result shows a

significant reduction of calcium in menopause women compared with younger age group as well as decrease estrogen level which leads to low absorption of calcium from duodenum which is the first part of small intestine compare with younger age group.¹⁴⁻¹⁸

CONCLUSION

Bad oral health problems are more in menopause women in comparison with productive age group, due to the difference in both groups, including dental caries, gingivitis, periodontitis respectively.

Recommendation: More attention to oral hygiene in menopause women to lower incidence of dental caries and periodontal health, beside to encourage giving calcium supplements to productive age groups plus pay more attention to oral hygiene, through oral hygiene education. to promote health of their oral cavity.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Nafi. A. Alani, Sabreen S. Abed
Drafting or Revising Critically:	Saad G. Hussein, Mortadha S. Abed
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.

Source of Funding: None

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Laparoscopic Management of Liver Hydatid Cyst: Current Experience of Single Center Study

Noori Hanoon Jasim¹, Muntadher Abdul Kareem Abdullah² and Mushtaq Chaseb Abu-Alhail³

ABSTRACT

Objective: To evaluate the feasibility and outcome of laparoscopic surgery in properly selected cases of liver hydatid cyst.

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the Department of Surgery, Basrah College of Medicine, Iraq from 1st June 2023 to 30th June 2025.

Methods: In this prospective study, twenty-seven 27 patients with liver hydatid disease were enrolled. All of them had undergone laparoscopic liver hydatid cyst surgical treatment.

Results: There were 17 females and 10 males with mean age 42.48 years. They presented with abdominal pain (19, 70.38%), asymptomatic (6, 22.22%), jaundice (2, 7.4%). There were 4 (14.81%) cases of cystobiliary communication; 2 patients with jaundice were preoperatively detected and treated by endoscopic retrograde cholangiopancreatography, 1 patient was intraoperatively detected during checking the cystic cavity by telescope which was treated by suturing using vicryl 2-0 and 1 patient was detected postoperatively by bile leak through intracystic drain which was treated by endoscopic retrograde cholangiopancreatography. Most patients had cyst size ≥ 8 cm, 17 (62.96%) cases. The mean operative time was 58.89 minutes. The mean Visual Analogue Scale score was 5.19 reflecting moderate severity of pain and thus mean duration of analgesia was 1.15 days and consequently the mean hospital stay was 1.59 days. Postoperative complications were noticed in 4 (14.81%) patients including cavity abscess, atelectasis, port site infection and postoperative bile leak.

Conclusion: Laparoscopic approach for appropriate liver hydatid cyst can be achieved safely with short hospital stay and short duration of analgesia.

Key Words: Liver hydatid cyst, Laparoscopic surgery, Spillage, Cystobiliary communication, Biliary leak

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INTRODUCTION

Surgical treatment is an essential modality for treatment of liver hydatid cyst (LHC). Additionally, albendazole pre- and postoperatively plays an important adjunct role to prevent recurrence.¹

¹. Department of ¹Department of Surgery, Basrah College of Medicine, Iraq

². Department of Medicine, Basrah College of Medicine, Iraq

³. Basrah Teaching Hospital, Basrah Health Directorate, Basrah, Iraq

Correspondence: Noori Hanoon Jasim, Department of Surgery, Basrah College of Medicine, Iraq.

Contact No: +9647812106971

Email: noorihanon@yahoo.com

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The surgical intervention includes different options for cyst treatment involving liver hydatid endocystectomy, pericystectomy, segmentectomy and occasionally liver lobectomy.²⁻⁴ Despite effectiveness of open surgical modality, numerous disadvantages are considered like increased pain severity postoperatively due to big incision, a long hospital stay, an increase possibility of wound infections, incisional hernia and bowel adhesions.⁵ After an advent and progressive improvement in laparoscopy, there were many recent published works reporting laparoscopic surgery (LS) for LHC.^{6,7} A reported advantage of LS for LHC is the capability of cyst telescoping to detect any cystobiliary communication or missed germinal membrane and thus avoid biliary leak and recurrence respectively.⁸ But, it is reported that the working area is restricted in comparison to open surgery for cyst manipulation increasing the fear of spillage and its serious consequences like anaphylactic shock and secondary hydatidosis.⁹ Generally, minimally invasive approach makes the post-operative pain lesser, the hospital stays shorter and thus rapid return to work.⁷

METHODS

This prospective study was conducted at Department of Surgery, Basrah College of Medicine, Iraq from 1st June 2023 to 30th June 2025 vide letter No. 1-12-5 dated 1st May 2023. A total of 27 patients who were admitted to surgical wards, were diagnosed as cases of LHC after history and physical examination, then, abdominal ultrasonography and confirmed by contrast abdominal computerized tomography (CT) scan. All patients had undergone elective laparoscopic liver hydatid surgery. Patients with LHC ≥ 5 cm, their ages ≥ 16 years old and fit for general anaesthesia were included. Patients with other types of cysts or recurrent LHC/s were excluded. Albendazole 10 mg/kg/d for 14 days preoperatively given for all patients and then albendazole was taken by all patients for 4 cycles postoperatively.¹⁰ All patients were assessed for risk of general anesthesia. Explanation of laparoscopic procedure was offered to all patients with possibility of conversion to open procedure and an informed consent was taken from all patients.

Patients' positions were supine for right lobe and trendelenburg for left lobe and pneumoperitoneum was created by using supra or infra-umbilical 10mm port achieving 12 mm Hg, other ports were positioned according to liver lobe affected as follow: in the epigastric region (sub-xyphoid) 12 mm port if the cyst was located in the right lobe and in left flank if cyst was located in the left lobe and 2 further 5mm working ports were positioned depending on liver lobe involved accordingly. An extra port was used according to cyst position to ensure presence of two suction tubes simultaneously during steps of puncture and aspiration to control spillage. Packs soaked with scolicidal agent 10% povidone iodine were placed around cystic area for spillage control. Then, cyst puncture was carefully performed for fluid aspiration and decompression using a special needle with 2 suction tubes was concurrently positioned in nearby area to control spillage. The aspirated fluid was observed for its color to detect any pus that indicated infected cyst or bile suggesting intrahepatic cystobiliary communication. Thereafter, 10% povidone iodine (equal amount of aspirated fluid) was injected inside the cyst and waiting for 10 minutes. Subsequently, aspiration of whole intracystic fluid treated with scolicidal agent. Consequently, cystostomy was achieved using monopolar hook in upper most area of cyst to avoid soiling. Furthermore, cavity was evacuated from the germinal membrane using grasper directly in an endobag. The cystic cavity was telescoped for any residual membrane or intrahepatic cystobiliary communication. If there is communication, then it was closed with 2-0 vicryl stitch. Additionally, deroofting of cyst was performed using ligasure and intracystic drain was used to manage the residual cavity. Subhepatic or subdiaphragmatic drains were

placed accordingly which were removed after 2-3 days while intracystic drains were usually removed after almost 7 days when no drainage. First visit after 2 weeks, then, the schedule was every 6 months for 18 months assessing patients clinically and radiologically for recurrence and cavity status. Follow up includes detection postoperative complications like: bile leak, atelectasis, cavity abscess, port site infection or hernia or recurrence. Pain on first post-operative day was assessed using visual analogue score (VAS) from 0-10 indicating "pain-free" till "worst-pain" respectively. Statistical analysis was conducted using SPSS-26

RESULTS

The mean age was 42.48 ± 13.61 years with range of (16-72). There were 17 (62.96%) females and 10 (37.04%) males with male/female equal to 1:1.7. Table 1 showed that the main presentation was right hypochondrial pain, anorexia and nausea with or without vomiting in 19 patients (70.38%). Then, asymptomatic patients who were accidentally discovered in 6 patients (22.22%). Two patients (7.40%) had jaundice and diagnosed by MRCP. They were successfully treated by ERCP prior LS. No one presented with fever or palpable mass.

Regarding number and site of LHC involved in this study, there were 20 patients (70.04%) representing the majority of patients had single right liver lobe hydatid cyst. Whereas, there were only 2 patients (7.4%) had multiple right liver lobe cysts. However, there were only 2 patients (7.4%) had single left lobe hydatid cyst which is apparently much less than the right lobe. Additionally, there was only 1 patient (3.7%) had multiple left liver cysts. Lastly, there were 2 patients (7.4%) had bilateral right and left lobe liver cysts. These cysts include 22 patients (81.48%) uncomplicated liver hydatid cysts and 5 complicated hydatid cysts; 1 patient with secondary infected liver hydatid cyst and filled with pus and 4 patients (14.81%) with cystobiliary communications (2 of them preoperatively detected by jaundice, 1 patient intraoperatively detected by cavity telescoping and 1 patient 2 weeks postoperatively detected by intracystic bile leak drain). LHC size ≥ 8 cm was reported in 17 patients (62.69%) [Table 2].

Table 3 shows that the mean of operative time for LS for LHC was 58.89 minutes. Regarding the intraoperative complications, interestingly, there were no spillage. Additionally, there were no intraoperative bleeding, anaphylactic shock and conversion to open surgery. However, there was 1 patient (3.7%) had cystobiliary communication detected while telescoping the cyst and treated by suturing using vicryl 2-0.

There were 15 patients (55.55%) spent 1 day in hospital, 8 patients (29.62%) spent 2 days in hospital while there were 4 patients (14.83%) spent 3 days in hospital. The mean of hospital stay was 1.59 days. The

mean of postoperative VAS score for assessing pain severity was 5.19 on the first day of hospitalisation reflecting that the pain was moderate in severity. The mean duration of injectable analgesia was 1.15 days (Table 4).

The postoperative complications were noticed in 4 patients (14.81%). One patient developed cavity abscess which was treated by percutaneous drainage and pigtail drain under ultrasound guide with antibiotics. In addition, there was 1 patient with atelectasis which was successfully treated by conservative treatment. Furthermore, there was 1 patient developed port site infection which was treated conservatively using antibiotics. Interestingly, one patient (3.7%) had bile leak by continuous draining bile through intracystic drain for 2 weeks which was successfully responded to treatment by ERCP. It is important to find that there was no case of recurrence during period of follow up stated in methodology (Table 5).

Table No. 1: Main presentations of patients with LHC

Symptoms	No.	%
Right hypochondrial pain, anorexia and nausea with or without vomiting	19	70.38
Symptomless	6	22.22
Palpable mass	-	-
Fever	-	-
Jaundice	2	7.4

Table No. 2: Number, location, size and type of LHC

Parameters	No.	%
Single cyst in R lobe	20	74.04
Multiple cysts in R lobe	2	7.40
Single cyst L lobe	2	7.40
Multiple cysts in L lobe	1	3.70
Bilateral	2	7.40
Uncomplicated	22	81.48
Complicated		
Cystobiliary communications	4	14.81
Secondary infection	1	3.71
Cyst size (cm)		
5- <8	10	37.04
≥ 8	17	62.96

Table No. 3: Mean operative time and intraoperative complications

Parameters or variables	
Operative time in minutes	58.89±8.01
Intraoperative spillage	-
Bleeding	-
Anaphylactic shock	-
Cystobiliary communication	1 (3.7%)
Conversion to open	-

Table No. 4: Shows duration of hospitalization stay, mean of hospital stay, mean of analgesia and VAS score on day one

Parameter	Patients underwent surgery		%
Hospital stay (days)	1	15	55.55
	2	8	29.62
	3	4	14.83
Mean of hospital stay in days	1.59± 0.75		
Mean of analgesia in days	1.15± 0.36		
Mean of VAS score on first day	5.19±1.04		

Table No. 5: Postoperative complications

Post-operative complications	No.	%
Cavity abscess	1	3.7
Atelectasis	1	3.7
Port site infection	1	3.7
Port site hernia	-	-
Bile leak	1	3.7
Recurrence	-	-
Total	4	14.81

DISCUSSION

It is evident that surgery often representing the crucial approach of treatment involving both open and laparoscopic techniques^{8,10} preserving medical therapy like albendazole for specific indications including prior and post-surgical intervention to prevent recurrence particularly if there is intraoperative spillage or in patients unfit for surgery.⁶ There is a recent rise of clinical tendency to manage liver hydatid cyst laparoscopically especially after raising surgeons' experience worldwide.^{6,7,10}

In the current study, the mean age was 42 years old which is consistent with many other studies.^{6,11} In our study, female percentage was more preponderant than males and this comes in accord with other study¹² and in contrast with others that report both sex equivalency¹¹ or male predominance.⁶

In this study, the commonest presentation was upper abdominal pain (70.38%) which is consistent with other studies.^{6,12} Additionally, 22.22% of our patients were asymptomatic and were detected accidentally which is similar to other study.⁶ In current study, the least presentation was jaundice 7.4% of patients with no fever or palpable mass. In contrast, Palanivelu et al⁶ report that 13 patients out of 66 total number in their series (19.7%) are presented with abdominal mass.

In present study, a single cyst in right hepatic lobe was more predominant. This is similar to the results of other published studies.^{6,7,11} There were 4 cases (14.81%) of cystobiliary communication. This is consistent with the rate of cystobiliary communication reported by other studies which ranges between 3.5%¹³ and 19%.¹⁴

Presence of cystobiliary communication is preoperatively confirmed by proper history and examination (jaundice and cholangitis), LFT and MRCP showing CBD dilatation together with presence of liver hydatid cyst.¹⁵

In the present study, the size of cyst in majority of patients (62.96%) was ≥ 8 cm. In contrast to study conducted by Masood et al⁷ who report that the number of patients with cystic size ≤ 10 cm are nearly similar to patients with cystic size > 10 cm despite the mean size of cyst is 8.8 ± 2.39 cm in their series. Kilic et al¹⁶ showed that the mean size of cystic lesion is 10.2 cm in cases with bile leak whereas it is 6.2 cm in cases without bile leak raising the likelihood that the cystic size is a risk factor for cystobiliary communications.

In current study, the mean operative time of LS for LHC was 58.89 minutes which is comparable to other studies conducted by Palanivelu et al⁶ and Shi¹⁷ and who report that the mean operative time is 57.19 minutes and 52 minutes respectively. However, it was less than other studies conducted by Masood et al⁷ and Minaev et al¹⁸ in which the operative time is of 104 minutes and 90 minutes respectively suggesting that the LS for LHC becomes shorter when it is used in less complex cases.

Intraoperatively, many incidental complications have been reported in other reports like spillage, bleeding, anaphylactic shock, cystobiliary communications.¹⁹ No one of these complications had been detected in our study except one case (3.7%) of cystobiliary communication discovered intraoperatively during cystic examination by telescope. Bektasoglu et al¹⁹ report that there are 3 patients out of 23 patients (13%) who are treated laparoscopically are converted to open surgery and 1 patient with anaphylactic shock. In contrast, neither conversion to open surgery nor anaphylactic shock had occurred in our study which is consistent with study reported by Masood et al.⁷

The major concern of laparoscopic surgeons is an intraoperative spillage and its serious sequelae like anaphylactic shock or recurrence in future and it is dealt with in many reports by albendazole treatment preoperatively, decompression of cyst by aspiration and injection of equal amount of scolical agents, pericystic placement of packs soaked with scolical agents, the first puncture at non-dependent upper most point with usage of double suction tubes near the point of aspiration to control spillage and lastly postoperative albendazole therapy.⁷ All these measures were adopted in our work.

Regarding the pain, the mean of VAS score on the first day postoperatively was 5.19 which aligns with the results reported by Masood et al⁷ who report the VAS score on first day is 6.36, reflecting that the severity is moderate in both. The moderate pain severity may be ascribed to the small wound access of laparoscopic technique resulting in reduction of tissue damage or

dissection as elucidated by Patil et al.²⁰ Therefore, post-operative hospital stay was 1-2 days in majority of patients (23 patients, 85.17%) with mean 1.59 days which is comparable to study conducted by Shi in which the hospital stay is 2.1 days.¹⁷ Thus, our patients had a short duration of analgesia requirement postoperatively (mean of 1.15 days). This comes in accords with studies conducted by Shi¹⁷ reporting that the durations and requirements for pain management are generally much decreased in LS intervention.

In our study, post-operative complications were reported in 4 patients (14.81%) which is comparable to results of Minaev et al¹⁸ who notice a complication rate of 14.3%. However, the complication rate is 6.6% in series of Masood et al.⁷ In our study, the following complications were detected: cavity abscess, atelectasis, port site infection and post-operative bile leak which were treated as mentioned in results with no port site hernia. These findings correspond with the research conducted by Masood et al.⁷ Though, a number of researchers have reported recurrence rate of LS is (1.1%)¹⁰, in our series there was no recurrence during period of follow up stated in methodology and that is similar to finding of Masood et al.⁷

CONCLUSION

Laparoscopic liver hydatid surgery can be feasible and safe therapy for LHC in case of proper selection of patients and following meticulous LS accompanied with pre- and postoperative albendazole treatment.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Noori Hanoon Jasim, Muntadher Abdul Kareem Abdullah
Drafting or Revising Critically:	Noori Hanoon Jasim, Mushtaq Chaseb Abu-Alhail
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Association of Postpartum Depression with Mode of Delivery: A Cross-Sectional Study at A Psychiatry Institute of Rawalpindi

Postpartum
Depression with
Mode of Delivery
among Women

Jasim Tariq¹, Abid Aftab², Izzah Khalid¹, Asif Azeem³, Isbah Gul³ and Tariq Raheem¹

ABSTRACT

Objective: To determine the association between postpartum depression and mode of delivery among women presenting to a psychiatry institute in Rawalpindi.

Study Design: Cross-sectional analytical study

Place and Duration of Study: This study was conducted at the Armed Forces Institute of Mental Health Rawalpindi December 16 till March 15, 2026.

Methods: This study was conducted including 210 postpartum women within 6 weeks of delivery. Postpartum depression was assessed using the Edinburgh Postnatal Depression Scale, with a score ≥ 13 indicating depression.

Results: The mean age of participants was 29.8 ± 5.7 years, and the overall frequency of postpartum depression was 40.0%. Depression was significantly more common in women undergoing cesarean section compared to vaginal delivery (57.1% vs 42.9%, $p = 0.002$), with emergency cesarean showing a stronger association. Women with postpartum depression had higher mean EPDS scores (16.8 ± 3.2 vs 8.2 ± 2.6 ; $p < 0.001$). Additional factors significantly associated with depression included age > 30 years, low socioeconomic status, unplanned pregnancy, primiparity, poor neonatal health, and inadequate social support ($p < 0.05$).

Conclusion: Postpartum depression is significantly associated with cesarean delivery, particularly emergency procedures, along with multiple demographic and psychosocial factors. Early screening and targeted interventions are essential to improve maternal mental health outcomes.

Key Words: Postpartum depression; Mode of delivery; Cesarean section; Vaginal delivery; EPDS; Maternal mental health.

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INTRODUCTION

Postpartum depression (PPD) is a mood disorder that usually occurs in about 10-20 percent of women after giving birth and is a leading cause of maternal morbidity¹. It has the following symptoms which include persistent low mood, fatigue, sleeping disturbances and lack of interest in daily activities which significantly affect maternal functioning and mother infant bonding². PPD has also been linked to unfavorable neonatal outcomes such as slow growth,

retarded cognitive and emotional developments, among others³. PPD etiology is multifactorial including hormonal alterations, psychological stressors and social factors. Quick changes in postpartum hormones, especially of estrogen and progesterone are known to affect mood regulation⁴. Besides this, deficit of social support, financial pressures, marital problems and unexpected pregnancy are also factors that have heightened risks of developing depressive symptoms⁵. Psychiatric history is also a strong predisposing factor that is already established⁶. Mode of delivery has been argued as a significant obstetric factor affecting the postpartum mental health. Risk factors of PPD may include cesarean section, particularly emergency operations because of the stress of surgery, slow recovery period, and adverse childbirth experiences⁷. On the other hand, vaginal birth is frequently related to faster recovery and improved mental consequences⁸. Nevertheless, the literature lacks consistency in its findings. There are reports that the incidence of PPD is higher after a cesarean section has taken place⁹, but a few also conclude that there is no significant association when controlling variables are taken into consideration¹⁰. This may differ because of different

¹. Resident Psychiatry / Head of Department Psychiatry²/ Consultant Psychiatrist³, Armed Forces Institute of Mental Health Rawalpindi.

Correspondence: Jasim Tariq, Resident Psychiatry, Armed Forces Institute of Mental Health Rawalpindi.

Contact No: 0344-3583157

Email: jasimtariq33@yahoo.com

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study designs, populations, and measurement instruments¹¹. Postpartum depression is not properly diagnosed in Pakistan and other low-resource environments because of stigma and poor mental care¹². Other factors like the sociocultural factors, including the gender roles and pressure of the family as well as lack of support systems on the mother may increase psychological distress on the mother¹³. Nonetheless, there is a lack of local data on the connection between mode of delivery and PPD¹⁴. This relationship is critical in determining the high-risk mothers and putting in place early screening measures¹⁵. Early diagnosis and treatment of PPD can enhance the maternal health and newborn outcomes¹⁶. Thus, the proposed research will evaluate the relationship between the mode of delivery and postpartum depression among women reporting to a psychiatry institute in Rawalpindi.

METHODS

This cross-sectional analytical study was conducted at Armed Forces Institute of Mental Health Rawalpindi December 16 till March 15, 2026, including 210 postpartum women presenting within 6 weeks after delivery. Patients were enrolled consecutively during the study period to determine the association between postpartum depression and mode of delivery.

Inclusion Criteria

- Women aged 18–45 years within 6 weeks postpartum
- Women who had delivered either by vaginal delivery or cesarean section
- Women presenting to the psychiatry institute for evaluation
- Women willing to participate and provide informed consent

Exclusion Criteria

- Women with a prior diagnosed psychiatric illness before pregnancy
- Women with severe postpartum medical or surgical complications
- Women with stillbirth or neonatal death
- Women with incomplete information or unwilling to participate

Data Collection: After obtaining institutional approval, data were collected using a structured proforma. Demographic variables included age, residence, education, occupation, and socioeconomic status. Obstetric variables included parity, planned or unplanned pregnancy, type and mode of delivery, and time since delivery. Postpartum depression was assessed using the Edinburgh Postnatal Depression Scale (EPDS), with a score of ≥ 13 considered indicative of depression. Additional information regarding family support and neonatal health status was also recorded.

Statistical Analysis: Data were entered and analyzed using SPSS version 26.0. Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequency and percentage. The association between postpartum depression and mode of delivery was assessed using the chi-square test. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

The mean age was 29.8 ± 5.7 years, with higher age in the PPD group (31.2 ± 5.9 vs 28.9 ± 5.4 years; $p = 0.006$). Women >30 years were more likely to have PPD (42.9%), while most non-PPD were ≤ 30 years (73.0%) ($p = 0.018$). Rural residence (50.0% vs 34.9%), lower education (52.4% vs 36.5%), and low socioeconomic status (57.1% vs 38.1%) were significantly associated with PPD ($p < 0.05$). Occupation showed no significant difference ($p = 0.081$).

Table No. 1. Demographic and Clinical Characteristics of Participants According to Postpartum Depression (N = 210)

Variable	Category	Overall (N=210)	No PPD (n=126)	PPD (n=84)
Age (years)	Mean $\pm$ SD	29.8 ± 5.7	28.9 ± 5.4	31.2 ± 5.9
Age Group	≤ 30 years	140 (66.7%)	92 (73.0%)	48 (57.1%)
	>30 years	70 (33.3%)	34 (27.0%)	36 (42.9%)
Residence	Urban	124 (59.0%)	82 (65.1%)	42 (50.0%)
	Rural	86 (41.0%)	44 (34.9%)	42 (50.0%)
Education	$\geq$ Secondary	120 (57.1%)	80 (63.5%)	40 (47.6%)
	$<$ Secondary	90 (42.9%)	46 (36.5%)	44 (52.4%)
Occupation	Housewife	162 (77.1%)	92 (73.0%)	70 (83.3%)
	Employed	48 (22.9%)	34 (27.0%)	14 (16.7%)
Socioeconomic Status	Low	96 (45.7%)	48 (38.1%)	48 (57.1%)
	Middle/High	114 (54.3%)	78 (61.9%)	36 (42.9%)

Primiparity (54.8% vs 41.3%; $p = 0.048$) and unplanned pregnancy (50.0% vs 31.7%; $p = 0.007$) were significantly associated with PPD. Cesarean delivery had higher depression rates (57.1% vs 42.9% in vaginal; $p = 0.002$), particularly emergency cesarean

(40.5% vs 15.9%; $p = 0.013$). Postpartum duration was not significant ($p = 0.154$), while poor neonatal health was more common in PPD (31.0% vs 12.7%; $p = 0.002$).

Table No. 2. Obstetric Characteristics According to Postpartum Depression (N = 210)

Variable	Category	Overall (N=210)	No PPD (n=126)	PPD (n=84)	p-value
Parity	Primiparous	98 (46.7%)	52 (41.3%)	46 (54.8%)	0.048
	Multiparous	112 (53.3%)	74 (58.7%)	38 (45.2%)	0.048
Pregnancy Type	Planned	128 (61.0%)	86 (68.3%)	42 (50.0%)	0.007
	Unplanned	82 (39.0%)	40 (31.7%)	42 (50.0%)	0.007
Mode of Delivery	Vaginal	118 (56.2%)	82 (65.1%)	36 (42.9%)	0.002
	Cesarean	92 (43.8%)	44 (34.9%)	48 (57.1%)	0.002
Type of Cesarean	Elective	38 (18.1%)	24 (19.0%)	14 (16.7%)	0.013
	Emergency	54 (25.7%)	20 (15.9%)	34 (40.5%)	0.013
Postpartum Duration	≤3 weeks	156 (74.3%)	98 (77.8%)	58 (69.0%)	0.154
	>3 weeks	54 (25.7%)	28 (22.2%)	26 (31.0%)	0.154
Baby Health	Healthy	168 (80.0%)	110 (87.3%)	58 (69.0%)	0.002
	Ill	42 (20.0%)	16 (12.7%)	26 (31.0%)	0.002

Table No. 3. Psychosocial and Clinical Factors Associated with Postpartum Depression (N = 210)

Variable	Category	Overall (N=210)	No PPD (n=126)	PPD (n=84)	p-value
EPDS Score	Mean ± SD	11.6 ± 4.8	8.2 ± 2.6	16.8 ± 3.2	<0.001
Family Support	Adequate	132 (62.9%)	96 (76.2%)	36 (42.9%)	<0.001
	Inadequate	78 (37.1%)	30 (23.8%)	48 (57.1%)	<0.001
Previous Depression	Yes	34 (16.2%)	10 (7.9%)	24 (28.6%)	<0.001
	No	176 (83.8%)	116 (92.1%)	60 (71.4%)	<0.001
Social Support	Present	142 (67.6%)	102 (81.0%)	40 (47.6%)	<0.001
	Absent	68 (32.4%)	24 (19.0%)	44 (52.4%)	<0.001

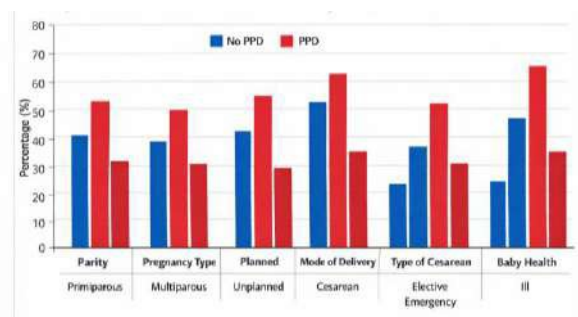


Figure No. 1. Distribution of Obstetric Factors According to Postpartum Depression Status (n = 210)

The mean EPDS score was higher in the PPD group (16.8 ± 3.2 vs 8.2 ± 2.6 ; $p < 0.001$). Inadequate family support (57.1% vs 23.8%), previous depression (28.6% vs 7.9%), and lack of social support (52.4% vs 19.0%) were all strongly associated with PPD ($p < 0.001$).

Mode of delivery showed a significant association with PPD ($p = 0.002$). Depression was more frequent after cesarean section (57.1%) compared to vaginal delivery (42.9%). Emergency cesarean had the highest association (40.5% vs 15.9%), while elective cesarean showed a weaker relationship ($p = 0.013$).

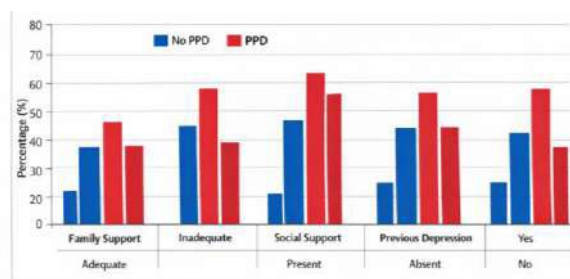


Figure No. 2. Psychosocial and Clinical Factors Associated with Postpartum Depression (n = 210)

Table No. 4. Association of Mode of Delivery with Postpartum Depression (N = 210)

Mode of Delivery	Overall (N=210)	No PPD (n=126)	PPD (n=84)	p-value
Vaginal Delivery	118 (56.2%)	82 (65.1%)	36 (42.9%)	0.002
Cesarean Section	92 (43.8%)	44 (34.9%)	48 (57.1%)	0.002
Elective Cesarean	38 (18.1%)	24 (19.0%)	14 (16.7%)	0.013
Emergency Cesarean	54 (25.7%)	20 (15.9%)	34 (40.5%)	0.013

DISCUSSION

This research study showed that postpartum depression was highly linked to various demographic, obstetric and psychosocial conditions whereby there was significantly high incidence among those women who delivered via cesarean section especially emergency delivery. The number of women having PPD (40.0%) in this study is rather high, and this could be attributed to the fact that the facility is a psychiatry institute that could have more women presenting with psychological distresses. Other studies previously also indicated high levels of postpartum depression in clinical or high-risk groups as opposed to community based samples¹⁷. The age was significantly related and older women (>30 years) were more likely to develop PPD. This could be associated with more psychosocial stresses, more expectations and more obstetric risk in this age group. The same conclusions have been drawn in previous studies in which advanced maternal age was correlated with more depressive symptoms in the postpartum period¹⁸. The status of socioeconomic and educational barriers also contributed greatly with less educated and low socioeconomic women having higher rates of PPD. These results indicate that maternal psychological vulnerability is caused by limited resources, less health awareness and financial stress. The past studies have continually emphasized the low socioeconomic status as a crucial factor leading to postpartum depression¹⁹. Cesarean section, mostly emergency cesarean, was among obstetric factors in which the PPD was found to be strongly associated. The women who had cesarean delivery were greatly affected as their depression was much higher (57.1) than those who gave birth through vaginal delivery (42.9). It was particularly the case with emergency procedures that were associated with greater psychological distress, which may have been caused by sudden complications, fear, and the inability to control the course of childbirth. The same trends have been seen in the past studies as cesarean birth particularly emergency birth was related to the increased postpartum depression risk²⁰. PPD was also greatly correlated with primiparity and unexpected pregnancy. The first-time mothers can be more anxious and unprepared, and the unexpected pregnancy can also be one of the sources of emotional stress and a lack of acceptance of motherhood. These results are consistent with other studies that have described the two variables as significant predictors of postpartum depression²¹. Psychosocial factors were most related. Lack of family support, social support, as well as history of depression in the past were found to be much higher in women with PPD. These results highlight the importance of emotional and social support systems, in order to safeguard the maternal mental health. The evidence provided by the previous literature has repeatedly shown that the social support is poor, and a past psychiatric history are some of the strongest predictors of postpartum depression²². There was also a significant association of neonatal health

status with mothers of sick babies experiencing depressive rates. This could either be as a result of heightened anxiety, care giving burden, and fear of the health of the child. Such parallels have been observed in earlier literature, with negative perinatal experiences adding to the maternal psychological distress levels. On the whole, the results of the conducted study indicate that postpartum depression is a multifactorial disease that is determined by demographic, obstetric, and psychosocial factors. Closely tied to the cesarean birth and emergency surgeries, the fact is that psychological screening and support of high-risk mothers should be the priority. These results are in line with the past studies and support the center of interest of including the mental health assessment in the general postpartum care.

