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Editorial

Relation of BPD Mother with Their Children

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

Borderline personality disorder (BPD) is a complex and severe psychiatric disorder characterized by mood dysregulation, interpersonal instability, self-image disturbance, and markedly impulsive behavior (e.g., aggression, self-injury, suicide)[1]. In addition, people with BPD may have chronic, frequent, random feelings of emptiness, fear, and so on. These symptoms often lead them to use unhealthy coping mechanisms in response to negative emotions, such as alcohol abuse[2]. BPD has a long course, which makes treatment difficult and may have a negative impact on patients' quality of life[3]. Due to its clinical challenge, BPD is by far the most studied category of personality disorder[4]. This disorder is present in 1−3% of the general population as well as in 10% of outpatients, 15−20% of inpatients, and 30−60% of patients with a diagnosed personality disorder, and has a suicide rate of up to 10%. Families of individuals with serious mental illness often experience distress, and those with relatives diagnosed with BPD tend to carry a heavier burden compared to other mental illnesses. As early as the 20th century, scholars began describing BPD and summarizing its symptoms. However, there was some debate regarding the precise definition of BPD.

According to the "Neuro-behavioral Model" proposed by Lieb[1], the process of BPD formation is very complex and is determined by the interaction of several factors. The interaction between different factors can be complex and dynamic. Genetic factors and adverse childhood experiences may contribute to emotional disorders and impulsivity, leading to dysfunctional behaviors and inner conflicts. These, in turn, can reinforce emotional dysregulation and impulsivity, exacerbating the preexisting conditions. Genetic factors are an important factor in the development of BPD[5]. Psychosocial factors, including adverse childhood experiences, have also been strongly associated with the development of BPD[6]. Emotional instability and impulsive behavior are even more common in patients with BPD[7]. The current study is based on the "Neuro-behavioral Model" and conducts a literature review of previous scientific research on BPD through bibliometric analysis to reorganize the influencing factors.

BPD symptoms in adolescents have been shown to respond to interventions with good results, so prevention and intervention for BPD is warranted[8]. Prevention and early intervention of BPD has been shown to provide many benefits, including reduced occurrence of secondary disorders, improved psychosocial functioning, and reduced risk of interpersonal conflict[9].

The etiology of BPD is closely related to many factors, and its pathogenesis is often ignored by clinicians. The exploration of risk factors has been an important research direction in the study. Some studies have found that BPD is largely the product of traumatic childhood experiences, which may lead to negative psychological effects on children growing up. It has also been found that the severity of borderline symptoms in parents is positively associated with poor parenting practices[10].

One of the most problematic aspects of having a mother with borderline personality disorder is dealing with their emotional volatility. Borderlines seek support and validation from their child, which they could never get from their own parents.

Emotional Instability and Insecurity: Unable to take charge of their emotions, BPD moms could hardly be worse models for their kids. Children learn to gain control of their feelings because they're taught how by parents who help them appreciate things from a broader, more balanced, and rational perspective. But maturationally arrested BPDs can't do this themselves, doubtless because of their own inherited and trauma-generated deficits. Given their non-chosen limitations, BPDs are doing the best they can. They don't consciously mean to harm their children, yet they're cursed with enormous blind spots that all too easily can be passed onto their progeny. For example, their uncontrollable mood swings and the indiscriminate intensity of their emotional reactions may be involuntary.

Irresponsibility in Caretaking: As already alluded to, in several ways BPDs unintentionally parentify their children. When they've been triggered and regressed to a childhood ego state, they can self-deludedly mistake their child for an adult. Consequently, they'll insist – with the almost limitless power they hold over their offspring – that the child offer them the validation never received when they were in the custody of their own ignorantly irresponsible parents. Additionally, or alternatively, the child may be assigned parental responsibility for their younger siblings. As a result, such children may struggle in their efforts to evolve a sense of autonomy distinct from this mutually dependent caregiving role.

Inability to Validate Their Child's Thoughts and Feelings: Desperately needing their child to confirm

their perspective, rarely supported by their own parents originally, BPDs have great difficulty validating their child's emotions and viewpoints when they diverge from their own. And when, therefore, they're compelled to disconfirm their offspring's reality, they can be understood as gaslighting their child.

The tragic outcome of their obliviousness is that the child is left afflicted with self-doubt, unable to trust the truth of their personal experience. Moreover, the child – accidentally abandoned emotionally – is left with a distorted sense of reality, reduced confidence and self-esteem, and mistrust in their own judgment. That, in turn, can create irresolvable difficulties in comfortably asserting reasonable boundaries with others. Because their cognitions and emotions go down different paths, their boundaries don't feel reasonable.

Modeling Dysfunctional Methods of Coping with Stress: As much as kids learn to cope with adversity through observing how their dominant parent has handled disappointments and failures, they're also highly subject to developing mental disorders aligned to their caretakers. Their mother's primitive, dysregulated coping devices may well become their own. Inevitably, just as was true earlier for their unresilient mother, they'll wind up unconsciously manifesting retaliatory behaviours almost guaranteed to jeopardise their later attachments.

The Solution to This Enduring Dilemma Is Complicated: Seldom is there any simple solution for the widespread problems experienced by children of borderlines. If they can, non-defensively and protractedly, engage with a highly proficient therapist and receive what might best be designated "corrective re-parenting", they may finally be able to cultivate healthier beliefs, attitudes, and communication skills untenable in their youth. Beyond that, establishing warm, supportive, and understanding relationships – from friends in whom they can safely confide – can significantly advance positive change. That is, with a liberating growth mindset, they can grasp more fully what happened to them in childhood and begin to revise residual feelings of distrust and hyper-vigilance.

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Original Article

Epilepsy in Pregnancy: Maternal and Fetal Outcomes of Antiepileptic Treatments

Epilepsy in Pregnancy

Ayesha Saleem[1], Rutaba Qadri[1], Zakia Bano[1], Mahwish Rizwan[2], Amanullah Khokhar[3] and Maryam Shahid[1]

ABSTRACT

Objective: To investigate the effects of various AEDs on maternal and fetal outcomes during pregnancy in a cohort of 135 women with epilepsy.

Study Design: A retrospective cohort study

Place and Duration of Study: This study was conducted at the K-health care hospital, Karachi during March 2023 to March 2024.

Methods: The cohort included 135 pregnant women diagnosed with epilepsy. Maternal seizure control, drug adherence, and fetal outcomes (e.g., congenital anomalies, birth weight) were analyzed.

Results: Maternal seizure control was achieved in 68% of patients, with a higher seizure-free rate in those on monotherapy compared to polytherapy. Fetal outcomes varied with the type of AED, with higher rates of congenital anomalies observed in polytherapy groups. Low birth weight was more common in pregnancies exposed to sodium valproate.

Conclusion: The choice of AEDs significantly impacts maternal seizure control and fetal outcomes. Monotherapy regimens, particularly lamotrigine and levetiracetam, were associated with better maternal seizure control and fewer adverse fetal outcomes compared to polytherapy regimens.

Key Words: Epilepsy, Pregnancy, Fetal Outcomes, Antiepileptic Treatments

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INTRODUCTION

Epilepsy is a chronic neurological disorder affecting approximately 50 million people worldwide, with women of childbearing age representing a significant proportion of this population. Pregnancy poses a unique set of challenges for women with epilepsy, as both the disease itself and the treatments required for its management can significantly influence maternal and fetal health. Seizures during pregnancy, particularly generalized tonic-clonic seizures, are associated with increased risks of trauma, placental abruption, status epilepticus, and even maternal mortality[1].

For the fetus, maternal seizures can result in intrauterine growth restriction, preterm birth, stillbirth, and long-term neurodevelopmental impairments, emphasizing the critical importance of maintaining seizure control during pregnancy[2]. The cornerstone of epilepsy management is the use of antiepileptic drugs (AEDs), which effectively reduce seizure frequency and severity. However, AEDs introduce a dual challenge during pregnancy: while they are essential for maintaining seizure control, many AEDs cross the placenta, potentially impacting fetal development. Older-generation AEDs, such as sodium valproate and phenytoin, are associated with higher risks of teratogenic effects, including major congenital malformations (MCMs) such as neural tube defects, cleft palate, cardiac abnormalities, and craniofacial dysmorphism[3]. These risks have been extensively documented in studies showing that the teratogenicity of sodium valproate, for instance, is dose-dependent, with higher doses correlating with increased risks of congenital anomalies[4]. In contrast, newer-generation AEDs like lamotrigine and levetiracetam have demonstrated improved safety profiles. Studies have shown that these drugs are associated with significantly lower rates of MCMs and neurodevelopmental impairments compared to older-generation AEDs. However, even these drugs require close monitoring during pregnancy to avoid complications such as subtherapeutic levels or potential drug-related adverse effects[5].

Physiological changes during pregnancy complicate AED management. Increased renal clearance, reduced

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protein binding, and enhanced hepatic metabolism lead to altered pharmacokinetics for many AEDs. For example, lamotrigine clearance can increase by 200-300% during pregnancy, resulting in decreased serum drug concentrations and an elevated risk of breakthrough seizures[6]. Therapeutic drug monitoring (TDM) has therefore become an essential component of epilepsy management during pregnancy, allowing clinicians to make precise dose adjustments to maintain therapeutic levels without increasing the risk of drug toxicity[7]. The psychosocial challenges faced by pregnant women with epilepsy further complicate management. Many women experience heightened anxiety about the potential teratogenic effects of AEDs and the impact of their condition on fetal health. This anxiety often leads to poor medication adherence, with some women discontinuing AEDs entirely, resulting in an increased risk of uncontrolled seizures. Societal stigma and lack of access to specialized care further exacerbate these issues, emphasizing the need for comprehensive patient education and support system[8]. Preconception counseling has emerged as a cornerstone of epilepsy management for women planning to conceive. This proactive approach allows clinicians to transition patients to safer AED regimens, initiate folic acid supplementation to reduce the risk of neural tube defects, and provide education about the risks and benefits of AED use during pregnancy. Studies have consistently shown that women who receive preconception counseling have significantly better maternal and fetal outcomes compared to others[9]. Despite advancements in epilepsy care, significant gaps remain in understanding the long-term neurodevelopmental effects of AED exposure in utero and the optimal management of refractory epilepsy during pregnancy. This study aims to address these gaps by evaluating maternal and fetal outcomes associated with AED use in a cohort of 135 pregnant women with epilepsy. By comparing outcomes between monotherapy and polytherapy regimens, the study seeks to provide evidence-based insights into safer and more effective treatment strategies for this population[10].

METHODS

A retrospective cohort study was conducted at K-health care hospital, Karachi during March 2023 to March 2024. Data were collected from medical records of 135 pregnant women diagnosed with epilepsy.

Inclusion Criteria:

- Pregnant women aged 18–40 years.
- Diagnosed with epilepsy before pregnancy.
- Receiving AEDs during pregnancy.

Exclusion Criteria:

- Women with other neurological disorders.
- Pregnancies with known chromosomal abnormalities.
- Incomplete medical records.

Data Collection: Clinical data were collected, including demographic information, type of epilepsy, AED regimen (monotherapy or polytherapy), maternal seizure frequency, drug adherence, and fetal outcomes. Outcomes assessed included congenital anomalies, low birth weight (<2.5 kg), preterm birth (<37 weeks), and perinatal mortality.

Statistical Analysis: Data were analyzed using SPSS version 25. Descriptive statistics were used for demographic and clinical variables. Chi-square and t-tests were employed to compare outcomes between AED regimens, with significance set at $p < 0.05$.

RESULTS

The cohort included 135 pregnant women with epilepsy, with a mean age of 29.8 years (±4.6). Focal epilepsy was the most common type, accounting for 62% of cases.

Table No. 1: Patient Demographics and Epilepsy Characteristics

Parameter	Value	Percentage (%)
Total Patients (n)	135	100
Mean Age (years)	29.8 ± 4.6	-
Type of Epilepsy		
- Focal Epilepsy	84	62
-Generalized Epilepsy	51	38
AED Regimen		
- Monotherapy	88	65
- Polytherapy	47	35

Maternal seizure control was achieved in 68% of patients, with a higher rate of seizure-free pregnancies in the monotherapy group (78%) compared to the polytherapy group (49%).

Table No. 2: Maternal Outcomes by AED Regimen

Outcome	Monotherapy (n = 88)	Polytherapy (n = 47)	p-value
Seizure-Free	78%	49%	0.002
Breakthrough Seizures	22%	51%	0.001
Status Epilepticus	1%	4%	0.05

Seizure control was significantly better in the monotherapy group, highlighting the importance of simplified treatment regimens during pregnancy. Polytherapy regimens, though sometimes necessary for refractory epilepsy, were associated with a higher incidence of breakthrough seizures and status epilepticus.

Congenital anomalies were more frequent in the polytherapy group (19%) compared to the monotherapy group (6%). Low birth weight and preterm births were also more common in pregnancies exposed to sodium valproate.

Table No. 3: Fetal Outcomes by AED Type

Outcome	Lamotrigine (n = 50)	Levetiracetam (n = 45)	Sodium Valproate (n = 40)	p-value
Congenital Anomalies (%)	4	7	18	0.01
Low Birth Weight (%)	6	8	22	0.001
Preterm Birth (%)	10	12	25	0.002

Sodium valproate was associated with the highest rates of adverse fetal outcomes, including congenital anomalies and low birth weight. Lamotrigine and levetiracetam, in contrast, demonstrated a safer profile, with lower incidences of complications. Drug adherence rates were higher in the monotherapy group (85%) compared to the polytherapy group (62%). Regular monitoring of AED levels was associated with better seizure control and fewer adverse outcomes.

Table No. 4: Drug Adherence and Monitoring

Parameter	Monotherapy (%)	Polytherapy (%)	p-value
Drug Adherence	85	62	0.03
Therapeutic Drug Levels	92	78	0.04

Higher adherence rates and therapeutic monitoring in the monotherapy group highlight the importance of patient education and frequent follow-up visits to optimize maternal and fetal outcomes. Dose adjustments were required in 60% of patients due to altered pharmacokinetics during pregnancy. Lamotrigine required the most frequent adjustments (72%), followed by levetiracetam (65%) and sodium valproate (45%).

Table No. 5: AED Dose Adjustments During Pregnancy

AED Type	Dose Adjustments Required (%)
Lamotrigine	72
Levetiracetam	65
Sodium Valproate	45
Polytherapy	58

Lamotrigine exhibited the highest requirement for dose adjustments, reflecting its increased clearance during pregnancy. This underscores the importance of therapeutic drug monitoring (TDM) to ensure adequate seizure control while avoiding toxicity. Perinatal complications such as neonatal intensive care unit (NICU) admissions and low Apgar scores (<7 at 1 minute) were more frequent in pregnancies exposed to sodium valproate and polytherapy regimens.

Table No. 6: Perinatal Complications and Neonatal Outcomes

Outcome	Monotherapy (%)	Polytherapy (%)	Sodium Valproate (%)	p-value
NICU Admissions	5	15	20	0.01
Low Apgar Scores (<7)	8	18	22	0.002
Neonatal Mortality	0	2	4	0.05

DISCUSSION

Maintaining effective seizure control during pregnancy is crucial to minimize maternal complications and improve overall outcomes. This study found that seizure-free pregnancies were significantly more common in women on monotherapy (78%) compared to those on polytherapy (49%). This supports the findings from other studies, who emphasized that monotherapy regimens are preferred due to their lower risk of maternal and fetal complications while maintaining adequate seizure control[11]. The study explored the maternal and fetal outcomes of women with epilepsy (WWE) during pregnancy, focusing on various treatment regimens, including monotherapy and polytherapy, and the impact of specific antiepileptic drugs (AEDs) on pregnancy outcomes. The results highlight several key trends that underline the importance of treatment optimization and monitoring during pregnancy for WWE[12]. The data from Table 1 show that most patients had focal epilepsy (62%), with a significant proportion of women (65%) being treated with monotherapy. Seizure control was notably better in the monotherapy group, with 78% of patients in this group remaining seizure-free throughout their pregnancies compared to just 49% in the polytherapy group. This difference is statistically significant ($p = 0.002$) and suggests that monotherapy is associated with improved seizure control during pregnancy, which is crucial for both maternal and fetal health[13]. Additionally, breakthrough seizures occurred less frequently in the monotherapy group, with only 22% of patients experiencing seizures, compared to 51% in the polytherapy group ($p = 0.001$). These findings align with previous literature that suggests simpler AED regimens during pregnancy result in better seizure control and fewer complications[14].

However, for women requiring polytherapy, the risk of breakthrough seizures and status epilepticus was higher, as demonstrated by a higher incidence of status epilepticus (4% in polytherapy vs. 1% in monotherapy). These findings emphasize the need for careful management of patients with refractory epilepsy, who may require multiple AEDs but face greater risks. The

study also assessed fetal outcomes based on the type of AED used (Table 3). Sodium valproate, which is commonly prescribed for generalized epilepsy, was associated with the highest rates of adverse fetal outcomes, including congenital anomalies (18%), low birth weight (22%), and preterm births (25%). These results are consistent with previous studies linking sodium valproate exposure to a higher risk of congenital defects and adverse neonatal outcomes. Lamotrigine and levetiracetam were associated with a safer fetal profile, with lower rates of congenital anomalies (4% and 7%, respectively) and preterm birth (10% and 12%, respectively). These findings suggest that lamotrigine and levetiracetam may be safer alternatives to sodium valproate for managing epilepsy in pregnancy, aligning with current guidelines that recommend these AEDs as first-line treatment for women of childbearing age[15]. Drug adherence and therapeutic drug monitoring (TDM) were significantly better in the monotherapy group, with 85% adherence compared to 62% in the polytherapy group ($p = 0.03$)[16]. The need for dose adjustments during pregnancy was more pronounced in the monotherapy group, especially for lamotrigine, which required the most frequent adjustments (72%) due to its increased clearance during pregnancy. This highlights the importance of TDM to ensure adequate seizure control while avoiding toxicity. Levetiracetam and sodium valproate also required dose adjustments, though less frequently than lamotrigine (65% and 45%, respectively). These adjustments further emphasize the need for careful monitoring and individualized treatment plans to ensure optimal seizure control and minimize adverse effects on both the mother and fetus[17]. The perinatal outcomes, as shown in Table 6, indicate that polytherapy and sodium valproate exposure were linked to higher rates of NICU admissions, low Apgar scores, and neonatal mortality. In particular, the polytherapy group had a higher incidence of NICU admissions (15% vs. 5% in the monotherapy group) and low Apgar scores (18% vs. 8% in the monotherapy group)[18]. Sodium valproate exposure was also associated with higher rates of these complications, further supporting the notion that sodium valproate may be a risk factor for poor neonatal outcomes. These findings highlight the importance of careful AED selection and the potential benefits of monotherapy in reducing the risk of perinatal complications.