CONCLUSION

It is concluded that postpartum depression is highly prevalent and significantly associated with mode of delivery, particularly cesarean section, with the strongest association observed in emergency procedures. Additionally, factors such as older maternal age, low socioeconomic status, lower education, primiparity, unplanned pregnancy, poor neonatal health, and inadequate social and family support were significantly linked with increased risk of postpartum depression. These findings emphasize that postpartum depression is a multifactorial condition, and early identification of high-risk mothers through routine screening especially among those undergoing cesarean delivery is essential to ensure timely intervention and improved maternal and neonatal outcomes.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Jasim Tariq, Abid Aftab, Izzah Khalid
Drafting or Revising Critically:	Asif Azeem, Isbah Gul, Tariq Raheem
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Nurses' Practices of Caring Toward Premature Infants at Neonatal Intensive Care Unit: Descriptive Study Research

Suror Hameed Aneed¹ and Hussein Fakher Kamel²

ABSTRACT

Objective: To assess of demographic features and practices of nurses providing about the premature baby needs at neonatal intensive care unit.

Study Design: Descriptive cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Pediatric Nursing, College of Nursing, Thi-Qar University, Iraq from 20th November 2024 to 10th April 2025.

Methods: A total 50 nurses in the neonatal intensive care units of teaching hospitals (Bent Al-Huda Hospital and Al-Mousawi Hospital) were enrolled.

Results: The nurses between 20-30 years have the largest. Bachelor's degrees in nursing were the majority of the educational level. 20% nurses have 6-10 years of experience and majority were 1-5 years experience in the neonatal intensive care unit. Skin care was assessed by 60% of the nurses, skin color, signs of skin infection and skin irritation were assessed. In contrast, 28% of the nurses studied did not assess the quality of care.

Conclusion: There was a significant relationship between nurses' practice score and age, the level of education, years of experience and experience in the neonatal intensive care unit.

Key Words: Nurse practices, Premature, Neonatal intensive care unit

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INTRODUCTION

Babies born prematurely are unique patients; they are subjected to rigorous and intrusive medical treatment in the highly mechanized setting of a neonatal intensive care unit (NICU). Their gestational age (GA) at birth has a significant impact on how their hospital stay turns out; the more immature the baby is at birth, the more difficult and intrusive the critical care he needs. In addition to the loss of their secure and dependable prenatal environment, preterm infants must deal with deprivation, stress, and overstimulation. Because they are unsure of their child's chances of life and how the early birth may affect their development, caregivers of premature babies also experience trauma. In addition, witnessing the invasive care their child needs can be very upsetting to parents.¹

¹ Department of Pediatric Nursing, College of Nursing, Thi-Qar University, Iraq

² Department of Pediatric Nursing, College of Nursing, University of Basrah, Iraq

Correspondence: Dr. Suror Hameed Aneed, Department of Pediatric Nursing, College of Nursing, Thi-Qar University, Iraq.

Email: surorneizy22@utq.edu.iq

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A high-risk baby is one who has a higher likelihood of morbidity due to disorders that arise during the embryo's growth, the mother's gestation, or issues that may arise during labor and delivery. Neonates born before the complete 37th week of pregnancy.²

Certain neonatal health issues, such as hypothermia, breathing difficulties, malnutrition, infection, hyperbilirubinemia, and even mortality, are more likely to occur in premature babies. A neonatal intensive care unit, which has specialized medical personnel and equipment to handle the various issues preterm neonates confront, is necessary for the care of many of these patients.³

Providing breathing assistance is part of the nursing role (see drug chart). Do the following evaluations. Check for murmurs in the heart sounds. Evaluate the perfusion and pulse. Keep an eye on your pulse pressure, heart rate, and blood pressure. Make sure you are getting enough calories, electrolytes, and hydration. Avoid infection and keep the environment at a neutral temperature.⁴

When it comes to helping premature babies who are in discomfort, pediatric nurses are essential, pain evaluation, treatment of pain, advocacy for mothers and newborns, and instruction for parents are all under the purview of nurses. Although nursing expertise is limited when it comes to caring for babies, the synthesis of nurses' experiences and viewpoints regarding the care of newborns in pain may help bring new insights to improve evaluation and treatment of pain for those who are at risk.⁵

METHODS

In the neonatal intensive care unit of pediatrics teaching organizations in Nasiriya city, nurses' practices in caring for premature infants were assessed using a descriptive (cross-sectional) research methodology. 50 nurses from Thi-Qar for the Al Moosawi Hospital and Bint Alhuda Teaching Hospital comprised the non-probability sample from 20th November 2024 to 10th April 2025 vide letter No. 4 dated 10-11-2024. The data was collected through face to face interview. Each interview took approximately 15-20 minutes to complete questionnaire form. The interviewing is carried out with each study sample who participated in the study. The device that the researcher created and built is based on prior research and the clinical context of the literature. Part I: Sociodemographic information includes seven items pertaining to the nurse's age, period of experience, and educational attainment, NICU experience, have you ever taken part in a training session on the requirements of premature babies? Course duration Part II: Nurses' practices regarding the needs of premature babies in the neonatal intensive care unit consists of (14) items. The Statistical Package of Social Science version-25 was used. Alpha Cronbach for the questionnaire's internal reliability and consistency was used. The Chi-Square test is used to determine if the noticed frequencies' random distribution matches the anticipated multiple category nominal scale.

RESULTS

The age group 20–30 is the biggest, accounting for 40%. Majority of nurses have Bachelor's degrees. Six to

ten years of experience accounted for 20% of the total years of experience. Majority have 26% had 1–5 years of NICU experience (Table 1).

Table No. 1: Sociodemographic characteristics of the nurses (N=50)

Demographic factor	No.	%
Age (years)		
<20	12	24.0
20 – 30	20	40.0
31 – 40 or more	18	36.0
Education Level		
Nursing high school graduate	10	20.0
Medical Institute of Nursing	19	38.0
Bachelor degree in nursing	20	40.0
Graduate	1	2.0
Years of experience (years)		
1-5	16	32.0
6-10	20	20.0
>10	14	28.0
Experience in NICU (years)		
1-5	32	64.0
6-10	13	26.0
11-15	5	10.0
>15	0	0.0
Have you participated in a training course related to the needs of a premature baby previously?		
Yes	10	20.0
No	40	80.0
Duration of course (week)		
< 1	2	4.0
≥ 2	8	16.0

Table No. 2: Distribution of study sample according to assess of nurses' practices in caring for premature infants (N=50)

Practices of nursing provided about the premature baby	Yes		No		I don't know	
	No.	%	No.	%	No.	%
Measuring Vital Signs	50	100.0	-	-	-	-
Bottle Feeding	50	100.0	-	-	-	-
Skin Care	30	60.0	14	28.0	6	12.0
Eye Care	40	80.0	6	12.0	4	8.0
Cord Care	42	84.0	6	12.0	2	4.0
Protection from Infection	24	48.0	18	36.0	8	16.0
Daily Care of Incubator	26	52.0	12	24.0	12	24.0
Assist in Laboratory Test	45	0.0	5	10.0	-	-
Administration of Medication	49	98.0	1	2.0	-	-
Keep Quite Environment	38	76.0	12	24.0	-	-
Maintain Parent-Neonate Bonding	10	20.0	34	68.0	6	12.0
Terminal Care of Incubator	26	52.0	12	24.0	12	24.0
Eyes and genitals should be covered when placing a premature baby under phototherapy	50	100.0	-	-	-	-
Hand hygiene is very important when caring for a premature baby, because the immune system in premature babies is immature so they are vulnerable to infection.	45	90.0	5	10.0	-	-

Table 2 showed that 60% of the nurses in the study evaluated skin care. Skin color, infection symptoms, and skin irritation were assessed. On the other hand, 28% of the nurses in the study did not evaluate. Eighty-four percent of the nurses in the study accurately provided cord care while under the influence of alcohol. However, 12% of them failed to offer care for the cord. In order to prevent infection, 48% of the nurses in the study donned gloves when they came into touch with bodily secretions and cleaned their hands both before and after tending to each newborn. The newborn cord stump was maintained dry and tidy by them. Additionally, isolate the infected baby, refrain from sharing neonatal equipment, and do not allow infected people to visit him. Every nurse in the study provides daily incubator care. Furthermore, 90% of nurses gave attention throughout laboratory tests. When administering medication, 98% of the nurses in the study made sure to follow aseptic technique, verify doctor's directions, and adhere to medication administration principles. On the other hand, 2% of them did not offer any assistance while taking medication.

Table No. 3: Correlations coefficient between socio demographic and nurses' practice score (N=50)

Sociodemographic	Nurses' Practice Score	
	X ²	P value
Age	22.0 56	0.06
Years of experience	16.776	0.001
level of education	36.702	0.000
Experience in NICU	35.072	0.001
Have you participated in a training course related to the needs of a premature baby previously?	27.678	0.004

Significant

The association between nurses' practice grade and demographic data was seen in table 3. For instance, the practice grade of nurses and age were significantly correlated. Additionally, there was a high correlation between years of experience, school level, and NICU experience.

DISCUSSION

In the present study, 40% nurses belonged the age group 20-30 (Table 1). The study's findings are consistent with the fact that a total of nursing employees were between the ages of 20 and 30. The majority of the study's nurses were female and in the under-30 age range.⁶ A great deal of nurses who participated in this study had a bachelor's degree in nursing, according to the study's findings, which also showed that bachelor's degrees in nursing made up 40% of the sample compared to other educational levels.⁷

In terms of years of experience, the largest group (representing 20%) had six to ten years. The current research supports the findings of the study. In terms of years of experience, eight years accounted for 20% of the total.^{8,9}

Since their percentage was anticipated to be 26% of the sample size, the majority had one to five years of experience in the NICU. According to the current study, the majority of nurses who worked in the preterm department had less than five years of experience. The study found that nurses knew a lot about complications and how to care for premature babies.^{10,11}

Table 2 showed the practices of nursing provided about the premature baby that 60% of the nurses in the study evaluated skin care. Skin color, infection symptoms, and skin irritation were assessed. On the other hand, 28% of the nurses in the study did not evaluate. Eighty-four percent of the nurses in the study accurately provided cord care while under the influence of alcohol. However, 12% of them failed to offer care for the cord. In order to prevent infection, 48% of the nurses in the study donned gloves when they came into touch with bodily secretions and cleaned their hands both before and after tending to each newborn. The newborn cord stump was maintained dry and tidy by them. Additionally, isolate the infected baby, refrain from sharing neonatal equipment, and do not allow infected people to visit him. Every nurse under study looks after the incubator on a daily basis. Furthermore, 90% of nurses gave attention throughout laboratory tests. When administering medication, 98% of the nurses in the study made sure to follow clean methods, verify doctor's directions, and adhere to medication administration principles. On the other hand, 2% of them did not offer any assistance while taking medication. According to the current study's findings, the majority of nurses lack training or understanding on septic the washing of hands practices; less than 15% did not receive preterm care instruction.^{12,13}

This study showed the connection between nurses' practice grade and demographic traits for instance, the practice level of nurses was significantly correlated with age, with a P-value of < 0.006 (Table 3). Additionally, there was a significant correlation between years of experience, level of schooling, NICU experience, and having previously completed a workshop on the needs of premature babies (P<0.000, P≤0.001, P≤0.001, and P≤0.004, respectively). The current study's findings support that. Every healthcare professional tries to apply what they have learned to provide ongoing care, ease the transition, and enhance the baby's and the family's results. There are found relationship between the level of education, years of experience from nurses.^{14,15}

CONCLUSION

The majority sample that the age group 20-30 is the largest age group, bachelor degrees in nursing were the

majority among the educational level, years of experience, 6–10 years were the most in this category and represented 20%. Regarding experience in the NICU, the majority was 1-5 years, as their percentage was estimates at 26% of the sample size. On the connection between nurses' practice level and demographic traits for example, nurses' practice score and age were significantly correlated, while their level of learning, years of experience, NICU experience, and prior participation in a training course on the needs of premature babies were all strongly correlated.

Recommendations: Phototherapy is effective in treating all cases of jaundice in the neonatal intensive care unit. Booklets on key procedures for premature neonates should be available at the unit. In-service training programs focused on all areas of care offered for newborns should be conducted. The study suggests the establishment of dedicated facilities for the care of premature infant units. The scientific level of nurses working in such units should be raised through rigorous training programs and courses. Pre-service training will assist newly hired nurses in modernizing and enhancing their job.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Suror Hameed Aneed, Hussein Fakher Kamel
Drafting or Revising Critically:	Suror Hameed Aneed, Hussein Fakher Kamel
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Effect of Combination of Different Postures and Pursed Lips Breathing on Dyspnea and Pulmonary Parameters among Patients with Asthma

Hayder Nawaf Abd Ali and Shatha Saadi Mohammed

Pursed Lips Breathing on Dyspnea and Pulmonary Parameters with Asthma

ABSTRACT

Objective: To evaluate the effects of combining prostration position with pursed-lip breathing in adult asthma patients.

Study Design: A quasi-experimental study

Place and Duration of Study: This study was conducted at the Emergency Department, Imam Hussein Medical City Karbala from 1st April 2025 to 30th September 2025.

Methods: 60 patients of intervention n=30 and control n=30. The patient's contribution to the study was positive, as the nursing intervention was implemented by the patient himself.

Results: The intervention group demonstrated significant improvements: respiratory rate decreased from (24.7) to (20.1) breaths/min ($p=0.001$), SpO₂ increased from 91.7% to 93.5% ($p<0.001$), and dyspnea scores reduced from 15.4 to 14.1 ($p=0.014$). No significant changes occurred in controls. Participants were predominantly middle-aged (46.7-50% aged 30-49), obese (36.7% Class I), with chronic asthma (40% duration 11-20 years) using ICS+LABAs (40%).

Conclusion: Prostrate position enhances diaphragmatic function and pursed-lip breathing reduces hyperinflation, supporting their integration into asthma care and education as a safe, effective intervention.

Key Words: Asthma, Prostration, Pursed-lip breathing

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INTRODUCTION

Chronic inflammation and edema of the airway mucosa, along with bronchial hyperresponsiveness, characterize asthma. Histamine and leukotrienes are released by triggers, causing symptoms. Some experience intermittent symptoms, while others may have long-term airway remodeling, leading to reduced lung function. Asthma patients may face coughing, dyspnea, wheezing, chest tightness, tachypnea, and nighttime or early morning coughing.¹

Asthma caused 397,150 deaths worldwide in 2015, including in the Middle East. In Iraq, the prevalence of allergies and asthma has increased due to factors such as electrical generators, oil pollution, vehicle emissions, and explosions.²

While there is a correlation between certain traits and asthma, the condition affects individuals of all ages and sexes. Men typically experience higher prevalence in youth, while women are more likely to develop severe asthma during adolescence.³ The economic impact of asthma on the United States is substantial. In the most recent survey, the total cost of asthma was \$82 billion. Today, the predicted total cost is significantly greater.⁴ Asthma incidence and prevalence are increasing, but regular use of inhaled corticosteroids reduces mortality and prevents the side effects of oral corticosteroids, while improving symptom control. New treatments and specific therapeutic targets are needed for severe asthma.⁵ Current studies on non-pharmacological asthma therapies are insufficient. We propose research to evaluate the effects of prostrating on dyspnea relief and pulmonary parameters in adult asthma patients.

METHODS

A quasi-experimental study was conducted at Emergency Department, Imam Hussein Medical City Karbala from 1st April 2025 to 30th September 2025 letter No. 77 dated 24-3-2025 with (non-equivalent pretest-posttest control-group) on 60 patients with asthma who selected purposively (non-probability sample) and divided into 2 groups (control and

College of Nursing, University of Babylon, Iraq.

Correspondence: Hayder Nawaf Abd Ali, College of Nursing/ University of Babylon, Iraq.

Contact No: +9647718575181

Email: haider84nawaf@gmail.com

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prostrate), 30 patients in each groups. Data was collected from three groups before the interventional procedure and re-evaluated dyspnea level and pulmonary parameters for patients in the study group (prostrate) after asked them to do the pursed lip breathing exercise 3 times in a row, then apply the prostrate position for 5 minutes, and then re-apply the pursed lip breathing exercise 3 times in a row. The hospitalized patients who were already diagnosed with asthma, both male and female sex, those who had dyspnea, and patients who are willing to participate were included. The participants in the experimental study, asthma patients who did not have shortness of breath and who refused to participate, children under the age of 18, the elderly who could not tolerate prone positions, individuals with mental disabilities, severe heart and lung conditions, pregnant women, and patients with fever were excluded. The prostrate position of the patient lies down so that his knees, forehead, and hands are close to the ground and the elbows are flexed and relaxed to bear the weight of the patient. The abdominal area remains unsupported so that the position of the patient is the same as the position of prostrate during prayer. The researcher measured the pulmonary parameters on his own and entered them into the study instrument as part of the interview approach used for data collection. The data was entered and analyzed through SPSS-24.

RESULTS

The mean of the patients' age was 54.4 ± 14 years. 46.7% of the patients in control group and 50% of them in prostrate group were age of (30-49) years. Males of the control and prostrate group were 53.3%, and 56.7%

respectively. 36.7% of control group and 30% of prostrate group were educated. 40% of control group were retired and 23.3% of prostrate group were factory workers. 43.4% and 40% of asthmatic patients in control and prostrate groups were previously smokers. Since all p-values are above the typical significance threshold (0.05), there are no statistically significant differences in demographic characteristics between the control and prostrate groups (Table 1).

There were 36.7% and 30% of the patients in the control and prostrate group had obesity class I. Also it revealed that 36.7% and 40% of the patients in the control and prostrate group had 11-20 years duration of suffering from asthma. 40% of patients in each group (control and prostrate) were use Inhaled (ICS) & (LABAs) as a chronic medication use for asthma. 53.3% and 63.3% of the patients in the control and prostrate group had non-allergic asthma attack. There are no statistically significant (>0.05) differences (Table 2).

There is no statistically significant ($p=.0926$) difference in respiratory rate between pretest and posttest in the control group while there is a significant (.001) difference in the experimental group (prostrate group). There is no statistically significant (.582) difference in SPO_2 between pretest and posttest in control group while there is a significant difference (.000) in prostrate group (Table 3).

There is no statistically significant difference in dyspnea between pretest and posttest in the control group ($df = 29$, $t = .368$, p value of .715) while there is a clear difference at the ($df = 29$, $t = 2.601$, p value of .014) in the prostrate group (Table 4).

Table No. 1: Demographical characteristics of the asthmatic patients

Characteristics		Control Group		Prostate Group		P value
		No.	%	No.	%	
Age (years)	30-49	14	46.7	15	50.0	.346
	50-69	11	36.7	12	40.0	
	≥ 70	5	16.6	3	10.0	
Gender	Male	16	53.3	17	56.7	.542
	Female	14	46.7	13	43.3	
Educational level	Illiterate	-	-	-	-	.218
	Educated	11	36.7	9	30.0	
	Primary	6	20.1	8	26.7	
	Intermediate	9	30.0	8	26.7	
	Institute	2	6.7	2	6.6	
	Collage or more	2	6.7	3	10.0	
Occupation	Construction Workers	4	13.3	3	10.0	.976
	Factory Workers	4	13.3	7	23.3	
	Cleaners and Janitors	4	13.3	4	13.3	
	Agriculture Workers	3	10.0	3	10.0	
	Retired	12	40.1	7	23.4	
	Housewife	3	10.0	6	20.0	

Table No. 2: Distribution of the asthmatic patients according their clinical data

Clinical data		Control Group		Prostate Group		P value
		No.	%	No.	%	
Body mass index	Normal	5	16.7	8	26.7	.489
	Overweight	4	13.2	5	16.7	
	Obesity I	11	36.7	9	30.0	
	Obesity II	8	26.7	7	23.3	
	Obesity III	2	6.7	1	3.3	
Duration of suffering from asthma (years)	1-10	8	26.7	10	33.3	.744
	11-20	11	36.7	12	40.0	
	≤ 21	11	36.7	8	26.7	
Chronic medication use for asthma	Inhaled Corticosteroids (ICS)	3	10.0	3	10.0	.218
	Long-acting beta-agonists	11	36.7	11	36.7	
	Short-acting beta-agonists (LABAs)	2	6.6	3	10.0	
	Inhaled (ICS) + (LABAs)	12	40.0	12	40.0	
	Inhaled (ICS) + Leukotriene receptor antagonists (LTRAs)	2	6.6	1	3.3	
Type of current asthmatic attack	Allergic asthma	10	33.3	9	30.0	.386
	Non- allergic asthma	16	53.3	19	63.3	
	Exercise-induced asthma	4	13.3	2	6.7	

Table No. 3: Effect of combination of prostrate position with pursed lip breathing on pulmonary parameters

Group	Pulmonary parameters	Paired sample t test					
		Mean		df	t value	p value	Significant
		Pre-test	Post-test				
Control	RR	25.8	25.7	29	.093	.926	NS
	SPO ₂	92.2	92.3	29	5.56	.582	NS
Prostate	RR	24.7	20.1	29	3.65	.001	S
	SPO ₂	91.7	93.5	29	4.69	.000	S

Table No. 4: Effect of combination of prostrate position with pursed lip breathing on dyspnea levels

Group	Paired sample t test						
	Pre-test		Post-test		df	t value	p value
	Mean	SD	Mean	SD			
Control	15.6	2.3	15.3	2.1	29	.368	.715 (NS)
Prostrate	15.4	2.12	14.1	2.67	29	2.601	.014 (S)

DISCUSSION

The predominance of middle-aged participants (30-49 years) aligns with previous research indicating that asthma symptoms often worsen in adulthood due to prolonged exposure to environmental and occupational triggers.⁶ Additionally, the higher proportion of male participants (53.3% in control, 56.7% in prostration group) may reflect occupational exposures, as males in this study were frequently engaged in high-risk jobs (factory workers, construction). This demographic trend is consistent with studies linking occupational hazards to asthma exacerbations.⁷

The educational background of participants (with 30-36.7% classified as "educated") suggests that health literacy may have influenced adherence to breathing techniques. Prior research indicates that patients with

higher education levels are more likely to effectively implement self-management strategies, including PLB.⁸ However, the lack of illiterate participants in this study limits generalizability to lower-literacy populations, who may require additional nursing support for proper technique adherence.

A significant proportion of participants in both groups were classified as obese (Class I: 36.7% control, 30% prostration group; Class II-III: 33.4% control, 26.6% prostration group). Obesity is a well-documented comorbidity in asthma, contributing to worsened symptoms due to mechanical restriction of the lungs, chronic low-grade inflammation, and reduced response to standard therapies.⁹ The high prevalence of obesity in this cohort suggests that posture-based interventions, such as the prostration position, may be particularly beneficial, as forward-leaning postures can alleviate

diaphragmatic compression and improve ventilation efficiency.¹⁰

Most participants had suffered from asthma for over a decade (11-20 years: 36.7% control, 40% prostration group; ≥ 21 years: 36.7% control, 26.7% prostration group), indicating a population with persistent disease. Long-term asthma is often associated with airway remodeling and reduced lung function, necessitating advanced therapeutic strategies.¹¹ The majority of patients in both groups relied on combination therapy with inhaled corticosteroids (ICS) and long-acting beta-agonists (LABAs) (40% each), reflecting current Global Initiative for Asthma (GINA) guidelines for moderate-to-severe asthma. The comparable medication profiles between groups strengthen the validity of the prostration/PLB intervention, as confounding by differential medication use is minimized.

Non-allergic asthma was the most common phenotype (53.3% control, 63.3% prostration group), which aligns with studies showing increased prevalence of this subtype in adults, particularly those with obesity or long-standing disease.¹² Non-allergic asthma is often less responsive to standard bronchodilators and more reliant on adjunctive therapies (breathing exercises) to manage symptoms.¹³ The predominance of this phenotype supports the rationale for testing non-pharmacological interventions like prostration/PLB, which may improve symptoms through mechanical rather than immunological pathways.

The experimental group showed a clinically and statistically significant reduction in respiratory rate (RR) from 24.7 to 20.1 breaths per minute ($p=0.001$), while the control group maintained nearly identical RR values (25.8 vs 25.7, $p=0.926$). This 4.6 breath/minute reduction in the experimental group represents a substantial improvement, as a normal adult RR ranges from 12-20 breaths per minute. The magnitude of this effect surpasses that seen in similar studies of breathing techniques for COPD patients suggesting particular efficacy for asthma populations.¹⁰

The mechanism behind this improvement likely involves multiple factors: The forward-leaning prostration position reduces accessory muscle use and improves diaphragmatic efficiency.¹⁴ PLB helps regulate breathing patterns by preventing airway collapse during expiration.¹⁵ The combination may synergistically reduce dynamic hyperinflation, a key contributor to tachypnea in acute asthma.

The experimental group demonstrated significant SpO_2 improvement from 91.7% to 93.5% ($p<0.001$), while the control group showed no meaningful change (92.2% to 92.3%, $p=0.582$). This 1.8% increase, while numerically modest, represents an important clinical improvement for several reasons. It moves patients from the borderline hypoxemic range (91-94%) into the normal range ($\geq 95\%$) this results come along with

Abed-Ali et al¹⁶ and Abed-Ali and Athbi.¹¹ The improvement occurred without supplemental oxygen. Similar studies using only PLB have shown smaller effects (0.5-1.0% increases). The oxygenation benefit stems from improved ventilation-perfusion matching, reduced respiratory rate for efficient gas exchange, and larger effect sizes than seen in similar COPD studies.¹⁰ Greater improvements than reported for PLB alone in asthma¹⁷ and supports growing evidence for postural interventions in obstructive lung diseases.¹⁸

The experimental group showed a clinically meaningful decrease in dyspnea scores (from 15.4 ± 2.12 to 14.1 ± 2.67), indicating improved breathing comfort. This aligns with previous research showing that forward-leaning postures (such as the prostration position) reduce accessory muscle use and improve diaphragmatic efficiency, thereby decreasing the work of breathing.¹⁸ Pursed-lip breathing (PLB) further enhances this effect by slowing expiration, preventing airway collapse, and improving oxygenation.¹⁵ The control group's dyspnea levels remained nearly unchanged (15.6 ± 2.3 to 15.3 ± 2.1 , $p=0.715$), confirming that standard care alone does not significantly impact perceived breathlessness in the short term. A reduction in dyspnea is crucial because breathlessness is one of the most distressing symptoms for asthma patients, often leading to anxiety and worsened respiratory function.⁹ The prostration + PLB technique is a non-pharmacological, low-cost intervention easily taught by nurses and used by patients, reducing dyspnea by optimizing lung expansion and addressing hyperinflation in asthma, a common issue in asthma that contributes to breathlessness these results agrees with Abed-Ali and Athbi.¹¹ PLB prolongs exhalation, reducing air trapping and dynamic hyperinflation.¹⁰ Slow, controlled breathing (as in PLB) may reduce sympathetic overactivity and modulate cortical processing of dyspnea, making it feel less severe.¹⁹ Structured breathing techniques can reduce anxiety, which often exacerbates dyspnea.²⁰ Similar effects have been seen in COPD patients using PLB and postural adjustments¹⁸, but this study extends the evidence to asthma patients. The magnitude of dyspnea reduction (~ 1.3 points) is comparable to some bronchodilator studies, suggesting this could be a useful adjunct to medication.¹⁷

CONCLUSION

Combining the prostration position with pursed-lip breathing significantly improves respiratory rate, SpO_2 , and dyspnea in adult asthma patients, offering a safe, non-pharmacological nursing intervention.

Recommendation: Integrating this technique into asthma self-management education, Training nurses to teach and supervise proper execution, and further research on long-term benefits in diverse asthma

populations. This intervention could enhance symptom control while reducing reliance on rescue medications.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Hayder Nawaf Abd Ali, Shatha Saadi Mohammed
Drafting or Revising Critically:	Hayder Nawaf Abd Ali, Shatha Saadi Mohammed
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Impact of Artificial Intelligence-Assisted Instruction on Classroom Behavior and Adaptive Functioning in Students with Learning Disabilities

AI Assisted
Instruction on
Classroom
Behavior in
Students with
Learning
Disabilities

Zainab Hassan Hussein and Amean A. Yasir

ABSTRACT

Objective: To evaluate the artificial intelligence-assisted instruction may influence classroom behavior and to explore its possible association with adaptive functioning in students with learning disabilities.

Study Design: A quasi-experimental study

Place and Duration of Study: This study was conducted at the Department of Community Health Nursing, College of Nursing, University of Babylon, Babylon Iraq from 01.02.2025 to January 2026.

Methods: A quasi-experimental design with pretest and posttest control groups was implement on a sample of 60 primary school students diagnosed with dyslexia, dyscalculia, or dysgraphia in Babylon, Iraq in the 01.02.2025 to January 2026 academic year letter No. 3434/QM/Approval/EFEF3 dated October 2, 2024 were enrolled. Participants were divided into an experimental group (n = 30), which received artificial intelligence-supported instruction for eight weeks, and a control group (n = 30), which continued with traditional teaching methods.

Results: Students in the experimental group demonstrated a statistically significant improvement in classroom behavior across the study period ($F(2,58) = 312.85$, $p < 0.001$, partial $\eta^2 = 0.915$), with notable progress from pretest to posttest that remained stable during follow-up assessment. In contrast, no statistically significant changes were observed in the control group ($p > 0.05$), indicating the limited effect of conventional instruction alone.

Conclusion: The adoption of artificial intelligence-based instructional methods in special education settings is therefore encouraged.

Key Words: Artificial intelligence, Learning disabilities, Classroom behaviour, Adaptive functioning, Special education

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INTRODUCTION

Artificial Intelligence (AI) technologies have become one of the most popular trends in the global education sector as a way to enhance the learning results and provide a more personalized instruction to students with the different learning requirements.¹

The field of AI has been opened up to a set of various educational technologies, such as adaptive learning systems, intelligent tutoring systems, simulation-based tools, and customized feedback applications.

Department of Community Health Nursing, College of Nursing, University of Babylon, Babylon Iraq.

Correspondence: Zainab Hassan Hussein, PhD Student in Community Health Nursing, College of Nursing, University of Babylon, Babylon Iraq.
Email: zainab.mohamed.1nurs1212@student.uobabylon.edu.iq

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These technologies are programmed in such a way that it takes into consideration the profile of a particular learner and able to respond to certain issues that are faced by students with learning disabilities such as dyslexia, attention problems and academic disorders involving reading and mathematics. It has been demonstrated in the previous literature that AI-based tools could offer individualized and adaptive learning assistance, particularly to students who fail to respond satisfactorily when using traditional learning methods.^{2,3} Moreover, these adaptive systems have shown statistically significant changes in the academic performance such as the performance of the learners in reading and mathematics among learners with learning disabilities.⁴

In the area of special education, the usefulness of AI is not confined solely to academic success but also to the possible impact it may have on the behavior of students, their engagement and their involvement in classroom tasks. The AIs have been identified to increase motivation, attention, and learning efficacy among students, which are all directly linked to behavioral functioning in a learning context.⁵ As an illustration, AI-based interventions involving selective attention

have positively impacted attention control and task-related behavior among elementary school students with learning issues, indicating that these technologies might be used to create a better classroom behavior and active engagement.⁶ Moreover, the systematic reviews of the AI usage in special education have revealed that the intervention could reinforce participation and engagement which are critical elements of positive classroom behavior and adjustment to school in students with special educational needs.⁷

Educational justifications of introducing AI into teaching and learning are based on the theory of adaptive learning, personal feedback and student-centered teaching. These views underline the necessity to react to the individual differences in the needs of students, their abilities and progress rates.⁸ By constantly updating student performance, AI technologies will be able to adapt learning content, learning velocity, and task challenge on the fly, thus delivering customized scaffolding which fosters cognitive in addition to behavioral growth.⁹ In this respect, AI-based teaching is consistent with general educational concepts of differentiated learning and inclusive pedagogy that strive to maximize learning experiences of every student by accommodating student differences.¹⁰

Although the effectiveness of AI in the education sector has been proven by an accumulating body of evidence, there are a number of methodological and practical shortcomings. The moderate to high risk of bias, relative lack of follow-up time and diversity in the implementation methods, among others, which must be cautiously taken into consideration during the interpretation of reported effects.¹¹ Moreover, the introduction of AI into special education attracts some critical concerns regarding teacher training, professional development, ethical application, and the necessity to maintain a human touch in the teaching decision-making process.¹² Based on these factors, more studies should be carried out to determine the educational and behavioral influence of AI-based teaching in students with learning disabilities. Specifically, the research of its impact on classroom conduct can also yield information about school-related features of adaptive functioning, where such a construct is not directly measured using standardized tests.

METHODS

This study was conducted on the special education services in the private primary schools in the Hilla, Babylon Governorate. The process of implementations involved three key components i.e. pretest, intervention and posttest. Sixty students studying in Hilla, Babylon Governorate, who has the special education classroom, was enrolled. All of them were formally diagnosed with dyslexia, dyscalculia, or dysgraphia and were included in the 2025-2026 academic year. The students were in

accordance with the set inclusion criteria and were separated into two matched groups. The experimental group comprised of 30 students who were provided with AI-assisted instruction and the control group had 30 students who were provided with traditional classroom instructions. Following the intervention took place in eight weeks, the behavioral observation grid was repeated in both groups, at two time points, Post-test I and Post-test II, to determine the changes in classroom behavior as time goes.

A behavioral observation grid and a structured questionnaire were utilized in order to measure the behavior of students with learning disabilities in the classroom. Socio-demographic data (age, sex, grade level, place of residence, and type of learning disability) was collected. The behavioral observation grid had 20 items on classroom behavior and was rated on a scale of 10 points in which 1 was behavior never exhibited and 10 behavior was strongly exhibited. The behaviors that were observed were punctuality, class participation, problem-solving, interest in classroom activities, cooperation with other classmates, communication as well as respect towards classroom rules. A combination of these tools made a complete evaluation of the classroom behavior of students before and after the intervention.

The content validity was determined by a panel of 20 experts in the universities of Iraq. The specialists checked the tools in terms of clarity, relevance, appropriateness, and wordings. According to their feedback, small changes were introduced in order to increase the accuracy and appropriateness of the items. The instruments were subsequently pilot-tested on 6 students who will constitute 10 percent of the sample in the study in order to determine the clarity, feasibility and time needed to administer the instruments. The analysis of reliability demonstrated good internal consistency with the behavioral observation grid Cronbach alpha coefficient of 0.80, which meant that the instrument can be used.

Statistical Package of the Social Sciences-28 was used to analyze the data. Chi-square tests, which are categorical tests, and independent-samples t-tests, which are continuous tests, were used. In order to investigate how the AI-assisted instructional program is effective in classroom behavior, a repeated-measures ANOVA was conducted at three measurement points, including pretest, Post-test I, and Post-test II. In situations where time effects were found to be significant, Bonferonni-adjusted post hoc comparison in pairs was done to establish that specific differences were occurring between measurement points. Effect sizes have also been determined to estimate the size of the intervention effect. Repeated-measures ANOVA was reported to give partial eta-squared (η^2) and pairwise comparisons were used to report Cohen d. All statistical tests were of the two tails statistical type and

a p-value below 0.05 was taken to be statistically significant.

RESULTS

Most students were 10–11 years old (60% in the study group and 66.7% in the control group), with mean ages of 11.4 ± 1.2 and 11.6 ± 1.3 years, respectively. Students were similarly distributed across 2nd and 3rd grades, and most of them lived in urban areas. The Chi-square test showed no significant differences between the two groups across all socio-demographic variables ($p > 0.05$), indicating that both groups were comparable at baseline (Table 1).

The most common type of learning disability was dyslexia in both groups, followed by dyscalculia and dysgraphia, with no significant differences between the study and control groups ($p > 0.05$). The mean pre-intervention academic performance was similar in both groups, indicating comparable baseline achievement. After the intervention, the study group demonstrated a noticeable improvement in academic performance compared with the control group, reflecting the positive effect of AI-based learning support (Table 2).

Overall behaviour scores of the study group, assessed using the Observation Grid, showed substantial improvement following the intervention. At pre-test, the majority of students (90.0%) scored in the low range (53.9 ± 18.60), with only 10.0% in the moderate range and none in the high range. After the intervention, Post-test I results demonstrated a marked increase, with 83.4% of students reaching the high range (165.4 ± 23.10) and only 3.3% remaining in the low range. In Post-test II, the gains were largely maintained, with 76.7% of students in the high range (158.65 ± 22.85) and 10.0% scoring in the low range (Table 3).

The repeated measures ANOVA for overall behaviour scores in the study group revealed a highly significant effect of time ($F(2, 58) = 312.85$, $p < 0.001$, partial $\eta^2 = 0.915$), indicating that students' behaviour improved significantly from pre-test to Post-test I and was largely maintained at Post-test II. The very large effect size demonstrates that the intervention had a substantial impact on enhancing students' overall behaviour in the school environment (Table 4).

Post-hoc pairwise comparisons with Bonferroni adjustment indicated significant improvements in students' overall behaviour scores. Specifically, scores increased markedly from pre-test to Post-test I (mean difference = -111.50 , 95% CI $[-123.50, -99.50]$, Cohen's $d = 5.20$, $p < 0.001$) and from pre-test to Post-test II (mean difference = -104.75 , 95% CI $[-116.70, -92.80]$, Cohen's $d = 4.85$, $p < 0.001$), reflecting extremely large effect sizes. No significant difference was found between Post-test I and Post-test II (mean difference = 6.75 , 95% CI $[-4.50, 18.00]$, Cohen's $d = 0.28$, $p = 0.52$), indicating that the improvements observed immediately after the intervention were largely maintained over time (Table 5).

The overall behaviour scores of the control group remained predominantly low throughout the study. At pre-test, 93.3% of students scored in the low range ($M = 48.75 \pm 17.22$), with only 6.7% in the moderate range and none in the high range. Post-test I and Post-test II showed slight increases in mean scores (60.90 ± 19.10 and 59.90 ± 19.74 respectively), but the majority of students (93.3%) continued to fall within the low range. The students' overall behaviour in the school environment showed minimal improvement over time (Table 6).

The repeated measures ANOVA for overall behaviour scores in the control group showed no significant effect of time ($F(2, 58) = 2.15$, $p = 0.12$, partial $\eta^2 = 0.069$), indicating that students' behaviour did not change meaningfully across pre-test, Post-test I, and Post-test II. Students' overall behaviour in the school environment remained largely stable over the study period (Table 7).

Post-hoc pairwise comparisons with Bonferroni adjustment indicated no significant differences in overall behaviour scores over time in the control group. The mean differences between pre-test and Post-test I (-12.15 , 95% CI $[-28.50, 4.20]$, Cohen's $d = 0.64$, $p = 0.12$), pre-test and Post-test II (-11.15 , 95% CI $[-27.40, 5.10]$, Cohen's $d = 0.58$, $p = 0.15$), and Post-test I and Post-test II (1.00 , 95% CI $[-10.20, 12.20]$, Cohen's $d = 0.05$, $p = 0.92$) were all non-significant and students' behaviour remained largely unchanged throughout the study period (Table 8).

Table No. 1: Sociodemographic information of the students (n=60)

Variable	Category	Study Group (n=30)	Control Group (n=30)	p-value
Age (years)	8–9	12 (40%)	10 (33.3%)	0.607
	10–11	18 (60%)	20 (66.7%)	
Sex	Male	16 (53.3%)	15 (50%)	0.796
	Female	14 (46.7%)	15 (50%)	
Grade Level	2nd	14 (46.7%)	13 (43.3%)	0.715
	3rd	16 (53.3%)	17 (56.7%)	
Residency	Urban	18 (60%)	17 (56.7%)	0.796
	Rural	12 (40%)	13 (43.3%)	

Table No. 2: Distribution of learning disability characteristics (n=60)

Variable	Category	Study Group (n=30)	Control Group (n=30)	p-value
Type of learning disability	Dyslexia	14 (46.7%)	13 (43.3%)	0.796
	Dyscalculia	10 (33.3%)	11 (36.7%)	
	Dysgraphia	6 (20%)	6 (20%)	
	Other	-	-	
Previous Academic Performance (Pre)		62.5±7.8	61.9±8.1	
Later Academic Performance (Post)		112.6±12.5	70.3±7.0	

Table No. 3: Overall students' behaviour scores in the school environment according to the observation grid (study group)

Weighted	Pre-test			Post-test I			Post-test II		
	No.	%	Mean±SD	No.	%	Mean±SD	No.	%	Mean±SD
Low	27	90.0	53.9±18.60	1	3.3	165.4±23.10	3	10.0	158.65±22.85
Moderate	3	10.0		4	13.3		4	13.3	
High	-	-		25	83.4		23	76.7	

Table No. 4: Repeated measures ANOVA for overall students' behaviour scores in the school environment (study group)

Source of Variation	SS	df	MS	F	p-value	Partial η^2
Time (Pre, Post I, Post II)	78,540.00	2	39,270.00	312.85	<0.001	0.915
Error (Within Subjects)	7,285.20	58	125.61			
Total	85,825.20	60				

Table No. 5: Post-hoc pairwise comparisons – study group (behaviour scores, Bonferroni-adjusted)

Comparison	Mean Difference	Cohen's d	95% CI	p-value
Pre-test vs Post-test I	-111.50	5.20	-123.50, -99.50	<0.001
Pre-test vs Post-test II	1104.75	4.85	-116.70, -92.80	<0.001
Post-test I vs Post-test II	6.75	0.28	-4.50, 18.00	0.52 (NS)

Table No. 6: Overall students' behaviour scores in the school environment according to the observation grid (control group, n=30)

Weighted	Pre-test			Post-test I			Post-test II		
	No.	%	Mean±SD	No.	%	Mean±SD	No.	%	Mean±SD
Low	28	93.3	48.75±17.22	28	93.3	60.90±19.10	28	93.3	59.90±19.74
Moderate	2	6.7		2	6.7		2	6.7	
High	-	-		-	-		-	-	

Table No. 7: Repeated measures ANOVA for overall students' behaviour scores in the school environment (control group)

Source of Variation	SS	df	MS	F	p-value	Partial η^2
Time (Pre, Post I, Post II)	1,285.60	2	642.80	2.15	0.12	0.069
Error (Within Subjects)	8,670.40	58	149.49			
Total	9,956.00	60				

Table No. 8: Post-hoc pairwise comparisons – control group (behaviour scores, Bonferroni-adjusted)

Comparison	Mean Difference	Cohen's d	95% CI	p-value
Pre-test vs Post-test I	-12.15	0.64	-28.50, 4.20	0.12 (NS)
Pre-test vs Post-test II	-11.15	0.58	-27.40, 5.10	0.15 (NS)
Post-test I vs Post-test II	1.00	0.05	-10.20, 12.20	0.92 (NS)

DISCUSSION

The current study indicated that the AI-based teaching intervention led to a significant improvement in classroom behavior among learners with learning disabilities. These improvements are unlikely to be attributed to baseline differences, as no statistically significant differences were found between the

experimental and control groups in terms of socio-demographic characteristics and types of learning disabilities prior to the intervention. This baseline equivalence strengthens the interpretation that the observed behavioral changes were primarily related to the AI-assisted instructional program rather than pre-existing group differences. At baseline, both groups were comparable in age, sex, grade level, and

residency, and showed similar distributions of learning disabilities, with dyslexia being the most prevalent. Such homogeneity supports the internal validity of the study design, consistent with previous research emphasizing the importance of group equivalence in intervention studies.¹³

This study showed that experimental group demonstrated significant improvements across all domains of classroom behavior, including engagement, participation, organization, punctuality, cooperation, communication, and compliance with classroom rules. These improvements were evident at Post-test I and largely maintained at Post-test II, indicating both immediate and sustained effects. In contrast, the control group showed only minimal changes, with behavior remaining predominantly within the low range. The shift in overall behavior levels further highlights the magnitude of the intervention effect. While most students in the experimental group were initially classified within the low behavioral range, the majority transitioned to the high range following the intervention, with this improvement sustained over time. This suggests that AI-assisted instruction can provide a structured and supportive learning environment that promotes positive behavioral outcomes. Similar findings have been reported by Hidayat-ur-Rehman¹⁴, who found that AI-based systems enhance student engagement, motivation, and self-regulation.

This study showed that highly significant effect of time in the experimental group, with a very large effect size, indicating substantial behavioral improvement across measurement points. Pairwise comparisons showed significant differences between pre-test and post-tests, while no significant difference was observed between Post-test I and Post-test II, suggesting stability of the intervention effects. In contrast, the control group showed no significant changes over time, indicating limited effectiveness of traditional instructional approaches. These findings are consistent with previous studies demonstrating that AI-based educational methods facilitate personalized learning and improve student engagement, particularly among learners with learning disabilities.¹⁵ The adaptive nature of AI-assisted instruction enables it to address individual learning needs more effectively than conventional teaching methods.

Although adaptive functioning was not directly assessed using a standardized measure, the observed improvements in classroom behavior may reflect enhancements in school-related adaptive functioning, particularly in domains such as task engagement, cooperation, communication, and rule-following. However, this interpretation should be approached with caution, as the study focused solely on classroom behavior. Alenezi¹⁶ and Benzizoune¹⁷ have highlighted that AI cannot fully replace the role of teachers in

providing emotional and social support. The findings of the present study support a complementary approach, where AI-based tools are integrated with teacher guidance to achieve optimal outcomes.

Overall, the magnitude and consistency of behavioral improvements observed in the experimental group suggest that AI-assisted instruction represents an effective strategy for enhancing classroom behavior among students with learning disabilities. These findings support the integration of AI-based interventions in special education settings and highlight the need for further research to explore their impact on broader aspects of adaptive functioning

CONCLUSION

Artificial intelligence-assisted teaching significantly improved classroom behavior among students with learning disabilities compared to traditional instruction. The experimental group demonstrated sustained improvements in engagement, organization, communication, and rule compliance across assessment phases. The effectiveness of AI-based instruction in supporting individualized learning and promoting positive behavioral outcomes in special education settings. Although adaptive functioning was not directly measured, the observed behavioral improvements may reflect related gains; however, this interpretation should be approached with caution.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Zainab Hassan Hussein, Amean A. Yasir
Drafting or Revising Critically:	Zainab Hassan Hussein, Amean A. Yasir
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Homocysteine Level and Some Biochemical Variables in Kidney Patients, Isolation and Partial Purification of Methionine Synthase Enzyme, Preparation of a Compound and its Effect on the Isolated Enzyme

Sabri Ali Sultan¹, Fadhel D. Khaled² and Yasser A.M Sulaiman³

ABSTRACT

Objective: To evaluate serum homocysteine, malondialdehyde, glutathione peroxidase, and tumor necrosis factor- α levels in hemodialysis and non-dialysis chronic kidney disease patients compared with healthy controls, and to assess their relationship with renal function parameters.

Study Design: Comparative study

Place and Duration of Study: This study was conducted at the Department of Pharmaceutical Chemistry, College of Pharmacy, Ninevah University, Iraq from 15th April to 15th October 2025.

Methods: A total of 90 blood samples were collected and divided into three groups (n = 30 each): hemodialysis patients (G1), non-dialysis chronic kidney disease patients (G2), and healthy controls (G3). Serum homocysteine, malondialdehyde, and tumor necrosis factor- α levels were measured using enzyme-linked immunosorbent assay techniques, while glutathione peroxidase activity and renal function tests were determined by a colorimetric method.

Results: Serum homocysteine levels were significantly higher in the hemodialysis group (G1) compared with the control group, whereas significantly lower levels were observed in the non-dialysis chronic kidney disease group (G2). Malondialdehyde concentrations were significantly elevated in hemodialysis patients, indicating increased lipid peroxidation. In contrast, glutathione peroxidase activity was significantly reduced in both patient groups compared with controls. Serum tumor necrosis factor- α levels were significantly increased in both patient groups. Renal function markers, including urea and creatinine, were also significantly elevated, particularly in the hemodialysis group.

Conclusion: Oxidative stress and inflammation intensify with chronic kidney disease progression and dialysis, and suggest that homocysteine may play a key role in linking impaired renal function with redox imbalance in chronic kidney disease patients.

Key Words: Homocysteine, Tumor necrosis factor- α , glutathione peroxidase, Malondialdehyde, Enzyme-linked immunosorbent assay

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INTRODUCTION

¹. Department of Pharmaceutical Chemistry, College of Pharmacy, Ninevah University, Iraq

². Department of Chemistry, College of Science, Tikrit University, Iraq

³. Department of Clinical Laboratory Science, College of Pharmacy, Tikrit University, Iraq

Correspondence: Sabri Ali Sultan, Department of Pharmaceutical Chemistry, College of Pharmacy, Ninevah University, Iraq.

Email: sabri.ali@uoninevah.edu.iq

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Chronic kidney disease (CKD) represents a major global health burden and is characterized by a persistent decline in glomerular filtration rate (GFR) and/or structural kidney damage lasting more than three months. Beyond the progressive loss of renal excretory function, CKD is increasingly recognized as a complex systemic disorder involving metabolic dysregulation, oxidative imbalance, endothelial dysfunction, and chronic low-grade inflammation.^{1,2}

One of the metabolic abnormalities frequently observed in CKD is hyperhomocysteinemia. Homocysteine is a sulfur-containing amino acid generated during methionine metabolism and normally undergoes remethylation to methionine or transsulfuration to cysteine. Impaired renal clearance, reduced enzymatic activity, and deficiencies in folate-dependent pathways, collectively contribute to elevated circulating

homocysteine levels in CKD patients.³ Increased homocysteine has been implicated in endothelial injury, vascular smooth muscle proliferation, and prothrombotic tendencies, thereby contributing to the markedly elevated cardiovascular risk observed in both dialysis and non-dialysis CKD populations.⁴

Oxidative stress plays a central mechanistic role in the progression of renal injury. It arises from an imbalance between reactive oxygen species (ROS) production and antioxidant defense systems. In CKD, multiple factors enhance ROS generation, including mitochondrial dysfunction, chronic inflammation, activation of the rennin-angiotensin system, and exposure to dialysis membranes in hemodialysis patients.⁵ Elevated levels of lipid peroxidation products such as malondialdehyde (MDA) and altered activity of antioxidant enzymes, including glutathione peroxidase and superoxide dismutase, have been consistently reported in individuals with impaired renal function.⁶

Chronic inflammation is another hallmark of CKD. Tumor necrosis factor- α (TNF- α) is a key pro-inflammatory cytokine involved in immune modulation, apoptosis, and intracellular signaling pathways. Circulating TNF- α concentrations are frequently elevated in CKD patients and have been associated with declining renal function, protein-energy wasting, and cardiovascular morbidity.⁷ In the context of hemodialysis, repeated blood-membrane interaction and complement activation further stimulate cytokine release, perpetuating a sustained inflammatory milieu.⁸ Importantly, growing evidence supports a biological interplay between hyperhomocysteinemia, oxidative stress, and inflammatory cytokines. Elevated homocysteine can enhance oxidative stress through auto-oxidation and reduced nitric oxide bioavailability, which in turn activates redox-sensitive transcription factors such as nuclear factor-kappa B (NF- κ B), promoting increased production of TNF- α and other inflammatory mediators.⁹ This interconnected network may contribute to endothelial dysfunction and progressive renal damage. Therefore, simultaneous evaluation of homocysteine, oxidative stress markers, TNF- α , and renal function parameters may provide a more integrated understanding of the metabolic-inflammatory axis in both hemodialysis and non-dialysis CKD patients.¹⁰

METHODS

This comparative study was conducted at Qayyarah General Hospital, Iraq from 15th April to 15th October 2025. Sixty people between the ages of 20 and 65 who had been diagnosed with CKD were enlisted and divided into two groups: those receiving regular hemodialysis (G1, n=30) and those not receiving dialysis (G2, n=30). Thirty individuals who seemed to be in good condition and were matched for age and sex with the patient groups made up the control group (G3).

There were a total of ninety competitors. Serum levels of homocysteine and MDA were determined by a competitive ELISA method. Measurement of TNF- α was performed using a sandwich ELISA technique based on antigen-antibody specific binding. Glutathione peroxidase activity was determined using a colorimetric method based on the Trinder reaction according to the principle described by Paglia and Valentine. In addition, serum urea, creatinine, and uric acid levels were measured using standard enzymatic colorimetric methods with commercially available diagnostic kits, following the manufacturer's instructions. The determination of urea was based on the urease-Berthelot reaction, creatinine was measured using the kinetic Jaffe method, and uric acid was determined by the uricase-peroxidase method.

Data were statistically analyzed using the Minitab software program (Version 17). Analysis of variance (ANOVA) was applied to assess significant differences among the studied groups. Mean values were compared using Duncan's Multiple Range Test at a significance level of $p \leq 0.05$. Pearson's correlation coefficient (r) was used to evaluate the relationship between plasma homocysteine levels and renal function biomarkers.

RESULTS

The significant biochemical changes associated with disease progression and dialysis and biochemical parameters, including homocysteine, MDA, GPx, TNF- α , and renal function markers. A significant ($P \leq 0.05$) elevation in serum homocysteine levels in hemodialysis patients (G1) compared to non-dialysis CKD patients (G2) and controls (G3). The average 819.8 ± 34.1 ng/ml in group G1, 492.0 ± 55.4 ng/ml in G2 and 573.0 ± 85.6 ng/ml in the control group (G3) respectively. This increase can be attributed to impaired renal clearance of homocysteine and dysfunction of its metabolic pathways, particularly remethylation and trans-sulfuration, which become more pronounced with progressive renal impairment. Serum malondialdehyde levels were significantly higher ($P \leq 0.05$) while the distribution pattern among groups in dialysis patients compared to non-dialysis patients and healthy groups. The mean values were 20.78 ± 5.35 ng/ml in group G1, 10.73 ± 4.66 ng/ml and 10.48 ± 4.03 ng/ml in the control group (G2, G3) respectively indicating enhanced lipid peroxidation and increased oxidative stress. Regarding antioxidant status, glutathione peroxidase (GPx) activity was significantly reduced in both patient groups compared with the control group. GPx activity decreased by approximately 33%, with mean values was 56.94 ± 9.84 IU/L in the first group and 58.47 ± 7.22 IU/L in the second group, versus 166.67 ± 5.06 IU/L in healthy controls (Table 1, Figs. 1-3).

The average level of urea were 116.67 ± 8.71 mg/dl in G1, 75.47 ± 6.04 mg/dl in G2, and 32.97 ± 5.69 mg/dl in the control group (G3). The creatinine levels were

7.02±2.39 mg/dl, 6.07±1.31 mg/dl, and 1.05±0.12 mg/dl, respectively. Both urea and creatinine concentrations were significantly higher in hemodialysis patients (G1) and non-dialysis CKD patients (G2) compared with controls ($p \leq 0.05$), with the highest levels observed in the dialysis group, indicating progressive impairment of renal function. The mean serum uric acid was 4.521±1.159 mg/dl in G1,

5.747±0.604 mg/dl in G2, and 4.193±0.418 mg/dl in G3. Unlike urea, creatinine and uric acid levels were significantly elevated in not dialysis CKD patients (G2) ($p \leq 0.05$) but decreased in hemodialysis patients (G1) compared to controls ($p \leq 0.05$). Overall, the findings of the present study indicate a clear association between impaired renal function, oxidative stress, and inflammation in patients with chronic kidney disease.

Table No. 1: Biochemical parameters in hemodialysis, non-dialysis CKD patients and controls

Variable	G1	G2	G3	P value
Homocysteine (ng/mL)	819.8±34.1	492.0±55.4	573.0±85.6	0.01*
MDA (ng/mL)	20.78±5.35	10.73±4.66	10.48±4.03	0.01*
GPx (IU/L)	56.94±9.84	58.47±7.22	166.67±5.06	0.01*
TNF- α (Pg/mL)	22.99±1.48	24.96±5.05	8.64±0.83	0.001*
Urea (mg/dl)	116.67±8.71	75.47±6.04	32.97±5.69	0.01*
Creatinine (mg/dl)	7.017±2.390	2.373±1.31	1.052±0.12	0.01*
Uric acid (mg/dl)	4.521±1.159	6.070 ± 0.604	5.12±0.418	0.01*

* $P \leq 0.05$ (Significant)

Table No. 2: Correlation between homocysteine and selected biochemical parameters in study groups

Parameters	G1	G2	G3
MDA	0.235	0.471	0.616
GPx	- 0.104	0.323	0.431
TNF- α	- 0.115	0.203	- 0.06
Urea	- 0.203	-0.234	0.382
Creatinine	- 0.044	-0.329	0.2
Uric acid	0.283	-0.003	0.064

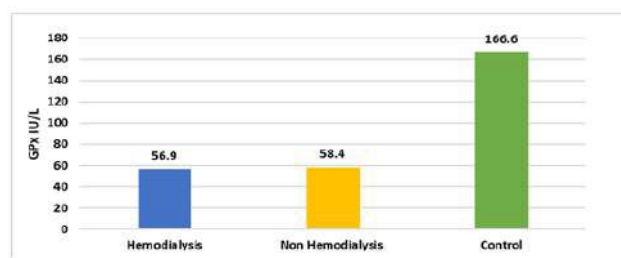


Figure No. 3: Glutathione peroxidase levels

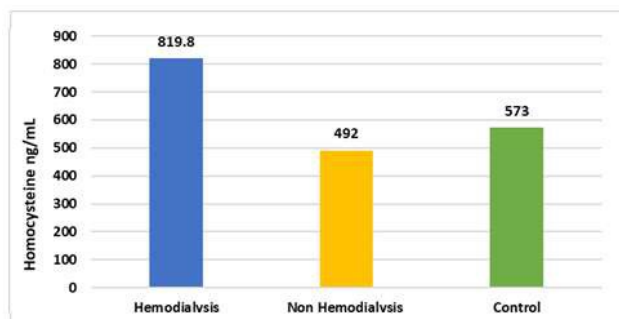


Figure No. 1: Homocysteine levels

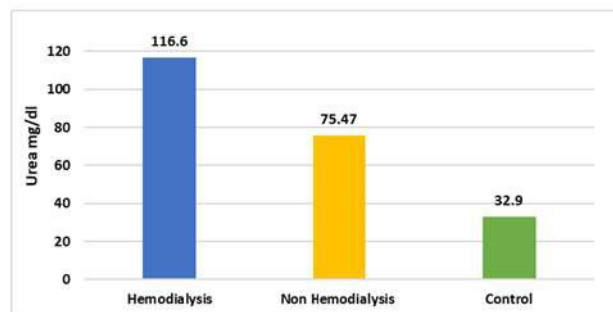


Figure No. 4: Urea levels

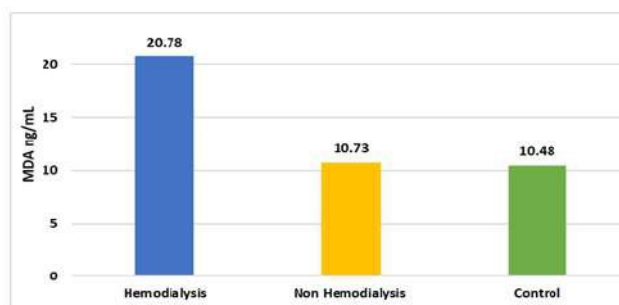


Figure No. 2: Malondialdehyde levels

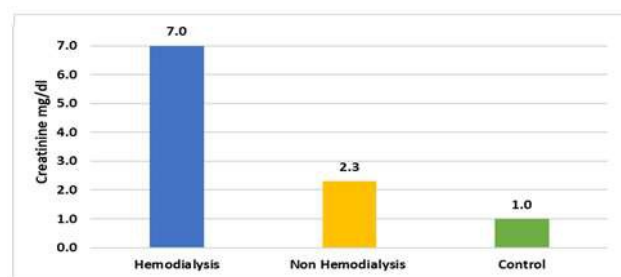


Figure No. 5: Creatinine levels

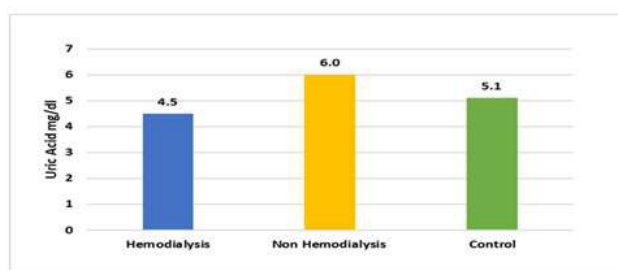


Figure No. 6: Uric acid levels

The significant elevation in serum homocysteine, MDA, TNF- α , urea, and creatinine levels, together with the marked reduction in GPx activity, suggests that CKD patients experience increased oxidative stress and inflammatory responses accompanied by diminished antioxidant defense mechanisms. The correlation analysis revealed a positive association between serum homocysteine and MDA levels across all studied groups, with the strongest correlation observed in the control group (Table 2, Figs. 4-6).