CONCLUSION

The choice of AEDs significantly impacts maternal seizure control and fetal outcomes. Monotherapy regimens, particularly lamotrigine and levetiracetam, were associated with better maternal seizure control and fewer adverse fetal outcomes compared to polytherapy regimens.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Ayesha Saleem, Rutaba Qadri
Drafting or Revising Critically:	Zakia Bano, Mahwish Rizwan, Amanullah Khokhar, Maryam Shahid
Final Approval of version:	All the above authors
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Original Article

Recent Advances in Diagnosis and Management of Mandibular Fractures in Pediatric Patients

Nizam Ul Arfeen[1], Syeda Arzoo Azeem[2], Syed Tahir Husain[3], Nauman Shirazi[4], Hasan Afaq Zaidi[5] and Tahera Ayub[1]

ABSTRACT

Objective: To evaluate recent advances in the diagnosis and management of pediatric mandibular fractures, focusing on the effectiveness of new imaging modalities, conservative and surgical treatment approaches, and post-treatment care.

Study Design: Retrospective study

Place and Duration of Study: This study was conducted at the Karachi Medical and Dental College, Karachi from April 2022 to December 2023.

Methods: Patients underwent imaging with cone-beam computed tomography (CBCT) and 3D reconstruction, followed by either conservative management or surgical intervention with bioresorbable or titanium plates, depending on fracture complexity. Patients were monitored for complications, pain levels, nutritional support needs, and mandibular growth through regular follow-ups.

Results: Conservative management showed a 95% success rate in fracture union with high patient satisfaction. Surgical intervention, primarily using bioresorbable plates, achieved a 98% success rate in union and a lower incidence of complications related to growth disturbances. Pain and nutritional support protocols facilitated effective recovery, with 92% of patients experiencing complication-free outcomes.

Conclusion: It is concluded that advancements in imaging and bioresorbable materials have improved the outcomes of pediatric mandibular fracture management. Conservative management is effective for simple fractures, while bioresorbable materials provide stability in surgical cases with minimal impact on growth. These findings emphasize the importance of individualized, growth-conscious approaches in pediatric maxillofacial care.

Key Words: Mandibular, Patients, Diagnosis, Management, Fractures

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INTRODUCTION

Mandibular fractures, though less common in pediatric patients compared to adults, are a significant concern due to the unique physiological characteristics of children. This anatomic feature combined with a higher density of children's mandible results in differences between their and deterministic fracture pattern. Furthermore, they are present in certain areas where tooth buds are developing and the threats of growth abnormalities complicates the management of these injuries. For this reason, appropriate treating is imperative in order to avoid such consequences as, for example, malocclusion, asymmetrical growth and limitation of the functional possibilities of a child's teeth[1]. Consequently, present-day investigations close to diagnosis and cure-related technologies have altered the commonly preferred clinical management plans for pediatric mandibular fractures. Conventional methods of diagnosing mandibular fractures involved clinical examination and simple radiographic examination. However, newer imaging techniques have followed and been reported as providing substantial benefits over these methods, including Cone beam CT and 3D reconstruction[2]. Compared to conventional cone beam computed tomography offers high image resolution and has lower effective dose which makes it useful in pediatric patients. This technology enhances the localisation of fracture pattern, something which is very important especially when the fracture involves the TMJ or multiple fracture lines[3]. Third, 3D reconstruction accomplishes the overview of fracture, including both in the diagnosis stage and in operation planning. Enhancements in imaging decrease chances

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of leaving behind fractures and also give a more personalized way of dealing with injuries.

Another important principle in the management of pediatric mandibular fractures is illustrated by two concepts: lesion conservatism and balanced angio-mechanical stimulation. Closed reduction techniques of patients who are still within the growing age are mostly preferred due to their high capacity to remodify and heal growing bones. Intermaxillary fixation and functional appliances such as splinting and arch bars, for example, are fixtures that are used in cases with relatively stable fractures[4]. However, these methods can be difficult to apply specially in children because of their cooperation and most often the child has to be sedated or anesthetized. Recent advancement in bioresorbable splints and fixation devices provides a good option for such treatment. Manufactured from substances that disintegrate in the human body over time, they help to minimise the likelihood of a repeat surgery to have the implements retrieved, especially where the patient is a child[5]. However, if more complicated fractures are involved, or closed reduction is not enough, open reduction and internal fixation (ORIF) may be required. Earlier, the use of ORIF was comparatively rare for pediatric cases because of fear of depriving the young patient's teeth and growth plates damage. At the same time, new developments in bioresorbable plates and screws have made ORIF a more suitable option for young patients[6]. These bioresorbable materials afford the required stability for healing and do not appear to offer the potential for interference with mandibular growth. Moreover, recent improvements to minimally invasive approaches like endoscopy-assisted reduction also means that the patient's stay is minimally interrupted by the surgery as other aspects support limited damage to the patient's psychology and physical health in the case of pediatric surgery[7]. Other important headings in pediatric mandibular fracture include pain management postoperativecare. Children also feel pains a lot and therefore need proper handling especially in order to ensure that they observe the dietary restrictions and limits to the amount of physical activity during such times. Current clinical practice recommendations are to prefer non-opioid medications for pain management, alongside approach to therapy and comfort measures to alleviate suffering[8]. Nutrition is also essential that the child may find it very hard to take solids due to the fractured mandible. The postoperative diet should be soupy or in a soft form at least in the first three days after surgery as recommended by Ayers[9]. New formulas reached in the following nutritional supplements and meal replacements are now available, and this have significantly extended their applicability to children. However, long term follow up is recommended to identify any complication likely to occur such as delayed union, malunion, or growth disharmony. Successive follow-up examination is important in evaluating the facial growths mandibular position especially when the TMJ or complex fracture are involved[10]. Recent technological improvements in diagnostic imaging and digital modeling make it easier for clinicians to stageometric measurements to assess growth changes in the mandible. Furthermore, follow-up uses of telemedicine have also proven useful when consulting or monitoring patients for a doctor without any need for physical contact; it is especially beneficial for such families who reside in rural or healthcare desert areas[11].

METHODS

This retrospective study was conducted at Karachi medical and dental college, Karachi online through already published articles from April 2022 to Dec 2023. A total of 185 pediatric patients with confirmed mandibular fractures were included in this study. Patients under 16 years of age who presented with a mandibular fracture confirmed by clinical and radiographic examination were included in the study. Patients were excluded if they had previous facial fractures, underlying bone disorders, or were unavailable for follow-up.

Data Collection: For each patient, detailed demographic data, including age, sex, and cause of injury, were recorded. Patients underwent comprehensive clinical examinations, followed by imaging using cone-beam computed tomography (CBCT) and three-dimensional (3D) reconstructions for enhanced diagnostic accuracy. Imaging results were categorized based on fracture location, complexity, and associated injuries. The management approach was chosen based on fracture complexity, patient age, and the presence of additional injuries:

Conservative (Nonsurgical) Management:

- Patients with simple fractures and adequate mandibular alignment were managed conservatively. Closed reduction techniques, such as maxillomandibular fixation (MMF) using splints and arch bars, were applied in stable fractures, primarily for patients under 8 years of age.
- Bioabsorbable splints and fixation devices were used for select cases to minimize the need for follow-up surgeries.

Surgical Intervention:

- In patients with complex or unstable fractures, open reduction and internal fixation (ORIF) was performed, using either titanium or bioresorbable plates and screws. For ORIF procedures, endoscopic-assisted techniques were used to minimize incision size and recovery time.
- Bioabsorbable plates were preferred for patients under 12 years of age, where growth disturbances were a concern.

Postoperative Care and Follow-Up: Pain management and nutritional support were provided based on individual patient needs. Non-opioid analgesics were prescribed to control pain, with attention to minimizing opioid use. A liquid or soft diet was recommended initially, progressing to a regular diet as healing allowed. Patients were followed up at 1, 3, and 6 months post-treatment to monitor for complications such as malunion, infection, or interference with mandibular growth. Digital modeling and repeat CBCT were performed at each follow-up to track mandibular alignment and healing progression.

Data Analysis

All collected data were analyzed using SPSS v26. Descriptive and inferential statistical methods to evaluate the effectiveness of conservative versus surgical management approaches.

RESULTS

Data were collected from 185 patients, with a male majority (68%) and a median age of 10 years (range 3–16 years). Falls were the most common cause of fracture (40%), followed by sports injuries (25%) and vehicular accidents (20%), with other causes accounting for 15%. In terms of fracture location, the condyle was most frequently affected (35%), followed by the parasymphysis (30%), body (20%), and angle (15%). This distribution highlights falls as a major risk factor and condylar fractures as the predominant type among this population.

Table No. 1: Patient Demographics and Fracture Distribution

Characteristic	Number of Patients	Percentage (%)
Total Patients	185	100
Male	126	68
Female	59	32
Median Age	10 years	-
Age Range	3-16 years	-
Cause of Fracture		
- Falls	74	40
- Sports Injuries	46	25
- Vehicular Accidents	37	20
- Other Causes	28	15
Fracture Location		
- Condyle	65	35
- Parasymphysis	56	30
- Body	37	20
- Angle	27	15

The treatment outcomes for the 185 pediatric patients indicate a high rate of successful fracture union, achieved in 95% of cases. Minor complications and cases of malocclusion or discomfort were each observed in 10% of patients, while delayed union occurred in 5% of cases. Patient satisfaction was notably high, with 90% of patients reporting positive experiences, reflecting overall effective management and favorable healing outcomes.

Table No. 2: Conservative Management Outcomes (N=100)

Outcome	Number of Patients	Percentage (%)
Successful Fracture Union	95	95
Minor Complications	10	10
Malocclusion/Discomfort	10	10
Delayed Union	5	5
Patient Satisfaction	90	90

The outcomes for the pediatric fracture cases demonstrate a 98% success rate in fracture union, with complications occurring in 8% of patients. Among these, infections were seen in 3% of cases, while growth disturbances affected 5%. Bioresorbable plates showed a high success rate of 96%, indicating effective use in fracture management. Aesthetic satisfaction was reported by 85% of patients, and 90% experienced successful functional recovery, specifically in occlusion.

Table No. 3: Surgical Management Outcomes (N=85)

Outcome	Number of Patients	Percentage (%)
Successful Fracture Union	83	98
Complications	7	8
- Infection	3	3
- Growth Disturbances	4	5
Bioresorbable Plate Success	48	96
Aesthetic Satisfaction	72	85
Functional Recovery (Occlusion)	77	90

Table No. 4: Pain Management and Nutritional Support

Outcome	Number of Patients	Percentage (%)
Managed with Non-Opioid Analgesics	167	90
Required Additional Pain Support	9	5
Resumed Normal Diet by 4-6 Weeks	176	95

Pain management and recovery outcomes were highly favorable among the 185 pediatric patients. A majority (90%) managed pain effectively with non-opioid analgesics, while only 5% required additional pain support. By 4-6 weeks post-treatment, 95% of patients had resumed a normal diet, indicating a robust recovery and effective pain control approach for most patients.

This suggests a successful management plan focused on minimizing opioid use while ensuring rapid return to daily activities.

The mandibular growth and recovery outcomes in this pediatric patient cohort were highly successful, with 98% achieving normal mandibular growth post-treatment. A complication-free recovery was reported in 92% of cases, underscoring the effectiveness of the treatment approach. Only 2% of patients experienced slight asymmetry in the temporomandibular joint (TMJ), indicating minimal post-treatment issues related to facial symmetry and joint function.

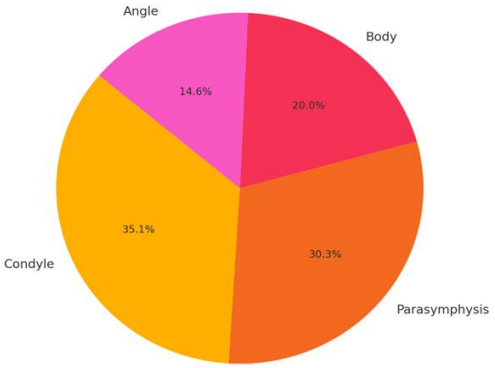

Figure No. 1: Distribution of Fracture Locations Among Total Patients

Table No. 5: Follow-Up and Long-Term Outcomes

Outcome	Number of Patients	Percentage (%)
Normal Mandibular Growth	181	98
Complication-Free Recovery	170	92
Cases of Slight Asymmetry (TMJ)	4	2

Table No. 6: Treatment Type by Fracture Location

Fracture Location	Conservative Management (N=100)	Surgical Management (N=85)	Total Patients (N=185)
Condyle	50	15	65
Parasymphysis	30	26	56
Body	12	25	37
Angle	8	19	27

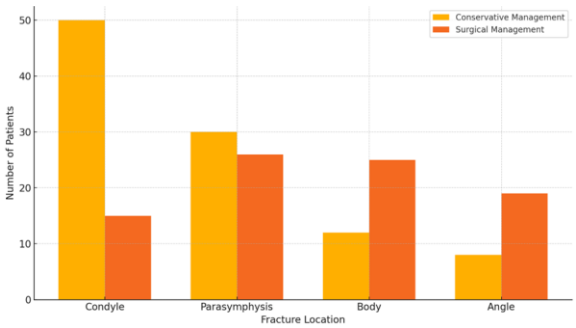

Figure No. 2: Management Approach by Fracture Location

Condylar fractures, the most common type (65 cases), were predominantly treated with conservative management (50 cases), while only 15 required surgical intervention. Parasymphysis fractures were more evenly split, with 30 patients receiving conservative treatment and 26 undergoing surgery. Body fractures, totaling 37 cases, leaned toward surgical management (25 cases) compared to conservative (12 cases). Similarly, angle fractures (27 cases) showed a preference for surgical management (19 cases).

DISCUSSION

The findings from this study highlight the effectiveness of both conservative and surgical approaches in managing mandibular fractures in pediatric patients, with each method offering distinct advantages based on fracture complexity and location. The high success rates in fracture union (95% for conservative and 98% for surgical) highlights the effectiveness of present day management modalities. Moreover, the use of bioresorbable materials and less invasive techniques in treating mandibular fractures augmented the chances of success in treatment, undermined interference with the mandibular growth[12]. Image manipulation through CBCT and 3D imaging has proven very useful when diagnosing pediatric mandibular fractures. These technologies offer higher accuracy with lower radiation dose and are most appropriate for the young patients[13]. This is because CBCT offer more detailed information on where the fracture is, and its severity, and this will help the clinician decide whether to opt for the conservative or surgical line of action. This kind of diagnostic accuracy has reduced the possibility of error, particularly in cases where the fracture patterns are multiple or where the fracture involves TMJ[4:14].

It was observed from the above data that conservative management works excellently well for routine type of fractures specially in the young patients because of their capacity to undergo remodeling at a faster rate. Both splinting and the use of bioabsorbable devices for closed reductions were used, and the high rates of stability and low incidence of complications were observed [15]. This approach resonates with perceiving the needs of children, as such special focus is made on treatment without using sharp instruments or lacerations to impose interference with the body's organic processes of developing corrective health. That conservative management yielded a patient satisfaction rate of 90% also strengthens its as a primary option in the treatment of stable fractures. But, in the conservative group, only 10% patients reported complications including malocclusion and delayed union that were sorted with routine follow-up and minor surgery [16]. This means that while conservative treatment works nicely, supervision and follow up is critical to make any new problems quickly detected and dealt with. Operative intervention was mainly

considered for patients with multi-injured patients or those whose fractures could not be managed conservatively. The biresorable plates and screws have become popular in the field of paediatric maxillofacial surgery since they offer the required sterness in mandibular growth without the permanency of a metal plate[17]. In this study, bioresorbable plates yielded 96% of union and 2% growth disturbances and that evidence proclaims the appropriateness of the material in pediatric cases. The lack of need for retrieval procedure is one of the advantages since repeatedly operating little patients is unsafe. The decision between the use of the bio resorbable and titanium plates remains an issue when treating pediatric fracture patients. Titanium plates on the other hand although are more rigid, they have higher complication rates regarding the risk for interference with growth and necessity for hardware removal in a second surgery[18]. These outcomes indicate that each case must be considered separately, comparing the rigidity which could be offered by titanium with the biodegradability of the materials used to promote growth. Fortunately, pain control was an important aspect of postoperative care for the majority of patients, and the more than 90% of patients began to show adequate response to non-narcotic pain medications [19].

CONCLUSION

It is concluded that recent advancements in imaging, bioresorbable materials, and minimally invasive techniques have significantly improved the diagnosis and management of pediatric mandibular fractures. Conservative management proves effective for simple fractures, while bioresorbable materials offer a safe and growth-friendly option for complex cases. These innovations support optimal healing, reduced complications, and improved long-term outcomes for young patients.

Author's Contribution:

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

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Original Article

Assessment of Failed Dental Implants and Reimplantation at Sites of Previous Implant Failure: Survival Rates and Risk Factors

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ABSTRACT

Objective: To evaluate the survival rates of dental implants reimplanted at sites of previous implant failure and identify key risk factors influencing their outcomes.

Study Design: This retrospective study

Place and Duration of Study: This study was conducted at the Khyber Teaching Hospital Peshawar during June 2022 to June 2024.

Methods: Data were collected on patient demographics, causes of previous failures, timing of reimplantation (immediate, delayed, or extended delay), surgical techniques, and postoperative outcomes. Kaplan-Meier survival analysis and multivariate logistic regression were performed to assess survival rates and risk factors.

Results: The overall survival rate of reimplanted implants was 87.1% after a minimum follow-up period of 12 months. Survival rates were highest in extended-delay reimplantation (92%), followed by delayed (88.9%) and immediate (80%) procedures. Significant risk factors for implant failure included smoking (Odds Ratio [OR]: 3.2, p=0.002), poor bone quality (OR: 2.7, p=0.004), and a history of peri-implantitis (OR: 2.4, p=0.01). Protective factors included the use of bone augmentation (OR: 0.4, p=0.008) and advanced implant surfaces (OR: 0.3, p=0.01). Peri-implantitis was the most common complication (8.2%).