DISCUSSION

Hyperhomocysteinemia is a well-recognized metabolic disturbance in CKD and has been shown to worsen as glomerular filtration rate declines, reaching its highest levels in patients undergoing hemodialysis.¹¹ The markedly elevated homocysteine concentrations observed in the hemodialysis group are consistent with previous reports indicating that dialysis is insufficient to fully normalize homocysteine levels, despite partial removal during treatment sessions. In addition, uremic toxicity and deficiencies of folate and B-complex vitamins may further disrupt homocysteine metabolism in these patients. Several studies have highlighted a strong association between elevated homocysteine levels and increased cardiovascular risk in patients with end-stage renal disease.¹² While patients with CKD not on dialysis showed significantly lower plasma homocysteine levels compared to dialysis patients and healthy individuals, this may be attributed to strict adherence to low-protein diets aimed at slowing the decline in kidney function, as well as variations in dietary intake and vitamin levels that affect homocysteine metabolism. Nevertheless, elevated homocysteine levels remain a clinically important biomarker in CKD, given their strong association with endothelial dysfunction and an increased risk of cardiovascular disease.^{13,14}

Serum malondialdehyde supports the concept that oxidative stress intensifies in advanced stages of kidney disease, particularly in patients receiving hemodialysis. Elevated MDA levels in this group may result from chronic inflammation, accumulation of uremic toxins, and repeated exposure to bioincompatible dialysis membranes, all of which promote excessive generation of reactive oxygen species.¹⁵ In contrast, no significant

difference in MDA levels was detected between non-dialyzed CKD patients and healthy controls, suggesting that oxidative damage becomes more evident in later stages of renal dysfunction. Similar findings have been reported in previous studies, which demonstrated that markers of oxidative stress are markedly elevated mainly in patients with end-stage renal disease rather than in those with early or moderate CKD.¹⁶ The significantly higher malondialdehyde levels observed in hemodialysis patients compared with non-dialyzed CKD patients may be attributed to dialysis-induced oxidative stress, as previously reported by Durak et al.¹⁷ Glutathione peroxidase reduction reflects a substantial impairment of the antioxidant defense system in patients with chronic kidney disease. The decreased GPx activity may be attributed to selenium deficiency, reduced enzymatic synthesis, and/or oxidative inactivation under uremic conditions. Consistent with the present findings, previous studies have reported significantly diminished GPx activity in both non-dialyzed CKD and hemodialysis patients, supporting the concept of a disrupted redox balance characterized by excessive oxidant generation and weakened antioxidant capacity.^{18,19}

The absence of a significant difference in GPx activity between hemodialysis and non-dialyzed patients suggests that impairment of antioxidant defenses may occur early in the course of chronic kidney disease and persist throughout disease progression. This sustained reduction in antioxidant capacity may increase susceptibility to oxidative injury, endothelial dysfunction, and subsequent cardiovascular complications.

Overall, the concurrent elevation of homocysteine and MDA levels, together with the reduction in GPx activity observed in the present study, supports the hypothesis that oxidative stress and impaired antioxidant defense play a central role in the pathophysiology of chronic kidney disease. These alterations appear to be more pronounced in hemodialysis patients, highlighting the contribution of dialysis-related factors to oxidative imbalance and systemic inflammation.²⁰

Elevated levels of tumor TNF- α in patients with CKD and those undergoing hemodialysis are primarily attributed to the persistent inflammatory state associated with renal dysfunction. CKD is increasingly recognized as a condition characterized by chronic low-grade systemic inflammation resulting from the accumulation of uremic toxins, oxidative stress, and immune system dysregulation. These factors stimulate immune cells, particularly monocytes and macrophages, to produce higher levels of pro-inflammatory cytokines such as TNF- α . Consequently, circulating TNF- α concentrations in CKD patients are significantly higher than those observed in healthy individuals.^{21,22}

Additionally, inflammatory cytokines including TNF- α have been shown to be strongly associated with the presence and severity of chronic kidney disease. Clinical studies demonstrated that serum TNF- α levels are significantly higher in CKD patients compared with healthy controls and are independently associated with reduced glomerular filtration rate and increased albuminuria.²³

The high increase in the renal functional indicators, especially, serum urea and creatinine, in patients under hemodialysis can be explained by the existence of advanced chronic kidney disease with a severe decrease in the level of glomerular filtration rate (GFR). The functional loss of nephrons with time causes functional impairment in the clearance of nitrogenous wastes products by the kidney, which ultimately makes it find its way into the circulatory system. Even though these metabolites are partially cleared by hemodialysis, they are not fully cleared and build up in between dialytic sessions which lead to continuously high levels. Moreover, higher protein metabolism, persistent inflammation and metabolic alterations that are likely to accompany end-stage renal disease can also contribute to urea levels, although serum creatinine is a dependable measure of reduced renal clearance capacity and disease progression in patients on dialysis.²⁴

Serum uric acid reflects the partial clearance of uric acid during dialysis sessions, whereas the kidneys decreased ability to excrete uric acid in non-dialysis CKD leads to its accumulation. Elevated uric acid in CKD has important clinical implications, as they contribute to oxidative stress, hypertension, and further progression of renal dysfunction.²⁵

The alterations may contribute to the progression of renal dysfunction and related complications, particularly in hemodialysis patients. The correlation analysis revealed a positive association between serum homocysteine and malondialdehyde (MDA) levels across all studied groups, with the strongest correlation observed in the control group (Table 2). This finding suggests a close link between hyperhomocysteinemia and oxidative stress, as elevated homocysteine levels are known to promote the generation of reactive oxygen species and lipid peroxidation.²⁶ In contrast, an inverse relationship was observed between homocysteine and GPx activity in the patient groups, indicating that increased homocysteine levels may be associated with impaired antioxidant defense mechanisms. This reduction in GPx activity could contribute to the accumulation of oxidative damage in CKD patients.²⁷

The relationship between homocysteine and TNF- α varied among the groups, reflecting the complex interaction between metabolic disturbances and inflammatory pathways in CKD. The observed alterations suggest that homocysteine may indirectly influence inflammatory responses through oxidative stress-mediated mechanisms.²⁸

Furthermore, weak and inconsistent correlations were found between homocysteine and renal function markers (urea, creatinine, and uric acid), which may indicate that homocysteine levels are influenced not only by renal impairment but also by additional metabolic and nutritional factors.²⁹

Overall, these findings support the hypothesis that homocysteine plays a central role in linking oxidative stress and inflammation in CKD, particularly in patients undergoing hemodialysis.³⁰

CONCLUSION

Patients with chronic kidney disease, particularly those undergoing hemodialysis, exhibit significant alterations in several biochemical and inflammatory markers compared with healthy controls. Serum homocysteine, malondialdehyde, tumor necrosis factor- α , urea, and creatinine levels were significantly elevated, whereas glutathione peroxidase activity was significantly reduced. The enhanced oxidative stress, inflammation, and impaired antioxidant defense mechanisms in chronic kidney disease patients.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Sabri Ali Sultan, Fadhel D. Khaled
Drafting or Revising Critically:	Sabri Ali Sultan, Yasser A.M Sulaiman
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Inculcating Compassion and Emotional Intelligence in Nursing Students: Building a Foundation for Empathetic Care

Syeda Aatika Batool, Madiha Mukhtar and Azeem Kaleem

Inculcating
Compassion and
Emotional
Intelligence in
Nursing Students

ABSTRACT

Objective: To examine the impact of a comprehensive educational program on emotional intelligence and compassion among nursing students at The University of Lahore.

Study Design: A quasi-experimental study

Place and Duration of Study: This study was conducted at the at Lahore School of Nursing, The University of Lahore, Pakistan from 20th March 2025 to 31st December 2025.

Methods: The study was a quasi-experimental study was conducted among 108 nursing students chosen using a universal sampling methodology. The participants were split into experimental (n=54) and control (n=54) groups. The experimental arm was given a structured learning intervention that included 60 minute sessions twice per week which included lectures, role plays, videos and scenario based learning on emotional intelligence and compassion, whilst the control group was not provided with anything. The Emotional Intelligence Evaluation Scale and the Compassion Scale were used to evaluate outcomes and the pre and post intervention scores were compared between the groups.

Results: There was a statistically significant change in emotional intelligence ($p=0.007$) and compassion ($p=0.015$). The experimental group had better scores in post-intervention EI (3.43 ± 0.61) than the control group (3.06 ± 0.64). Likewise, the scores in compassion were greatest in the experimental group (4.02 ± 1.13) than in the control (3.05 ± 0.62) and pre-intervention (3.33 ± 0.53).

Conclusion: The educational intervention was structured and found to be highly effective at enhancing emotional intelligence and compassion amongst nursing students, as well as at promoting crucial competencies to provide empathetic and patient-centered care to patients.

Key Words: Compassion, Emotional intelligence, Nursing students, Educational intervention

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INTRODUCTION

Compassionate care has gained growing acknowledgment as a crucial aspect of nursing practice. Traditionally, Florence Nightingale has placed emphasis on compassion as a key ethical virtue and a necessity to good nursing. Compassion as a professional value is also supported by the International Council of Nurses in modern healthcare, which has an impact on clinical decision-making and providing high-quality and patient-centered care.

Lahore School of Nursing, Faculty of Allied Health Sciences, The University of Lahore.

Correspondence: Syeda Aatika Batool, Lahore School of Nursing, Faculty of Allied Health Sciences, The University of Lahore.

Contact No: 03334938527

Email: aatikabaqari@gmail.com

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Compassion is a profound level of understanding the suffering of patients and a strong wish to help patients, which is the basis of caring and therapeutic relationships. The nursing practice is by nature a pressure situation where nurses are exposed to critical illness, death, demanding workloads and time constraints. All these difficulties make emotional stress and emotional regulation and resilience among nurses significant.¹ Emotional intelligence (EI) as the capacity to perceive, understand and control personal and other people emotions is an important aspect of nursing practice. It improves interpersonal communication, promotes clinical decision-making, and improves patient outcomes through developing effective nurse-patient relationships.² Moreover, EI helps nurses to withstand stressful situations at work, adjust to the changing clinical setting, and stay psychologically healthy.³

There is evidence indicating that compassion and emotional intelligence are both critical determinants of clinical competence, because they combine knowledge, skills, values, and attitudes to efficient nursing care.² These attributes are however affected by personal and organizational factors such as training, role modeling,

and work environment.⁴ Although it is important, research has shown that nursing students tend to show moderate levels of compassion and emotional intelligence, which is why special educational interventions are needed.⁵ Furthermore, it was revealed that emotional intelligence can serve as a buffer to compassion fatigue and burnout, prevalent among healthcare professionals who are under the considerable influence of emotional stress over an extended period.⁶ Structured training programs, role-play and learning through simulation have been suggested as educational methods of improving these competencies among nursing students.⁵

Considering the increased focus on patient-centered care and the emotional aspects of clinical practice, structured interventions that will help to foster compassion and emotional intelligence in nursing education are inevitable. Thus, the purpose of the current study is to examine the impact of a designed didactic intervention on compassion and emotional intelligence in nursing students.

METHODS

The quasi-experimental study was carried at Lahore School of Nursing, The University of Lahore from 20th March 2025 to 31st December 2025 in a sample of 108 nursing students of 3rd year who were selected using the universal sampling method. The participants were separated into experimental (n=54) and control (n=54) groups. The experimental group underwent a designed educational intervention, comprising of 60 minutes sessions with twice a week, involving lectures, role plays, videos, and scenario based learning about emotional intelligence and compassion, whereas the control group did not receive any intervention. The inclusion Criteria was 3rd year BSc students. Nursing students who cleared their 2nd year examination, have basic communication skills to actively engage in intervention plan activities. The exclusion criteria were 3rd year nursing students who are away or absent longer time i.e. 01 week during the course, diagnosed with psychological illness before. Individuals who have undergone previous training/certifications on compassion/emotional intelligence to ensure the ability to retain baseline level to be used with intervention evaluation. The educational process was aimed at the improvement of the emotional intelligence and compassion and included 60-minute sessions that were performed twice a week. The intervention involved some structured lectures about emotional intelligence and compassion, and the role they can play in clinical practice. Along with didactic instruction, interactive techniques like role-plays, video-based learning, and scenario-based discussions were included to promote experiential learning and the development of skills. Standardized and validated instruments were used to perform the outcome assessment. To assess emotional

intelligence, the Emotional Intelligence Evaluation Scale created by Hall⁷ was used and it has 30 items in five subscales, which are emotional awareness, emotion management, self-motivation, empathy, and social skills. Compassion was measured based on the Compassion Scale created by Pommier⁸, comprising of 24 items divided into six sub scales: kindness, indifference, common humanity (intentional sharing), separation, mindfulness (conscious awareness) and disengagement. The two tools are found to be good in reliability with Cronbachs alpha of 0.89 in emotional intelligence and 0.85 in compassion reported in earlier validation of the two tools among the nursing students.^{8,9} Pre-intervention and post-intervention data were taken and compared to the control group and experimental group to measure the impact of the educational program on the levels of emotional intelligence and compassion. SPSS version 27 was used to analyze the data. The Kolmogorov Smirnov test was used to test the normality of the data distribution. Kruskal Wallis H test was used to compare pre- and post-intervention within groups. A p-value of below 0.05 was taken to be statistically significant.

RESULTS

Most of the participants were between the ages of 18 and 22 (82.4%), which showed that the group of participants was mostly young. The percentage of males (58.3%) was slightly higher than the percentage of females (41.7%). The majority of participants were middle socioeconomic group (76.9%), nuclear families (68.5%), indicating a fairly homogenous background. On the issue of career motivation, family influence was the most frequently used reason (36.1%) then the personal interest (22.2%) and the need to be employed early (19.4%). These results show that socio-demographic variables as well as external factors are influential in determining career decisions by nursing students. (Table 1)

Table 2 demonstrates statistically significant differences among the pre-intervention, control, and experimental groups for both emotional intelligence and compassion scores. For emotional intelligence, a significant difference was observed ($p=0.007$). The experimental group showed higher mean scores (3.43 ± 0.61) compared to the control group (3.06 ± 0.64), indicating a positive effect of the intervention. Although the pre-intervention mean was higher (4.05 ± 0.82), the post-intervention improvement in the experimental group relative to the control group suggests the effectiveness of the educational program. Similarly, for the Compassion Scale, a statistically significant difference was found ($p=0.015$). The experimental group achieved the highest mean score (4.02 ± 1.13), exceeding both the pre-intervention (3.33 ± 0.53) and control group scores (3.05 ± 0.62).

Table No. 1: Sociodemographic characteristics of study participants (n=108)

Variable	Category	No.	%
Age (years)	18-22	89	82.4
	23-27	16	14.8
	28-32	3	2.7
Gender	Male	63	58.3
	Female	45	41.7
Family type	Nuclear	74	68.5
	Extended	34	31.5
Socioeconomic status	Lower class	18	16.6
	Middle class	83	76.9
	Upper class	7	6.4
Reason for Choosing Nursing	Family wish	39	36.1
	Personal interest	24	22.2
	Quick profession	21	19.4
	Job availability	18	16.6
	Health-related field	3	2.7
	To serve humanity	3	2.7

Table No. 2: Overall mean difference and score comparison of control and experimental groups with Kruskal–Wallis Test

Components	Groups	Size	Score	Mean±SD	Sig (p-value)
Emotional Intelligence	Pre-Intervention	N = 108	121.64	4.05±0.82	0.007
	Controlled	N = 54	70.31	3.06±0.64	
	Experimental	N = 54	185.57	3.43±0.61	
Compassion Scale	Pre-Intervention	N = 108	80.01	3.33±0.53	0.015
	Controlled	N = 54	73.31	3.05±0.62	
	Experimental	N = 54	120.57	4.02±1.13	

Overall, these findings indicate that the structured educational intervention significantly improved both emotional intelligence and compassion among nursing students compared to the control group.

DISCUSSION

The current research has shown that a well-designed education program had a significant positive effect on the emotional intelligence and compassion levels in nursing students. The results indicated statistically significant difference between groups in emotional intelligence ($p=0.007$) and compassion ($p=0.015$) with high mean scores being recorded in the experimental group compared to the control group. The findings emphasize the usefulness of specific educational interventions in improving the key psychosocial skills needed in patient-centered care. The high level of improvement in compassion that was found in this study is in line with the recent literature. One study done in Iran found out that empathy-based educational intervention led to significant increase in compassion among nursing students and both cognitive and affective elements of empathy were significantly improved after the intervention.¹⁰

Equally, Xue et al¹¹ showed that professionalism, empathy, and humanistic care skills among nursing

students were significantly enhanced through structured compassion-focused training, compared to controls, supporting the importance of educational interventions in cultivating compassionate care. Such results are consistent with the present research since the intervention group demonstrated a greater level of compassion which proves the effectiveness of structured training in the development of empathetic interaction in clinical practice. In terms of emotional intelligence, this study has found the same results as the other studies conducted in this area that show that educational and simulation-based interventions are effective in improving emotional intelligence in nursing students. The group of Arrogante et al¹² showed large improvements in emotional attention, clarity, and regulation after high-fidelity simulation training, which makes the role of experiential learning in the development of emotional skills a priority. Ko et al¹³ discovered that structured interventions yielded durable emotional competence improvement over time and the effect was significant at the follow-up assessments. These results can be compared to those of the current study, in which the experimental group exhibited much greater emotional intelligence scores than the control group, which proves the beneficial influence of planned educational programs. Moreover, our findings are backed by the fact that a strong connection was

observed between emotional intelligence and decreased stress, burnout, and compassion fatigue among health care workers. Filipponi et al¹⁴ found out that the better emotional intelligence, the less compassion fatigue and better coping strategies, which corresponds to the protective nature of emotional intelligence in clinical practice. This highlights the need to incorporate emotional intelligence training in nursing programs to improve professional abilities, as well as, psychological health. The results of this research indicate that the intervention was especially effective in improving cognitive and behavioral levels of compassion and emotional intelligence. Learning approaches such as role-play, scenario learning, and interactive sessions could have led to better self-awareness, empathy, and emotional regulation of the participants. These results reinforce the importance of incorporating experiential and student-centered learning approaches in nursing education.

CONCLUSION

The systematic learning program greatly enhanced emotional intelligence and compassion in nursing students. Experimental scores were greater than control ones, which evidenced the adequacy of specific educational tools to promote the main competencies in empathetic and patient-centered care.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Syeda Aatika Batool, Madiha Mukhtar
Drafting or Revising Critically:	Syeda Aatika Batool, Azeem Kaleem
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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The Outcomes of Kulkarni's Dorsal Onlay Buccal Mucosal Graft Urethroplasty in Patients with Anterior Urethral Stricture: A Single Center Experience

Majed A Mohammad¹ and Hussain Odey Fahad²

ABSTRACT

Objective: To assess the success & the complications of Kulkarni's dorsal onlay buccal mucosal graft urethroplasty in patients with anterior urethral stricture.

Study Design: Prospective trial study

Place and Duration of Study: This study was conducted at the Basra Urology Center, Iraq between April 2022 and September 2024.

Methods: 20 patients with anterior urethral stricture received Kulkarni's dorsal onlay buccal mucosal graft urethroplasty. Retrograde urethrogram was done one week after removing the Foley's catheter, and urine flowmetry is usually done 3 & 6 months following the urethroplasty. Patients were kept on follow-up every 3 & 6 months.

Results: The averages of age was 40.65 years, urethral stricture length was 4.25 cm, operative time was (175±7.78 minutes, hospitalization period was 2.35±0.81 days, American Urological Association Symptom Score was (22.1±3.22) and Q max was 5.47±0.69 ml/s. Successful urethroplasty was achieved in 17 (85%) patients, while 3 patients (15%) had recurrent stricture. There was an improvement in the average maximal urine flow rate to 16.87±0.87 ml/s and 16.42±0.67 ml/s postoperatively at 3 and 6 months respectively. The improvement in the Q max was neither correlated with patients' age nor with the stricture length. The American Urological Association Symptom Score was improved to 5.15±1.26 and 6.20±1.00 postoperatively at three and six months.

Conclusion: The dorsal onlay buccal mucosal graft urethroplasty procedure, developed by Kulkarni, shown a low risk of complications and a high success rate.

Key Words: Buccal mucosa, Urethral stricture, Urethroplasty; American Urological Association Symptom Score

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INTRODUCTION

Numerous surgical approaches have been used to treat urethral stricture throughout the history of urology. Procedures that provide a long-lasting result, little morbidity, and minimal sexual adverse effects have been the cornerstone of treatment. With failure rates of 20% to 30%, local flaps of the penile and scrotal skin were the mainstay of early treatment for urethral stricture illness.¹ The buccal mucosa was referred to as the perfect graft tissue when Sapezhko initially used buccal mucosal grafts (BMGs) for urethral repair in the

early 19th century due to its robust epithelium, resistance to infection, and simplicity of transfer.^{1,2}

The dorsal onlay technique with BMGs for bulbar urethral strictures was made famous.³ Kulkarni et al⁴ reported a unilateral dorsal onlay with BMGs. Buccal mucosa is currently the most common graft used in substitute urethroplasty.⁵ Scarring causes the urethra's lumen to narrow, a condition known as urethral stricture, which can obstruct the lower urinary system. By producing micturition issues and destroying the entire urinary system, this obstruction can have a major negative effect on the patient's quality of life and cause irreversible kidney damage.⁶

The symptoms of the patients must be evaluated, potential causes should be noted, prior therapies and problems should be noted, and related factors that could affect the surgical outcome should be identified.⁷ The majority of presenting symptoms 54.3% were lower urinary tract symptoms. Urinary retention 22.3%, catheterization difficulties 4.8%, and urinary tract infections UTI 6.1% were other less frequent presentations.⁸

Weak stream 49%, inadequate emptying 27%, and urine frequency 20% were the most prevalent complaints. 73% of patients have postvoid dribble.⁹

¹. Department of Urology, College of Medicine, University of Basra Iraq

². Department of Urology, Basra Teaching Hospital, Basra, Iraq

Correspondence: Majed A Mohammad, Department of Urology, College of Medicine, University of Basra Iraq.
Contact No: +9641392433
Email: majed.muhammed@uobasrah.edu.iq

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Another typical symptom that affects 22.9-71% of people is pain.^{1,2} More severe symptoms of the lower urinary system are associated with pain, which is typically felt in the bladder and/or urethra. Pain is more common in younger boys and usually goes away following reconstructive surgery.¹⁰ Other manifestations include incontinence 1-4%, urgency 14%, urethral abscess or necrotizing fasciitis 2.3% and visible hematuria 3.1-5%.⁸ This study aimed to assess the success and the complication rate of BMG urethroplasty by dorsal onlay (Kulkarni technique) in anterior urethral stricture.

METHODS

This prospective study was done in the Basra Urology Center between April 2022 and September 2024 vide letter No. 341 dated 15th March 2022. Twenty individuals with anterior urethral stricture underwent buccal mucosa graft urethroplasty using Kulkarni's technique. All the patients underwent at least a single urethrotomy. Selected patients were kept on suprapubic catheters. Preoperative assessment included history and physical examination, general urine examination, renal function test, retrograde urethrogram, uroflowmetry, and urethroscopy (not routinely done). Individuals who have anterior urethral stricture, regardless of the cause of the stricture were included. Those with a history of failed previous urethroplasty were excluded.

Firstly, the patient is intubated either orally or by the nose. In order to prevent peroneal nerve damage, the patient is put in a basic lithotomy posture with their heels properly positioned to reduce pressure on their calves. The skin of the scrotum, perineum, and suprapubic region is cleaned, shaved, and covered. Using different sets of tools, two surgical teams operate concurrently at the donor and recipient locations. The standard approach involves harvesting the oral mucosal graft from the cheek and using 4/0 polyglactin sutures to seal the donor site in a running way. 7 Fr is used to do a urethroscopy.

Semirigid ureteroscope with a guide wire insertion, which confirms the exact proximal end of the stricture and helps guide the extent of urethrotomy. A small well-lubricated Foley's catheter (10-12 Fr) was inserted, which helps in urethral delineation and orientation during surgery. The central tendon of the perineum and the bulbospongiosus muscle remain intact when the bulbar urethra separates from the corpora cavernosa just along the left side, starting at the distal tract where no muscles are present. Because the urethra is entirely integrated into the corpora cavernosa, its lateral vascular blood supply is maintained along the right side. It is possible to execute penile invagination into the perineal wound for penile or pan-urethral strictures. With the urethra slightly mobilized toward the left. The surface of the lateral urethra is exposed. After mobilization is complete, the dorsal urethral surface is sliced along the midline to determine the distal extent of the stenosis.

The urethrotomy is then extended both proximally and distally to incise the stricture over its whole length. After being cut to the proper size based on the urethrotomy's length and width, the oral mucosal graft is spread firmly across the tunica albuginea. Using 4/0 polyglactin sutures, the urethrotomy's proximal and distal apices are attached to the two graft apices. The urethral mucosal plate's left edge is sutured to the oral transplant's right margin in a running pattern. Inserted is a silicone catheter featuring a Foley 16 F groove. The bulbospongiosus muscle is left intact as the urethra rotates back to its original place over the graft. Using interrupted 4/0 polyglactin sutures, the urethral margins are secured to the corpora cavernosa over the left side graft. The urethra and muscles cover the graft fully at the end of the surgery. For three weeks, the catheter remains in place. All patients are kept on injectable followed by oral antibiotics for a few days.

Urine flowmetry is typically performed three and six months after urethroplasty, and calibration using Foley's catheters and RUG was completed one week after the removal of the Foley's catheter, three & six months postoperatively, patients were monitored for the emergence of any obstructive urinary symptoms that would suggest the need for a repeat RUG or urethroscopy. Normal micturition without the necessity for any additional procedures (endoluminal or open reconstructive) was considered a successful urethroplasty. The data was entered and analyzed by SPSS-24. Spearman correlation coefficient was applied. $P < 0.05$ was considered significant.

RESULTS

The mean age was 40.65 with a range of 18-63 years, buccal mucosal graft urethroplasty using Kulkarni's dorsal onlay technique. 55% of strictures were idiopathic, 30% were caused by BXO/lichen sclerosis and inflammation, and 15% were caused by trauma (Table 1).

The strictures site was penile in 50% of patients, bulbar in 40%, and panurethral in 10% of patients, and the mean length of the stricture was 4.25 cm. The average AUASS was 22.1 ± 3.22 and mean Q max (ml/s) was 5.74 ± 0.69 . The associated comorbidities were found in 40% of patients, 20% of them have DM, 10% have HTN and 10% have IHD (Table 2). The average duration of the procedure was 175.85 ± 7.78 minutes, and the average length of hospitalization was 2.35 ± 0.81 days (Table 3).

Three patients experienced postoperative wound infections, all of which were effectively treated by changing antibiotics in response to a wound swab sensitivity test and culture. Two patients experienced post-void dribbling, which was treatable with conservative measures. Incontinence of urine, de novo erectile dysfunction, or surgical diverticulum formation did not occur. Successful urethroplasty was achieved in 17 (85%) patients, while three patients (15%) developed strictures at three- and six-months period of follow up. Reduced urine flow (peak urine flow < 15

ml/s), dysuria, and recurrent UTIs were observed in patients with recurrent strictures.

Table No. 1: The reasons for the anterior urethral stricture (N=20)

Cause	No.	%
Idiopathic	11	55
BXO/lichensclerosis/inflammatory	6	30
Iatrogenic	3	15

Table No. 2: Pre-operative parameters

Pre-operative parameters	Value
Mean age (range 18-63 years)	40.65±13.58
Mean stricture length (range 2.3-8 cm)	4.25±1.37
Stricture site	
Penile	10 (50%)
Bulbar	8 (40%)
Pan urethral	2 (10%)
Mean AUASS	22.1±3.22
Mean Q max(ml/s)	5.74±0.69
Associated comorbidities	
DM	4 (20%)
HTN	2 (10%)
IHD	2 (10%)
No comorbidities	12 (60%)

Table No. 3: parameters of the patients post-operatively

Post-operative parameters	Mean±SD
Mean time of operation (minutes)	175.85±7.78
Mean hospital stays (days)	2.35±0.81

Table No. 4: Outcomes and Complications of the operation

Complications	No.	%
No complication	12	60.0
Surgical site infection	3	15.0
Post void dribbling	2	10.0
Recurrent stricture (failure at 3 months)	2	10.0
Recurrent stricture (failure at 6 months)	1	5.0

All of the failed instances reacted favorably to DVIU; One exhibited two stenotic rings at the proximal and distal sites of anastomosis, and two developed a distal anastomotic stricture (Table 4). The improvement in the Q max was neither correlated with patients' age nor with the stricture length (Table 5).