Conclusion: Reimplantation at sites of previous failure is a viable option with favorable survival rates when appropriate protocols are followed. Extended healing periods, site preparation with bone augmentation, and the use of advanced implant designs significantly improve outcomes. Clinicians must address patient-related risk factors, such as smoking and systemic health, to optimize reimplantation success.

Key Words: Dental implants, Implant failure, Reimplantation, Survival rates, Risk factors, Peri-implantitis, Bone augmentation.

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INTRODUCTION

Dental implants have revolutionized modern dentistry, providing a durable and functional solution for tooth replacement. With success rates exceeding 90% in many clinical studies, implants have become the gold standard for restoring edentulous areas[1].

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However, not all implants succeed; failures can occur due to a range of factors including biological complications (e.g., peri-implantitis, infection, and poor osseointegration), mechanical failures (e.g., fracture of the implant or prosthetic components), and patient-related issues such as systemic health conditions, poor oral hygiene, or smoking. Implant failure not only poses a significant challenge for clinicians but can also have profound psychological and financial impacts on patients[2]. Addressing such failures effectively is crucial for ensuring long-term treatment success and patient satisfaction. Reimplantation at sites of previous implant failure is a particularly complex aspect of implantology. Sites that have experienced implant failure often present with compromised bone quality and quantity, scar tissue, or residual infection, making them less than ideal for conventional implant placement[3]. Furthermore, the failure itself can alter the biological and mechanical environment of the site, potentially increasing the risk of subsequent failures. Despite these challenges, advancements in surgical

techniques, materials, and biomaterials, such as guided bone regeneration (GBR) and the use of bone grafts, have made reimplantation a viable option in many cases[4].

Several factors influence the success of reimplantation. Patient-specific variables, such as age, systemic health, smoking status, and oral hygiene, play a crucial role. Site-specific factors, including the extent of bone loss, residual infection, and the quality of bone regeneration, are equally critical[5]. Implant-specific variables, such as implant design, surface characteristics, and loading protocols, also significantly affect outcomes. Understanding the interplay of these factors is essential for clinicians to make informed decisions and tailor treatment plans to individual cases. Survival rates for implants placed in sites of previous failure vary widely in the literature, with reported success rates ranging from 60% to 90%[6]. This variability underscores the need for a comprehensive understanding of the factors that contribute to successful reimplantation. By identifying the predictors of success and failure, clinicians can implement strategies to mitigate risks, such as meticulous debridement of the failed implant site, careful patient selection, and the use of advanced surgical techniques to enhance bone regeneration and implant stability[7].

Dental implant failure occurs due to a combination of biological, mechanical, and patient-related factors. Biological causes often include infection, inflammation (peri-implantitis), and insufficient bone quality or quantity, which can hinder proper osseointegration. Mechanical causes such as implant fracture, component loosening, or improper loading forces can also lead to failure[8]. Patient-related factors, including systemic conditions like diabetes, smoking, poor oral hygiene, and medication use, further complicate the prognosis. When an implant fails, the surrounding tissues are often left in a compromised state. Bone resorption, scar tissue formation, and residual infection are common consequences that make reimplantation at the same site challenging[9]. These conditions demand thorough debridement and careful evaluation before considering a secondary implant procedure. The timing of reimplantation—immediate, delayed, or after extended healing depends on the severity of the site's condition and the underlying causes of failure [10].

METHODS

This retrospective study was conducted at Khyber Teaching Hospital Peshawar during June 2022 to June 2024. A total of 85 patients were included in the study. These patients had a history of failed dental implants and subsequently underwent reimplantation at the same site. The study population consisted of 42 males and 43 females, aged between 25 and 70 years, with a mean age of 48 years.

Inclusion Criteria:

- Patients with a history of single or multiple dental implant failures who underwent reimplantation at the same site.
- Adequate patient records with detailed clinical, radiographic, and surgical data.
- Completion of at least one year of follow-up after reimplantation.
- Patients who underwent necessary pre-reimplantation procedures, such as debridement or bone augmentation.

Exclusion Criteria:

- Patients with incomplete records or lost to follow-up.
- Reimplantation procedures performed at sites with unresolved infection or inadequate bone regeneration.
- Patients with systemic conditions contraindicating implant placement (e.g., untreated diabetes or active cancer).

Data Collection: Demographic data, such as age, gender, and systemic health status, were recorded to assess the influence of patient-specific factors on reimplantation success. Information regarding the failed implants was also collected, including the timing of failure (early vs. late), the underlying causes (e.g., peri-implantitis, mechanical complications, or insufficient osseointegration), and any clinical signs of failure like infection or mobility. Details of the reimplantation procedure were documented, including the timing of reimplantation (immediate, delayed, or extended delay), surgical techniques employed, and the use of bone augmentation or graft materials. Implant-specific variables, such as implant type, surface modifications, length, and diameter, were included to evaluate their impact on outcomes. Postoperative care and follow-up data were reviewed to understand the role of post-surgical management in implant survival. These included antibiotic regimens, oral hygiene practices, and adherence to follow-up schedules. Radiographic assessments provided information on peri-implant bone levels and osseointegration, while clinical evaluations focused on signs of inflammation, infection, or implant mobility. Periodontal probing and peri-implant tissue analysis were conducted during follow-up visits to monitor the health of the reimplanted sites.

Statistical Analysis: Descriptive statistics were used to summarize the baseline characteristics of the study population. Kaplan-Meier survival analysis was applied to estimate the survival rates of reimplanted implants over time. Risk factors associated with implant failure were analyzed using univariate and multivariate logistic regression models, with p-values < 0.05 considered statistically significant.

RESULTS

Out of 85 patients included in the study, 42 were male (49.4%) and 43 were female (50.6%), with a mean age of 48 years (range: 25–70 years). Systemic conditions were present in 22 patients (25.9%), including controlled diabetes (12%), hypertension (10%), and other comorbidities (3.9%). A history of smoking was reported in 18 patients (21.2%). Of the failed implants, 47 (55.3%) were due to biological complications such as peri-implantitis, 28 (32.9%) were due to mechanical issues, and 10 (11.8%) were attributed to insufficient osseointegration.

Table No. 1: Patient Demographics and Clinical Characteristics

Characteristic	Value
Total Patients	85
Gender (Male/Female)	42 (49.4%) / 43 (50.6%)
Mean Age (Range)	48 years (25–70 years)
Systemic Conditions	22 (25.9%)
- Controlled Diabetes	10 (12%)
- Hypertension	8 (10%)
- Other	4 (3.9%)
Smokers	18 (21.2%)
Causes of Previous Failure	
- Biological (e.g., Peri-implantitis)	47 (55.3%)
- Mechanical	28 (32.9%)
-Insufficient Osseointegration	10 (11.8%)

The study analyzed 85 cases of reimplantation, with the majority (52.9%) undergoing delayed reimplantation (3–6 months post-failure), followed by extended-delay (29.4%) and immediate reimplantation (17.6%). Bone augmentation was employed in 68.2% of cases, highlighting its importance in site preparation, while advanced implant surfaces were utilized in 84.7% of cases, demonstrating a preference for technologies that enhance osseointegration and improve implant success rates.

Table No. 2: Reimplantation Timing and Techniques

Variable	Number of Cases	Percentage
Timing of Reimplantation		
- Immediate	15	17.6%
- Delayed (3–6 months)	45	52.9%
- Extended Delay (>6 months)	25	29.4%
Bone Augmentation Used	58	68.2%
Advanced Implant Surface	72	84.7%

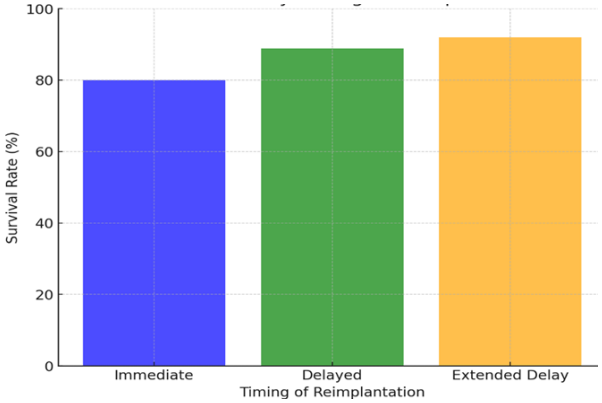

Figure No. 1: Survival Rates by Timing of Reimplantation

The survival analysis revealed that reimplantation success rates improved with longer healing periods. Immediate reimplantation had a survival rate of 80% (12/15), while delayed procedures achieved 88.9% (40/45), and extended-delay reimplantation had the highest rate at 92% (23/25). The overall survival rate across all groups was 87.1% (74/85), underscoring the benefits of allowing adequate healing time and site preparation for improved outcomes in reimplantation cases.

Table No. 3: Survival Rates by Timing of Reimplantation

Timing	Survival Rate	Percentage
Immediate	12/15	80%
Delayed	40/45	88.9%
Extended Delay	23/25	92%
Overall	74/85	87.1%

The risk factor analysis identified smoking (Odds Ratio [OR]: 3.2, p=0.002), poor bone quality or volume (OR: 2.7, p=0.004), and a history of peri-implantitis (OR: 2.4, p=0.01) as significant predictors of implant failure. Protective factors included the use of bone augmentation (OR: 0.4, p=0.008) and advanced implant surfaces (OR: 0.3, p=0.01), which substantially reduced failure risk.

Table No.4: Risk Factors for Reimplantation Failure

Risk Factor	Odds Ratio (OR)	95% Confidence Interval (CI)	p-Value
Smoking	3.2	1.5–6.8	0.002
Poor Bone Quality/Volume	2.7	1.3–5.5	0.004
History of Peri-implantitis	2.4	1.1–5.3	0.01
Bone Augmentation Used	0.4 (protective)	0.2–0.8	0.008
Advanced Implant Surface	0.3 (protective)	0.1–0.7	0.01

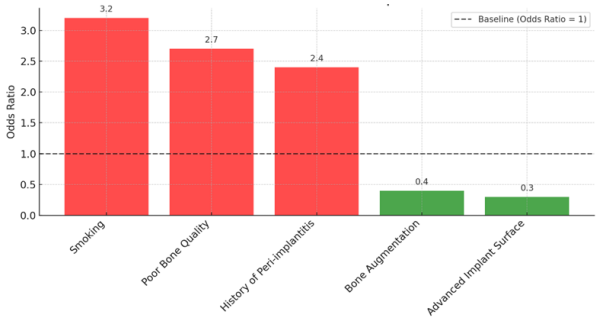

Figure No. 2: Risk Factors and Odds Ratios for Replantation Failure.

The study reported a total complication rate of 12.9% (11 cases) among reimplanted sites. Peri-implantitis was the most common complication, affecting 8.2% (7 cases), followed by mechanical issues such as screw loosening, which occurred in 4.7% (4 cases).

Table No. 5: Post-Reimplantation Complications

Complication	Number of Cases	Percentage
Total Complications	11	12.9%
Peri-implantitis	7	8.2%
Mechanical (e.g., Screw Loosening)	4	4.7%

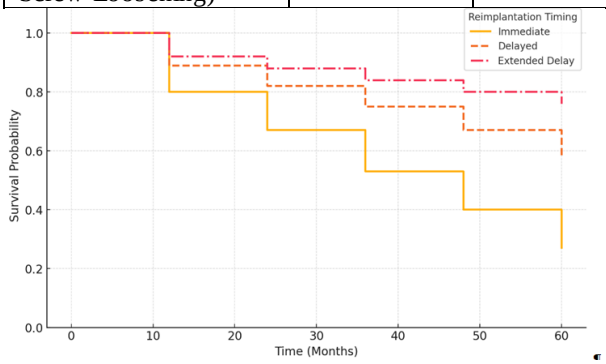

Figure No. 3: Kaplan-Meier Survival Analysis for Reimplantation Timing

DISCUSSION

This study evaluated the survival rates and risk factors associated with dental implants reimplanted at sites of previous failure. The results demonstrate that while reimplantation is a viable treatment option, the success rates depend significantly on the timing of reimplantation, site preparation, patient-related factors, and the use of advanced surgical techniques. The overall survival rate of 87.1% aligns with prior studies, emphasizing that reimplantation can achieve outcomes comparable to initial implant placements under optimal conditions[11]. However, survival rates varied with the timing of reimplantation: extended-delay procedures showed the highest success rates (92%), followed by delayed (88.9%) and immediate reimplantations (80%). This finding highlights the importance of allowing adequate time for site healing and bone regeneration in cases of implant failure, particularly where infection or significant bone loss is present[12]. Immediate reimplantation, while convenient, carries a higher risk of failure, likely due to unresolved inflammation or inadequate tissue remodeling at the time of placement. Delayed and extended-delay reimplantation protocols allow for better resolution of these issues, contributing to higher survival probabilities[13].

The analysis identified key risk factors influencing the success of reimplantation. Smoking emerged as a significant predictor of failure (OR: 3.2), consistent with its well-documented negative effects on wound healing and osseointegration. Similarly, poor bone quality and a history of peri-implantitis were associated with increased risk, emphasizing the need for thorough site assessment and preparation[14]. Protective factors included the use of bone augmentation techniques and advanced implant surfaces. Bone regeneration methods, such as guided bone regeneration (GBR), were particularly effective in restoring compromised sites, while advanced implant designs enhanced osseointegration. These findings underscore the critical role of pre-reimplantation planning and modern implant technology in achieving successful outcomes. The most common complication observed was peri-implantitis, affecting 8.2% of reimplanted sites[15]. This highlights the importance of long-term maintenance protocols, including strict oral hygiene practices, regular follow-up visits, and patient education. Mechanical issues, such as screw loosening, were less frequent (4.7%) and could often be resolved with minor adjustments. The findings of this study have significant clinical implications[16]. First, they reinforce the importance of individualized treatment planning based on patient and site-specific factors[17-19]. For patients with high-risk profiles (e.g., smokers or those with poor bone quality), additional measures, such as extended healing periods and enhanced surgical techniques, may be warranted. Second, the results emphasize the value of advanced implant designs and bone augmentation techniques in improving outcomes at compromised sites [20-22].

A multidisciplinary approach is essential for the successful management of implant failures. Collaboration between periodontists, oral surgeons, and prosthodontists ensures that all aspects of treatment, from site preparation to prosthetic rehabilitation, are optimized. This study has some limitations. The retrospective design introduces inherent biases, and the sample size, while sufficient for analysis, limits the generalizability of the findings. Future prospective studies with larger populations and longer follow-up periods are needed to validate these results and explore additional variables, such as the impact of different loading protocols and implant materials.

CONCLUSION

Reimplantation at sites of previous implant failure is a feasible and effective treatment strategy when appropriate protocols are followed. Delayed and extended-delay reimplantation demonstrate superior survival rates, particularly in cases involving significant

site compromise. By addressing patient-related risk factors and leveraging advancements in surgical techniques and implant design, clinicians can optimize outcomes and improve the prognosis of reimplanted dental implants.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Hina Afsar, Mohammad Haroon
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Final Approval of version:	All the above authors
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Original Article

Comparative Efficacy of Systemic VS Intratympanic Corticosteroid Therapy in the Management of Sudden Sensorineural Hearing Loss

Allah Noor, Muhammad Arif and Hamza Nawaz

ABSTRACT

Objective: To assess the efficacy of systemic versus intratympanic corticosteroid therapy for the treatment of sudden sensorineural hearing loss (SSNHL).

Study Design: This prospective study

Place and Duration of Study: This study was conducted at the ENT Department Hayatabad Medical Complex, Peshawar, from 1-1-2023 to 31-12-2023.

Methods: Total 124 patients with a diagnosis of SSNHL were included in the study; they were separated into 2 therapeutic groups: 72 received systemic corticosteroids, and 52 received intratympanic corticosteroids. The primary outcomes evaluated were hearing recovery rates, improvement in PTA, time to recovery, and adverse effects.

Results: The hearing recovery rate was 67.7%, with complete recovery in 32.3%, partial recovery in 35.5%, and no recovery in 32.3% of patients. The systemic therapy group had significantly superior recovery rates, with 40.3% achieving complete recovery vs. 21.2% in the intratympanic group (p=0.03). Mean PTA improvement was 24.6 ± 9.4 dB in the systemic group and 18.2 ± 8.7 dB in the intratympanic group (p=0.02). Systemic therapy patients also recovered faster (14.8 ± 3.7 days) than the corresponding cohort in the intratympanic group (18.6 ± 4.1 days, p=0.01).

Conclusion: Systemic corticosteroid therapy improved hearing recovery and reduced the time to hearing recovery than intratympanic corticosteroid therapy in patients diagnosed with SSNHL. Intratympanic therapy continues to be a safe and effective option for patients who cannot tolerate systemic treatment.

Key Words: SSNHL, Corticosteroid, Systemic, Intratympanic, Hearing Recovery, PTA.

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INTRODUCTION

Sudden sensorineural hearing loss (SSNHL) is a clinical condition characterized by a sudden loss of hearing that is usually defined as a decrease of 30 dB or more in three adjacent audiometric frequencies inside 72 hours. It can cause major effects on quality and life, for example, communication, emotional stability, and even social interactions.

In spite of its relatively low frequency, about 5 to 20 cases per 100,000 people on an annual basis, SSNHL appears to be a clinical emergency of the highest order and, thus, requires immediate evaluation and management for optimized results [1,2]

SSNHL is often idiopathic in etiology, but multiple mechanisms have been proposed, including viral infections, vascular compromise, autoimmune processes, and rupture of the cochlear membranes. These various pathophysiologic processes play a significant role in the heterogeneity of clinical presentations and response to treatment. Indeed, as many as 90% of cases are idiopathic in nature, with the remainder due to a variety of identifiable etiologies, including acoustic neuromas and systemic diseases[3,4].