At three and six months, the AUASS dramatically dropped from a mean of 22.1±3.22 before surgery to 5.15±1.26 and 6.20±1.00 afterward ($p<0.001$). The mean peak urine flow rate (Q max) increased from 5.74±0.69 ml/s before surgery to 16.87±0.87 ml/s and 16.42±0.67 ml/s after surgery at three and six months, respectively ($p<0.001$) [Table 6]

Table No. 5: Correlation between patient age, stricture length, and Q max improvement

Variable	Q max improvement	
	R*	P value
Age	0.421	0.065
Stricture length	R*	0.167
	P value	0.481

R*Spearman's correlation coefficient

Table No. 6: Follow-up parameters

Follow-up parameters	Mean±SD	P value
AUASS (preoperative)	22.1±3.22	<0.001
AUASS (at 3 months)	5.15±0.26	
AUASS (at 6 months)	6.20±1.00	
Q max (ml/s) preoperative	5.74±0.69	<0.001
Q max (ml/s) over three months	16.87±0.87	
Q max (ml/s) over six months	16.42±0.67	

DISCUSSION

The gold standard for treating USD is urethroplasty, which has the highest documented success rates and is reasonably priced. In contemporary practice, a wide range of urethroplasty techniques are employed. However, regardless of the method, the common objectives are durability (long-term outcomes), safety (minimum adverse effects), and efficacy (normal voiding without obstruction).¹¹

The stricture's location, duration, and causedetermine the various urethroplasty methods, as demonstrated by Hapson et al.¹² Nevertheless, increased morbidity and stricture recurrence are associated with many of the methods.¹³ Many reconstructive urologists eventually dislike resection and spatulated end-to-end anastomosis, exceptfor traumatic causes of urethral strictures following appropriate counselling.¹⁴ Substitution urethroplasty should be used to treat anterior urethral strictures longer than 2 cm to prevent the development of chordees after surgery. Graft distortion, diverticulum formation, and recurrent stricture are among the problems that have been linked to the use of In replacement urethroplasty procedures, free skin grafts are used as patch or tube grafts.¹⁵

Urinary stasis and ejaculatory dysfunction are more likely to result from fistula, saculation, and diverticula formation following ventral onlay graft. The improved vascularity across the corporal bodies and stronger mechanical support for improved graft uptake, as well as a lower likelihood of sacculatation and fistula formation, are advantages of the dorsal onlay graft technique for the stricture of the anterior urethra.¹⁶

Bagchi et al¹⁷ assessed 42 patients with stricture of the anterior urethra (mean age 38.7 years, ranging from 17 to 62 years) who had BMG urethroplasty using Kulkarni's dorsal onlay technique over a six-month follow-up period (16). 57.1% of strictures were idiopathic, 30.9% were BXO/lichen sclerosis and

inflammatory, and 11.9% were iatrogenic. 80.9% of people were successful. Success is defined by Bagchi et al¹⁷ as requiring no additional procedures after surgery and having a maximal flow rate of more than 15 ml/s during the follow-up period. Forty-eight patients with a follow-up period of one to five years were included in Pathak et al¹⁸, which found a success rate of 79%.

In their trial, which comprised 68 patients with a mean age of 28.16±14.12 and a 12-month follow-up period, Prakash et al¹⁹ found a 91% success rate. Kartal et al²⁰ reported the Kulkarni technique, the success rate was 87.1%.²⁰ Islam et al²¹ included 12 patients with a 48-month follow-up period, had an 83% success rate employing the Kulkarni approach.

All these studies have a success rate comparable to our study (85%). Success rate was defined by Prakash et al¹⁹ as the final follow-up revealed no stricture, no obstructive symptoms, a maximum flow rate >15 ml/s, a urethral diameter >12 Fr, and no need for further treatment. The success rate in research by Pathak et al¹⁸ was characterized as no voiding symptoms, no urethrography abnormalities, a maximum flow rate of more than 15 ml/s, and no need for further intervention. In Bagchi et al¹⁷ The average duration of the operation was 175±22.6 minutes, and the average period of hospitalization was 4.5±2.2 days, which was comparable to our study (175.85±7.78 min) & the hospital stay was (2.35±0.81days). Prakash et al¹⁹ reported mean time of operation was (143.3 min), which was shorter than our study. Kartal et al²⁰ reported the average length of hospital stay and surgery were 179.5±30 min and 3.5±1.2 days, which were comparable to our study.

Numerous parameters, including site, length, degree of spongiofibrosis, number of strictures, and presence of BXO, affect the results of urethroplasty. Risk factors for recurrence include a lengthy history of USD, numerous prior surgeries that resulted in severe spongiofibrosis, periurethral fibrosis, and false passages.²²

Regarding urinary flow rate, Bagchi et al¹⁷, at three and six months after surgery, the mean peak urine flow rate (Q max) increased ranging from 5.65±2.47 ml/s on average to 17.75±4.05 ml/s and 16.82±3.42 ml/s separately. Pisapati et al²³ reported the mean peak urinary flow rate (Q max) improved from 6.8 (5.3-7.7) preoperatively to 20.2 (12.3-23.4) postoperatively in a period of follow-up of 17 months.

Islam et al reported an improvement in maximum flow rate (Q max) from 6-10 ml/s preoperatively to >15 ml/s in 93.5 % of patients in a period of follow-up of 3 and 6 months postoperatively.²¹ In our study mean urinary flow rate (Q max) improved from 5.74±0.69ml/s preoperatively to 16.87±0.87 ml/s and 16.42±0.67 ml/s postoperatively in 3 and 6 months. The improvement in the Q max was neither correlated with patients' age nor with the stricture length. Regarding the improvement in AUASS score, Bagchi et al¹⁷ reported a significant decrease from a mean of 22.1±5.06 preoperatively to 5.16±3.84 and 6.05±4.12 postoperatively at 3 and 6

months. Spencer et al²⁴ reported a decrease in AUASS score from 23 (7-24) to 10 (1-17) on a follow-up period of 44 months.

In the present study, the AUASS decreased considerably from a mean of 22.1±3.22 before surgery to 5.15±1.26 and 6.20 ±1.00 postoperatively at 3 and 6 months (p value <0.001), which is comparable to Bagchi's results. Regarding the complications of surgery, Bagchi et al¹⁷ reported surgical site infection in 3 patients (7.14%), and Prakash et al¹⁹ reported wound infection in 2 patients (2.94%).

According to Kartal et al²⁰ experience, there was no wound infection following Kulkarni's urethroplasty. In this study, we had three patients (15%) who suffered from wound infection, which were all effectively treated by switching antibiotics based on sensitivity and culture.

Regarding postoperative post-void dribbling, Bagchi et al¹⁷ reported that five patients (11.9%) developed post-void dribbling, whereas Prakash et al¹⁹ reported that two patients (2.94%) had post-void dribbling. In our study, two patients (10%) developed post-void dribbling, and all of them were managed conservatively. Regarding postoperative recurrent stricture, Bagchi et al¹⁷ reported that eight patients (19%) developed stricture at 3 and 6 months, all of them responded well to DVIU.

Zumrutbas et al²⁵ reported that six patients (17%) had recurrence, one of them managed by urethral dilatation, two of them were managed by DVIU, one by meatoplasty & the remaining underwent re-urethroplasty. Wan et al²³ reported that five patients (14.3%) developed recurrent stricture, two of them were managed by DVIU & the remaining three patients were managed by staged urethroplasty. In our study, three patients (15%) developed recurrent stricture at three and six months of follow-up, all of them were managed successfully with DVIU.

Bagchi et al¹⁷ reported no diverticulum formation postoperatively, incontinence of urine, or erectile dysfunction, which is similar to our study. In our study, all patients experienced good donor site healing through primary closure. The absence of long-term morbidity is consistent with the findings of Kartal et al.²⁰ In Bagchi et al¹⁷ experience, one patient (2.4%) experienced donor site complications and had temporary trouble opening his mouth.

CONCLUSION

Kulkarni's method of one-sided oral mucosa graft urethroplasty is a reliable, acceptable surgery with a high success rate and few complications.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Majed A Mohammed, Hussain Odey Fahad
Drafting or Revising Critically:	Majed A Mohammed, Hussain Odey Fahad
Final Approval of version:	All the above authors

Agreement to accountable for all aspects of work:	All the above authors
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Association of Sertraline and Escitalopram With Antidepressant Induced Hyponatremia Among Coronary Artery Disease Patients at a Tertiary Care Hospital of Rawalpindi

Sertraline and
Escitalopram
With
Antidepressant
Induced
Hyponatremia

Jasim Tariq¹, Abid Aftab², Izzah Khalid¹, Asif Azeem³, Isbah Gul³ and Tariq Raheem¹

ABSTRACT

Objective: To determine the association of sertraline and escitalopram with antidepressant-induced hyponatremia among coronary artery disease patients.

Study Design: Cross-sectional analytical study

Place and Duration of Study: This study was conducted at the Armed Forces Institute of Mental Health Rawalpindi December 16 till March 15, 2026.

Methods: This study was conducted including 220 patients with coronary artery disease receiving sertraline or escitalopram. Demographic variables included age, gender, and socioeconomic status. Clinical variables included type and duration of coronary artery disease, comorbidities such as hypertension and diabetes, and concurrent medications.

Results: The mean age was 61.4 ± 10.8 years, and hyponatremia was observed in 26.4% of patients. Hyponatremia was more frequent with escitalopram compared to sertraline (65.5% vs 34.5%, $p = 0.003$). Patients with hyponatremia had lower serum sodium (131.1 ± 3.1 vs 139.2 ± 2.8 mEq/L; $p < 0.001$) and higher creatinine levels (2.0 ± 0.9 vs 1.4 ± 0.6 mg/dL; $p < 0.001$). Heart failure, diuretic use, high-dose SSRI therapy, and polypharmacy were significantly associated with hyponatremia ($p < 0.05$). **Conclusion:** Antidepressant-induced hyponatremia is significantly associated with escitalopram use and multiple clinical risk factors in coronary artery disease patients. Regular monitoring and careful drug selection are essential to reduce complications

Key Words: Coronary artery disease; Hyponatremia; Sertraline; Escitalopram; SSRIs; Electrolyte imbalance

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INTRODUCTION

Depression is also an example of comorbidity in coronary cardiac patients with coronary artery disease (CAD), where a significant proportion of patients with cardiac diseases have depression that leads to worse clinical outcomes, morbidity and mortality¹. It hurts in compliance to treatment, lifestyle change, and general quality of life among the cardiac patients².

¹. Resident Psychiatry / Head of Department Psychiatry²/ Consultant Psychiatrist³, Armed Forces Institute of Mental Health Rawalpindi.

Correspondence: Jasim Tariq, Resident Psychiatry, Armed Forces Institute of Mental Health Rawalpindi.
Contact No: 0344-3583157
Email: jasimtariq33@yahoo.com

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The most common example of such a drug is selective serotonin reuptake inhibitors (SSRIs), especially sertraline and escitalopram, which are recommended by their effectiveness and rather good cardiovascular safety record³. However, SSRIs are linked with unwanted effects, hyponatremia is one of them, and it is a clinically important condition⁴. The syndrome of inappropriate antidiuretic hormone secretion is the most widespread mediator of antidepressant-induced hyponatremia, which causes the dilutional sodium imbalance⁵. Though not severe in most cases, it may develop into severe problems like confusion, seizures, and risk of falls particularly in susceptible groups⁶. Elderly individuals, polypharmacy and regular taking of diuretics are specific risk factors to the patients with CAD⁷. This might result in further augmentation of the risk of hyponatremia and even make clinical management more challenging in such patients with the addition of SSRIs⁸. The symptoms of hyponatremia can be confused with symptoms of cardiac or depressive symptoms and, therefore, not recognized in time⁹.

Sertraline and escitalopram are the most popular SSRIs, yet the relative risk of each of them triggering hyponatremia is still unclear¹⁰. There have been studies indicating differences in the risk of SSRIs and then there are those which show similarity in the safety profiles¹¹. The lack of consistency also emphasizes the necessity to conduct additional assessment, especially among high-risk groups like CAD patients¹². Data of the occurrence of antidepressant-induced hyponatremia in low- and middle-income countries such as Pakistan are scanty, even though there is an emerging trend of using SSRIs in cardiac patients¹³. These factors can be localized, including comorbidities, medication habits, and access to healthcare and other relevant factors that might affect the presence and the rate of this complication¹⁴. This association is relevant to the safer prescribing and monitoring practices¹⁵. The patient at-risk can be identified at an early stage to reduce complications and enhance patient outcomes¹⁶. Thus, this research will evaluate the correlation between sertraline and escitalopram and antidepressant induced hyponatremia CAD patients in the tertiary care hospital of Rawalpindi.

METHODS

This cross-sectional analytical study was conducted at Armed Forces Institute of Mental Health Rawalpindi December 16 till March 15, 2026, including 220 patients diagnosed with coronary artery disease and receiving antidepressant therapy with either sertraline or escitalopram. Patients admitted to cardiology wards or attending outpatient services were enrolled consecutively during the study period to determine the association between specific SSRIs and antidepressant-induced hyponatremia.

Inclusion Criteria

- Patients aged ≥ 18 years with confirmed coronary artery disease
- Patients receiving sertraline or escitalopram for diagnosed depression
- Patients with baseline and follow-up serum sodium levels available

- Patients willing to participate and provide informed consent

Exclusion Criteria

- Patients with pre-existing hyponatremia prior to initiation of antidepressant therapy
- Patients with conditions known to cause hyponatremia (e.g., severe renal failure, liver cirrhosis, SIADH due to other causes)
- Patients on medications strongly associated with hyponatremia (e.g., carbamazepine, thiazide diuretics without adjustment)
- Patients with incomplete clinical or laboratory data

Data Collection: After institutional approval, data were collected using a structured proforma. Demographic variables included age, gender, and socioeconomic status. Clinical variables included type and duration of coronary artery disease, comorbidities such as hypertension and diabetes, and concurrent medications. Details of antidepressant therapy, including type (sertraline or escitalopram), dosage, and duration of use, were recorded. Laboratory data included baseline and follow-up serum sodium levels. Hyponatremia was defined as serum sodium level < 135 mEq/L. Patients were categorized based on the presence or absence of hyponatremia following antidepressant use.

Statistical Analysis: Data were entered and analyzed using SPSS version 25.0. Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequency and percentage. Comparison between sertraline and escitalopram groups regarding occurrence of hyponatremia was performed using chi-square test. Independent t-test was used for comparison of mean sodium levels where appropriate. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

The mean age was 61.4 ± 10.8 years, with higher age in patients with hyponatremia (65.2 ± 11.1 vs 59.8 ± 10.2 years; $p = 0.002$).

Table No. 1. Demographic and Clinical Characteristics of CAD Patients According to Hyponatremia (N = 220)

Variable	Category	Overall (N=220)	No Hyponatremia (n=162)	Hyponatremia (n=58)	p-value
Age (years)	Mean $\pm$ SD	61.4 ± 10.8	59.8 ± 10.2	65.2 ± 11.1	0.002
Age Group	≤ 60 years	104 (47.3%)	84 (51.9%)	20 (34.5%)	0.019
	> 60 years	116 (52.7%)	78 (48.1%)	38 (65.5%)	0.019
Gender	Male	138 (62.7%)	104 (64.2%)	34 (58.6%)	0.442
	Female	82 (37.3%)	58 (35.8%)	24 (41.4%)	0.442
Hypertension	Present	148 (67.3%)	102 (63.0%)	46 (79.3%)	0.018
Diabetes Mellitus	Present	126 (57.3%)	88 (54.3%)	38 (65.5%)	0.124
Heart Failure	Present	72 (32.7%)	42 (25.9%)	30 (51.7%)	< 0.001
Diuretic Use	Yes	94 (42.7%)	58 (35.8%)	36 (62.1%)	< 0.001
Length of Stay (days)	Mean $\pm$ SD	7.9 ± 3.6	7.1 ± 3.2	9.8 ± 4.1	< 0.001

A greater proportion of patients aged >60 years had hyponatremia (65.5% vs 48.1%) ($p = 0.019$). Hypertension (79.3% vs 63.0%; $p = 0.018$), heart failure (51.7% vs 25.9%; $p < 0.001$), and diuretic use (62.1% vs 35.8%; $p < 0.001$) were significantly more common in the hyponatremia group. These patients also had longer hospital stays (9.8 ± 4.1 vs 7.1 ± 3.2 days; $p < 0.001$), while gender and diabetes showed no significant association.

Hyponatremia was significantly more frequent in patients receiving escitalopram compared to sertraline (65.5% vs 34.5%; $p = 0.003$). Longer antidepressant use (≥ 2 weeks) was associated with higher hyponatremia rates (75.9% vs 60.5%; $p = 0.031$). High-dose SSRI use was also more common in hyponatremic patients (41.4% vs 24.7%; $p = 0.017$). Additionally, polypharmacy (≥ 5 drugs) was significantly associated with hyponatremia (75.9% vs 56.8%; $p = 0.009$).

Table 2. Antidepressant Exposure and Hyponatremia (N = 220)

Variable	Category	Overall (N=220)	No Hyponatremia (n=162)	Hyponatremia (n=58)	p-value
Antidepressant	Sertraline	112 (50.9%)	92 (56.8%)	20 (34.5%)	0.003
	Escitalopram	108 (49.1%)	70 (43.2%)	38 (65.5%)	0.003
Duration of Use	<2 weeks	78 (35.5%)	64 (39.5%)	14 (24.1%)	0.031
	≥ 2 weeks	142 (64.5%)	98 (60.5%)	44 (75.9%)	0.031
Dose Category	Standard Dose	156 (70.9%)	122 (75.3%)	34 (58.6%)	0.017
	High Dose	64 (29.1%)	40 (24.7%)	24 (41.4%)	0.017
Polypharmacy	≥ 5 drugs	136 (61.8%)	92 (56.8%)	44 (75.9%)	0.009
	<5 drugs	84 (38.2%)	70 (43.2%)	14 (24.1%)	0.009

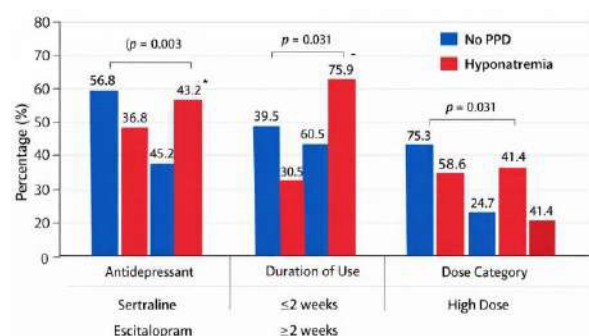


Figure 1. Antidepressant Exposure and Risk of Hyponatremia Among Coronary Artery Disease Patients (n = 220)

Table No. 3. Laboratory Parameters in Patients With and Without Hyponatremia (N = 220)

Laboratory Parameter	Overall Mean $\pm$ SD	No Hyponatremia Mean $\pm$ SD	Hyponatremia Mean $\pm$ SD	p-value
Serum Sodium (mEq/L)	136.8 $\pm$ 4.2	139.2 $\pm$ 2.8	131.1 $\pm$ 3.1	<0.001
Serum Potassium (mEq/L)	4.2 $\pm$ 0.6	4.3 $\pm$ 0.5	3.9 $\pm$ 0.7	0.001
Serum Creatinine (mg/dL)	1.6 $\pm$ 0.8	1.4 $\pm$ 0.6	2.0 $\pm$ 0.9	<0.001
Blood Urea (mg/dL)	42.6 $\pm$ 15.3	38.9 $\pm$ 13.7	52.4 $\pm$ 17.1	<0.001
Serum Osmolality (mOsm/kg)	282.5 $\pm$ 9.4	286.1 $\pm$ 7.8	272.3 $\pm$ 10.5	<0.001
Urine Sodium (mEq/L)	38.7 $\pm$ 12.6	34.2 $\pm$ 10.4	49.5 $\pm$ 13.8	<0.001
Serum Albumin (g/dL)	3.3 $\pm$ 0.6	3.5 $\pm$ 0.5	2.9 $\pm$ 0.6	<0.001

On multivariate analysis, heart failure (OR = 2.94, $p = 0.001$), diuretic use (OR = 2.67, $p = 0.003$), escitalopram use (OR = 2.21, $p = 0.013$), high-dose SSRI (OR = 1.96, $p = 0.036$), and polypharmacy (OR = 2.15, $p = 0.021$) were independent predictors of

hyponatremia. Patients with hyponatremia had significantly lower serum sodium levels (131.1 ± 3.1 vs 139.2 ± 2.8 mEq/L; $p < 0.001$). They also showed lower potassium (3.9 ± 0.7 vs 4.3 ± 0.5 mEq/L; $p = 0.001$) and albumin levels (2.9 ± 0.6 vs 3.5 ± 0.5 g/dL; $p < 0.001$). Conversely, creatinine (2.0 ± 0.9 vs 1.4 ± 0.6 mg/dL), blood urea (52.4 ± 17.1 vs 38.9 ± 13.7 mg/dL), and urine sodium (49.5 ± 13.8 vs 34.2 ± 10.4 mEq/L) were significantly higher in the hyponatremia group ($p < 0.001$). Serum osmolality was also lower (272.3 ± 10.5 vs 286.1 ± 7.8 mOsm/kg; $p < 0.001$).

hyponatremia. Age >60 years also showed a significant association (OR = 1.88, $p = 0.042$), while gender, hypertension, and duration of use were not statistically significant.

Table 4. Multivariate Analysis of Factors Associated with Hyponatremia (N = 220)

Variable	Adjusted OR	95% CI	p-value
Age >60 years	1.88	1.02 – 3.46	0.042
Female Gender	1.24	0.66 – 2.32	0.501
Hypertension	1.76	0.91 – 3.41	0.091
Heart Failure	2.94	1.54 – 5.61	0.001
Diuretic Use	2.67	1.41 – 5.05	0.003
Escitalopram Use	2.21	1.18 – 4.13	0.013
Duration ≥ 2 weeks	1.79	0.95 – 3.36	0.071
High Dose SSRI	1.96	1.04 – 3.69	0.036
Polypharmacy (≥ 5 drugs)	2.15	1.12 – 4.12	0.021

DISCUSSION

This research showed that there was a strong correlation between the use of SSRI and the antidepressant-induced hyponatremia in patients with coronary artery disease, where escitalopram was more prone to induce hyponatremia than sertraline. The prevalence of hyponatremia in the entire cohort points out its clinical importance in the patients with cardiac conditions who are under antidepressant therapy. The same results have been mentioned in the earlier studies where the administration of SSRI was correlated with the risk of experiencing hyponatremia, especially in the circumstances of populations of patients with medical illnesses¹⁷. Advanced age was found as a significant risk factor and patients over 60 years demonstrated higher hyponatremia prevalence and a much higher mean age in the hyponatremic group. This can be explained by the age-related alterations in renal functioning, greater susceptibility to antidiuretic hormone, and greater susceptibility to comorbid conditions. Other studies in the past have considered the advanced age as a persistent predictor of hyponatremia caused by SSRI¹⁸. Patients with hyponatremia had comorbid conditions, especially heart failure and hypertension. This close correlation with heart failure could be attributed to underlying fluid imbalance and neuro hormonal stimulation, which predisposes to sodium imbalances. Besides this, the use of diuretics was much greater in the hyponatremia group that further predisposed it by acting as a heightened loss of sodium and a loss of volume. Prior studies have reported similar associations between diuretics, heart failure and hyponatremia¹⁹. Escitalopram, relative to sertraline, had a greater percentage of hyponatremia, indicating that maybe there is a dissimilar risk pattern in SSRIs. The increased risk was also associated with longer duration of use and increased doses, which means that it is a dose- and exposure-dependent risk. Other studies have found similar results, with some SSRIs and higher dosage increased chances of hyponatremia²⁰.

Findings in this laboratory study were in line with the characteristics of dilutional hyponatremia that encompassed inadequately low serum sodium and

osmolality in addition to an increase in the urine sodium levels that validated a mechanism of the inappropriate antidiuretic hormone secretion. High levels of creatinine and blood urea in the hyponatremia group also indicate poor renal functioning and fluid balance. This pattern of biochemical changes has been observed in earlier studies that examined the hyponatremia induced by the use of the SSRIs²¹. The multivariate analysis demonstrated that heart failure, diuretic use, escitalopram therapy, high-dose SSRI use, and polypharmacy were independent predictors of hyponatremia, which confirms the multifactorial nature of hyponatremia. Polypharmacy is a significant factor that implies possible interactions of drugs and cumulative effects on sodium balance. It has also been found that previous studies have highlighted the significance of various medications and comorbidities in the risk escalation of hyponatremia²². In general, the results suggest that patient factors, drug factors, and clinical factors combine to cause hyponatremia caused by antidepressants in CAD patients. The increased risk of escitalopram and the ability to alter it through dose and co-morbid drugs, highlights the importance of selecting and monitoring antidepressant therapy carefully. These findings are in line with the past studies and serve to underscore the need to regularly monitor the electrolytes in high-risk cardiac patients on SSRIs.

CONCLUSION

It is concluded that antidepressant-induced hyponatremia is a significant clinical concern among patients with coronary artery disease receiving SSRI therapy, with a higher association observed in those treated with escitalopram compared to sertraline. Advanced age, heart failure, diuretic use, high-dose antidepressant therapy, and polypharmacy were identified as important contributing factors. These findings highlight that hyponatremia is a multifactorial condition in CAD patients and emphasize the need for careful selection of antidepressants, dose optimization, and close monitoring of serum sodium levels, particularly in high-risk individuals, to prevent complications and improve clinical outcomes.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Jasim Tariq, Abid Aftab, Izzah Khalid
Drafting or Revising Critically:	Asif Azeem, Isbah Gul, Tariq Raheem
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Frequency of Stillbirth Among Women with Regular and Irregular Antenatal Visits Presenting in the Third Trimester of Pregnancy

Neelum Aziz, Sumera, Samreen Hasan and Arsh

Stillbirth Among Women with Regular and Irregular Antenatal Visits

ABSTRACT

Objective: To determine the frequency of stillbirth among women with regular and irregular antenatal visits presenting in the third trimester of pregnancy.

Study Design: Comparative cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Obstetrics and Gynecology, Lady Reading Hospital, Peshawar, over a period of six months from 8 October 2021 to 8 April 2022.

Methods: A total of 160 pregnant women aged 18–35 years presenting in the third trimester were included through non-probability consecutive sampling. Data regarding age, body mass index, parity, residence, occupation, socioeconomic status, education, antenatal visit status, and pregnancy outcome were recorded on a structured proforma. Participants were categorized into regular and irregular antenatal visit groups.

Results: The mean maternal age was 28.0 ± 5.03 years, and the mean body mass index was 27.0 ± 2.59 kg/m². Of the 160 participants, 72 (45.0%) had regular antenatal visits and 88 (55.0%) had irregular antenatal visits. The overall frequency of stillbirth was 13 (8.1%). Stillbirth occurred in 3 (4.2%) women with regular antenatal visits and in 10 (11.4%) women with irregular antenatal visits. Although stillbirth was more frequent among women with irregular antenatal attendance, the difference was not statistically significant ($p=0.097$).

Conclusion: Stillbirth was more frequent among women with irregular antenatal visits than among those with regular antenatal visits, although the observed difference was not statistically significant. Regular and timely antenatal follow-up during the third trimester may still have important clinical value in reducing preventable fetal loss.

Key Words: Stillbirth, antenatal visits, antenatal care, third trimester, pregnancy outcome, maternal health

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INTRODUCTION

Stillbirth is a significant yet neglected adverse pregnancy outcome and still has an impact on depicting maternal and fetal health care inequalities across the globe. According to recent estimates in the world, the burden has been particularly high in low- and middle-income nations, with South Asia being one of the most affected regions¹. The lack of timely detection of risks, the continuity of care provided to a mother, and the quality of obstetric services remain the persistent factors that cause the death of fetuses due to the lack of preventive measures².

Department of Gynaecology & Obstetrics, Lady Reading Hospital Peshawar.

Correspondence: Dr. Neelum Aziz, FCPS Gynaecology & Obstetrics Lady Reading Hospital Peshawar,
Contact No: 03358317768
Email: drneelumaziz@gmail.com

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ANC represents the main platform on which maternal complications, fetal compromise, and modifiable risks in pregnancy could be detected before causing negative perinatal outcomes. ANC can also provide access to monitoring of blood pressure, screening of anemia, diabetes, fetal growth, warning signs counseling, and timely referral in addition to connecting them to the health system^{3,4}. Existing evidence indicates that ANC advantage does not only depend on the number of visits, but also on the timing of visits, their frequency and quality. Prophylactic, diagnostic, and curative measures applied in pregnancy can decrease the risk of stillbirth, but poor-quality ANC is prevalent in most low-resource environments despite presumed access to services^{5,6}.

ANC attendance is essential in particular as inconsistent or insufficient follow-up can postpone the identification of conditions that have a strong relationship with stillbirth, such as hypertensive disorders, fetal growth restriction, placental dysfunction, maternal infection, and metabolic complications⁷. Research in low-resource environments has demonstrated that the use of ANC in addition to the quality thereof are both linked to the risk of stillbirth, whereas substandard prenatal care and

subpar adherence to recommended visit timetables are associated with increased odds of fetal mortality⁸. Women in most of these environments can enroll in ANC, but they do not attend regularly, are given partial evaluations, and show up late during pregnancy, thus depriving themselves of all important prevention and intervention chances.

This is particularly susceptible in the third trimester in which fetal growth abnormalities, placental inadequacy, hypertensive disease, oligohydramnios, and decreased fetal movements tend to be most evident in late pregnancy⁹. Recent research has focused on the significance of reduced fetal movements as an indicator of fetal compromise, and fetal growth restriction and placental pathology has been found to be always linked with higher risk of stillbirth¹⁰. Such results substantiate the importance of regular ANC contacts in the third trimester and close monitoring of high-risk pregnancies. Stillbirth is still a significant health issue in Pakistan. Despite the increased ANC coverage, there is little local evidence on the effect of the frequency of antenatal visits during the third trimester in terms of its impact on stillbirth prevalence. Thus, the research was performed to identify the prevalence of stillbirth in women who have routine and abnormal antenatal check-ups during the third trimester of pregnancy.

METHODS

This is a comparative cross-sectional study that was conducted in the Department of Obstetrics and Gynecology, Lady Reading Hospital, Peshawar, between 8 October 2021 and 8 April 2022. The aim was to establish the rate of stillbirth in women who had regular and irregular antenatal visits in third trimester of pregnancy.

The sample consisted of 160 pregnant women between the ages of 18-35 years and who reported to outpatient department of Obs & Gyne during the third trimester. The calculation of sample size was based on the WHO formula of comparison of two proportions at a 95% confidence level and 80% power of the study based on the anticipated stillbirth frequencies of those that had been observed in earlier studies [11]. The respondents were categorized into two groups of 80 women who had regular antenatal visits (group A) and 80 women who had irregular antenatal visits (group B).

Women with singleton pregnancies in the third trimester (≥ 28 gestation weeks) were included in the study. Women with multiple pregnancy, congenital anomalies of the fetus, no idea of the date, previous trauma, incomplete antenatal record, and major coexisting medical disease were excluded. Individuals who failed to give consent to participate were also excluded.