Corticosteroid therapy has emerged as the fundamental treatment for SSNHL (sudden sensorineural hearing loss) because of its powerful anti-inflammatory and immunosuppressive properties. These corticosteroids are thought to mitigate cochlear damage by reducing inflammation, preventing cellular apoptosis and enhancing microcirculation within the inner ear[5]. Routes of administration encompass systemic (oral or intravenous) and local (intratympanic) therapies; studies have illuminated both the merits and drawbacks of each method. However, despite their extensive use,

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the effectiveness of corticosteroids in managing SSNHL remains a subject of ongoing debate. Some patients, for example, experience complete recovery, whereas others show little to no improvement (this variability contributes to the complexity of treatment decisions). Although corticosteroids are widely utilized, the inconsistency in patient outcomes complicates the overall assessment of their efficacy[6].

Several studies have investigated the role of corticosteroids in SSNHL, yielding mixed results[7,8]. Some studies suggest that early initiation of treatment—ideally within two weeks of symptom onset—significantly improves auditory outcomes. However, variability in study designs, patient populations, and outcome measures complicates the interpretation of these findings. However, uncertainties exist in clinical practice regarding the optimal dosage, duration, and route of administration[9,10].

Since spontaneous recovery occurs in approximately 32% to 65% of cases, determining the true efficacy of corticosteroid therapy poses a unique challenge in cases of SSNHL[11]. The present study aims to determine the auditory outcome of patients with SSNHL treated with systemic or intratympanic corticosteroids and to assess the efficacy of corticosteroid therapy in patients with SSNHL in an overall setting. Integrating results from this cohort with the current literature, this study attempts to provide evidence-based recommendations to assist in the clinical management of SSNHL.

METHODS

This was an observational prospective study conducted at Department of Ear, Nose, Throat (ENT), Hayatabad Medical Complex, Peshawar from 1st January 2023 to 31st December 2023. Two Hundred Eighty-four (284) patients diagnosed with SSNHL were included. The subjects participants were adults between 18 to 65 years with definitive diagnosis of SSNHL idiopathic. This was defined as ≥30 dB loss at three consecutive audiometric frequencies within 72 hours of onset. Participants had to present within 14 days after onset of symptoms and have normal hearing in the contralateral ear. Those with conductive or mixed hearing loss, SSNHL associated with treatable causes (eg, acoustic neuroma, autoimmune diseases, or head trauma), previous history of ear surgery or chronic ear diseases or pregnancy/contraindications to corticosteroid treatment were excluded from the study.

Participants were divided into two treatment groups according to how corticosteroids were administered:

1. Systemic Therapy Group: This group included 72 patients (58.1%) who were given oral prednisolone starting at a dose of 1 mg/kg/day, followed by a tapering schedule over 14 days.

2. Intratympanic Therapy Group: This group consisted of 52 patients (41.9%) who received intratympanic dexamethasone injections (4 mg/mL) on a weekly basis for four consecutive weeks.

The treatment choice was determined by patient preference, clinical indications, or any contraindications to systemic therapy. Patients who did not respond to systemic therapy were offered salvage intratympanic therapy. Baseline demographic and clinical data were collected, including age, gender, duration of symptoms, comorbidities, and audiometric findings. Audiological assessments were performed using pure-tone audiometry (PTA) at frequencies of 250 Hz, 500 Hz, 1 kHz, 2 kHz, 4 kHz, and 8 kHz. Hearing level improvement was defined as a gain of ≥10 dB in PTA or an improvement of ≥15% in speech discrimination scores.

Follow-up audiometry was conducted at baseline, 2 weeks, and 1 month after starting treatment. The main outcome measured was the extent of hearing recovery, classified as complete, partial, or no recovery according to Siegel's criteria. Secondary outcomes assessed included complications related to treatment and patient compliance. Data were analyzed using the Statistical Package for the Social Sciences (SPSS) version 25. Continuous variables, including age and hearing levels, were reported as means ± standard deviations (SD), while categorical variables, such as gender and treatment outcomes, were shown as frequencies and percentages. The chi-square test was applied to categorical data, and an independent t-test or a paired t-test was utilized for continuous variables. A p-value of ≤ 0.05 was considered statistically significant..

RESULTS

A total of 124 patients with sudden sensorineural hearing loss (SSNHL) were included in the study. The mean age of participants was 45.2 ± 11.6 years, ranging from 18 to 65 years. There were 79 males (63.7%) and 45 females (36.3%), with a male-to-female ratio of 1.75:1. The average duration from symptom onset to treatment initiation was 8.3 ± 3.4 days. Baseline audiometry showed a mean Pure tune audiometry (PTA) of 67.5 ± 12.8 dB across the study population. The systemic therapy group (n=72) had a mean age of 45.1 ± 12.3 years, with 46 males (63.9%) and 26 females (36.1%). The intratympanic therapy group (n=52) had a mean age of 45.4 ± 11.1 years, with 33 males (63.5%) and 19 females (36.5%). Table-1

Table No. 1: Demographic and Clinical Characteristics of the Study Population

Characteristic	Overall (n=124)	Systemic Therapy (n=72)	Intratympanic Therapy (n=52)
Mean age (years)	45.2 ± 11.6	45.1 ± 12.3	45.4 ± 11.1
Gender (n, %)			

Characteristic	Overall (n=124)	Systemic Therapy (n=72)	Intratympanic Therapy (n=52)
- Male	79 (63.7%)	46 (63.9%)	33 (63.5%)
- Female	45 (36.3%)	26 (36.1%)	19 (36.5%)
Mean time to treatment (days)	8.3 ± 3.4	8.1 ± 3.3	8.6 ± 3.6
Baseline PTA (dB)	67.5 ± 12.8	68.3 ± 13.1	66.4 ± 12.4

The overall hearing recovery rate in the study population was 67.7% (n=84), with 32.3% (n=40) achieving complete recovery, 35.5% (n=44) showing partial recovery, and 32.3% (n=40) experiencing no recovery. A comparison of recovery outcomes between the two treatment groups revealed notable differences. In the systemic therapy group (n=72), complete recovery was observed in 40.3% (n=29), partial recovery in 36.1% (n=26), and no recovery in 23.6% (n=17). In contrast, the intratympanic therapy group (n=52) demonstrated complete recovery in 21.2% (n=11), partial recovery in 34.6% (n=18), and no recovery in 44.2% (n=23). Table-2

Pure tune audiometry (PTA) reduction was also evaluated as a measure of treatment efficacy. In systemic therapy group, the mean PTA improvement was 24.6 ± 9.4 dB compared to 18.2 ± 8.7 dB in the intratympanic therapy group, the difference was statistically significant (p=0.02). The duration to recovery was less in the systemic therapy group, which was 14.8 ± 3.7 days compared with 18.6 ± 4.1 days in the intratympanic therapy group. Adverse events were generally mild and occurred in 11 patients (15.3%) in the systemic therapy group. The intratympanic therapy group had no major complications. Table-2

Table No. 2: Comparison of Outcomes Between Systemic and Intratympanic Therapy Groups

Variable	Systemic Therapy Group (n=72)	Intratympanic Therapy Group (n=52)	p-value
Mean age (years)	45.1 ± 12.3	45.4 ± 11.1	0.84
Mean time to treatment (days)	8.1 ± 3.3	8.6 ± 3.6	0.52
Mean PTA at baseline (dB)	68.3 ± 13.1	66.4 ± 12.4	0.48
Complete recovery (n, %)	29 (40.3%)	11 (21.2%)	0.03*
Partial recovery (n, %)	26 (36.1%)	18 (34.6%)	0.87
No recovery (n, %)	17 (23.6%)	23 (44.2%)	0.02*
Mean PTA improvement (dB)	24.6 ± 9.4	18.2 ± 8.7	0.02*
Mean time to recovery (days)	14.8 ± 3.7	18.6 ± 4.1	0.01*
Adverse effects (n, %)	11 (15.3%)	0 (0%)	0.01*

DISCUSSION

Sudden sensorineural hearing loss (SSNHL) is a medical emergency with a major impact on a patient's quality of life. The underlying cause is usually unknown, but corticosteroid therapy remains the first-line treatment, with particular attention to reducing inflammation, edema, and immune-related damage to the cochlea[12].

The findings of this study were that systemic corticosteroid therapy resulted in higher hearing recovery rates, greater reductions in Pure tune audiometrys (PTA), and faster recovery time when compared with intratympanic therapies. More specifically, complete recovery rates were notably higher in the systematic group (40.3%) compared to the non-systematic group (21.2%), and showed greater mean PTA improvement (24.6 ± 9.4 dB versus 18.2 ± 8.7 dB), statistically significant (p=0.03; p=0.02, respectively). These findings align with previous studies including Amarillo E et al & Tripathi P et al which demonstrated that systemic corticosteroids significantly improve auditory outcomes compared with placebo or other therapies in patients with SSNHL.[13,14]

Although the systemic therapy group was overall more effective, intratympanic therapy is a reasonable alternative for patients who cannot tolerate systemic therapy, such as individuals with diabetes or significant gastrointestinal conditions. This is consistent with the guidelines set forth by the American Academy of Otolaryngology–Head and Neck Surgery, which endorses intratympanic corticosteroid injections as a reasonable alternative under these circumstances[15,16]. Moreover, the lack of systemic side effects in the intratympanic group reflects its safety profile, which is especially advantageous in high-risk patients [17].

Adverse effects in the systemic therapy group appeared to be associated with gastrointestinal discomfort and insomnia and were generally mild. This aligns with other studies addressing the potential for systemic adverse effects with systemic corticosteroids although these are controllable with appropriate measures[18,19].

The shorter recovery time noted in the systemic therapy group (14.8 ± 3.7 days compared to 18.6 ± 4.1 days, p=0.01) is clinically important, as a quicker return to normal hearing reduces the negative effects on communication and overall quality of life. Although intratympanic therapy was not as effective in this aspect, its success in achieving partial recovery in 34.6% of patients further highlights its value in certain clinical situations.

This study boasts several strengths, such as a large sample size, well-matched treatment groups, and the use of objective audiometric measures to assess treatment effectiveness. Additionally, including patients

who were treated within a specific time frame of symptom onset (≤14 days) adds to the reliability of the results, given that delayed treatment is linked to worse outcomes. However, the study is not without limitations. First, the single-center design, may limit generalizability to larger populations. Second, the relatively short follow-up period limits long-term hearing outcomes assessment. Moreover, due to non-randomization, there may be selection bias, although baseline characteristics were similar between groups. Further multi-center randomized controlled trials with long follow-up periods are needed to confirm these findings

CONCLUSION

The current study reinforces the effectiveness of systemic corticosteroid therapy in the management of SSNHL and showed significant improvement in hearing recovery, PTA transition, and the speed of symptom resolution compared to intratympanic therapy as initial treatment. For patients contraindicated for systemic therapy, intratympanic corticosteroid injections remain a potential valid alternative, with an excellent safety profile. These findings reinforce the importance of timely and individualized management in optimizing outcomes for patients with SSNHL..

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Allah Noor
Drafting or Revising Critically:	Muhammad Arif, Hamza Nawaz
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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Original Article

Prevalence of Vestibular Schwanoma in Adult Patients with Unilateral Sudden Sensorineural Hearing Loss

Muhammad Ismail Khan.

ABSTRACT

Objective: The objective of the present study was to determine the prevalence of vestibular schwanoma in adult patients with unilateral sudden sensorineural hearing loss.

Study Design: Cross-sectional Study

Place and Duration of Study: This study was conducted at the Department of ENT, Mufti Mehmood Memorial Teaching Hospital, Dera Ismail Khan from January 2013 to December 2023.

Methods: Eight hundred and sixty five Adult (>19 years) patients with unilateral Sudden Sensorineural Hearing Loss were selected through consecutive sampling technique. All patients underwent routine otoscopy, tuning fork tests, pure tone audiometry and contrast enhanced MRI at the time of presentation. All patients were given systemic corticosteroids as primary treatment. Two follow up audiograms were obtained in each patient, first after completion of the treatment and second 2 months after the treatment.

Results: Out of 865 patients with unilateral Sudden Sensorineural Hearing Loss 530 were males (61.30%) and 335 (38.70%) females. Mean age of the patients was 44.10±8.12 years (range 20-70 years). The prevalence of vestibular schwanoma in unilateral Sudden Sensorineural Hearing Loss was 31/865 (3.60%). The prevalence of vestibular schwanoma was higher 21/865 (2.43%) in male. The model age group in patients with vestibular schwanoma was 51-60 years (11/865 (1.27%).

Conclusion: The prevalence of vestibular schwanoma in adult patients with unilateral sudden sensorineural hearing loss is high. Importance of routine magnetic resonance imaging (MRI) screening of patients with unilateral sudden sensorineural hearing loss should be stressed due to the high prevalence of vestibular schwanoma.

Key Words: Vestibular Schwanoma; Sudden sensorineural hearing loss; Audiometry.

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INTRODUCTION

Vestibular schwanoma (VS) is a benign tumor arising from the vestibular nerves, mostly from superior vestibular nerve. Approximately 1% cases of sudden sensorineural hearing loss (SSNHL) are due to retro-cochlear lesions like neoplasms, demyelinating diseases, or stroke. Hearing loss on the affected side may be the most common and early symptom of this benign tumor. Although hearing loss is usually gradual, but a sudden hearing loss can occur in 7-20% of the cases at some stage in these neoplams.[1] The prevalence of VS in patients suffering from SSNHL is about 1.9% to 10.2%.[2,3]

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The investigation of choice for the diagnosis of VS is contrast enhanced magnetic resonance imaging (MRI). Early MRI helps patients both in seeking early treatment as well as functional preservation of the auditory and facial nerves.[4]

The objective of the present study was to determine the prevalence of vestibular schwanoma in adult patients with unilateral sudden sensorineural hearing loss.

METHODS

Design, Setting, Duration & Approval: This cross-sectional study was carried out in the Department of ENT, Mufti Mehmood Memorial Teaching Hospital, Dera Ismail Khan, Pakistan from January 2013 to December 2023. An informed consent was taken from each patient after explaining the benefits and risks involved during the study. A written Ethical approval for the present study was obtained from Institutional Ethical Committee of the hospital.

Population & Sapling: A sample of 865 adult (>19 years) patients of sudden sensorineural hearing loss (SSNH) was selected from the outdoor Department of ENT, Mufti Mehmood Memorial Teaching Hospital, Dera Ismail Khan, Pakistan through consecutive sampling technique.

Inclusion criteria: All adult (>19 years) patients with unilateral Sudden Sensorineural Hearing Loss were eligible for inclusion.

Exclusion criteria: All adult patients with bilateral sudden sensorineural hearing loss were excluded. Cases without a follow-up audiometric assessment were also dropped from the study.

Procedure: Sudden sensorineural hearing loss was defined as sudden onset of hearing loss of >30 dB over three consecutive frequencies in pure tone audiometry, which happened progressively over few days.

A detailed history with special emphasis on hearing loss, tinnitis and vertigo was obtained. All patients underwent routine otoscopy with a standard otoscope, tuning fork tests and pure tone audiometry at the time of presentation. In each patient the hearing level was assessed on Pure tone audiometry for the speech frequencies i.e (500, 1000, 2000, and 4000 Hz).

A contrast enhanced magnetic resonance imaging (MRI) of 1.5 Tesla of the internal acoustic meatus and brain was performed in all patients at the initial consultation. All the images were reviewed and reported by a consultant radiologist. The tumor size was classified into 5 grades on the size picked on MRI according to the New and Modified Reporting Systems from the Consensus Meeting on Systems for Reporting Results in Vestibular Schwanoma Classification as follows: grade 1 (1-10 mm), grade 2 (11-20 mm), grade 3 (21-30 mm), grade 4 (31-40 mm) and grade 5 (> 40 mm).

Systemic oral corticosteroids as primary treatment was given to all patients, tapered over 10-14 days (60mg of prednisone daily for 4 days which was tapered by 10mg every 2 days). Two follow up audiograms were obtained in each patient, first after completion of the treatment and second 3 months after the completion of treatment.

Data Collection Plan: For each patient a written Performa was used comprising of the following variables. All variables were entered into the data editor of SPSS 16 (SPSS.Inc,Chicago,Illinois,USA).

Data was collected for demographic variables: sex, age in years and age groups. Sex had two attributes of males and females. Age groups had four attributes: >19-40 years, 41-50 years, 51-60 years, and >60 years.

Research variables were history of unilateral sudden hearing loss, side involved, prevalence of vestibular schwanoma in unilateral SSNHL and size of the tumor.

Age group was ordinal; age in years was a numeric data while all the rest were nominal data.

Data Analysis Plan: Nominal and ordinal data was expressed as count and percentage for the sample (sample statistics). Population parameters were expressed as 95% confidence interval of proportion using Wilson score interval method through an online statistical calculator "Statistic Kingdom" (https://www.statskingdom.com/proportion-confidence-interval-calculator.html).. Numeric data was expressed as mean, minimum, maximum, range and standard deviation. Keeping in view the objectives and design of the study, no further analysis was applicable.

RESULTS

Demographics: Out of 865 patients with Sudden Sensorineural Hearing Loss (SSNH) 530 were men (61.30%) & 335 (38.70%) women. Mean age of the patients was 44.10±8.12 years (range 20-70 years). The modal age group was 51-60 years. Out of 865 patients, the age group >19-40 years included 293 (33.90%), 41-50 years included 420 (48.55%), 51-60 years included 115 (13.30%), and 61-70 years included 37 (04.25%) patients.