Non-probability consecutive sampling technique was used to recruit the study participants in the obstetric unit. Informed written consent was received after which data were collected on a predesigned proforma. Data on

maternal age, parity, gestational age, pattern of antenatal visits and pregnancy outcome were recorded. The status of antenatal visits was based on patient history and available antenatal documentation. Women who visited the antenatal care on the recommended schedule were defined as having regular antenatal visits and those with no or poor antenatal follow-up visits were defined as having irregular antenatal visits.

The major outcome was stillbirth, which was defined as giving birth to a fetus, which did not have any signs of life at the age of viability or later. Delivery records were used to establish pregnancy outcome. Categorical variables were computed using frequencies and percentages whereas continuous variables were computed using means and standard deviation. The chi-square test was used to compare the number of stillbirths in the two groups. Age, parity, and gestational age were stratified and a p-value ≤ 0.05 was considered statistically significant. Data analysis was done on SPSS version 26.0. The study received ethical approval of the institutional review board, and patient data confidentiality was maintained.

RESULTS

A total of 160 women presenting in the third trimester of pregnancy were enrolled. The mean maternal age was 28.0 ± 5.03 years, and most participants (66.3%) were aged 18–28 years. The mean BMI was 27.0 ± 2.59 kg/m², with 58.8% women having BMI > 27 kg/m². Primiparous women constituted 61.3% of the study population. Most women were from rural areas (65.0%), were housewives (71.9%), belonged to poor socioeconomic class (48.8%), and were illiterate (66.9%). Table-1

Table No. 1: Baseline demographic, obstetric, and socioeconomic characteristics of the study population (n = 160)

Variable	Category	n (%)
Age (years)	18–28	106 (66.3)
	29–35	54 (33.8)
BMI (kg/m ²)	≤ 27	66 (41.3)
	> 27	94 (58.8)
Parity	Primipara	98 (61.3)
	Multipara	62 (38.8)
Residence	Rural	104 (65.0)
	Urban	56 (35.0)
Occupation	Working woman	45 (28.1)
	Housewife	115 (71.9)
Socioeconomic status	Poor	78 (48.8)
	Middle class	69 (43.1)
	Rich	13 (8.1)
Education	Illiterate	107 (66.9)
	Literate	53 (33.1)

Mean age: 28.0 ± 5.03 years

Mean BMI: 27.0 ± 2.59 kg/m²

Regarding antenatal care utilization, 45% women had regular antenatal visits, whereas 55.0% had irregular antenatal visits. Table-2

Table No. 2: Antenatal visit status and pregnancy outcome (n = 160)

Variable	Category	n (%)
Antenatal visits	Regular	72 (45.0)
	Irregular	88 (55.0)
Stillbirth	Yes	13 (8.1)
	No	147 (91.9)

The overall frequency of stillbirth was 8.1%. Stillbirth occurred in 4.2% of women with regular antenatal visits and in 11.4% of women with irregular antenatal visits. Although stillbirth was more frequent among women with irregular antenatal attendance, the difference was not statistically significant ($p = 0.097$). Table-3

Table No. 3: Association between antenatal visit status and stillbirth (n = 160)

Antenatal visits	Stillbirth Yes n (%)	Stillbirth No n (%)	Total	p-value
Regular	3 (4.2)	69 (95.8)	72	0.097
Irregular	10 (11.4)	78 (88.6)	88	
Total	13 (8.1)	147 (91.9)	160	

Chi-square test applied

Table No. 4: Stratification of stillbirth with respect to study variables (n = 160)

Variable	Category	Stillbirth Yes n (%)	Stillbirth No n (%)	p-value
Age	18–28 years	9 (8.5)	97 (91.5)	0.813
	29–35 years	4 (7.4)	50 (92.6)	
BMI	$\leq 27 \text{ kg/m}^2$	6 (9.1)	60 (90.9)	0.708
	$> 27 \text{ kg/m}^2$	7 (7.4)	87 (92.6)	
Parity	Primipara	8 (8.2)	90 (91.8)	0.982
	Multipara	5 (8.1)	57 (91.9)	
Residence	Rural	7 (6.7)	97 (93.3)	0.379
	Urban	6 (10.7)	50 (89.3)	
Occupation	Working woman	5 (11.1)	40 (88.9)	0.387
	Housewife	8 (7.0)	107 (93.0)	
Socioeconomic status	Poor	6 (7.7)	72 (92.3)	0.974
	Middle class	6 (8.7)	63 (91.3)	
Education	Rich	1 (7.7)	12 (92.3)	0.422
	Illiterate	10 (9.3)	97 (90.7)	
	Literate	3 (5.7)	50 (94.3)	

Chi-square test applied

Stratified analysis showed no statistically significant association of stillbirth with age, BMI, parity,

residence, occupation, socioeconomic status, or education level ($p > 0.05$). Table-4.

DISCUSSION

The current study determined the prevalence of stillbirth in regular and irregular antenatal visitation women who presented during the third trimester of pregnancy. The general rate of stillbirth was 8.1% and the rate was found to be higher among women with irregular antenatal visits than it was among women who had regular antenatal visits (11.4% vs 4.2%), although the relationship was not statistically significant ($p=0.097$). This difference is (although statistically insignificant) still clinically significant and indicates that poor follow-up of antenatal care could be one of the factors of poor fetal outcomes. More recent data in Pakistan and other contexts has also demonstrated that incomplete or less than optimal antenatal care is linked to the increased risk of still birth and avoidable fetal death^{12,13}.

Our findings are consistent in direction with recent literature. A longitudinal cohort study in Karachi showed that poor use of antenatal care was correlated with stillbirth, with the importance of regular maternal follow-up in the area¹⁴. Similarly, failure to comply with guideline-based prenatal visits schedules has been associated with greater risk of stillbirth especially when the pregnancy is characterized by hypertensive diseases. It was also shown by a multi centre observational study that the benefit of antenatal care is not only determined by attendance, but also by the quality and completeness of services provided at each visit, including screening, counseling, and timely detection of risk¹⁵. This could be the reason why there are groups of women that have adverse results even when they are classified as having received antenatal care.

Since most of the women in the current study lived in rural areas, were housewives, had low or moderate socioeconomic level, and lacked literacy, they fell into socially vulnerable categories. These traits are important because they often influence health-seeking behavior, awareness of warning signs, and access to skilled obstetric services. Even though the analysis in our study did not reveal a statistically significant correlation, we find the same pattern that social determinants of maternal factors are noteworthy in the outcome of pregnancy. However, recent studies have consistently linked stillbirth to social disadvantage, such as poverty, low educational attainment, and low access to maternal healthcare^{16,17}.

Our study did not reveal a substantial correlation between stillbirth and maternal age, BMI or parity. Perhaps this is partly because the sample size is relatively small and the incidences of stillbirth are few. Moreover, 18-35 years age range was used to exclude other women at the more extreme maternal ages, where

the association with stillbirth is frequently more pronounced, but these relationships may not necessarily be visible in smaller hospital-based studies with broad BMI categories^{18,19}.

Our findings have particular clinical value because each participant was reported in the third trimester. Fetal growth restriction, placental insufficiency, hypertensive illness, and reduced mobility can all be seen in the latter stages of pregnancy. Thus, regular monitoring of pregnant women at this time may provide an opportunity to intervene and avoid fetal death^{20,21}. Missed opportunities for late-pregnancy checkups and risk management may have contributed to the higher percentage of stillbirths among women with irregular prenatal visits in our study.

This study offers a valuable local data in the form of a tertiary care hospital in Peshawar and highlights the necessity of enhancing the continuity and quality of antenatal care in the area in which the connection of the regularity of an antenatal care and stillbirth remain under-studied. The comparative design made it possible to directly compare the stillbirth rate between women with regular and irregular antenatal visits and demographic, socioeconomic, and obstetric variables were measured in a standardized way, which enhanced the internal consistency of the results. Also, the emphasis on women who deliver during the third trimester is medically significant since it is during this time frame that most of the avoidable reasons why babies become stillborn are identified, and early monitoring can potentially affect the results. Nevertheless, the research also possesses limitations. Since it is a non-probability consecutive sampling, non-probability, and single-center hospital study, it might not be completely applicable to the rest of the population. The small sample size and the few incidences of stillbirths might have contributed to the low statistical power and this fact could have led to the absence of statistical significance even though an observed difference arose between the groups. Moreover, the status of the antenatal visits was evaluated based on the patient history and the records provided, which can have brought forth the biases of recollection and documentation. The content, quality, and timing of antenatal care were not also thoroughly assessed in the study; neither did it thoroughly address all obstetric and medical confounding factors, which could have been important contributors to the risk of stillbirth.

CONCLUSION

The incidence of stillbirth was higher in women with irregular antenatal visits as compared to women with regular antenatal follow-up during the third trimester though the difference between the two was not statistically significant. These results indicate that the continuity of the antenatal care can be of significant

clinical value in the context of both the early prediction of maternal and fetal complications and in the elimination of the preventable fetal loss. Amplifying routine antenatal care especially in late pregnancy combined with a focus on the quality and the completeness of the care in each antenatal visit could change the fetus outcomes of such low-resource settings. Additional multicenter studies should be carried out in large scale to determine the independent contribution of inconsistent antenatal attendance to the risks of still birth among Pakistani women.

Recommendations: Further randomized, multi-center studies with extended follow-up are recommended to validate and generalize these findings.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Neelum Aziz, Sumera
Drafting or Revising Critically:	Samreen Hasan, Arsh
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Comparative Analysis of Measured Outcomes of Acute Asthma Patients in Karachi Undergoing Treatment with Inhaled β Agonists with or without Corticosteroids

Noor-ul-Ain Kiran, Samia Perwaiz Khan and Nousheen Iqbal

Improvement in
Pulmonary
Function in
Acute Asthma by
Post
Bronchodilator
Affectivity

ABSTRACT

Objective: To compare the outcome in acute asthma patients post treatment with inhaled beta agonists alone or in combination with corticosteroids.

Study Design: Prospective cohort study.

Place and Duration of Study: This study was conducted at the Medicare Cardiac & General Hospital, Karachi, from October 2024-till July 2025.

Methods: Out of a total of hundred patients with symptoms of asthma visiting OPD, were recommended spirometry test by the Pulmonologist. By spirometry, pulmonary functions were recorded, forced vital capacity, and forced expiratory volume in one second. Forced expiratory volume in one second/ forced vital capacity. Graph 1, 2 represent normal or obstructive lung diseases.

Results: General characteristics of these participants normal and asthmatic were, male(n=62) female (n= 38), age (mean: 31 + 12 vs 44± 15.9 years) , ethnicity of both groups were same(Pakistani), BMI (mean 23.58± 0.6 vs 27.17± 4.52 kg/ m²) shown in table 1. Pulmonary function test by spirometry was performed to record FVC, FEV₁, FEV₁/ FVC, PEF for groups with normal function and asthma patients t test was applied to compare both groups in table 1. Changes recorded in FEV₁/ FVC ratio post bronchodilator administered inhaled salbutamol alone (mean 75.96 ± 4.9), compared to salbutamol and corticosteroids (mean 79.82 ± 1.23) significance was determined by applying t-test (p < 0.005) table 2.

Conclusion: The study concludes that the outcomes of acute asthma treatment with inhaled β agonists in combination with inhaled corticosteroids were much better as compared to beta agonist alone.

Key Words: Spirometry, bronchodilators, beta agonists, corticosteroids

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INTRODUCTION

Asthma is now a serious global health issue, respiratory symptoms are wheezing, productive cough, chest tightness, and shortness of breath¹, and these are typical features of Asthma. Spirometry serves as a valuable tool in diagnosis and management of asthma and COPD.² It is one of most common respiratory obstructive diseases in different ethnicity all over the world¹. People suffering from asthma are in all age ranges³.

Department of Pharmacology, Pulmonology, Sohail University, Karachi.

Correspondence: Noor Ul Ain Kiran, Lecturer, Department of Pharmacology, Pulmonology, Sohail University, Karachi.

Contact No: 0300-5457742

Email: drkirannazar110@gmail.com

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Asthma prevalence worldwide has seen a rapid increase in last few decades⁴. Studies³⁻⁵ have shown that asthma prevalence has rapidly increased in various regions of the world⁴. Nearly 4.3% population of Pakistan are suffering from asthma². Rise in asthma patients in Pakistan are similar to other countries in the south Asia. The rise of seasonal asthma cases is particularly notable in certain regions of the country². Majority of the recurrent episodes of asthma are caused by various indoor and outdoor allergens in air. Although some other risk factors are leading to occupational asthma due to unhealthy work surroundings, the major factors are environmental pollution and stressful life, contributing significantly to the rapid rise in asthma cases⁸. According to Global initiative for asthma (GINA) – guidelines² and recommendations, therapeutics for asthma³ are inhaled β 2-agonists, corticosteroids, muscarinic antagonists, leukotriene inhibitors, and some other expensive options as well but asthma still remains difficult to manage. The Pakistan Chest Society regularly revises its asthma guidelines, placing emphasis on training doctors and educating patients. The allergy and asthma institute Pakistan

(AAIP) conducted a research and provides training for both academic and clinical practice in this field⁵. The AAIP is currently researching asthma, allergies and other chronic respiratory diseases (CRDs) in Pakistan, in association with the Respiratory Health Institute in the UK⁵. Asthma has been identified as serious health issue leading to frequent hospital admissions and results in heavy financial burden for lower income countries such as Pakistan. According to the WHO data published in 2020⁶, deaths due to asthma reached a staggering 20,750 or 1.42% of total deaths⁸ in Pakistan. A range of etiological factors, such as social and environmental factors that influence health, genetic susceptibility and outdoor air pollution, plays a role in asthma morbidity and mortality. Among these the deteriorating air quality index across the country requires particular attention as a major contributor to Asthma-related morbidity⁷. Airway inflammation in asthma is present in both central and peripheral airways. Hence optimal pulmonary deposition of medication is an important factor in achieving effective therapeutic outcomes⁴. The bronchial smooth muscle is directly supplied by the parasympathetic nervous system associated with muscarinic receptor stimulation and cause of bronchoconstriction³. Although the airways do not receive direct sympathetic innervation, the bronchi are rich in beta-2 adrenergic receptors. Therefore, both cholinergic and adrenergic receptors are important targets in bronchodilator therapy. Bronchodilation can occur through two main mechanisms³. First, stimulation of beta-2 adrenergic receptors directly relaxes bronchial smooth muscle. Second, muscarinic receptor antagonists (anticholinergic drugs) competitively block the action of acetylcholine at cholinergic receptors, leading to smooth muscle relaxation and subsequent bronchodilation³.

In acute asthma attack, patients often use short acting beta agonists (SABAs) after short intervals, numerous times⁹. However, SABA alone has poor effect on bronchial airway inflammation, and frequent usage of SABA's is linked to poor asthma control and a higher risk of severe exacerbations, fixed dose albuterol-budesonide has shown⁹ better asthma management. As severe asthma attack (status asthmaticus) is associated with significant morbidity and mortality, therefore, prevention of exacerbations is a critical priority in the asthma management. According to a study done in UK⁹ patients with uncontrolled moderate to severe asthma who were already receiving different inhaled glucocorticoid-based maintenance therapies, the risk of severe asthma exacerbations was lower with a fixed dose combination of 180 ug albuterol and 160 ug budesonide compared with albuterol alone. In 2021 a retrospective study was done at the Aga Khan University Hospital, Karachi, Pakistan, in which one hundred and fourteen children aged 6-11 years old, were participants. The participants were divided into 3

groups, 1st group with low dose, long-acting beta agonist-inhaled corticosteroid (LABA-ICS), 2nd group with very low dose formoterol-ICS, 3rd group with medium dose ICS and Inhaled corticosteroids-leukotriene receptor antagonists (ICS-LTRA). It was a comparative study conducted on pediatric asthma patients of three therapeutic option¹⁰. Among the three treatment groups, ICS- LABA group patients had the best values of Forced expiratory volume in one second and forced expiratory volume in 1 second /Forced vital capacity ratio after pulmonary function tests at 3 months follow-up as compared to ICS-LTRA and ICS group¹⁰.

However, the efficacy and side effects of SABA and inhaled corticosteroids combination remains unknown in acute asthma adult population of Karachi, Pakistan. In this study the effectiveness and outcome of β -Agonists and inhaled corticosteroids and their effects on FEV1, pulmonary function tests in the population were observed. In primary care, spirometry plays very important role in the diagnosis and management of COPD and asthma. In a study¹², the spirometry data, collected from asthma patients was compared with data collected from individuals who were nonsmokers without lung diseases. The lung size is larger in males than in females of the same age, height, and ethnicity. The study was aimed to compare the improvement in spirometry values (Forced expiratory volume in 1 second, forced vital capacity, and ratio of Forced expiratory volume in 1 second /Forced vital capacity) between patients treated with: Beta agonists alone and Combination therapy (beta agonists + corticosteroids). Second treatment modality leads to the more significant improvement in pulmonary function parameters in acute asthma patients in Karachi.

METHODS

Setting: Medicare Cardiac & General Hospital.

Study Design: Prospective cohort study.

Participants: Patients with symptoms asthma, Karachi.

Sample Size: 100 participants, with symptoms of asthma (cough, wheeze).

Sampling technique: convenience sampling.

Bronchodilation: Participants divided into groups inhaled salbutamol with or without corticosteroids.

Outcome Measures: bronchodilation, there were statistically significant differences in Forced expiratory volume in 1 second, forced vital capacity, and ratio of Forced expiratory volume in 1 second /Forced vital capacity among the two treatment groups after a standard intervention.

Data Collection: Medical records review, patient history, spirometry test and follow-up assessments.

Inclusion criteria: Participants must have a confirmed diagnosis of asthma as per established diagnostic criteria, with characteristics of asthma such that are

recurrent wheezing, coughing, chest tightness, and variable airflow obstruction.

Exclusion Criteria: All patients with respiratory diseases other than asthma, including chronic obstructive pulmonary disease (COPD) or restrictive lung diseases (cystic fibrosis) were excluded to ensure homogeneity of the study population.

Spirometry: By use of portable spirometer, maintain an upright posture throughout the process. Securing the mouthpiece firmly to prevent any air leaks. After 2 puffs of salbutamol or combination wait for 10-15 min before recording the values.

Interpretation: -

FEV1/FVC ratio

? FEV1/FVC < 70% (or less than the Lower limit of normal): Obstructive Pattern (COPD, Asthma)

? $\geq 70\%$: Normal or Restrictive disease

Statistical Analysis: The data of hundred participants was entered in SPSS Version 25.0. Descriptive analysis variables were age, gender, BMI, FVC, FEV1, FVC/FEV1, PEF for two groups. By applying t-test for

pre and post bronchodilator response in groups (Pre and Post Salbutamol alone or salbutamol and corticosteroid therapy).

Ethical Considerations & ERC approval: Approval was obtained from the Ethical Review Board (ERB), Sohail University prior to the commencement of the study. Informed consent was obtained from all participants. Protocol #: 00032/24.

RESULTS

A total of hundred patients with asthma visiting Medicare Cardiac and General hospital between October 2024 to July 2025 were recommended spirometry by pulmonologist. Baseline characteristics of these patient's gender, age, ethnicity, BMI are shown in Table 1. Pulmonary function test by portable spirometer to record FVC, FEV1, FEV1/FVC, PEF for both groups pre and post salbutamol alone and with inhaled corticosteroids as given in Table 2. Improvement in post bronchodilator response was observed more significantly in combination group (Post Inhale beta agonist and corticosteroids group).

Table No.1: Baseline Characteristics of participants

VARIABLES N=100	Normal	Asthma	p-value
Age(years)	16- 60 (mean 31 $\pm$ 12.61)	12 – 63 (mean 44 $\pm$ 15.9)	<0.00*
Gender M:F	30:20	24: 26	0.2
Ethnicity	Pakistani	Pakistani	0.1
BMI (m ² /kg)	24 $\pm$ 0.6 (mean 23.58 $\pm$ 0.6)	27 $\pm$ 4.52 (mean 27.17 $\pm$ 4.52)	<0.00*
SPIROMETRY			
FVC (L)	2.89 – 5.17 (mean 3.98 $\pm$ 0.60)	1.28 $\pm$ 3.70 (mean 2.19 $\pm$ 0.45)	<0.00*
FEV ₁ (L)	1.49- 4.89 (mean 3.63 $\pm$ 0.75)	1.05- 1.30 (mean 1.87 $\pm$ 0.77)	<0.00*
FEV ₁ / FVC (%)	70- 89 (mean 72.84 $\pm$ 8.15)	51- 67 (mean 66.6 $\pm$ 14.98)	<0.00*
PEF (L)	3. 00- 9.02 (mean 6.33 $\pm$ 1.68)	1.38 – 5.79 (mean 3.79 $\pm$ 1.26)	<0.00*

*p-value – 0.05 was considered statistically significant.

Table No.2: Pulmonary function tests as recorded by performing spirometry before & Post-bronchodilator therapy

Spirometry FEV ₁ /FVC	Pre-Bronchodilator Response (%)	Post-Bronchodilator Response (%)	P-value
Inhaled Salbutamol group (n =35) (mild- severe obstruction)	51 – 67 (mean 66.96 $\pm$ 12)	67-90 (mean 75.96 $\pm$ 4.9 1)	<0.00*
Inhaled Salbutamol+ Steroids (n =35) (mild- severe obstruction)	52- 69 (mean 66.96)	70- 90 (mean 79.82 $\pm$ 123)	<0.00*
Inhaled Salbutamol group (n =35) Inhaled Salbutamol+ Steroids (n =35)	51 – 67 (mean 66.96 $\pm$ 12) 52- 60 (mean 66.96)	67-90 (mean 75.96 $\pm$ 4.9 1) 70- 90 (mean 79.82 $\pm$ 123)	<0.00*

*p-value – 0.05 was considered statistically significant. t-test was applied.

DISCUSSION

Total of hundred patients with asthma symptoms were included in this study. The age range of all participants was between 12-63 years, and male: female ratio was found 2:1. The range of FVC was normal vs asthma (mean 3.98 $\pm$ 0.6 vs 2.19 $\pm$ 0.45 L), FEV₁ (mean 3.63 vs 1.87 L) and FEV₁/FVC (mean 73% vs 67 %) for spirometry. Improvement in FEV1/FVC bronchodilation, salbutamol alone pre and post (mean

67 vs 76%) as compared to combination group pre and post (mean 67% vs 80%) respectively. Inhaled therapy salbutamol and corticosteroids had a greater advantage with least adverse effects. The use of inhaled salbutamol and corticosteroids together gave significant improvement in outcome of the two groups (moderate-severe) asthma. As it has been shown by study¹² inhaled bronchodilators having several advantages over oral and intravenous routes of administration. Post corticosteroid and salbutamol therapy had shown to improve pulmonary function in 80-100% of these

patients. Whereas Salbutamol alone improvement seen in 70-90% only. Spirometry¹¹⁻¹² was found to be a useful tool in diagnosis of lung diseases and severity of asthma (mild- moderate- severe) and the effectivity of bronchodilation. It is advised to bring in a pulmonary function technologist from an affiliated pulmonary lab to offer education and mentorship. Additionally, it is essential that personnel conduct testing regularly to maintain proficiency and ensure quality results. In this study well trained PFT technologist performed the tests. Thus, study shows, spirometry is beneficial tool to determine the outcome of therapy of beta 2 agonist and ICS, as a bronchodilator they increase lung vital capacity, forced expiratory volume in one second in moderate – severe asthma patients. Study done by Sim et al¹³ reported that patients with lung disease, severity and intensity by performing spirometry was a beneficial tool.¹³

The difference in lung size between gender, age, racial differences in lung capacity must also be considered when performing spirometry testing. Most notably patients of African and south Asian origin are expected to have smaller lungs than Caucasians, Latinos and North Asian population. Studies has shown¹⁴⁻¹⁵ that the great beneficial effects of inhaler used in lung diseases not only benefit the pharmacokinetics; absorption. distribution, bioavailability also more clinical safe. Inhalation therapy with corticosteroids and long-acting β_2 -agonists are very important in asthma management.¹⁵⁻¹⁶ Forced expiratory volume in one second is most beneficial measured by spirometry for assessment of therapy outcome for improvement in pulmonary functions.¹⁷ Study¹⁸ shows combination of beta agonists with corticosteroids are more beneficial in reducing the risk of acute respiratory distress syndrome by reducing inflammation and lung secretions. Beta agonist alone do not reduce inflammation and secretions and higher dose can lead to adverse-effects¹⁹. ICS are unavailable or not affordable in low- and middle-income countries, uncontrolled asthma has been one of major cause of morbidity and mortality, arrangements should not be non- affordable²⁰.

CONCLUSION

The study concludes, in acute asthma therapy compared to beta agonists alone, combination of inhaled beta agonists and corticosteroids combination has shown much results.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Noor-ul-Ain Kiran, Samia Perwaiz Khan
Drafting or Revising Critically:	Noor-ul-Ain Kiran, Nousheen Iqbal
Final Approval of version:	All the above authors
Agreement to accountable	All the above authors

for all aspects of work:	
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Development of an AI-Based Risk Prediction Model for Sepsis Mortality Using Routine Laboratory Parameters

AI-Based Risk
Prediction Model
for Sepsis
Mortality
Using RLP

Shehroze Rauf Shakoori, Momina Asif, Aila Fatima, Muhammad Abdullah Khan, Alishba Murtaza and Taimoor Ali

ABSTRACT

Objective: To develop an AI-based risk prediction model for sepsis mortality using routine laboratory parameters among patients admitted to teaching hospitals of Lahore.

Study Design: Multicenter hospital-based analytical study

Place and Duration of Study: This study was conducted at the Amna Inayat Medical College, Lahore from December 2024 to February 2026.

Methods: This was a multicenter hospital-based analytical study conducted at teaching hospitals of Lahore, including 250 adult patients diagnosed with sepsis according to the Sepsis-3 criteria.

Results: The mean age of patients was 56.8 ± 17.2 years, and overall mortality was 29.6%. Non-survivors had significantly higher serum lactate (5.4 ± 1.9 mmol/L), creatinine (2.4 ± 1.0 mg/dL), procalcitonin (10.4 ± 3.6 ng/mL), and C-reactive protein levels compared with survivors ($p < 0.001$). Gradient boosting demonstrated the best predictive performance with 88.0% accuracy and an AUC of 0.93.

Conclusion: AI-based models using routine laboratory parameters provide accurate prediction of sepsis mortality and may assist clinicians in early identification of high-risk patients.

Key Words: Sepsis; Artificial intelligence; Mortality prediction; Machine learning; Laboratory biomarkers.

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INTRODUCTION

Sepsis is a life-threatening disorder, which is manifested by dysfunction of organs due to the dysregulated host response to an infection and is one of the primary causes of death in hospitalized patients around the globe¹. Even with the current developments in treatment with antimicrobials and critical care, sepsis remains a major burden to morbidity and mortality worldwide, especially in populations with low and middle incomes². Early detection of high-risk patients at the risk of deaths is necessary to inform early treatment and enhance clinical outcomes³.

The most common examples of traditional scoring systems are the Sequential Organ Failure Assessment (SOFA), quick SOFA (qSOFA) as well as the Acute Physiology and Chronic Health Evaluation (APACHE) systems that can be used to assess the level of the

disease and its prognosis in the case of a septic patient⁴. Nonetheless, these systems demand numerous clinical parameters and do not necessarily give adequate rapidity or precision risk prediction in emergency care⁵. The recent developments in the field of artificial intelligence and machine learning have brought new opportunities in order to enhance the clinical prediction models. The AI-based methods have the ability of processing large datasets and also detecting complex relationships between clinical variables that would otherwise not be revealed using the traditional statistical methods⁶. These models can be used to help clinicians to risk stratify septic patients that they see early by incorporating routinely available laboratory parameters⁷.

Sepsis associated with metabolic imbalance, liver dysfunction, and systemic inflammation can be detected by routine laboratory evidence of complete blood count, serum lactate, creatinine, inflammatory markers, and liver functionality tests⁸. Integrating these parameters into AI-based models can improve the accuracy of predictions and still be applicable in a medical facility in everyday operations⁹. It has already been demonstrated in previous studies that machine learning algorithms can be more effective in forecasting sepsis mortality and clinical decision-making than traditional scoring systems¹⁰. These models can be of interest especially in healthcare systems with limited resources, as they are not dependent on sophisticated diagnostic

Medical Students, Amna Inayat Medical College, Lahore.

Correspondence: Taimoor Ali, Medical Student; Amna Inayat Medical College, Lahore.

Contact No: 03021455477

Email: ataimoor829@gmail.com

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equipment and instead on the regularly accessible laboratory results¹¹. The use of AI-based prediction tools can thus be useful in assisting clinicians to track high-risk patients more promptly and enhance resources distribution in critical care facilities^{12,13}. Nevertheless, there is a scarcity of information on the process of creating AI-based sepsis mortality prediction models utilizing regular laboratory parameters in the Pakistani hospital cohorts¹⁴. Patient differences and healthcare setting differences could have an impact on predictive accuracy and therefore models developed locally are necessary¹⁵.

METHODS

This was a multicenter hospital-based analytical study conducted at teaching hospitals of Lahore from December 2024 to February 2026, including 250 adult patients diagnosed with sepsis according to the Sepsis-3 criteria. Patients admitted to emergency departments, medical wards, and intensive care units with clinical and laboratory evidence of infection and organ dysfunction were enrolled consecutively during the study period to develop an artificial intelligence-based model for predicting sepsis mortality using routinely available laboratory parameters.

Inclusion Criteria

- Patients aged ≥ 18 years diagnosed with sepsis based on Sepsis-3 criteria.
- Patients admitted to emergency departments, medical wards, or intensive care units of participating hospitals.
- Patients with complete baseline laboratory investigations available at admission.

Exclusion Criteria

- Patients with incomplete clinical or laboratory records.
- Patients discharged against medical advice or transferred before outcome determination.
- Patients with terminal malignancy or advanced chronic diseases affecting short-term mortality independently of sepsis.

Data Collection: After institutional approval, demographic and clinical information was collected from hospital records using a structured data extraction form. Baseline variables included age, gender, comorbidities, site of infection, and admission location. Routine laboratory parameters recorded within the first 24 hours of admission included hemoglobin level, total leukocyte count, platelet count, serum lactate, serum creatinine, blood urea nitrogen, C-reactive protein, procalcitonin, bilirubin, and serum albumin. Clinical outcomes including survival status, length of hospital stay, and need for intensive care support were documented. Data preprocessing involved cleaning, normalization, and handling of missing values before model development.