Prevalence of Vestibular Schwanoma in SSNH: Out of total 865 patients of sudden sensorineural hearing loss, 31 (3.58%) patients had vestibular schwanoma. (Table 1)

Table No. 1: Prevalence of Vestibular Schwanoma in Unilateral Sudden Sensorineural Hearing Loss (n=865)

Variable	Attributes	Sample Statistics		95% Confidence Interval	
		Frequency	Percentage	Lower bound	Upper bound
Presence of vestibular schwanoma in SSNH	Yes	31	03.58%	02.53	05.04
	No	834	96.42%	94.95	97.46
	Total	865	100%	Parameters estimates	

Distribution of Vestibular Schwanoma in Unilateral SSNH by sex and age groups: The prevalence of vestibular schwanoma in unilateral SSNH was higher 21/865 (02.43%) in men than 10/865 (01.15%) women. It was highest 11/865 (1.27%) in age group 51-60 years followed by 8/865 (0.92%) in 41-50 years. (Table 2)

Table No. 2: Distribution of Vestibular Schwanoma in Unilateral SSNH by sex and age groups (n=31/865)

Variable	Attributes	Sample size	Sample Statistics(n=31)		95% Confidence Interval	
			Frequency	Percentage	Lower bound	Upper bound
Sex	Men	530	21	21*100/865=02.43	01.59	03.68
	Women	335	10	10*100/865=01.15	00.62	02.11
Age groups	>19-40	293	7	7*100/865=00.81	00.39	01.66
	41-50	420	8	8*100/865=00.92	00.46	01.81

(years)	51-60	115	11	11*100/865=01.27	00.52	02.01
	61-70	37	5	5*100/865=00.58	00.24	01.34
VS in Unilateral SSNH present			31	3.58%	02.53	05.04
VS in Unilateral SSNH absent			834	96.42%	94.95	97.46
Total			865	100%	Parameters estimates	

VS: Vestibular schwanoma, SSNH: Sudden sensorineural hearing loss

Distribution of Vestibular Schwanoma in Unilateral SSNH by laterality and grade:

The prevalence of vestibular schwanoma in unilateral SSNH was higher 17/865 (1.96%) on left side than 14/865 (1.62%) right side. By tumor size, most 12/865 (1.39%) of the patients were in grade 1, followed by 9/865 (1.04%) in grade 2, 7/865 (0.81%) in grade 3, 2/865 (0.23%) in grade 4 and 1/865 (0.11%) in grade 5. (Table 3)

Table No. 3: Distribution of Vestibular Schwanoma in Unilateral SSNH by laterality and grade (n=31/865)

Variable	Attributes	Sample Statistics		95% Confidence Interval	
		Frequency	Percentage	Lower bound	Upper bound
Laterality	Left	17	17*100/865=01.96	01.04	02.89
	Right	14	10*100/865=01.62	00.77	02.45
Grade	1	12	12*100/865=01.39	00.60	02.16
	2	09	09*100/865=01.04	00.36	01.71
	3	07	07*100/865=00.81	00.21	01.40
	4	02	02*100/865=00.23	00.06	00.83
	5	01	01*100/865=00.11	00.02	00.65
VS in SSNH present		31	03.58%	02.53	05.04
VS in SSNH absent		834	96.42%	94.95	97.46
Total		865	100%	Parameters estimates	

VS: Vestibular schwanoma, SSNH: Sudden sensorineural hearing loss

DISCUSSION

Patients with Vestibular Schwanoma may present with sudden sensorineural hearing loss although it has several other presentations as well. In the present study the true frequency of Vestibular Schwanoma was 3.60% but literature has documented a prevalence of VS of about 1.9% to 10.2% in patients suffering from SSNHL[2,3]

a variable prevalence of VS among patients treated for SSNHL ranging from 1.9% to 10.2%.[3-5] The higher percentage (3.60%) in our study may be attributed to higher average age of the patients in our study & secondly due to use of MRI in all patients presented with unilateral sudden hearing loss.[6]

The age range (20-70 years) of the patients in the present study is similar to that in a local and international studies.[7,8,10] Contrary to our results, a retrospective study of 542 patients included patients of 28 to 57 years.[9]

Our study revealed male preponderance like other two other studies.[5,7] But two other international studies have reported female preponderance in their studies.[9,10] The higher incidence in men in our study is more likely because of our dominant male society who seek earlier treatment for audio vestibular symptoms.[7]

Almost matching with the results of the current study (54.85%), another study has also reported VS more on left side.[5] Contrary to these reports another international study reported an equal involvement on both sides.[11]

We recommended contrast enhanced MRI in all patients with unilateral sudden SNHL for screening VS in these cases due to its high accuracy and easy availability. On the other side non-contrast screening protocols have been developed to reduce the cost, contrast reactions and patient screening time but false negatives occur in very small tumors especially when the tumor size is less than <4mm.[12]

In our study majority of the patients (54.85%) had grade1 tumors (1-10mm). These findings are in agreement with those reported by Song M and his colleagues.[13] Almost similar results were also reported by Jeong KH and his colleagues.[14] However another study found that size of the tumor has no effect on sudden sensorineural hearing loss. Keeping in view the slow growth of these tumors, the hearing loss should also be progressive. But hemorrhage or cystic degeneration in these tumors lead to sudden increase in the size of the tumor causing compression of the cochlear nerve leading to sudden hearing loss.[15] Early detection of these tumors may be addressed well by hearing preservation surgery or even only by radiation treatment.[16]

CONCLUSION

The prevalence of Vestibular Schwanoma in adult patients with unilateral sudden sensorineural hearing

loss is high. Importance of routine magnetic resonance imaging screening of patients with unilateral sudden sensorineural hearing loss should be stressed due to the high prevalence of Vestibular Schwanoma.

Limitation: The main limitation of our study was a small sample size with point prevalence. A cohort study with a larger sample size over a long duration should be carried out.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Muhammad Ismail Khan
Drafting or Revising Critically:	Muhammad Ismail Khan
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Compare the Laparoscopic versus Open Appendectomy in Al-Diwaniyah Teaching Hospital

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ABSTRACT

Objective: To compare the outcomes of laparoscopic appendectomy (LA) and open appendectomy (OA) in patients with acute appendicitis at Al-Diwaniyah Teaching Hospital.

Study Design: Prospective study

Place and Duration of Study: This study was conducted at the AL-Diwaniyah Teaching Hospital, Al-Diwaniyah City Iraq from 1st May 2021 to 30th April 2022.

Methods: One hundred patients with a clinical diagnosis of appendicitis were chosen. They were divided in two groups; group A treated with laparoscopic appendectomy and group B managed with open appendectomy.

Results: The average operative time was 45min in group Abetween 30 to 60 minutes while in group B, the average was 25min.Regarding the complicationspostoperatively, were mainly observed in group B as compared to group A. Paralytic ileus was 2 (4%) in group A.

Conclusion: Laparoscopic appendicectomy is regarding as a safe and effective technique with lower postoperative pain, less hospital stay then less cost, quicker recovery and best looking scar than in classical Open appendectomy.

Key Words: Laparoscopic appendectomy, Open appendectomy, Appendicitis

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INTRODUCTION

Acute appendicitis (AA) is mainly diagnosed clinically. The first appendectomy in the history was done in New York in 1886, and since that time, appendectomy was regarded as the commonest emergency surgery. Early and proper appendectomy has considered as the gold standard treatment for AA because of the highly risk of developmentof seriouscomplications.[1]

Appendicitis is regarded as the main emergency case in surgerythat accounts about of 7-10% and is regarded as the major occurrence in child and adolescentages,with age range from 10 to 30 years, and majority of patient need surgical intervention with appendicectomy to prevent possibility of perforation of the appendix.[2] The classical l surgical incision in open appendicectomy OA includes a minorwound (about 4-6 cm) in the lower right segment of the abdominal wall, called a grid iron incision.

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Other approaches may include laparoscopic method (laparoscopic appendicectomy), which perform in most cases with 3minute incisions (each about 1.5 cm). Then surgeoninserts probesfor a camera and specialized laparoscopic toolswithin the abdominal cavity after inflation with CQ2 gas and excised the appendix as in the open traditional surgery.[3]

Open surgical appendectomy is a smooth and mostlyusedprocedure for cases of acute appendicitis in the last years, but from about 15 yearsago, laparoscopic appendectomy is becoming more popular, in spite of it is not as famous as laparoscopic cholecystectomy.[4]The first laparscopic appendicectomy was performed by a German gynecologist surgeon Semma in 1983. Laparscopyin cases of suspected appendicitis are regarded as a safe and effective procedure.[1,4]

Using the laparoscopy gives a great assessment and large operative field of the peritoneumspace more than that in the classic grid-iron incision. The technique gives a good vision that resulted in full assessment of the para-colic areas and the pelvisorgans that is not easy to be performwith the OA.[5]

Inspite that traditional appendectomy has low risk of complications with low risk of complications and death, the laparoscopy has less invasive approach with bestbenefits in the postoperative period like small wound size and low risk of infection, less postoperative pain, and less postoperative recovery time result in less hospital cost, with other additional benefit mainly for femalescases as it enhances the diagnosisassessment

and lowering the after operationpelvic adhesionthat may end with infertility problems in addition to better aesthetic results.[6] It has been done to make comparison of OA with LA, but the benefit of laparoscopy in appendectomy is underdiscussion till now.

Till now it has not regarded as the most popularprocedure for dealing withacute appendicitis as gall stone surgery. Debate still exists about the beneficial effect of laparoscopic appendicectomy as compared to a conventional open procedure. The majority of patients with appendices are treated by the open approach in the UK.[7]

Laparoscopic appendectomy is a delicate and safe procedure with lowrisk of complications; it is also a great training procedure in laparoscopic field and, with best experience, takes a shorter time thanin open procedure. In cases of negative appendectomieswhich are mostfrequent in fertile age women and can be accompanied with significant morbidity;therefore, laparoscopy has a diagnostic role here and, when the appendicitis is the cause, then appendix can be removed safely by laparoscopy.[8]

We applied this prospective study to make a comparisonbetween thefinalresults of open appendectomy and laparoscopic appendectomy regarding the pain in the postoperativeperiod, recovery and the need of analgesics, incidence of infection of the wound and hospital admission time, reflecting including early resume the normal work.[9]

METHODS

In thisreview was done in AL-Diwaniyah teaching hospital in Al-Diwaniyah city, from May 2021 to May 2022. One hundred Patients with a clinical diagnosis of appendicitis were chosen (60 male and 40 female) there afterdistributed as a group A (50 patients treated with lap.appendectomy LA and group B (50 patients managed with open appendectomy OA). Exclusion criteriathat applied in this study were including patientsless than 10 years, patients withfeatures of acute peritonitis, cases with asuspected right iliac fossa mass that may diagnosed as appendicular mass or abscess, and cases of laparoscopy that converted to open appendectomy.

All patients had detailed information regarding the study and the risk of conversion to open surgery in the group of laparoscopic procedure. The ages of patients in the study were range between 15–45 years old. Cases with suspicion presented with right lower abdominal pain or withpain around umbilicus that migrate to right iliac fossa within 24 hours. Painand nausea with or without anorexia, vomitingand elevated temperature in some cases were explained. On abdominal examination tenderness in the right lower abdomen withrebound tenderness and in some casesa cough impulse and Rovsings sign, mild increase in temperaturelower than 38 C. Regarding laboratory tests, leukocytosis in most cases more than 10^4 cells/ml, and general urine examination and chest x-ray were performedin all cases. Regarding ultrasound studyof the abdomen mainly needed in femalesin order to excludeother diagnosis thatgiven a picture similar toacute appendicitis. Prophylactic antibiotic were given to all patients by using ceftriaxone (1000 mgtwice daily) and metronidazole vial. Cases of OA weredone by a classical McBurneys approach.

In LA cases, using the typical technique by three ports which includes two 10 mm ports (umbilical and right lower abdomen) and one 5mm (left iliac fossa) ports were used. Post insufflation of peritoneumwith CO2, the intra-abdominalspace was examined to allocate the appendix and exclude other differential pathology. Divide the mesoappendix by using ligasure or bipolar cautery and appendix excised using endoclip and then appendix extrudedwith a laparoscopic bag. Close the wounds of port sites. Excised appendices were sent for histopathology.

Follow up postoperatively with checking bowel sounds at 6 hours interval, when positive, can allow a fluid diet to patient and then allowing patients going home.Time of operation from starting of anesthesia until discharge from the hospital started.Postoperative analgesia includes the numbersof intravenous or intramuscular injections needed. Thecomplications in the postoperative period whichmay be including respiratory, gastrointestinal, and vascular. In our study, all those creteria were calculated between Laparoscopic appendectomy and open appendectomy. The data was entered and analyzed through SPSS-25.

RESULTS

Average age in both groups was 15-45 years and 30 years is the mean age in both groups.Men to women ratio were not the same in both groups, in group A was (1.3:1) and(1.2:1)was in group B. there minor differences in age, sex in both groups which is no significant.Main clinical features are shiftinglower right abdominal pain and rebound tenderness; other characteristics include nausea, anorexia and mild fever, there were no significant dereferences in the two groups (Table 1). The average operative time was 45min in group Abetween 30 to 60 minutes while in group B, the average was 25minutes between 20 to 30minutes. It is clear that operative time was less in group B, the p value was $P < 0.001$ (Table 2).

The using of postoperative analgesia was assessed by calculation the number of analgesicinjections used postoperativelyat time of the hospital staying before discharge. More need for analgesia in group B than in group A, $p < 0.001$ which is significant (Table 3).

Return of normal bowelactivity was explained by the spontaneous passage of flatus and detection of bowel sounds;in cases of LA the range was 10 hours while in

OA group the range was 18 hours, the p<0.001,which is significant (Table 4).

About the initiation of oral fluids diet, it was about 14 hours in cases of group A LA while it was about and 22 hours after OA in group B. Regarding the duration of admission postoperatively,in group A the mean hospital staying was 24 hours, while in group B it was 2 days, p <0.001which is significant (Table 5).

Regarding postoperative complications, mainly observed in group B as compared to group A. Regarding paralytic ileus was 2 (4%) in group A ,and 5 (10%) in group While the wound infection was 15(16%) in group B and 3(6%) in group A.The chest infectionwas (zero) in group A and 1 (2%) in group B. Deep venous thrombosis (DVT) was (zero) in both groups. using intra-abdominal drain was in 3 cases in group A (6%) while in group B, in 17 case (34%). Mortality rate was zero in both groups which is of significant value p<0.001 (Table 6).

Table No. 1: Clinical features of acute appendicitis

Clinical feature	Group A		Group B	
	No.	%	No.	%
Shifting pain	35	70.0	33	66.0
Rebound tenderness	45	90.0	47	94.0
Anorexia	25	50.0	27	54.0
Nausea	15	30.0	13	26.0
Vomiting	10	20.0	11	22.0
Fever	5	10.0	6	12.0

Table No. 2: Comparison of duration of the operation

Time (minutes)	Group A		Group B	
	No.	%	No.	%
25	-	-	18	36.0
30	-	-	19	38.0
35	1	2.0	10	20.0
40	1	2.0	2	4.0
45	20	40.0	1	2.0
50	15	30.0	-	-
55	9	18.0	-	-
60	4	8.0	-	-

Table No. 3: Need for postoperative analgesic injection

No. of analgesic injection	Group A		Group B	
	No.	%	No.	%
1	30	60.0	50	100.0
2	5	10.0	30	60.0
3	1	2.0	25	50.0
4	-	-	10	20.0
>4	-	-	4	8.0

Table No. 4: Return of normal bowel movement

Bowel sounds (hour)	Group A		Group B	
	No.	%	No.	%
8	2	4.0	-	-
10	15	30.0	7	14.0
12	24	48.0	8	16.0
14	8	16.0	20	40.0
16	1	2.0	10	20.0
18	-	-	3	6.0
20	-	-	2	4.0

Table No. 5: Duration of postoperative hospital staying

Duration of hospital stay (hours)	Group A		Group B	
	No.	%	No.	%
8	2	4.0	-	-
12	2	4.0	1	2.0
24	40	80.0	10	20.0
48	6	12.0	35	70.0
72	-	-	4	8.0

Table No. 6: Postoperative complications rate

Complication	Group A		Group B	
	No.	%	No.	%
Paralytic ileus	2	4.0	5	10.0
Wound infection	3	6.0	15	30.0
Chest infection	-	-	1	2.0
DVT	-	-	-	-
Drain using	3	6.0	17	34.0
Mortality	-	-	-	-

DISCUSSION

Laparoscopic appendectomy has a progressive way to be a gold standard and approving its superiority over the open appendectomy (OA) and in spite of OA is the first choiceto deal with acute appendicitis and is hence the most common urgentsurgical operation performed, but with progression of minimally invasive techniques, LA had more attention worldwide. The first LA was reported in 1983 and from that time was considered accurate with high safety and low reported of complication rates around1.2%.

Laparoscopic appendectomy gives a well exploration of the peritoneal cavity and can be examine totally more than as in the classical open appendectomy. This procedure permits a thorough and rapid inspection of total peritoneum, the paracolic regions and pelvic cavity which is difficult to be performed with open grid iron inscion.[10]

Many researchers regard emergency laparoscopy is a greatoption for the management of acute abdomen casesthat may be of benefit inlowering the costs and risk of complications andimprovingend results and more comfortable for patients.[11]

The diagnostic accuracy inlaparoscopic appendectomy is very good in patients with suspected appendicitis therefore it is highly recommended procedure. There are multiple studies that showing that laparoscopy regards a great diagnostic stoolthat reducesthe unnecessary appendectomies in fertile age female.[12]

A multiplenumbers of studies have been carried out in India that makes a comparison between open and lap. appendicectomy. In the majority of the reviews,the result was that LA preferable than OA. According to a manyreviews applied in Nawaz SharifHospital, Lahore in 2011, which showed that the time of operation was lowerin LA.This not as that in review where the operative time is more in LA as in our study we calculated the time of surgery from the time of insufflation of peritoneal cavity until the time of deflation. In this study, the mean operationduration was forty fiveminutes. In LA, while in OA is25 min. which was determinedbythe surgeon experience and the efficacy of the assistant team.[10,13]

Inourstudy the more operativeduration in laparoscopic appendicectomy may be resulted fromextra needs as preparing thelaparoscopic tools,gas inflation, ports insertion and a period for diagnostic laparoscopy.[14]

In other study that was done in 2002, Multan.it was also showed that LA,in spite of it is a new and expensive more coastyprocedure, was a great substitute for the OA as it had an additionalfeature that facilitate full visualization of abdominal cavity in young female patient when there suspicion about the diagnosis between other gynecological causes.

A study done by Al-Aubaidi[12] in Iraq at 2011 showed that the averageduration of operationin OA was nearly25 min lessthan in LA group. With the mean analgesic used postoperatively in laparoscopic patientswere 1.3; and regarding the complications afterthe procedure were few and detected more in OApatients. Staying of hospital was 24 hours in laparoscopic group. In other study performed by Pokalaet al[15] revealed that LA consumed a moretime, about (95.1±44.1 minutes) than OA which about (65.8±32.5 minutes).

About the need for analgesia in our study was less in group A about 1.5 doses and is near to the result in the study conducted by Kamalet al[10] was 1.4 doses.