AI Model Development: The dataset was randomly divided into training (70%) and testing (30%) sets. Machine learning algorithms including logistic regression, random forest, and gradient boosting models were applied to develop the mortality prediction model. Feature selection techniques were used to identify the most significant laboratory predictors associated with sepsis mortality. Model performance was evaluated using accuracy, sensitivity, specificity, precision, and area under the receiver operating characteristic curve (AUC-ROC).

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS version 26 and Python-based machine learning libraries. Continuous variables were expressed as mean $\pm$ standard deviation, while categorical variables were presented as frequency and percentage. Comparisons between survivor and non-survivor groups were performed using independent t-test or chi-square test where appropriate. The predictive performance of the AI models was assessed using ROC curve analysis, with a p-value < 0.05 .

RESULTS

A total of 250 sepsis patients were analyzed with a mean age of 56.8 ± 17.2 years. Survivors had a lower mean age (54.3 ± 16.1) compared with non-survivors (62.4 ± 18.5 ; $p = 0.004$). Patients aged ≤ 60 years constituted 56.0% while those > 60 years were 44.0%, with higher mortality in older patients (58.1%). Males represented 59.2% of the cohort. ICU admission occurred in 29.6% overall but was significantly higher among non-survivors (45.9% vs. 22.7%; $p < 0.001$). Chronic kidney disease was also more frequent in non-survivors (27.0% vs. 11.9%; $p = 0.003$). The mean hospital stay was 9.6 ± 4.3 days, longer among non-survivors (11.1 ± 5.0 vs. 8.9 ± 3.8 ; $p = 0.002$). Table 1. Significant laboratory differences were observed between groups. Mean hemoglobin was lower in non-survivors (9.9 ± 2.2 g/dL) than survivors (11.2 ± 1.9 ; $p < 0.001$). Leukocyte counts were higher in non-survivors ($16.4 \pm 5.7 \times 10^9/L$) compared with survivors (13.8 ± 4.9 ; $p = 0.002$). Platelet counts were reduced in non-survivors ($159 \pm 81 \times 10^9/L$ vs. 206 ± 74 ; $p < 0.001$). Serum lactate levels were markedly elevated in non-survivors (5.4 ± 1.9 mmol/L) compared with survivors (3.2 ± 1.4 ; $p < 0.001$). Similarly, creatinine (2.4 ± 1.0 vs. 1.5 ± 0.7 mg/dL), CRP (116.5 ± 41.7 vs. 88.3 ± 34.6 mg/L), and procalcitonin (10.4 ± 3.6 vs. 6.3 ± 2.8 ng/mL) were significantly higher among non-survivors ($p < 0.001$). Serum albumin was lower in non-survivors (2.6 ± 0.5 vs. 3.2 ± 0.5 g/dL; $p < 0.001$). Table 2.

Among the machine learning models, gradient boosting demonstrated the best performance with 88.0% accuracy, 84.7% sensitivity, 89.8% specificity, and AUC of 0.93. Random forest also performed strongly with 86.4% accuracy and AUC of 0.91. Support vector

machine achieved 83.6% accuracy with AUC of 0.88, while logistic regression showed the lowest predictive ability with 79.2% accuracy and AUC of 0.83.

Table No. 1. Demographic and Clinical Characteristics of Sepsis Patients (N = 250)

Variable	Category	Overall (N=250)	Survivors (n=176)	Non-Survivors (n=74)	p-value
Age (years)	Mean $\pm$ SD	56.8 $\pm$ 17.2	54.3 $\pm$ 16.1	62.4 $\pm$ 18.5	0.004
Age Group	≤ 60 years	140 (56.0%)	109 (61.9%)	31 (41.9%)	0.003
	> 60 years	110 (44.0%)	67 (38.1%)	43 (58.1%)	0.003
Gender	Male	148 (59.2%)	100 (56.8%)	48 (64.9%)	0.241
	Female	102 (40.8%)	76 (43.2%)	26 (35.1%)	0.241
ICU Admission	Yes	74 (29.6%)	40 (22.7%)	34 (45.9%)	< 0.001
Diabetes Mellitus	Present	96 (38.4%)	62 (35.2%)	34 (45.9%)	0.118
Hypertension	Present	112 (44.8%)	72 (40.9%)	40 (54.1%)	0.063
Chronic Kidney Disease	Present	41 (16.4%)	21 (11.9%)	20 (27.0%)	0.003
Length of Hospital Stay (days)	Mean $\pm$ SD	9.6 $\pm$ 4.3	8.9 $\pm$ 3.8	11.1 $\pm$ 5.0	0.002

Table No.2: Admission Laboratory Parameters in Survivors vs Non-Survivors

Laboratory Parameter	Overall Mean $\pm$ SD	Survivors Mean $\pm$ SD	Non-Survivors Mean $\pm$ SD	p-value
Hemoglobin (g/dL)	10.8 $\pm$ 2.1	11.2 $\pm$ 1.9	9.9 $\pm$ 2.2	< 0.001
Leukocyte Count ($\times 10^9/L$)	14.6 $\pm$ 5.3	13.8 $\pm$ 4.9	16.4 $\pm$ 5.7	0.002
Platelet Count ($\times 10^9/L$)	192 $\pm$ 78	206 $\pm$ 74	159 $\pm$ 81	< 0.001
Serum Lactate (mmol/L)	3.9 $\pm$ 1.7	3.2 $\pm$ 1.4	5.4 $\pm$ 1.9	< 0.001
Serum Creatinine (mg/dL)	1.8 $\pm$ 0.9	1.5 $\pm$ 0.7	2.4 $\pm$ 1.0	< 0.001
C-Reactive Protein (mg/L)	96.7 $\pm$ 38.5	88.3 $\pm$ 34.6	116.5 $\pm$ 41.7	< 0.001
Procalcitonin (ng/mL)	7.6 $\pm$ 3.4	6.3 $\pm$ 2.8	10.4 $\pm$ 3.6	< 0.001
Serum Albumin (g/dL)	3.0 $\pm$ 0.6	3.2 $\pm$ 0.5	2.6 $\pm$ 0.5	< 0.001

Table No. 3. Performance of AI Models for Sepsis Mortality Prediction

Model	Accuracy (%)	Sensitivity (%)	Specificity (%)	Precision (%)	AUC
Logistic Regression	79.2	74.3	81.8	70.6	0.83
Random Forest	86.4	82.4	88.1	79.5	0.91
Gradient Boosting	88.0	84.7	89.8	81.9	0.93
Support Vector Machine	83.6	78.3	85.9	74.8	0.88

Legend: Receiver operating characteristic (ROC) curves comparing the predictive performance of machine learning models for sepsis mortality. Gradient boosting achieved the highest discrimination ability (AUC = 0.93), followed by random forest (AUC = 0.91), support vector machine (AUC = 0.88), and logistic regression (AUC = 0.83).

Feature importance analysis identified serum lactate as the strongest mortality predictor (importance score 0.28; OR 2.41, 95% CI: 1.78–3.26; $p < 0.001$). Procalcitonin (0.23; OR 2.08), serum creatinine (0.19; OR 1.86), and CRP (0.15; OR 1.64) were also significant predictors. Lower platelet count (importance 0.11; OR 0.72) and lower albumin (importance 0.10; OR 0.64) were associated with increased mortality risk. Leukocyte count also contributed to prediction (importance 0.09; OR 1.32; $p = 0.015$). These variables formed the key inputs for the AI mortality prediction model.

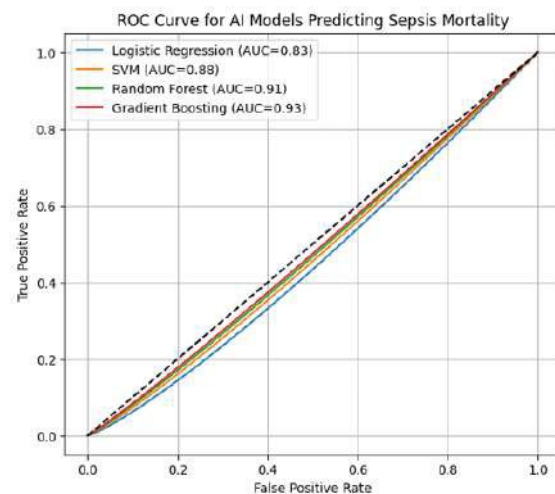


Figure No.1: ROC Curves of AI Models for Sepsis Mortality Prediction

Legend: Receiver operating characteristic (ROC) curves comparing the predictive performance of machine learning models for sepsis mortality. Gradient boosting achieved the highest discrimination ability (AUC = 0.93), followed by random forest (AUC = 0.91), support vector machine (AUC = 0.88), and logistic regression (AUC = 0.83).

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Table No. 4: Key Predictors of Sepsis Mortality Identified by the AI Model

Predictor Variable	Importance Score	Odds Ratio (95% CI)	p-value
Serum Lactate	0.28	2.41 (1.78–3.26)	<0.001
Procalcitonin	0.23	2.08 (1.54–2.91)	<0.001
Serum Creatinine	0.19	1.86 (1.37–2.53)	<0.001
C-Reactive Protein	0.15	1.64 (1.21–2.18)	0.002
Platelet Count	0.11	0.72 (0.56–0.91)	0.008
Serum Albumin	0.10	0.64 (0.49–0.83)	0.001

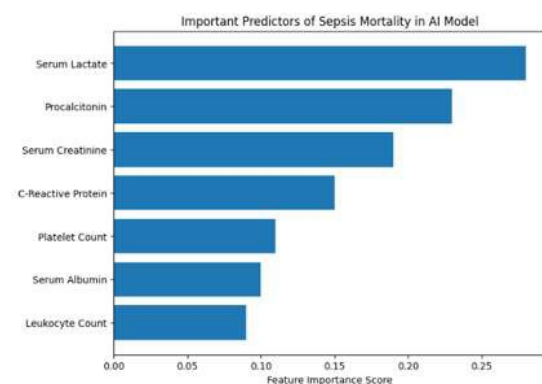


Figure No.2: Feature Importance Ranking for Mortality Prediction

Legend: Feature importance ranking from the AI-based mortality prediction model. Serum lactate had the highest predictive contribution followed by procalcitonin and serum creatinine, indicating that markers of tissue hypoperfusion, inflammation, and organ dysfunction play key roles in predicting sepsis mortality.

DISCUSSION

This paper has formulated an AI-based sepsis mortality predictive model on the use of routine laboratory parameters of patients admitted to teaching hospitals in Lahore. These results established a mortality rate of 29.6 with non-survivors being much older (62.4 ± 18.5 years) than the survivors (54.3 ± 16.1 years). Strong association with mortality had been found with older age and increased ICU admissions (45.9% vs. 22.7). The same has been observed in other previous studies where advanced age and admission due to critical care was noted as significant predictors of poor outcomes in septic patients¹⁶. Laboratory results also showed that there were big variations in the survivors and non-survivors. The dead patients exhibited an increase in the leukocyte count ($16.4 \pm 5.7 \times 10^9/L$), serum lactate (5.4 ± 1.9 mmol/L), serum creatinine (2.4 ± 1.0 mg/dL) and inflammatory markers such as C-reactive protein (116.5 ± 41.7 mg/L) and procalcitonin (10.4 ± 3.6 ng/mL). On the contrary, the number of platelets ($159 \pm 81 \times 10^9/L$) and serum albumin (2.6 ± 0.5 g/dL) were lower and significant in non-survivors. Past studies have also established that high levels of lactate, inflammatory biomarkers and organ dysfunction indicators are closely linked with high risk of mortality in sepsis^{17,18}. The performance analysis of AI model revealed that gradient boosting was the most accurate model with the predictive accuracy of 88.0% and AUC of 0.93, and then random forest had the predictive accuracy of 86.4 and an AUC of 0.91. Logistic regression had a relatively poorer level of performance (79.2% accuracy). Such findings can be attributed to the past studies that have shown machine learning algorithms like gradient boosting and random forest can tend to be more effective than other statistical models in predicting the occurrence of sepsis¹⁹.

The analysis of feature importance showed that serum lactate is the most significant predictor of mortality (OR 2.41), procalcitonin (OR 2.08), serum creatinine (OR 1.86), and C-reactive protein (OR 1.64). Protective relationships were observed between platelet count and serum albumin, so thrombocytopenia and hypoalbuminemia were associated with poor outcomes. This is not the first time this kind of predictor came up with various studies showing that metabolic, inflammatory, and organ dysfunction biomarkers were the main predictors of mortality when it comes to sepsis²⁰. In general, the results are consistent with the emerging evidence that AI-driven prediction algorithms on top of routinely collected laboratory parameters are capable of delivering reliable early risk stratification among patients in the state of septic shock. The use of such models in clinical practice can help clinicians to recognize high-risk patients sooner and make better decisions during emergencies.

CONCLUSION

It is concluded that routine laboratory parameters combined with artificial intelligence-based algorithms can effectively predict mortality risk in patients with sepsis. Elevated serum lactate, procalcitonin, creatinine,

and inflammatory markers were strongly associated with poor outcomes, while lower platelet counts and serum albumin were also linked to increased mortality. Among the evaluated models, gradient boosting demonstrated the highest predictive accuracy. These findings suggest that AI-driven prediction tools using readily available laboratory data may support early risk stratification and clinical decision-making in sepsis management within tertiary care hospitals.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Shehroze Rauf Shakoori, Momina Asif, Aila Fatima
Drafting or Revising Critically:	Muhammad Abdullah Khan, Alishba Murtaza, Taimoor Ali
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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Prevalence of Diurnal Enuresis in Children Aged 5-12 Years in Al-Diwaniyah, Iraq

Prevalence of
Diurnal
Enuresis in
Children

Ahmed Ali Obaid¹, Ahmed Abdul Ameer Alwan¹ and Shiren Ali Al-Hamzawi²

ABSTRACT

Objective: To assess the prevalence of diurnal enuresis among children aged 5-12 years in Al-Diwaniyah.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Al-Diwaniyah Teaching Hospital and Al-Diwaniyah Maternity and Pediatrics Hospital, in central part of Iraq from 1st January 2024 to 1st July 2025.

Methods: 200 children of the age 5-12 years were enrolled. Seven cases were excluded due to other medical causes. The children have been interviewed, and the children have been assessed clinically. Urine test and lumbosacral X-ray were done.

Results: Twelve (6%) children were diagnosed with diurnal enuresis. The highest prevalence was at the age group of 5-8 years 75% with a steady decline by the age of 12 (8%). Males were more frequently affected 66.7% and females represent 33.3% of the cases. Primary diurnal enuresis accounted for 75% of the cases, while secondary diurnal enuresis was 25%.

Conclusion: A minority of school-aged children in Al-Diwaniyah were affected, especially younger boys. The commonest type of diurnal enuresis was the primary one.

Keywords: Diurnal enuresis, Prevalence, Children, Urinary tract infection

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INTRODUCTION

Diurnal enuresis (DE) is a substantial but under recognized condition in childhood, specifically in the developing countries. Mastering control of bladder and bowel is a complex and gradual process that occurs over a period of months for the typical toddler. Infants in general void small amounts of urine every hour and this is commonly stimulated by the process of feeding to diagnose a case of diurnal enuresis the child must show a chronological or developmental age of at least 5 years. The diagnosis of enuresis is done only after the exclusion of medical conditions. Infants void frequently, but as bladder capacity increases during toddler years, cortical inhibitory pathways mature and voluntary control emerges. Normally, sequence of the control over bladder and bowel function is nocturnal bowel control, diurnal bowel control, diurnal bladder control, and nocturnal bladder control.

The developmental route of toilet training is affected by a variety of factors among them are intellectual ability, neurological growth, social maturity, cultural practices, and parents–children psychological interaction. Diurnal enuresis is described as involuntary urination during waking hours beyond the usual age of bladder control.¹ Generally the clinical criteria require a minimum of two wetting periods per week for three months or more in the absence of underlying medical disorders.² Compared with nocturnal enuresis, DE has received less attention in research, despite being linked to delayed bladder maturation, psychosocial stresses, urinary tract infections, and behavioral comorbidities. The prevalence of diurnal enuresis decreases with the increase of age. The previous international studies accounted a prevalence ranging from 2 percent to 5 percent among the age of school children, with higher percentage was in younger children and in the developing countries.³⁻⁵ The purpose of the present study was to address the prevalence of diurnal enuresis in children who live in Al-Diwaniyah, Iraq.

¹. Department of Surgery / Gynecology and Obstetrics², College of Medicine, University of Al-Qadisiyah, Iraq.

Correspondence: Ahmed Ali Obaid, Department of Surgery, College of Medicine, University of Al-Qadisiyah, Iraq.
Email: ahmed.a.obaid@qu.edu.iq

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METHODS

This cross-sectional study was conducted at Al-Diwaniyah Teaching Hospital and Al-Diwaniyah Maternity and Pediatrics Hospital, Iraq from 15th September 2024 to 15th March 2025 letter No. 3434/QM/Approval/JSDJNEHU dated September 7, 2024. The study was using convenience sampling of those children who were attending outpatient

department in two main hospitals: Two hundred children between the age of 5-12 years were enrolled. Children with known neurological disorders, congenital urinary tract anomalies, or urinary tract infection confirmed by laboratory investigations were excluded. Data were obtained through structured parents' interview. Clinical examination, Laboratory urine analysis, and lumbosacral X-ray were done. Prevalence was analyzed according to age, sex, and diurnal enuresis subtypes (primary vs. secondary). The analyses of data were done by the use of Statistical Package for the Social Sciences 27.0. Descriptive statistics were used as percentages and frequencies and for assessing the association between diurnal enuresis and sex, Chi-square (χ^2) test was used. A p-value of <0.05 was of statistical significance.

RESULTS

There were 120 (60%) males and 80 (40%) females. Diurnal enuresis was observed in 12 cases, giving prevalence of 6%. The results of this study revealed that affected males were outnumbering females, 8 out of 120 (6.7%) for males and 4 out of 80 (5%) for female but the difference was not of statistical significance ($\chi^2 = 0.23$, $p = 0.62$) [Table 1].

The predominant subtype was primary diurnal enuresis constituting 9 (75%) cases, while secondary diurnal enuresis was found in 3 (25%) cases (Table 2).

The distribution of diurnal enuresis cases was clearly concentrated in the age group of 5-8 years and constitutes (75%) of the study sample while there is a decline in the occurrence of diurnal enuresis with the increase of age (Table 3)

Table No. 1: Prevalence of diurnal enuresis according to sex

Gender	No.	Cases of diurnal enuresis	Prevalence
Males	120	8	6.7%
Females	80	4	5.0
Total	200	12	6.0

$\chi^2 = 0.23$, $p = 0.62$

Table No. 2: Subtypes of diurnal enuresis

Subtype	Cases	Percent
Primary diurnal enuresis	9	75.0
Secondary diurnal enuresis	3	25.0
Total	12	100.0

Table No. 3: Distribution of diurnal enuresis according to the age group

Age (years)	No.	%
5-8	9	75.0
9-11	2	16.7
12	1	8.3
Total	12	100.0

DISCUSSION

The present study identified a prevalence of diurnal enuresis among the age of school children in Al-Diwaniyah. This percentage of diurnal enuresis is consistent with other Iraqi research that generally reported prevalence ranging between 4% and 7%.⁶⁻¹⁰ However, in comparison with other international studies this figure is lower than that reported 8%-10% by them.¹¹⁻¹³ This discrepancy may be ascribed underreporting of diurnal enuresis because of being socially stigmatized or due to the differences in the study.

The higher prevalence in 5-year-olds reflects incomplete bladder maturation, which improves progressively with age while the decline in prevalence with the increase of age supports the concept that diurnal enuresis considerably resolves as the capacity of the bladder improves.⁸

Within the context of the region many behavioral and environmental factors may have a contribution to diurnal enuresis persistence. These factors are cultural expectations in practicing toilet training, limited access to school toilet, which may discourage urination regularly, long class hours with limitation of bath breaks. In addition to that the province's climate which is characterized by being hot probably affects hydration of children and voiding manner. These factors with the psychosocial and other stressors such as academic pressure, overcrowding, parental awareness patterns may give a possible explanation for the prevalence and decline in diurnal enuresis with age development.^{5,7}

In this study boys were slightly higher than girls were and this is in alignment with findings from other studies^{13,14}, despite the fact that the difference was not statistically significant. The most suitable explanations are the slower urogenital maturation in boys and the differences in report that is given by the parents. All cases of diurnal enuresis attributed to neurological disorders, congenital urinary tract abnormalities, urinary tract infections or other organic causes, were excluded to secure that the study is focusing on the functional nature of diurnal enuresis. In general the predominance of primary diurnal enuresis compared to secondary diurnal enuresis reflects the trend that is reported in both Iraqi and international literature. Secondary diurnal enuresis is more commonly linked with other medical conditions, psychological stressors and traumas, emotional distress and behavioral disturbances as it is stated in previous literatures.^{11,12,15}

Limitations of the study: On interpretation of the results of this study, several limitations should be taken in consideration: First, the study was a hospital-based convenience sampling method and this limits the generalization of results to the broader group of

children in Al-Diwaniyah. Second, the number of those diagnosed with diurnal enuresis is so small and this may reduce the ability to detect significant associations of the variables (e.g. age and sex). Third parent's reports through interviews may lead to recall bias particularly for stigmatizing conditions as diurnal enuresis.

CONCLUSION

Diurnal enuresis affects a minority of children aged between 5–12 years in Al-Diwaniyah and the highest prevalence was among younger age group. Primary diurnal enuresis is more prevalent than secondary one though statistically not significant and males are outnumbering females. Early identification and recognition with the education of parents are of paramount importance, particularly at the age of school entrance.

Recommendations

1. Children under the age of eight years are routinely screened for enuresis.
2. Comprehensive psychological and medical assessment for children with secondary diurnal enuresis.
3. Education of parents about normal bladder development and early intervention.
4. Further studies in Iraq are required to provide further epidemiological data about diurnal enuresis.

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

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Association Between Addiction Severity and Sleep Quality among Patients with Substance Use Disorders: A Secondary Analysis of a Virtual Reality Intervention Study

Ahmed Mishaal Mohammed¹ and Amean A. Yasir²

ABSTRACT

Objective: To evaluate the relationship between the severity of addiction and sleep quality among patients actively receiving substance use disorder treatment.

Study Design: Cross-sectional quasi-experimental study

Place and Duration of Study: This study was conducted at the National Addiction Rehabilitation Center in Mosul, Iraq from 15th September 2024 to 15th February 2025.

Methods: 60 patients were enrolled. The participants were divided into an intervention group receiving virtual reality relaxation therapy (n = 30) and a control group receiving routine care (n = 30). Assessments were performed using the Addiction Severity Index (ASI) to measure addiction levels and the Pittsburgh Sleep Quality Index (PSQI) to evaluate sleep quality.

Results: The sample demonstrated widespread sleep disruption, with 86.7% of participants reporting poor sleep and an overall mean PSQI score of 12.7±2.5. A significant positive correlation was identified between addiction severity and PSQI scores (r=0.51, p<0.001), indicating that higher addiction severity correlates with poorer sleep. Furthermore, linear regression analysis confirmed that both the severity of addiction (0.47, p<0.001) and the duration of substance use (0.32, p=0.003) were significant predictors of sleep disturbances.

Conclusion: There is a robust association between addiction severity and poor sleep quality in patients with SUD. Integrating targeted sleep management protocols into standard addiction treatment could significantly enhance overall recovery outcomes and reduce the likelihood of relapse.

Key Words: Insomnia, Rehabilitation, Psychological health

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INTRODUCTION

Substance use disorders (SUD) are also one of the key problems of global public health impacting millions of people every day and causing a significant burden of morbidity, mortality, and dysfunction of society.¹ Persistent use of psychoactive drugs may cause enduring neurobiological changes impacting mental activity, emotional control, and physiological activities such as sleeping regulation.^{2,3} The reports of sleep disturbances are thus also common in people who are

dependent on substances and are believed to be one of the most common clinical complications prevalent in the addiction treatment and recovery.⁴

Somatic and/or substance use disorders Insomnia, prolonged sleep latency, reduced sleep efficiency, fragmented sleep, and disrupted rapid eye movement (REM) sleep are among the sleep problems among people with substance use disorders.⁵ Past epidemiology research has revealed that about 70-90% of the people receiving a substance dependence treatment suffer serious sleeping issues.⁶ The disturbances can be experienced when one is under active substance use, withdrawal, and even during the prolonged abstinence period since the neurobiological changes in the central nervous system are persistent.⁷ These drugs include opioids, stimulants, alcohol, and sedative-hypnotics, which influence the sleep regulation systems; they are dopamine, serotonin, and gamma-aminobutyric acid (GABA) systems.⁸ Their interference can cause changes in circadian rhythm and sleep architecture, which are the causes of chronic insomnia and poor sleep quality.⁹

Sleep quality of the individuals with substance use disorders has been linked to many adverse consequences. It has been established that sleep

¹. Department of Psychiatric and Mental Health, College of Nursing, University of Babylon, Babylon, Iraq.

². Department of Family and Community Health Nursing, College of Nursing, University of Babylon, Babylon, Iraq.

Correspondence: Ahmed Mishaal Mohammed, Department of Psychiatric and Mental Health, College of Nursing, University of Babylon, Babylon, Iraq.

Email: nur660.ahmed.mshal@student.uobabylon.edu.iq

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disturbances can make psychological distress more prevalent, worsen cognitive abilities, and make mood unstable.¹⁰ In addition, chronic insomnia has been found to be another factor that is predictive of relapse in people who are recovering substance dependence.¹¹ Therefore, sleep problems are also becoming an urgent area of clinical intervention in the course of the addiction treatment programs.¹²

Another factor that could affect patient sleep is addiction severity. The neurophysiological disruption, psychological distress, and social impairment of persons with more severe substance dependence is more frequent than in persons with less severe substance use problems.¹³ The Addiction Severity Index (ASI) is regarded as one of the most commonly used tools in addiction studies and clinical settings to determine the extent of substance consumption and how it affects different areas of functioning.¹⁴

In the past, researchers have proposed that participants who score high in terms of addiction severity are more likely to report more serious sleeping disorders.¹⁵ The neurobiological processes of this association could be the long-term changes in the brain reward systems, the maladaptation of circadian mechanisms, and the elevated aspects of stress and anxiety in people with severe substance dependence.¹⁶

Although this relationship faces increasing evidence on its importance, there is little research available on the interaction between the severity of addiction and sleep disturbances in Middle Eastern societies, especially with regard to patients receiving treatment in rehabilitation facilities. The knowledge about the correlation between the degree of addiction and the quality of sleep can assist healthcare specialists in creating specific intervention to enhance sleep wellness and promote recovery outcomes in persons with substance use disorders.¹⁷

Thus, the current study was conducted to determine the relationship between the degree of addiction and the quality of sleep in patients who are receiving treatment of substance use disorders in Mosul, Iraq.

METHODS

The cross-sectional quasi-experimental intervention study was carried out in the National Addiction Rehabilitation Center at Mosul, Iraq from 15th September 2024 to 15th February 2025. vide letter No.44 Dated 12.09.2024. It is a special center that is able to offer inpatient treatment and rehabilitation programs to patients diagnosed with substance use disorders. The facility has extensive addiction treatment initiatives, which comprise medical care, psychological guidance, and behavioral counseling. The choice of the setting to carry out the study enabled patients undergoing organised treatment of substance dependence to be accessed hence enabling the severity of the addiction and sleep disturbances to be evaluated in a fitting environment. A total of 60 patients

diagnosed with substance use disorders being treated in the rehabilitation center in the time of the study. They were initially identified as the larger study aimed to test the productivity of virtual reality-based relaxation therapy in individuals with the substance dependence in context of sleep disturbance reduction. As per the overall intervention study, the study participants were separated into two equal groups. The intervention group comprised 30 patients who underwent virtual reality relaxation therapy sessions and the control group comprised 30 patients who had the regular treatment as offered by the rehabilitation center. They were carried out by using the data obtained in both groups to determine the relationship between the level of addiction and the quality of sleep. The participants were to be diagnosed with substance use disorders based on the diagnostic criteria, the age of the eligible participants was to be 18-50 years, having disturbances in sleep during the time of recruitment and to give informed consent and show readiness to undergo the process were included.

The Sleep quality was measured by means of a Pittsburgh Sleep Quality Index (PSQI), a common standardized self-report measure that is supposed to assess the sleep quality in the last month. PSQI has seven items that measure various sleeping factors such as subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleeping disturbances, sleep medication use, and dysfunction daytime. All the components are rated out of 0 to 3 and the scores of the components are added up to get the final score that is out of 0 to 21. A high score means worse sleep, and a global score more than five is usually seen to refer to poor sleep.

The severity of addiction was measured with the help of the Addiction Severity Index (ASI), a structured clinical assessment instrument that determines the degree of substance being used and how it affects other spheres of the life of a particular person. The ASI evaluates a number of areas, such as medical status, employment and assistance, alcohol/drug use, legal status, family and social relationships, and psychiatric status. The instrument is a very thorough assessment of the severity of addiction, which is highly utilized both in clinical and research environments to assess patients with substance use disorder. The data was analyzed with the use of IBM SPSS-26. The Pearson correlation analysis was examined to determine the correlation between severity of the addiction and the scores of the sleep quality. Moreover, linear regression analysis has been conducted to reveal possible predictors of sleep disturbances of the participants. A p-value <0.05 was considered as a statistically significant value.

RESULTS

The demographic characteristics of participants were similar across the two groups, indicating homogeneity in baseline characteristics (Table 1). The majority of participants exhibited severe addiction levels, reflecting the clinical nature of the rehabilitation setting (Table 2).

Most participants experienced poor sleep quality according to PSQI classification (Table 3).