In our series the risk of infection is similar in an other study, which showed that the risk of wound infections in cases of the laparoscopygroup was 8.4% compare to that in the OA group which was 24.5%.Gupta and Cliff[16] also reported that the risk of wound infections was much lesser in LA (15.4%) than in cases of OA (31%).Which may be explained bynoting that in laparoscopic appendectomy there is little touching of the bowel and other organ directly by the surgeon hands and instruments as comparison in OA. Also, the gut is rarely come intouch with the wound of the abdominal wall at the time of LA where the appendix is dealt with ininternally.

In our study theapproximate hospital stay in group A was 1 day and 2 days in group B and this result is a slightmore than that mentioned in a study by Kamal et al[10] and Yau et al[14] but is nearto the result showed in an other study. Pokalaet al[15] had also reported more hospital stay than our series and reported a clear difference regarding the hospital admission between groups of LA which was (4.34±4.84 days and, 7.31±9.35 days in the OA group.

The return of normal bowel movement and starting of fluid diets with return of normal activity following appendectomy is better in cases of LA than in OA in our study. And this also the findings in multiple other series .the minimally invasive procedures including (LA) by definition it must allow for a more quick recovery, less admission time, and quicker recovery time.[17-20]

CONCLUSION

Laparoscopic appendicectomy is regarding as a safe and effective technique with lower postoperative pain, less hospital stay then less cost, quicker recovery and bestlooking scar than in classical OA. Also there was less need for postoperative analgesic treatment, so it is characterized early mobility of patient and less risk of complications with early return to normal life.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Ali Abdul Hussein Handooz
Drafting or Revising Critically:	Ali Fawzi Abdalsahib, Doaa Faris Jabaz
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Assessment Alpha-1-Antitrypsin and Correlation with Liver Enzymes in Non-Alcoholic Fatty Liver Patients in Thi-Qar Province, Iraq

Muna Hameed Kazem, Jamal Harbi Hussein Alsaadi

ABSTRACT

Objective: The research aims to evaluate the relationship between alpha-1-antitrypsin and liver enzymes alanine aminotransferase and aspartate aminotransferase in patients with fatty liver disease.
Study Design: Comparative study.
Place and Duration of Study: This study was conducted at the University of Thi-Qar, Al-Nasiriyah Teaching Hospital, Iraq from 1st December 2023 to 1st May 2024
Methods: Serum Alpha-1-antitripsin, alanine aminotransferase and aspartate aminotransferase levels were measured in 96 volunteers, 23 healthy control group members and 73 patients. An internist physician made the diagnosis for the patients. Patients with non-alcoholic fatty liver disease are the instances that were included, fatty liver to diabetes mellitus and hypertension. Individuals with fatty liver disease caused by alcoholism, or fatty liver along with other illnesses like cardiac and kidneys were excluded.
Results: Significant decrease in the concentration of alpha-1-antitripsin in patient's groups in comparison to the control group ($p \leq 0.05$). Notable rise in the concentration of alanine aminotransferase in patient's group comparison to controls groups ($p \leq 0.05$).notable rise in the concentration of aspartate aminotransferase in patient's group comparison to controls groups ($p \leq 0.05$).
Conclusion: The negative correlation between alpha-1-antitripsin and aspartate aminotransferase in the fatty liver group and the association factor (r= -0.13). A negative relationship between Alpha-1-antitripsin and alanine aminotransferase in the fatty liver group and the association factor (r= -0.26).
Key Words: Non-alcoholic fatty liver disease (NAFLD), Alpha-1-antitripsin (AAT), Alanine aminotransferase (ALT), Aspartate aminotransferase(AST)

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INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is a growing global health concern due to its connection to insulin-resistant metabolic diseases and heart ailments. NAFLD is characterized by chronic buildup of lipids in the liver, insulin resistance, and steatosis.[1] It can lead to malignancy of the liver, cirrhosis, and non-alcoholic steatohepatitis (NASH), and simple steatosis of the liver.[2] Despite its prevalence, only 5% of NAFLD patients are aware of it, compared to 38% of those suffering from viral liver disease.[3]

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Antioxidants play a critical role in the body's defense to combat free radicals.[4] Reduced antioxidant activity and higher blood oxidative markers like MDA are correlated in people with non-alcoholic fatty liver disease (NAFLD)

Alpha-1-antitrypsin (AAAT), an average-sized glycoprotein, is a key enzyme in identifying liver problems, hepatic inflammation, and heart failure. The site of action is made up of serine and methionine at locations 358 and 359, respectively, and extends from its spherical form. Locations 46, 83, and 247 contain residues of asparagine (Asn). Bind the mature molecule to the protein, which is made up of three branching carbohydrate side chains and a core chain with 394 amino acids. The molecule's half-life is greatly extended, and its electrophoretic heterogeneity is defined by carbohydrates.[5]

Elevated ALT levels indicate serious liver disorders, such as toxic liver necrosis or hepatitis. Alanine Aminotransferase (ALT) is most concentrated in the liver and plays a crucial role in identifying liver problems, hepatic inflammation, and heart failure.[6]

Aspartate aminotransferase (AST) is a distinct isoenzyme type that differs genetically. Elevated mitochondrial AST has been associated with chronic liver illnesses, such as hepatic tissue degeneration and necrosis. Elevated AST levels are common in people with cirrhosis, even in liver conditions where a high ALT is often observed.[7]

METHODS

The study, conducted from from 1st December 2023 to 1st May 2024, involved 96 volunteers from the University of Thi-Qar, Al-Nasiriyah Teaching Hospital, and private laboratories, Iraq. The participants were divided into four groups: 28 cases of fatty liver, 22 cases of DM and fatty liver, 23 individuals with diabetes and hypertension, and 23 controls. The ultrasound device detects illness, and men and women give 5 milliliters of blood intravenously. Serum is separated using centrifugation-based separation, then chilled at -20°C for testing chemical indicators. The data was entered and analyzed through SPSS-25.

RESULTS

The important decrease in the concentration of Alpha-1-antitripsin in the patient groups relative to the baseline group ($p \leq 0.05$). There was no noticeable variation in the amount of focus of alpha-1-antitripsinamong every patient's group ($p \leq 0.05$) Table No. 2).

The increase in the concentration of ALT in the patient groups relative to the baseline group ($p \leq 0.05$). There was no discernible difference in the concentration of ALT between fatty liver and fatty liver with DM groups ($p \leq 0.05$) [Table 3].

Figure 1 showed a negative correlation between Alpha-1-antitripsin and ALT in the fatty liver group in association factor (r= -0.26), negative correlation in the fatty liver with DM group in association factor (r= -0.19) and negative correlation in the fatty liver with DM and HTN group in association factor (r= -0.22)

An important increase in the concentration of AST in the patient groups relative to the baseline group ($p \leq 0.05$). There was no discernible difference in the concentration of AST between fatty liver with DM and fatty liver with DM and HTN groups ($p \leq 0.05$) [Table No. 4].

Table No. 1: Descriptive statistics of the patients

Group	BMI (kg/m^2)	Age (years)
Fatty liver	31.38±4.82	44.53±13.81
Fatty liver with DM	32.64±5.19	50.00±7.69
Fatty liver with DM and HTN	35.66±3.6.88	56.82±12.48
Controls	28.24±4.85	51.65±12.38

Table No. 2: Serum Alpha-1-antitripsin levels of control and patient's groups

Group	No.	Alpha-1-antitripsin (mg/mL)
Fatty liver	28	1.75±0.27
Fatty liver with DM	22	1.85±0.29
Fatty liver with DM and HTN	23	1.71±0.27
Controls	23	2.02±0.50
LSD		0.16

Table No. 3: Serum ALT levels of control and patient's groups

Group	No.	ALT (U/L)
Fatty liver	28	30.24±4.1
Fatty liver with DM	22	31.20±5.64
Fatty liver with DM and HTN	23	35.78±6.07
Controls	23	20.77±6.05
LSD		2.45

Table No. 4: Serum AST levels of control and patient's groups

Group	No.	ALT (U/L)
Fatty liver	28	26.76±3.51
Fatty liver with DM	22	32.63±5.39
Fatty liver with DM and HTN	23	30.71±3.99
Controls	23	19.78±5.76
LSD		2.11

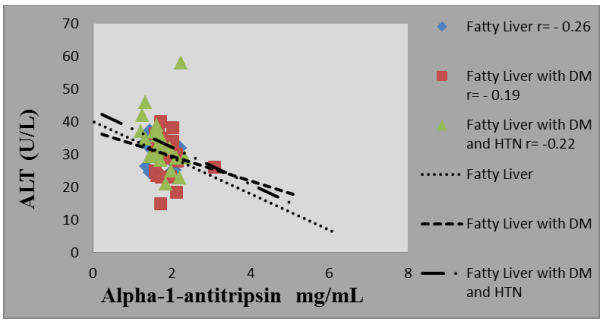

Figure No. 1: Correlation between alpha-1-antitripsin and ALT in the patient's groups.

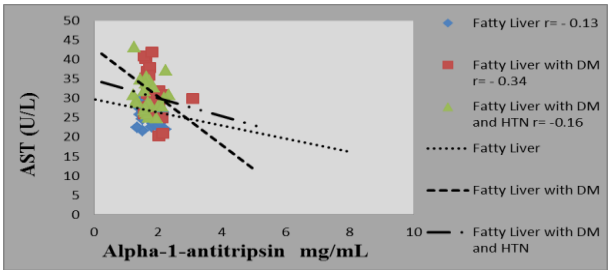

Figure No. 2: Correlation between alpha-1-antitripsin and AST in the patient's groups

Figure 2 indicates a negative relationship between Alpha-1-antitripsin and AST in the fatty liver group in

association factor (r= -0.13), negative relationship in the fatty liver with DM group in association factor (r= -0.34) and a negative relationship in the fatty liver with DM and HTN group in association factor (r= -0.16)

DISCUSSION

The liver's cells release the protein AAT, which protects pulmonary tissue from proteolytic enzymes.[8] AAT is a highly variable gene with over 120 variations, including 60 deficiencies. The most prevalent defective alleles are S and Z respectively.[9] The Z variant alters the protein's tertiary structure, leading to polymerization and mis-folding, causing protein build up in the hepatocellular endoplasmic reticulum.[10] This accumulation can lead to liver damage, apoptosis, and fibrosis.[11] The majority of individuals with liver illness are homozygous for the dysfunctional Z allele, but heterozygotes may have varying levels of liver inflammation.[12] The most common cause of alpha-1 antitrypsin deficiency (AATD) is the Z mutant version of AAT (ZAAT), an inadequate allele of the gene SERPINA1. This mutation causes ZAAT to misfold, accumulate, and cause endoplasmic reticulum stress in hepatocytes, leading to chronic liver illness.[13] This validates the study's findings of Hamesch et al.[14]
NAFLD is a common liver disease with higher average liver enzyme quantities.[15] Alanine aminotransferase is a key indicator of NAFLD with elevated levels associated with severe histopathological ranges.[16] Hypertension, high blood sugar, and abnormal triglycerides, total cholesterol, and adiposity are also associated with elevated ALT.[17] Serum ALT is strongly correlated with insulin resistance, glucose tolerance, and other metabolic disorders. AST, a composite measure, is used to detect hepatic steatosis but does not represent a clinical diagnosis. Many studies indicate that increasing abdominal size Adipose tissue is associated with elevated liver enzymes.[18]

CONCLUSION

An important decrease in the concentration of alpha-1-antitripsin in patients' groups compared to controls group ($p \leq 0.05$), a negative relationship between alpha-1-antitripsin and AST in the fatty liver group with association factor (r= -0.13) and negative relationship between alpha-1-antitripsin and ALT in the fatty liver group with association factor (r= -0.26).

Author's Contribution:

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Drafting or Revising Critically:	Jamal Harbi Hussein Alsaadi
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Evaluation of Uric Acid Level in Albino Rabbits Treated with Ivy Leaves Extract

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ABSTRACT

Objective: Evaluate the effect of dried Ivy leaves extract on blood uric acid in Albino Rabbits.

Study Design: Experimental study

Place and Duration of Study: This study was conducted at the Pharmacology Research Department of University of Karachi, duration of study was 2 months from 20 June 2019 to 19 Aug 2019.

Methods: Dried Ivy leaves extract was given to Rabbits and they were consigned in 2 groups, group A was given normal saline and it was control group while group B, treatment group, was given Ivy leaves extract. Blood samples were drawn from control and treated groups and Uric acids levels were tested on day 7, 15 and 30 respectively.

Results: As it is evident from results that animals treated with Ivy leaves extract showed significant reduction in normal serum uric acid level compared to control group. Mean level of Uric Acid Level mg/dl at Day 7 in groups 1 and 2 was 5.10±0.51 and 4.78±0.27, at day 30 in group 1 and 2 was 4.98±0.34 and 3.76±0.32 and at day 60 in groups 1 and 2 was 5.06±0.48 and 3.46±0.48 it shows significant difference among the groups ($p<0.001$).

Conclusion: Current study showed that some acidic compounds and amino acids present in Ivy leaves extract can impair reabsorption of uric acid which ultimately increases its elimination so uric acid concentration decreased significantly in treated groups given Ivy leaves extract.

Key Words: Albino Rabbits, Ivy leaves, Uric Acid

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INTRODUCTION

It has proved from different research tasks both epidemiologically and medically that increased intake of naturally obtained fruits and leafy green vegetables might reduce the risk of highly fatal chronic diseases like tumors of different body organs and cardiovascular events such as angina, myocardial infarcts and stroke[1,2]. It is also understood that role of different ingredients derived from plant origin in nanotechnology is not sufficiently known also their consequences in the field of health and health industries is unidentified, in spite of advances in pharmacological discipline of herbal extracts, recent developments worldwide have specified active naturally extracted components from plant sources that not just exhibit decreased side effects but also yield numerous health advantages. It has unlocked modern road maps in the discipline of bio medics, some published studies have partly or entirely replaced nano capsulated drugs synthesized from photochemical compounds (plant derived drugs) which may enhance pharmacological effects and provide additional biological features[3,4].

Hedera helix l is associated with family Araliaceae, it is frequently called as English Ivy or simply Ivy, in conventional treatment of respiratory diseases extract of newly emerged leaves of plant has been recommended for many years[5]. There are various pharmacological formulations, preprations and dosage forms of Ivy leaf extract are found including liquid, semisolid, solid and these forms are conveniently made accessible for patients to cure diseases [6,7].

Habitat of plant conforms is often found along roadside, abandoned fields, railroads areas, gardens, and different waste areas. I. hederacea frequently grows in warm climatic areas, Ivy plant originates in different parts of Asia like Pakistan, India and Kashmir[8,9]. Various phenols such as sinapic acid-hexoside, erulic acid, coumaric acid-hexoside and ferulic acid-hexoside were found in hederacea helix leaves, according to the mass spectral characteristics, following amino acids are also present in hedera leaves Leucine= 6.59, Isoleucine=5.03, Glycine =5. 36, Glutamic acid=22.71 and Tyrosine =2.58.

It is studied by most of the investigators believe that high intake of proteins cause increases the excretion of uric acid but exact mechanism of its excretion is not clear. Mares has mentioned that increased level of uric

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acid in urine due to high dietary feeding of amino acids results from deterioration of many nuclei of digestive cells which are involved in assimilation of ingested proteins. Taylor and Rose proved in their study that uric acid level increases in urine after ingestion of high protein diet but urinary creatinine level does not alter. Mosier and Christman specifically mentioned that amino acid glycine significantly increases urinary uric acid concentration but it does not affect creatinine level. Hedera helix plant is widely consumed for cure of different joint diseases like rheumatoid arthritis, osteoporosis and other degenerative arthritis for treatment of these disorders higher share is from Ivy leaves. Fleck is a skin disease usually expressed on face it can be best treated with this plant, Ivy plant is also commonly used for different skin whitening creams mixed with some other medicinal plants [10,11].

Based on above information that high dietary protein intake can increase uric acid excretion through urine, our study also rely on these facts as Ivy leaves extract contain many amino acids specially glycine and this amino acid increases excretion of uric acid markedly. So it can be studied that food substances rich in protein amino acid content and different acidic substances can decrease blood uric acid level like acetyl salicylic acid and can be beneficial in gout diseases.

METHODS

For the perseverance of study healthy rabbits were used, them prolong biochemical effect like blood concentration of uric acid studied. The weight of animals ranges between 1200 to 1800 grams, they were from different gender and alienated uniformly in two groups.

Group A is control group (Normal saline 6ml/kg).

Group B is test group given Ivy extract at the dose of 0.0125 ml/kg [12].

Dried Ivy leaves extract was given on daily basis for sixty days. One-week time period was permitted to all animals to acclimatize under normal favorable laboratory condition, they were also under strict observation for any ulceration on skin, lack of activity, edema, diarrhea and hair loss.

Extract preparation: Extract of Ivy leaves can be prepared with following steps, first fresh leaves of plant were filtered with the aid of mesh #60 then it was crushed and powder form was obtained. Extractor was employed to formulate the extract and water has to be used as solvent in the ratio of 1:10 with herb and finally infusion was acquired and sieved.

Test Collection: Test collection method was done with obtaining blood from rabbits on regular intervals like 7th, 30th, and 60thday of study for measuring variations in blood uric acid levels. Total amount of blood collected from each animal is 5 ml and it was injected in jell tubes for the assessment of uric acid level.

Rate of mortality was checked for 60 days' time period in animals getting extract of dried Ivy leaves and it was zero percent.

Statistical analysis: TUKES POST HOC TEST has been used to evaluate significance of mean.

P <0.05 considered as significant.

P<0.01 considered as very significant.

P<0.001 considered as highly significant.

RESULTS

Uric acid level: Uric Acid conc. in mg/dl as Mean and comparison on day 7 in both groups

Uric Acid Level as mean in mg/dl on Day 7 in group 1 and 2 was 5.10±0.51 and 4.78±0.27 it shows notable difference among groups (p<0.001). Correlation of Group 1 and Group 2 exhibited insignificant difference (p=0.326) as shown in Table 1 and Figure 1.

Uric Acid conc in mg/dl as Mean and comparison on day 30 in both groups

Uric Acid Level as mean in mg/dl on Day 30 in group 1 and 2 was 4.98±0.34 and3.76±0.32 with marked difference among groups (p<0.001). Correlation of Group 1 and Group 2 presented significant difference (p<0.001) as shown in Table 1 and Figure 2.

Uric Acid conc in mg/dl as Mean and comparison on day 60 in both groups

Table No. 1: Showing mean and comparison between the groups

	Day7	Day 30	Day 60
Mean group1 Mean group 2	5.10±0.51 4.78±0.27	4.98±0.34 3.76±0.32	5.06±0.48 3.46±0.48
Comparison between group1 and group2	Insignificant difference TUKES POST HOC TEST used	Significant	Significant

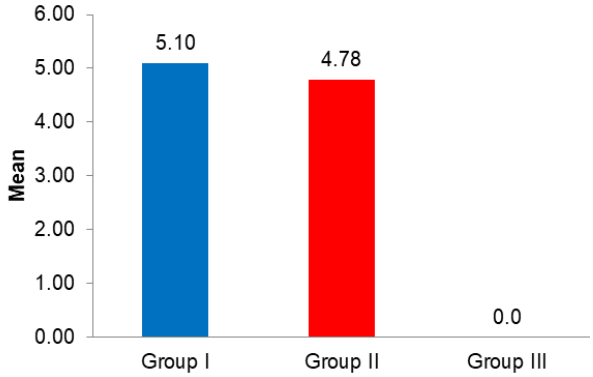

Figure No. 1: Uric Acid level as mean concentration in mg/dl at day 7 in different groups

Uric Acid Level as mean in mg/dl on Day 60 in group 1 and 2 was 5.06±0.48 and 3.46±0.48. difference is marked among the groups (p<0.001). Correlation of

Group 1 and Group 2 presented marked difference ($p<0.001$) as shown in Table 1 and Figure 3.

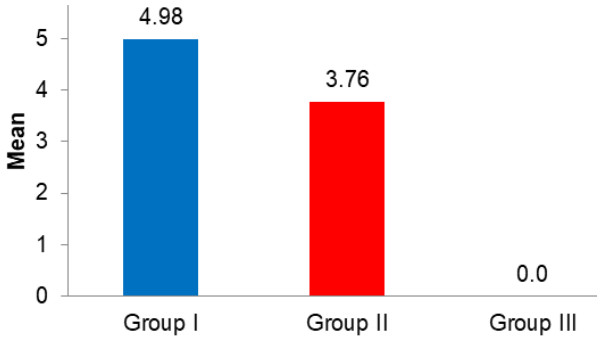

Figure No. 2: Uric Acid level as mean concentration in mg/dl at day 30 in different groups

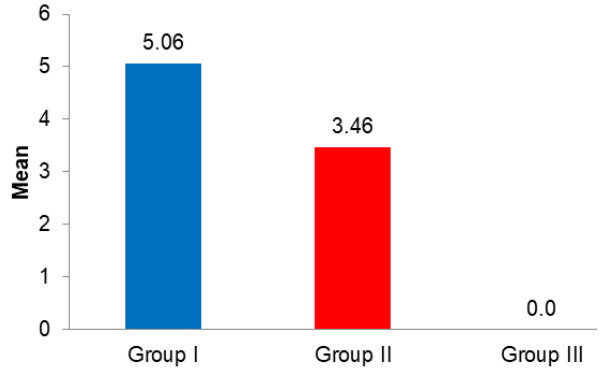

Figure No. 3: Uric Acid level as mean concentration in mg/dl at day 60 in different groups

DISCUSSION

Biochemical Formula of uric acid is C5-H4-N4-O3. It consist of oxygen, carbon, hydrogen and nitrogen and it is a heterocyclic ring compound. Uric acid is the metabolic product of purines. Purines naturally produced in the body and can be taken from diet also. Higher levels of uric acid start to deposit in joints as sodium urate crystals and can be the result of pathological condition gout. Uric acid can form different salts and ionic compounds called as acidic urates and urates, ammonium acid urate is one of the compound of uric acid which can deposit in spaces of joints and starts inflammatory process known as arthritis. Formation of uric acid begins with breakdown of nucleotide purine in the body and it is one of the components of urine. Higher values of blood uric acid may lead to gout, and it can cause some other medical disorders, like formation of ammonium acid urate crystals in joints and diabetes. Reference range of uric acid in blood lies between 3.4 and 7.2. Raised or decreased levels of uric acid are known as hypouricemia and hyperuricemia respectively. There are certain factors which can increase level of uric acid in body like diet rich in purine, sucrose, fructose corn soup, dieting or weight loss (rapidly) may temporarily elevate uric acid levels.

It was already proved by Taylor that high intake of protein in diet can increase uric acid excretion in urine our study is also in accordance with Taylor and it might occur due to interaction of amino acids at proximal convulated tubules of kidney. Christman and Moiser have also proved in their study that glycine amino acid inhibits reabsorption of uric acid at proximal convulated tubules it also causes secretion of uric acid thus can increase uric acid level in urine current study is also in favor of Christman and Moiser study because Ivy leaves extract also contain many amino acids and acidic compounds that might increase urinary excretion of uric acid.

Certain acidic substances may increase blood uric acid level like acetylsalicylic acid interfere with uric acid excretion at proximal convulated tubule as shown by terkeltaub in his study which is in favor of this study that acidic substances and amino acids can also interfere with excretion of uric acid [13].

Gout is the diseased condition which is characterized as higher levels of uric acid in blood and it get deposited in spaces of joints usually small joints of foot. The usual symptoms of gout include arthritis with severe pain in joints, redness swelling and inflammation begins where crystals of uric acid has been deposited. Reduction of uric acid level might occur due to amino acids found in Ivy leaves extract as these amino acids along with some acidic molecules might affect uric acid reabsorption at proximal convoluted tubules. It is apparent from this research that uric acid level is markedly less in rabbits given Ivy leaves (extract) which manifest that its extract cause fruitful effects in gout.

CONCLUSION

Different acidic substances are present in Ivy leaves extract which interacts with uric acid at proximal convulated tubules of kidney. These substances absorb back and cause secretion of uric acid in tubular lumen. Serum uric acid concentration is significantly less in treated groups given Ivy leaves extract as compared to control group.

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Original Article

Incidence and Clinical Patterns of Leprosy in Interior Sindh; Retrospective Study

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ABSTRACT

Objective: Incidence and Clinical Patterns of Leprosy in Interior Sindh: A Four-Year Retrospective Analysis.

Study Design: A case-control retrospective study

Place and Duration of Study: This study examines newly diagnosed leprosy cases in interior Sindh and was conducted at the Pathology Department CMC (SMBBMU), Larkana from August 2023 to July 2024.

Methods: The study comprised newly diagnosed leprosy patients from 17 designated locations. Cases were people who were diagnosed with leprosy based on clinical signs and laboratory results. All cases' demographic information, such as age, gender, regional distribution, and clinical trends, were obtained. All data was analysed using the SPSS 26 version software.

Results: A total of 239 new leprosy cases were registered across all leprosy centers in interior Sindh between 2019 and 2022. Male patients accounted for 154 cases (64.43%), outnumbering female patients, who comprised 85 cases (35.56%). The mean age of the patients was 42.44 ± 10.22 years, ranging from 3 to 59 years. Notably, the 15–30-year-old age group was the most affected. During the four-year study period, the most common forms of leprosy observed were borderline tuberculoid (BT) in 92 cases (38.49%), tuberculoid tuberculoid (TT) in 72 cases (30.12%), borderline lepromatous (BL) in 48 cases (20.08%), borderline borderline (BB) in 16 cases (6.69%), and lepromatous lepromatous (LL) in 11 cases (4.6%). Additionally, multibacillary (MB) cases were more prevalent, with 172 cases (71.96%), while paucibacillary (PB) cases accounted for 67 cases (28.03%).

Conclusion: To eliminate the stigma associated with the illness by educating the public about the fact that it is a bacterial disease that is readily curable.

Key Words: Incidence, Clinical, Leprosy centers.

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INTRODUCTION

Leprosy is a chronic infectious illness caused by Mycobacterium leprae or lepromatosis that spreads by aerosols from the nose and mouth after close and regular contact with untreated individuals. Stigmatisation and prejudice disrupt people's life, therefore early detection is critical for disease management. [1]

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Because of the sluggish development of the Mycobacterium leprae germs, leprosy symptoms might show up to 20 years after infection, making early detection and treatment difficult. [2]

Despite the availability of curative therapy, leprosy remains a global problem, with no change in yearly incidence over the last decade. The WHO South East Asia area is the most severely hit, accounting for more than 70% of new cases. Noncompliance with multi-drug therapy is one reason why leprosy continues to spread. [3]

Leprosy is frequently associated with socioeconomic determinants of health, and despite effective therapy, over 200,000 new cases were reported worldwide in 2019. Early identification is critical for efficient leprosy control because it limits the spread of infection and prevents impairments. [1]

In 2004, 407,791 new cases were found, according to a WHO report. Leprosy had been eradicated as a public health concern around the world in 2000. When leprosy was first discovered in India in December 2005, at a prevalence rate of less than 1 per 10,000, the WHO indicated that the prevalence was 181941 at the start of 2012. [4]

In 2023, 184 nations, regions, and territories contributed leprosy data, resulting in 182,815 new cases, with 72,845 (39.8%) females and 10,322 (5.6%) children. Despite curative treatment being available, leprosy is still prevalent worldwide, with little change in annual cases observed in the past decade. The WHO South East Asia region is the worst affected, accounting for over 70% of new cases. One reason leprosy transmission still occurs is non-adherence to multi-drug therapy.

This suggests that nations in the African (AFR) and Southeast Asian (SEAR) regions have the highest rates of detecting new cases. India, Brazil, and Indonesia continued to report the most new cases (>10,000) out of the 127 countries that submitted data in 2020; out of the 124 countries that provided data on child cases, SEAR reported 62% of all new child cases.[5]

The decrease in the number of new cases has occurred gradually. According to statistics from 2023, Brazil, India, and Indonesia continue to record more than 10,000 new cases, while 12 other countries, including Bangladesh, Myanmar, Nepal, Nigeria, the Philippines, Somalia, and Sri Lanka, report 1,000-10,000 new cases. Fifty-six nations reported zero instances, while 112 reported less than 1000 new cases.[6]

Recent developments have drawn attention to IRIS (Immune Reconstitution Inflammatory Syndrome in HIV-positive) or leprosy reversal patients. IRIS frequently happens after beginning highly active antiretroviral treatment (HAART).[7]

Some armadillos in the southern United States are naturally infected with the bacterium that causes Hansen's disease in humans, but the risk is very low, and the majority of individuals who come into contact with armadillos are at little risk of leprosy.[8] Man-to-man transmission of M. leprae predominates because patient diagnosis and treatment are crucial to halting the chain of transmission.[9]

The WHO system has taken the position of the Ridley and Jobling scale, which categorizes illnesses as either paucibacillary or multi.[10] The disease's patterns range from tuberculoid (paucibacillary), which has few skin lesions and a noticeable cell-mediated response, to lepromatous (multibacillary), which has many weak cell-mediated immunities against M. leprae.

Operational definition of selected leprosy patients: the diagnosis was based upon two factors,

Any two signs of leprosy

Localized skin lesions

Raised or flat Light or pigmented.

Sensory loss in the lesion

Thickened peripheral nerves

Laboratory test

Laboratory acid-fast test positivity in a slit skin smear or biopsy (histopathological) report according to WHO criteria

Leprosy is a significant health problem in developing countries such as Sindh, Pakistan. It can lead to serious disabilities if not treated properly. Understanding leprosy incidence in Sindh is crucial for identifying high-risk areas, improving detection, and developing better intervention strategies. Understanding socioeconomic conditions like poverty and lack of healthcare can help allocate resources effectively. Early detection and prevention are key to reducing disabilities and stigma. Epidemiological data can aid in healthcare planning and funding for leprosy control programs.

METHODS

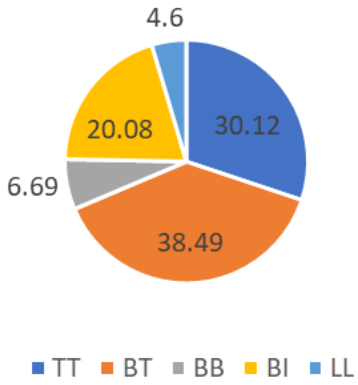
This retrospective study was conducted at Pathology department CMC (SMBBMU) Larkana, over a period from August 2023 to July 2024. Newly diagnosed leprosy cases were collected from various leprosy centers and clinics in interior Sindh over a four-year period (2019–2022). Patient data were extracted from medical records maintained at leprosy centers, including demographic variables such as age, gender, and residence. Leprosy cases were clinically classified based on the Ridley-Jopling classification into Borderline Tuberculoid (BT), Tuberculoid Tuberculoid (TT), Borderline Lepromatous (BL), Borderline Borderline (BB), and Lepromatous Lepromatous (LL). Additionally, cases were further categorized into Multibacillary (MB) and Paucibacillary (PB) according to WHO guidelines based on the Bacillary Index. Diagnosis was confirmed based on the presence of at least two cardinal signs of leprosy along with laboratory confirmation, including acid-fast positivity in a slit skin smear or biopsy report. This standardized methodology ensured the accurate classification and assessment of leprosy incidence in Sindh.

RESULTS

In the study, a total of 239 new cases were collected from seventeen different leprosy centers and clinics located in different districts of interior Sindh during the period of four years, i.e., from 2019 to 2022.

Table No.1: Demographic characteristics of study population

Variable	n(%)	
Gender	Male	154 (64.43 %)
	Female	85 (35.56%)
Age	1-15 years	57 (23.85%)
	15-30 years	86 (35.98%)
	31-45 years	74 (30.96%)
	45 years and above	22 (9.20%)
Residence	Urban	82 (34.31%)
	Rural	157 (65.69%)



Graph No.1: Different Types of Leprosy

According to gender-wise data, male patients (64.43%) seemed to be somewhat more than female patients 85(35.56%). The mean age of all leprosy cases was 42.44 ± 10.22 years and ranged from 3 years to 59 years, while in the study, according to the 15–30-year-old age group 86 (35.9%), it affected more patients than 31–45-year-old patients 74(30.96%), and 57(23.85%) and 22(9.2%) seemed to be in the 1–15 years and 45 years and above groups. In addition, 157(65.69%) patients belonged to rural communities, and the remaining 82(34.31%) belonged to urban communities in the study.

In the study, the different types of leprosy, such as tuberculoid 86(35.98%), borderline tuberculoid 74(30.96%), borderline borderline (BB) 57(23.85%), borderline lepromatous (BL) 22 (9.2%), and lepromatous lepromatous (LL) 14 (3.69%), were the most prevalent forms of the illness in the said four-year period. Paucibacillary (PB) cases made up 67(28.04%), and multibacillary (MB) instances made up 172(70.96%). The year-wise leprosy data and types were presented in Tables 2, 3, 4, 5, and graph1 respectively.

Table No.2: Various Types of Leprosy year-wise 2019

CENTERS 2019	Types						Types		
Leprocy Center	T.T	BT	BB	BI	LL	Total	M.bac	P.bac	Total
LMC(Jam)	1	4	0	0	1	6	6	3	9
LFD (Hyd)	5	1	0	1	0	7	3	3	6
Thana Bola khan	2	2	0	1	0	5	3	2	5
Kotri KT	3	2	0	0	0	5	3	3	6
Thatta	1	0	0	0	0	1	0	1	1
Dadu	2	0	0	0	0	2	0	2	2
Mirpur Khas	0	1	1	3	0	5	5	0	5
Badin	0	0	1	0	0	1	1	0	1
Sanghar	0	0	2	1	0	3	4	0	4
Nawabshah	2	2	0	2	0	6	4	2	6
Sakrand	0	2	0	2	0	4	4	0	4
Khairpur	0	3	0	0	0	3	3	0	3
Lakana	0	3	0	2	1	6	6	0	6
Shikarpur	0	0	1	2	1	4	4	0	4
Jacababad	1	0	0	0	2	3	2	1	3
KK	3	4	1	3	0	11	5	2	7
Mirpur Mathelo	1	3	0	0	0	4	3	1	4
Total	21	27	6	17	5	76	56	20	76

Table No.3: Various Types of Leprosy year-wise 2020

Centers 2020	Types						Type		
Leprocy Center	T.T	BT	BB	BI	LL	Total	M.bac	P.bac	Total
LMC(Jam)	1	1	0	0	0	2	0	1	1
LFD (Hyd)	1	1	0	0	0	2	2	2	4
T B khan	1	1	0	0	0	2	1	0	1
Kotri KT	1	0	1	0	0	2	1	2	3
Thatta	1	1	0	1	1	4	1	0	1
Dadu	0	0	1	2	0	3	4	1	5
Mirpur Khas	0	0	0	0	0	0	3	0	3
Badin	1	0	0	0	0	1	1	0	1
Sanghar	1	1	0	1	0	3	2	1	3
Nawabshah	1	2	0	0	0	3	2	1	3

Sakrand	1	1	0	0	0	2	2	2	4
Khairpur	1	1	0	0	0	2	0	0	0
Lakana	1	4	0	1	0	6	3	1	4
Shikarpur	0	1	0	1	1	3	2	1	3
Jacababad	0	1	0	1	0	2	2	0	2
KK	0	1	0	0	0	1	1	0	1
M.Mathelo	1	1	0	0	0	2	1	0	1
Total	12	17	2	7	2	40	28	12	40

Table No.4: Various Types of Leprosy year-wise 2021

Centers 2021	Types						Type		
Leprocy Center	T.T	BT	BB	BI	LL	Total	M.bac	P.bac	Total
LMC(Jam)	1	1	0	1	0	3	3	1	4
LFD (Hyd)	2	1	1	1	0	5	4	1	5
T B khan	0	1	0	0	1	2	1	0	0
Kotri KT	1	1	0	0	0	2	2	2	4
Thatta	2	0	0	1	0	3	1	1	2
Dadu	2	2	1	1	1	7	3	1	4
Mirpur Khas	0	0	0	2	0	2	1	1	2
Badin	0	0	0	0	1	1	0	0	0
Sanghar	0	1	0	0	0	1	0	0	0
Nawabshah	0	1	0	1	0	2	1	1	2
Sakrand	1	2	1	1	0	5	3	1	4
Khairpur	1	2	0	0	0	3	2	0	2
Lakana	2	2	1	1	0	6	5	1	6
Shikarpur	1	3	0	0	0	4	2	1	3
Jacababad	1	2	0	0	0	3	2	2	4
KK	2	2	0	0	0	4	5	2	7
M.Mathelo	0	0	0	0	0	0	2	1	3
Total	16	21	4	9	3	53	37	16	53

Table No.5: Various Types of Leprosy year-wise 2022

Centers 2022	Types						Type		
Leprocy Center	T.T	BT	BB	BI	LL	Total	M.bac	P.bac	Total
LMC(Jam)	2	0	0	0	0	2	1	1	2
LFD (Hyd)	2	1	1	1	1	6	4	2	6
T B khan	1	3	0	0	0	4	4	1	5
Kotri KT	1	1	0	0	0	2	3	1	4
Thatta	1	0	0	2	0	3	3	1	4
Dadu	1	2	0	1	0	4	3	1	4
Mirpur Khas	1	3	1	1	0	6	4	1	5
Badin	0	0	0	0	0	0	0	1	1
Sanghar	2	1	1	2	0	6	4	2	6
Nawabshah	2	2	0	2	0	6	3	2	5
Sakrand	1	2	0	0	0	3	3	0	3
Khairpur	2	0	0	1	0	3	2	1	3
Lakana	1	5	1	2	0	9	5	3	8
Shikarpur	2	3	0	1	0	6	4	0	4
Jacababad	1	2	0	1	0	4	3	1	4
KK	2	1	0	0	0	3	2	1	3
M.Mathelo	1	1	0	1	0	3	3	0	3
Total	23	27	4	15	1	70	51	19	70

DISCUSSION

According to health data, it is observed that leprosy due to M. leprae infection affects 239 individuals, making it essential to have an effective leprosy control program. Due to the high prevalence of leprosy in the world's poorest regions, environmental variables such as unsanitary living conditions, overpopulation, and starvation may also be factors that favor the infection.[11]

Leprosy has been declining slowly but steadily in Pakistan, with the current prevalence ranging from 250 to 350 cases per year. For many years, Sindh province has borne the largest burden of serious illness, accounting for almost 40% of total new cases each year. Leprosy data for Pakistan highlight a long-term trend of fewer new cases being discovered, although more work is still needed to eradicate this disease. There were 397 new leprosy cases discovered in 2016, 40 of which were reported to be new cases.[12]

Following the policy of "the sooner the better," which calls for early diagnosis and adherence to multiple drug therapies, clinical workups on leprosy are conducted in all clinics and centers across the nation, including the districts of interior Sindh and nearby, which is an endemic region for leprosy in Pakistan.[13]

Clinics and centers play a critical role in diagnosis, registration, management, information, and record-keeping for the strategic plan to control illness in the region.