Table No. 1: Sociodemographic characteristics of participants (N = 60)

Variable	Intervention (n=30)	Control (n=30)
Age (years)	31.8±6.4	32.5±6.9
Gender		
Male	27 (90%)	26 (86.7%)
Female	3 (10%)	4 (13.3%)
Marital status		
Single	18 (60%)	17 (56.7%)
Married	12 (40%)	13 (43.3%)

Table No. 2: Addiction severity levels

Addiction Severity	No.	%
Moderate	22	36.7
Severe	38	63.3

Table No. 3: Sleep quality distribution

Sleep Quality	No.	%
Good sleep quality	8	13.3
Poor sleep quality	52	86.7

Table No. 4: Correlation between addiction severity and sleep quality

Variable	r	p-value
Addiction severity vs PSQI	0.51	<0.001

Table No. 5: Regression analysis predicting sleep quality

Predictor	β	Standard Error	p-value
Addiction severity	0.47	0.11	<0.001
Age	0.09	0.07	0.21
Duration of substance use	0.32	0.10	0.003

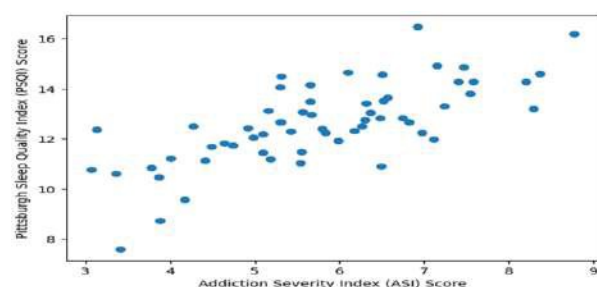


Figure No. 1: Relationship between addiction severity and sleep quality

A moderate positive correlation was found between addiction severity and sleep disturbances (Table 4). Addiction severity and duration of substance use were significant predictors of poor sleep quality (Table 5). The positive association between Addiction Severity Index (ASI) scores and Pittsburgh Sleep Quality Index (PSQI) scores among patients with substance use

disorders (Fig. 1). Regression analysis demonstrates the positive linear relationship between addiction severity and sleep disturbance (Fig. 2).

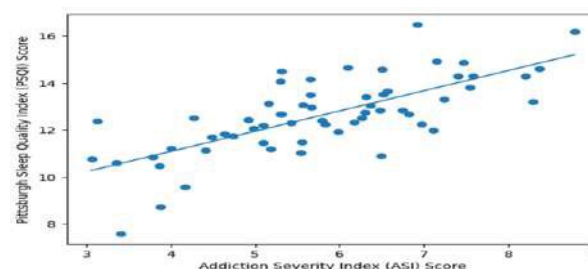


Figure No. 2: Linear regression between addiction severity and sleep quality

DISCUSSION

The current research investigated the level of the addiction and the quality of sleep among patients with substance use disorders in the treatment process. The results revealed that most participants had low quality of sleep, PSQI score of 12.7 on average showed that there was a high level of sleep deprivation in the population of the study. The results are in line with other studies that suggest that sleep disorders are very common in patients with substance use disorders.¹⁸

In the current research almost 86.7 percent of those interviewed reported poor sleep quality by PSQI categories. Prior studies that have been done on people undergoing treatment of addiction have also shown similar prevalence rates, with more than three-quarters of the patients being reported to have sleep disturbances.¹⁹ Persistent insomnia and sleep fragmentation is proven to be a result of chronic exposure to psychoactive substances by discontinuing normal sleep architecture, and circadian cycling.²⁰

Findings of this study also showed that there was a strong positive relationship between the severity of addiction and sleep disturbances. The patients scoring higher on the addiction severity scales reported the poor sleep quality more. These results align with other studies that propose more profound substance dependence to correlate with increased physiological and psychological dysfunction that could be linked with sleep disturbances.²¹

There are a number of biological processes that could help in the explanation of a correlation between the severity of addiction and sleep disturbances. Chronic substance use can modify the work of neurotransmitters that are used in the regulation of sleep, such as dopamine, serotonin and GABA.²² Such alterations in the neurochemical system can result in the disruption of sleep-wake system and poor sleep in people with severe substance dependence.

The other possible cause of the observed relationship is psychological stress connected with an extreme addiction. Anxiety, depression, and emotional distress are more frequently seen in the individuals with the

high severity of addiction.²³ These are psychological factors that have been closely associated with insomnia and other sleeping disturbances.²⁴

The current paper also revealed that the time of substance use was also a strong predictor of sleep disruptions. The longer the duration of the use of the substances, the more likely the patients were to report poor sleep quality. This has been observed in the past research that suggested that chronic exposure to substances can cause chronic changes in brain activity and attire sleep.²⁵

Clinically, the results of this study underscore the need to examine the quality of sleep to be used in the process of treating an addiction. The treatment of sleep disorders can help to enhance the psychological well-being and treatment outcomes of persons affected by substance use disorders. As the previous research has shown, the method of enhancing the quality of sleep can be used to help decrease the risk of relapse and promote long-term recovery.²⁶

Cognitive behavioral therapy of insomnia, mindfulness-based therapies, and relaxation methods are all non-pharmacological interventions that have been found to enhance the quality of sleep in substance use disorder victims.²⁷ The new technologies like the use of virtual reality to create relaxation therapy can also offer good potential in enhancing sleep health in addiction treatment environments.

CONCLUSION

The severity of substance use disorder addictions is strongly correlated with low sleep quality in substance use disorder people. Patients who are highly addicted are more likely to suffer sleeps disturbance and sleep management approaches should be included in the addiction treatment programs.

Recommendations: Medical staff members need to evaluate patients with addiction status on their sleep quality regularly. The rehabilitation programs should include interventions that enhance the quality of sleep. It is advised that future research should be conducted on a larger scale with longitudinal designs.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Ahmed Mishaal Mohammed, Amean A. Yasir
Drafting or Revising Critically:	Ahmed Mishaal Mohammed, Amean A. Yasir
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Impact of Water Quality and Maternal Diet on Pregnancy Outcomes in Al-Hawija

Ali Kareem Durib

Impact of Water Quality and Maternal Diet on Pregnancy

ABSTRACT

Objective: To determine the effect of the geological nature of drinking water, dietary habits and effect on changing the sex ratio of fetuses through its effect on the pH of the cervix.

Study Design: comparative study

Place and Duration of Study: This study was conducted at the Middle Technical University, Baghdad Iraq from 1st August 2023 to 31st August 2024.

Methods: This comparative study was conducted at Middle Technical University, Baghdad Iraq. Two hundred and fifty women were enrolled among them 150 from Hawija area and 100 from Kirkuk city.

Results: There were 110 (73.3%) males and 40 (26.7%) females in Hawija area and 70 (70%) males and 30 (30%) females in Kirkuk city. The significant increases in the levels of calcium, magnesium and potassium were in the raw water of Al-Hawija area as compared to Kirkuk city. There was no significant difference in the level of sodium in the raw water of Al-Hawija area as compared to Kirkuk city.

Conclusion: There is a difference in the sex ratio of births and acidity of the cervix between women in Kirkuk city and Hawija city. The presence of a significant difference in the percentage of calcium, magnesium, sodium and potassium in the water supplied.

Key Words: Water pollution, Dietary habits, Sex difference, Cervical pH

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INTRODUCTION

The sex of the fetus is determined by the male cells (sperm) produced by the man, as the testicles produce two types of sex cells, one of which contains the X chromosome (female sperm) and the other contains the Y chromosome (male sperm). A woman produces one type of sex cell (the egg) that carries the X chromosome. When the egg carrying the X chromosome meets the sperm carrying the X chromosome, the sex of the fetus will be female (XX). However, if the egg meets the sperm carrying the Y chromosome, the sex of the fetus will be male (XY). Therefore, the sex of the newborn is determined from the first moment of fertilization.^{1,2}

Scientific research has shown that female sperm (carrying the X chromosome) have a better ability to tolerate the acidic vaginal pH than male sperm

(carrying the Y chromosome)^{3,4}, which means that female sperm have a greater chance of survival than male sperm in the vaginal environment and the cervix with an acidic pH.⁵ The cells lining the vagina secrete lactic acid and hydrogen peroxide, which act as a protective barrier against bacterial and fungal infections, as it works to lower the vaginal pH level to 3.5-4.5, which is unsuitable for bacterial and fungal growth^{6,7}, while the pH that incubates sperm ranges from 6.9 in the testes to 7.14 in semen.^{8,9} The cervix also acts as a reservoir for sperm for a short period of approximately two days. It is noted that sperm are active and effective 24 hours after sexual intercourse and in the inner region of the cervix in large quantities. These sperm can move into the uterus and fertilize the egg, as the appropriate degree for the cervical acidity scale is between 3.6-2.7. If the cervical acidity is less than 3.6, this causes paralysis or death of sperm inside the cervix.^{10,11}

Sex determination has been the subject of many scientific studies for a long time, as advances in genetics have revealed the existence of some sex-linked genetic diseases (X-linked diseases) that affect only one sex, in addition to common diseases that are not sex-linked but are more common in males, such as autism.¹² Therefore, research and studies continued to arrive at the possibility of determining the sex of fetuses. Among these studies, a method of following diets emerged that leads to increasing the level of calcium and magnesium (CaMg) to the ratio of sodium and potassium (NaK) in

Department of Anesthesia, Medical Technical Institute, Middle Technical University, Baghdad, Iraq.

Correspondence: Ali Kareem Durib, Department of Anesthesia, Medical Technical Institute, Middle Technical University, Baghdad, Iraq.

Email: ali_kareem37@yahoo.com

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food and drinking water leading to an increase in the chances of giving birth to females, while increasing the level of sodium and potassium (NaK) to the ratio of calcium and magnesium (CaMg) leads to an increase in the chances of giving birth to males¹³, as Ca⁺ and Mg ions work to increase the acidity of the vagina and cervix, while Na⁺ and K⁺ ions work to increase the alkalinity of the vagina and cervix.^{14,15} Considering the geological nature of Al-Hawija district, which is mostly composed of limestone rocks rich in calcium, which has the ability to dissolve in the water passing through it and is prepared for drinking water for all areas of the district^{16,17}, in addition to the fact that all agricultural drains in the region carry water from agricultural lands to which chemical fertilizers are constantly added and poured into drinking water sources, which led to the erosion of these ions from agricultural lands of a calcareous nature and their collection in drinking water sources, which led to a change in the proportion of these ions when they reached the population compared to the drinking water supplied to the city of Kirkuk, which passes through lined waterways and is far from the sources of pollution with agricultural fertilizers in the lands, in addition to the different dietary habits of each of the two study groups, as the first group (Al-Hawija women) relied heavily in its nutrition on dairy products rich in calcium and magnesium as a basic food, while the second group (Kirkuk women) relied on diversity in food, which provided the entry of larger quantities of sodium and potassium into the body compared to calcium sources and magnesium.

METHODS

This comparative study was conducted at Middle Technical University, Baghdad Iraq from 1st August 2023 to 31st August 2024 vide letter No. 130/QM/Approval/9393JFDNF Dated 15.07.2023. Two hundred and fifty women were enrolled among them 150 from Hawija area and 100 from Kirkuk city. Their ages ranged from 18-38 years, who gave birth to a higher percentage of females than males for women in Hawija, while the samples were taken from women in Kirkuk who gave birth to a higher percentage of males than females. The cervical pH of the women in the study group was measured. Drinking water samples affecting the cervical pH were also taken from the water sources supplied to Al-Hawija district, namely the water of Al-Hawija irrigation project, in addition to drinking water samples from Kirkuk city, where two water samples were collected (a raw water sample, a prepared water sample) from each of the mentioned sources in the seasons (winter, spring, summer). Then, chemical analyses were conducted for these samples and the levels of Ca⁺, Mg⁺, Na⁺, K⁺ were measured. Data was also collected on the dietary habits of each of the women in the study group. The results of the first group were compared with the results of the second

group. The cervical pH level was measured using special strips. A sterile swab was inserted into the cervix, taking care not to touch the vaginal wall. The swab was then wiped on the measuring strip, and the results were compared with a special measuring ruler. The data was entered and analyzed through SPSS-25.

RESULTS

There were 110 (73.3%) males and 40 (26.7%) females in Hawija area and 70 (70%) males and 30 (30%) females in Kirkuk city (Table 1).

Figure 1 showed a significant increase in the level of calcium in the raw water of Al-Hawija area for the years 2021-2024 at a rate of (51.100±9.163), (43.40±6.90), (46.23±5.35), (53.80±8.69) mg/L respectively compared to the level of calcium in the raw water of Kirkuk city at a rate of (41.700±5.889), (35.40±3.95), (41.57±4.31), (41.20±1.75) mg/L respectively. It also showed a significant increase in the level of calcium in the water supplied to the Al-Hawija area for the same years at a rate of (52.40±6.85), (41.80±7.70), (45.96±5.24), (52.81±7.94) mg/L respectively compared to the water supplied to the city of Kirkuk at a rate of (42.30±4.06), (36.51±3.62), (41.94±5.53), (43.00±1.95) ml/L at a significant level (p≤0.05).

The significant increase in the level of magnesium in the raw water of the Hawija area for the years was 2021-2024 at a rate of (17.850±6.189), (17.431±5.162), (17.272±2.058), (20.971±3.771) mg/L respectively compared to the raw water of the city of Kirkuk at a rate of (13.681±3.871), (14.201±1.688), (14.937±1.228), (17.740±2.381) mg/L respectively. It also shows a significant increase in the magnesium level of the water supplied in the Hawija area at a rate of (16.941±2.986), (17.993±3.898), (17.546±2.019), (21.130±3.534) mg/L compared to the water supplied to the city of Kirkuk at a rate of (13.942±4.167), (14.480±1.078), (14.719±1.093), (17.890 ±2.457) mg/L respectively for the same years (Fig. 2).

There was no significant difference in the level of sodium in the raw water of Al-Hawija area for the years 2021-2024, with a rate of (6.605±2.016), (9.334±3.001), (7.742±1.176), (9.051±0.708) mg/L, respectively, compared to the level of sodium in the raw water of Kirkuk city, with a rate of (7.010±0.817), (10.355±2.133), (7.628±1.451), (9.021±0.453) mg/L, respectively, for the same years. The figure also shows that there is no significant difference in the sodium level between the water supplied to the Hawija area and the water supplied to the city of Kirkuk for the same years at a rate of (6.251±2.121), (9.334±2.237), (6.726±1.407), (8.841±0.518) compared to the water supplied to the city of Kirkuk at a rate of (7.510±0.547), (10.757±1.546), (6.951±1.612), (9.011±0.491) mg/L respectively for the same years (Fig. 3).

Table No. 1: Frequency of genders in cities (n=250)

Gender	Hawija city (n=150)		Kirkuk city (n=100)	
	No.	%	No.	%
Male	110	73.3	70	70.0
Female	40	26.7	30	30.0

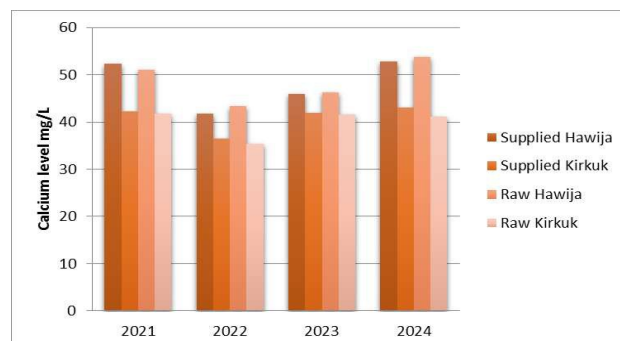
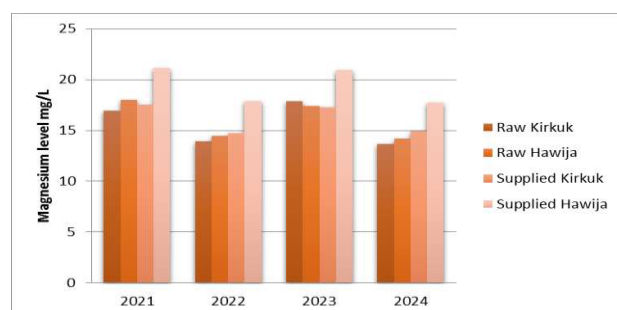
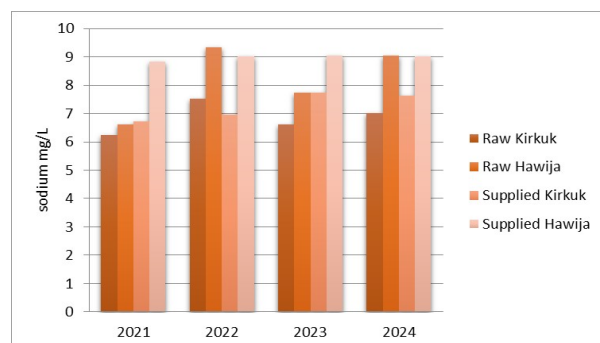
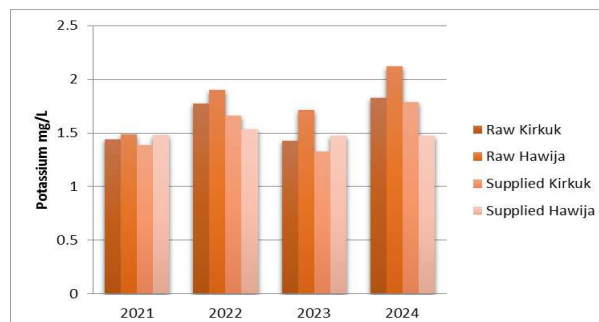
**Figure No. 1: Comparison of the level of calcium mg/L in prepared and raw water****Figure No. 2: Comparison of the magnesium level mg/L in prepared and raw water****Figure No. 3: Comparison of the level of sodium mg/L in prepared and raw water**

Figure 4 showed a significant increase in the level of potassium in the raw water of Kirkuk city for the years 2021-2024 at a rate of (1.826 ± 0.159) , (2.123 ± 0.548) , (1.788 ± 0.191) , (1.473 ± 0.083) mg/L respectively compared to the level of potassium in the raw water of Al-Hawija area at a rate of (1.427 ± 0.088) , (1.714 ± 0.244) , (1.324 ± 0.214) , (1.471 ± 0.081) mg/L respectively for the same years. It also shows a significant increase in the potassium level in the water supplied to Kirkuk city at a rate of (1.776 ± 0.117) , (1.902 ± 0.549) , (1.657 ± 0.195) , (1.531 ± 0.049) mg/L

respectively compared to the water supplied to Al-Hawija area at a rate of (1.439 ± 0.091) , (1.488 ± 0.146) , (1.386 ± 0.216) , (1.482 ± 0.078) mg/L respectively for the same years at a significant level ($p \leq 0.05$).

**Figure No. 4: Comparison of the level of potassium mg/L in prepared and raw water.**

DISCUSSION

The results of our study showed a significant difference in the ratio of males to females between Kirkuk city and Hawija district. In light of what we have reached through this study, the reason for this difference could be one of the reasons for it is the difference in the acidity of the cervix and the sexual canal in women, which our results showed a decrease in the acidity of the cervix in Hawija women compared to Kirkuk women. The cervix has an alkaline environment that is ideal for the movement and activity of sperm with the Y chromosome, unlike the acidic environment, which is harsh and unsuitable for their movement and activity, while sperm with the X chromosome resist the acidic environment.¹⁹ In light of the results of our study, there is a significant difference in the percentage of calcium and magnesium between the water supplied to the city of Kirkuk, which was lower than the percentage in the water of the Hawija district. Diet is one of the most important trends in scientific research to solve all health problems, and it is what researchers have resorted to solve the problem of determining the sex of the fetus. Many studies have focused on the role of high levels of calcium and magnesium compared to sodium and potassium in the diet, and their role in increasing the chance of conceiving females, and this percentage reflects the increased chance of conceiving males.^{20,21}

The difference in the proportions of these mineral salts between the water supplied to Kirkuk compared to the water supplied to Al-Hawija district may be attributed to the geological nature of the land and the nature of the canals supplied for the water, in addition to the quantities of organic and chemical agricultural fertilizers, which are considered the largest pollutant of drinking water in Al-Hawija district.^{20,21} The lack of health awareness and ignorance of the dangers of using this polluted water is considered an additional reason

for the significant difference in the variation in the proportion of fetal sex.

CONCLUSION

There is a difference in the sex ratio of births between Kirkuk city and Hawija district and indicated that there is a difference in the acidity of the cervix between women of Kirkuk city and Hawija district in addition to the presence of a significant difference in the percentage of calcium, magnesium, sodium and potassium in the water supplied to Kirkuk city and Hawija district.

Author's Contribution:

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

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Comparison of Conventional Laparoscopic Cholecystectomy with Clips and Laparoscopic Cholecystectomy Using Ligasure (High Energy Vessel Sealing Devices) Without Clips in Terms of Hemostasis

Conventional
Laparoscopic
Cholecystectomy
with Clips and
Laparoscopic
Cholecystectomy

Muhammad Usama Tariq¹, Muhammad Azhar², Sana Bashir¹ and Asad Janjua¹

ABSTRACT

Objective: To determine and compare mean intraoperative blood loss and mean time for achieving hemostasis in patients undergoing laparoscopic cholecystectomy using clips versus LigaSure vessel sealing system.

Study Design: Randomized clinical trial study

Place and Duration of Study: This study was conducted at the Department of Surgery, Pakistan Ordnance Factories Hospital, Wah Cantt, over a period of six months from November 2025 till January 2026.

Methods: A total of 114 patients between 18–60 years of age undergoing elective laparoscopic cholecystectomy were included in this study using non-probability consecutive sampling and randomized into two equal groups. Group A underwent cystic artery ligation with titanium clips, while Group B underwent vessel sealing using LigaSure. Intraoperative blood loss and time for achieving hemostasis were recorded and analyzed using the independent samples t-test.

Results: Patients in the LigaSure group demonstrated significantly lower mean intraoperative blood loss and shorter mean time to achieve hemostasis compared to the clip group ($p \leq 0.05$).

Conclusion: LigaSure is a safe and effective alternative to titanium clips for cystic artery control in laparoscopic cholecystectomy and may provide superior hemostatic outcomes.

Key Words: Laparoscopic cholecystectomy, LigaSure, titanium clips, hemostasis, blood loss

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INTRODUCTION

Laparoscopic cholecystectomy has been established as the gold standard surgical technique for symptomatic cholelithiasis since its introduction by Mühe in 1985. Over the decades of refinements in operative technique and instrumentation have resulted in better safety and efficiency, and also decreased complications. A critical step in laparoscopic cholecystectomy is to secure control of the cystic artery and cystic duct because the inadequate hemostasis may result in intraoperative hemorrhage, poor surgical field visualization, bile duct injuries and the need to convert to open surgery¹.

¹. Resident General Surgery / Assoc. Prof. of Surgery², Wah Medical College, POF Hospital Wah Cantt

Correspondence: Dr. Muhammad Usama Tariq, Resident General Surgery, Wah Medical College, POF Hospital Wah Cantt.

Contact No: tariqosama26@gmail.com

Email: 03405432504

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Conventionally the titanium clips are used for sealing cystic artery because they are readily available, cost-effective, and easy to apply. Despite their widespread use, their complications such as clip slippage, its migration, bile duct injury, and the late complications such as formation of choledocholithiasis have been reported by many^{2,3}. Also, in the presence of acute inflammation, dense adhesions, or a frozen Calot's triangle, the safe clip application to the target may be technically challenging.⁴

Over the years, the evolution of energy devices in surgery has significantly improved the minimally invasive surgery. For example, advanced bipolar vessel sealing systems such as LigaSure seal the vessels by denaturing the collagen and elastin within the vessel wall, providing a reliable hemostasis for vessels having diameter up to 7 mm^{5,6}. The use of LigaSure has been successfully implied in thyroidectomy, hysterectomy, colorectal surgery, thoracic surgery, and soft tissue procedures, with evidence showing decreased blood loss and better surgical outcomes^{7,8}.

Specifically considering laparoscopic cholecystectomy, the use of ultrasonic and advanced energy devices has resulted in decreased operative time, improved surgical field visibility, and decreased blood loss as compared to

conventional techniques such as titanium clips application^{9,10}. However, limited local and international studies exist on this important topic which directly compare LigaSure use with conventional titanium clips, particularly with regards to objective parameters such as intraoperative hemorrhage and time for achieving hemostasis. This study was designed to fill this gap and provide the evidence relevant to surgical practice in resource-limited settings.

METHODS

This randomized clinical trial was conducted in the Department of Surgery, Pakistan Ordnance Factories Hospital Wah Cantt, over three months duration. Ethical approval for this study was obtained from the Institutional Ethical Review Board of Pakistan Ordnance Factories Hospital Wah Cantt, before starting the study. Written informed consent was obtained from all the participants after explaining the nature, purpose, benefits, and potential risks of the study. Confidentiality of patient data was maintained throughout the process, and participants reserved the right to withdraw at any stage of study without consequence to their treatment.

A total of 114 patients between 18 to 60 years of age undergoing elective laparoscopic cholecystectomy for any indication were enrolled using non-probability consecutive sampling. Written informed consent was obtained from all patients. Those requiring conversion to open cholecystectomy, those with known inherited or acquired bleeding diathesis, and those undergoing another concomitant major surgical procedure were excluded to minimize the confounding factors.

Following enrollment, the patients were randomly allocated to two groups using the lottery method. Group A underwent cystic artery ligation using conventional titanium clips. Group B underwent cystic artery control using the LigaSure vessel sealing system without clip application.

All procedures were performed using a standardized four-port technique by the same consultant surgeon to eliminate inter-operator variability. The same type and size of titanium clips and the same LigaSure device settings were used throughout the study to maintain consistency. Calot's triangle dissection was performed according to the critical view of safety principle in all cases.

Intraoperative blood loss was calculated by measuring the difference between pre- and post-procedure weight of suction bottles, gauze pieces, and abdominal sponges using a standardized weighing scale. Time for achieving hemostasis was calculated from the onset of bleeding from the cystic artery, if any, until complete cessation. These measurements were recorded intraoperatively by a trained observer blinded to group allocation to minimize observer bias.

All patients received standard perioperative care according to institutional protocol. Intraoperative complications were documented. Patients requiring conversion to open surgery were excluded from final analysis as per predefined criteria.

Data were entered and analyzed using SPSS version 26. Quantitative variables were expressed as mean $\pm$ standard deviation. The independent samples t-test was applied to compare intraoperative blood loss and time to achieve hemostasis between the two groups. A p-value ≤ 0.05 was considered statistically significant.

RESULTS

A total of 114 patients were included, with 57 in each group. The two groups were comparable with respect to baseline demographic characteristics, including age, gender distribution, and body mass index, minimizing confounding effects on outcomes (Table I).

Table No. I: Baseline Characteristics of Patients

Variable	Group A (Clips, n=57)	Group B(LigaSure, n=57)
Age (years)	43.2 $\pm$ 9.1	42.6 $\pm$ 8.8
Gender (M/F)	21 / 36	23 / 34
BMI (kg/m ²)	27.4 $\pm$ 3.2	27.1 $\pm$ 3.0

(Values are presented as mean $\pm$ standard deviation or as numbers.)

Intraoperative outcomes are presented in Table II. Patients in the LigaSure group demonstrated significantly lower mean intraoperative blood loss and shorter mean time to achieve hemostasis compared to the clip group. Mean operative time was comparable between the two groups.

Table No.2: Comparison of Intraoperative Outcomes

Outcome	Group A (Clips, n=57)	Group B (LigaSure, n=57)	p-value
Intraoperative blood loss (ml)	42.3 $\pm$ 10.5	18.7 $\pm$ 6.2	<0.001
Time to achieve haemostasis (sec)	85.4 $\pm$ 18.2	32.6 $\pm$ 8.9	<0.001
Operative time (min)	48.6 $\pm$ 11.3	46.2 $\pm$ 10.8	0.24

(Values are presented as mean $\pm$ standard deviation. p-values calculated using independent samples t-test.)

DISCUSSION

This randomized clinical trial shows that the use of LigaSure for cystic artery sealing during laparoscopic cholecystectomy is associated with improved

hemostasis compared to the conventional titanium clips. The observed reduction in intraoperative blood loss and shorter time required to achieve the hemostasis in the LigaSure group shows that advanced bipolar vessel sealing devices provide more reliable vascular control. Effective hemostasis is particularly important in laparoscopic cholecystectomy, where even small volume of hemorrhage can significantly decrease the field visualization and increase operative difficulty. LigaSure achieves vessel sealing through controlled bipolar energy delivery, resulting in permanent fusion of collagen and elastin fibers within the vessel wall. This mechanism likely accounts for the better hemostasis observed in the present study.

Our findings are consistent with previous reports. For example, the several studies demonstrated significantly reduced intraoperative blood loss and operative time in laparoscopic cholecystectomy performed using high-energy devices compared to conventional techniques¹¹. Studies have reported improved visualization and reduced blood loss with ultrasonic dissection in laparoscopic cholecystectomy¹². Although many studies have focused on ultrasonic devices, available evidence suggests that LigaSure also provides the comparable efficacy and safety¹³.

Concerns regarding thermal injury to adjacent structures, particularly the bile duct, have been raised with energy-based devices. However, several studies have shown that when used correctly, LigaSure does not increase the risk of bile duct injury or postoperative bile leak when compared to the conventional methods¹⁴. No bile duct injuries or major complications were observed in the present study.

An important strength of this study is the assessment of time for achieving hemostasis, an outcome that is not frequently reported in the existing studies. Shorter time required to achieve hemostasis may translate into improved efficiency, reduced surgeon's fatigue, and potentially lower conversion to open cholecystectomy rates in difficult cases¹⁵.

The findings of this study are especially relevant in our local context, where titanium clips remain the standard of care. While the initial cost of LigaSure may seem higher, its potential benefits in terms of efficiency and reduced hemorrhage may justify its use particularly in selected cases, such as acute cholecystitis or in case of difficult dissection¹⁶.

This study has some limitations however, as it was conducted at a single center with a relatively short follow-up period. Also, the long-term outcomes, cost-effectiveness, and postoperative pain were not evaluated. So multicenter studies with larger sample sizes and longer follow-up periods are recommended to validate these findings further and assess its generalizability.

CONCLUSION

LigaSure is a safe and effective alternative to titanium clips for cystic artery control during laparoscopic cholecystectomy. Its use is associated with decreased intraoperative hemorrhage and comparatively shorter time required to achieve hemostasis than titanium clips, especially in technically challenging cases.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Muhammad Usama Tariq, Muhammad Azhar
Drafting or Revising Critically:	Sana Bashir, Asad Janjua
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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INTRODUCTION

The start of the introduction should be Relevant. Reasons and Importance of the study should be clear. Give only strictly pertinent References and do not include data or conclusions from the work being reported.

MATERIALS AND METHODS

- ? If the method is already exist give reference but if new give its detail information. If use of any drug, give its generic name. For patient, give age and sex. Statistical method must be mentioned
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- ? Present finding, variations and similarities with other studies in the field. New and important aspects of your study and conclusions you should mentioned here that the hypothesis of your study is true, false or no conclusion can be derived.

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- ? • In this link write the goals of the study.

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ACKNOWLEDGMENTS

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Prof. Dr. Azhar Masud Bhatti,
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ADDRESS FOR SUBMISSION OF ARTICLES:

75-P, Phase-VIII, Defence Housing Authority, Lahore.
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