In this study, 239 leprosy cases were identified, of which 64% were male and 36% were female. A study conducted at the leprosy center in Karachi, shows 77% male and 23% female means a 3:2.1 ratio.[14]

A similar outcome was observed in a study conducted in China from 2010 to 2015, during which time 2900 new cases were discovered.[15] Although the age distribution of the patients appeared to be identical, an Indian retrospective study revealed a significant association between the different age groups.[16] Among these all cases, 134 were probably delayed diagnosed after 1 year, and this observation correlates with these studies.[17]

This can coincide with the WHO's objective of eradication whenever skilled technical staff members is working on the project, and general statistics on the subject frequently face issues with dependability due to missing data, differing policies for particular groups, and difficulty in diagnosis. It is necessary for the team involved to control the disease through NGOs and public institutes in the country.

CONCLUSION

In a leprosy-endemic area, such data can help plan an effective control program in the region. Effective health interventions will be required among communities and health personnel to reduce morbidity and mortality.

Author's Contribution:

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

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Original Article

Comparison Between Dexmedetomidine Plus Bupivacaine and Simple Bupivacaine for Post-Operative Pain Relief Among Pregnant Women Undergoing Cesarean Section Under Spinal

Salman Athar Qureshi, Faiqa Qurban and Muhammad Usman Ilyas

ABSTRACT

Objective: To compare the effects of Bupivacaine plus dexmedetomidine versus Bupivacaine in terms of postoperative pain relief in c-section patients under spinal anesthesia.

Study Design: Randomized Controlled Trial study

Place and Duration of Study: This study was conducted at the Department of Anesthesiology / ICU, DHQ Teaching Hospital Gujranwala from August-21 to September 22.

Methods: After Hospital Ethical Committee approval, 60 eligible inpatients were enrolled. Group D received 1.5 ml of hyperbaric 0.75% bupivacaine plus 1 ml of dexmedetomidine (10 mcg/ml), while Group B received only 1.5 ml of hyperbaric bupivacaine. The first analgesic requirement, pain intensity, vitals, and side effects were recorded. Analgesia was given only if pain was reported: paracetamol 1g IV for mild pain, ketorolac 30 mg IV for moderate pain, and nalbuphine 4-6 mg IV for severe pain.

Results: The mean patient age was 25.77 ± 5 years. In Group D (n=30), 6 (20%) required ketorolac 30 mg IV, 15 (50%) needed paracetamol 1 g IV, and 9 (30%) required no analgesia within 120 minutes postoperatively. In Group B (n=30), 9 (30%) required nalbuphine 4-6 mg IV, 6 (20%) needed ketorolac, 8 (27%) required paracetamol, and 7 (23%) required no analgesia. The Chi-square test showed no significant difference in comorbidities ($p=0.44$) or baseline HR, DBP, SBP, and MAP ($p>0.05$). However, HR, DBP, SBP, and MAP differed significantly between groups throughout the study ($p<0.001$).

Conclusion: The use of dexmedetomidine with Bupivacine significantly reduce the need of analgesia as compared to Bupivacaine alone.

Key Words: Dexmedetomidine, Bupivacaine , Post operative analgesia, Spinal anesthesia

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INTRODUCTION

Dexmedetomidine a new drug introduced in market which claims to provide better analgesia and prolongation of post operative pain relief.[1] The efficacy of Dexmedetomidine has been assessed in terms of post operative pain relief when used with Bupivacaine in subarachnoid block for cesarean section patients. Its administration with Bupivacaine also reduces the chance of neurotoxicty.

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It also provides good analgesia with minimum interaction with other drugs. Dexmedetomidine administration also reduces the chances of shivering in post operative anesthetized patient.[2,3]

Studies have shown that this combination enhances pain relief, extends analgesic duration, reduces opioid consumption, and improves patient satisfaction.[4] One of the primary benefits of dexmedetomidine is its ability to prolong analgesic duration. Patients receiving only bupivacaine typically require rescue analgesics around 7 hours after the subarachnoid block. However, when dexmedetomidine is added, the duration of analgesia extends significantly, often lasting up to 9 hours or more.[5] Some studies even report that the analgesic effect nearly doubles compared to bupivacaine alone. Pain control is a key advantage, as patients receiving bupivacaine with dexmedetomidine experience consistently lower postoperative Visual Analog Scale (VAS) pain scores compared to those receiving bupivacaine alone. The enhanced pain relief becomes

noticeable within the first hour after surgery and remains superior throughout the postoperative period.[6]

The safety profile of this combination is also favorable. Both groups maintain hemodynamic stability, with no significant differences in blood pressure or oxygen saturation levels. Importantly, dexmedetomidine does not lead to an increased incidence of adverse effects such as hypotension or bradycardia. Additionally, patients receiving dexmedetomidine report a lower incidence of adverse effects. Neonatal health outcomes remain unaffected, further supporting the safety of this combination for cesarean section patients.

Another important benefit of dexmedetomidine is its opioid-sparing effect. Patients receiving this combination require fewer rescue opioid doses postoperatively compared to those in the bupivacaine-only group.[7] This reduction in opioid use helps minimize opioid-related side effects and enhances overall recovery. Moreover, maternal satisfaction is higher in the dexmedetomidine group due to prolonged pain relief and a decreased need for additional analgesics.[8] The improved comfort and reduced opioid consumption contribute to a better overall postoperative experience.

This study evaluated the effectiveness of pre-operative administration of Dexmedetomidine in post Operative pain in patient undergoing Cesarean Section with Spinal Anesthesia. Dexmedetomidine mixed with Bupivacainehas been given intratheacal and their effect has been compared with cases in which only Bupivacaine given intrathecal for cesarean sections and the post operative pain relief has been assessed.

METHODS

In this study, postoperative pain intensity of pain was measured using the Numeric Rating Scale (NRS) and the Verbal Rating Scale (VRS), where patients were asked to rate their pain on a scale of 0 to 10. The study duration was twelve months following the approval of the synopsis. The calculated sample size comprised 80 patients, with 40 in each group. The sample size was determined using the formula $n=Z^2 Pq/d^2$, where Z=1.96 at a 95.9% confidence interval, P=the proportion of patients requiring analgesia, q=1-0.959, and d=0.05. The sampling technique employed was non-probability purposive sampling.

The inclusion criteria for this study encompassed patients aged 18-40 years, weighing between 45-85 kg, and undergoing cesarean section under spinal anesthesia. Patients with a history of previous spinal surgery, diagnosed pregnancy-induced or essential hypertension, and diabetes mellitus were excluded. The patients were divided into two groups: Group B, which received 1.5 ml of 0.75% hyperbaric Bupivacaine, and Group D, which received 1.5 ml of 0.75% hyperbaric Bupivacaine combined with 10 mcg of Dexmedetomidine.

Following approval from the hospital's ethical committee, 60 patients who met the inclusion and exclusion criteria were recruited from the inpatient department. Baseline data, including name, age, weight, and hospital registration number, were recorded. The patients were randomly assigned to one of the two groups using the draw method before the induction of anesthesia.

All patients received spinal anesthesia using a 25G Quincke needle at the L3-L4 or L4-L5 space in a sitting position. Patients in Group D were administered 1.5 ml of hyperbaric 0.75% Bupivacaine along with 1 ml of Dexmedetomidine (10 mcg/ml), whereas Group B received only 1.5 ml of hyperbaric Bupivacaine. After the administration of spinal anesthesia, patients were placed in a supine position and observed for sensory and motor block. The duration of surgery was recorded.

Postoperative pain assessment was conducted at predefined time intervals: 30 minutes, 60 minutes, 120 minutes, 240 minutes, 360 minutes, and 720 minutes following spinal anesthesia. At each of these time points, patients were asked to rate their pain intensity. The time of the first request for analgesia was noted, along with pain severity, heart rate, blood pressure. Pain intensity was classified according to the predefined operational definitions. No analgesic was administered to patients who reported no pain. For mild pain, Paracetamol 1 g intravenous infusion was used; for moderate pain, Ketorolac 30 mg intravenous was given; and for severe pain, Nalbuphine 4-6 mg was administered. All data were meticulously recorded on a structured proforma.

Quantitative variables such as age, numeric rating system scores, blood pressure, heart rate, and the number of analgesic doses were presented as mean ± standard deviation (SD). An independent t-test was applied for the comparison of quantitative variables between the two groups. Qualitative variables, including pain severity, visual rating scores, and time to first analgesia, were presented as frequencies and percentages. A t-test was also used for comparing these categorical variables.

RESULTS

A total of 60 participants were enrolled in this study from the Department of Anesthesiology and Intensive Care Unit (ICU) at DHQ Teaching Hospital, Gujranwala, affiliated with the University of Health Sciences, Lahore, Pakistan. The mean age of the participants was 25.00 ± 5.99 years. In Group D (Bupivacaine + Dexmedetomidine), out of 30 participants, 6 required Ketorolac (30 mg), 15 required Paracetamol (1 g), and 9 did not require any analgesia. In Group B (Bupivacaine alone), out of 30 participants, 9 required Nalbuphine (4-6 mg), 6 required Ketorolac (30 mg), 8 required Paracetamol (1 g), and 7 did not require any analgesia.

The overall mean Numeric Rating Scale (NRS) pain score for all patients was 1.30 ± 0.93, with a minimum score of 0 and a maximum score of 3. A comparison of pain scores between the two groups revealed that the mean NRS pain score in Group D was 0.80 ± 0.71, whereas in Group B, it was 1.80 ± 0.84. This difference was statistically significant (p-value < 0.001) (Table 1).

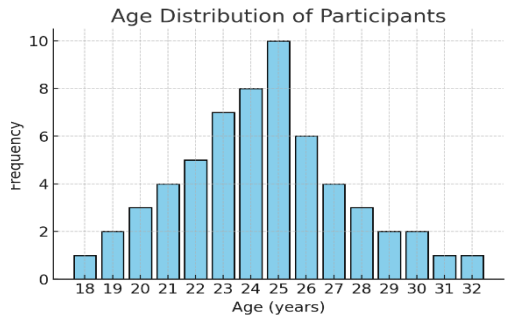

Figure No. 1: Age Distribution (Histogram) – Shows the frequency of participants in different age groups.

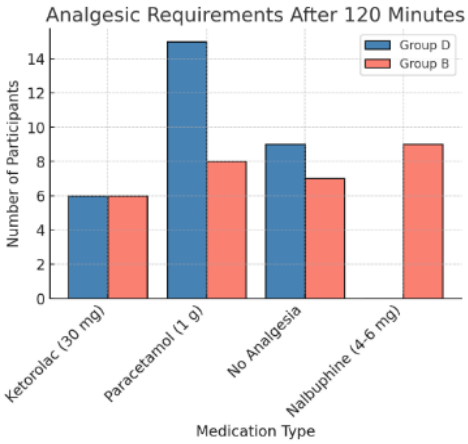

Figure No. 2: Analgesic Requirements (Stacked Bar Chart) – Compares the number of participants requiring different analgesics between Group D and Group B.

Table No. 1: showing the details of the NRS Pain Scores between Groups

Study Group	n	Mean NRS Score	Standard Deviation	p-value
Group D (Bupivacaine + Dexmedetomidine)	30	0.80	0.71	<0.001
Group B (Bupivacaine Alone)	30	1.80	0.84	

DISCUSSION

The addition of either Nalbuphine or Dexmedetomidine to epidural Bupivacaine significantly enhances postoperative analgesia; however, Dexmedetomidine offers several advantages, making it the superior choice. It provides a faster onset of pain relief by acting on α2-adrenergic receptors, which reduce nerve excitability and enhance local anesthetic effects. Additionally, Dexmedetomidine ensures a longer duration of analgesia by modulating nociceptive transmission in the spinal cord and central nervous system, reducing the need for rescue analgesics.[10] Compared to Nalbuphine, which, as an opioid, can cause pruritus, nausea, and mild respiratory depression, Dexmedetomidine demonstrates better hemodynamic stability and fewer sedation-related side effects. Furthermore, due to its ability to provide better pain control, fewer adverse effects, and reduced dependence on additional analgesics, Dexmedetomidine results in higher patient satisfaction.[11] Given its superior analgesic profile and safety, Dexmedetomidine emerges as the preferred epidural adjuvant for postoperative pain management in lower limb orthopedic surgeries, offering an effective and well-tolerated option in multimodal pain management strategies.[12]

Data collection was done at Department of Anesthesia DHQ Hospital, Gujranwala. In this study, mean age of patients was 25.77 ± 5 years. Out of 30 participants of group D only 6 need ketorolac 30mg I/V(20%) & 15 participants need 1 gm I/V Paracetamol (50%) while 9 participants need no analgesic (30%) after first 120 min of post op care. On the other hand out of 30 participants of group B,9 participants need nelbuphine 4-6 mg(30%), 06 participants need ketorolac 30 mg I/V (20%), 8 participants need 1gm paracetamol (27%) and only 7 participants need no analgesic (23%) after first 120 min of post op care. On statistical analysis using the Chi-square test, it was found that the co-morbidities between those in groups A and B were not statistically significant (p = 0.44). There was no significant difference in baseline values between HR, DBP, SBP, and MAP groups (p-value > 0.05). Throughout the study, there was a statistically significant difference in HR, DBP, SBP, and MAP between Group (A) and Group (BP) (p < 0.001).

One study by Houman Teymourian et al[13] concluded that intrathecal usage of the dexmedetomidine as adjuvant therapy with bupivacaine during obstetric surgeries like c-sections provide very impressive analgesic properties both intra or post-operative periods by showing no significant effect on the child APGAR scores or any sort of adverse reactions. The bupivacaine group showed delayed initiation of pain post-operatively and also sedation score based on Ramsay sedation score was improved with values initially as 0 to 3 and then 1 to 4. The APGAR score was insignificant within the two groups under consideration.

But significant distinction found regarding BIS among the two groups during their c-sections.

In another study by Sun et al[14] demonstrated that using bupivacaine with dexmedetomidine showed similar results as using fentanyl with bupivacaine regarding APGAR score with insignificant difference among both groups.

A study by Hala Ezzat Abdelnaim et al found that injecting a dexmedetomidine–bupivacaine mixture into the wound before making the skin incision reduces the need for anesthesia during surgery, provides longer-lasting pain relief.[15] One study by Urvashi Yadav et al[16] documented that analgesia duration was significant among patient with group D showing higher value (19.93 ± 3.2) as compared to group B (12.13 ± 1.8) with lesser demand of analgesia among group D individuals in comparison to group B respondents. The total rescue analgesics requirement in group D was 62.51 ± 39.13 and in other one (group B) was 95.68 ± 33.5 with significant p-value <0.05.

A recent study by Deshwal et al[17] found that adding dexmedetomidine to ropivacaine for wound infiltration in microdiscectomy patients provides effective postoperative pain relief while maintaining stable hemodynamics and avoiding sedation. Dexmedetomidine has been widely used as an adjuvant to local anesthetics in various surgeries, consistently showing similar benefits.

This discussion and our results suggest that dexmedetomidine enhances the analgesic duration and reduces the need for postoperative analgesics. The combination of bupivacaine and dexmedetomidine provides superior postoperative analgesia compared to bupivacaine alone, making it a more effective option for pain management in C-section patients under spinal anesthesia.

CONCLUSION

These results demonstrate that the addition of dexmedetomidine to bupivacaine in spinal anesthesia significantly improves postoperative analgesia, reducing pain scores and the need for stronger analgesics.

LIMITATIONS: One of the key limitations of this study is its relatively small sample size, which may limit the generalizability of the findings. Additionally, the study was conducted at a single center, which may introduce selection bias and restrict the applicability of the results to broader populations. Another limitation is the relatively short follow-up period, which prevents an assessment of long-term analgesic efficacy and potential delayed adverse effects of dexmedetomidine. The study also did not account for potential confounding factors such as variations in individual pain tolerance, postoperative care differences, and anesthesia provider experience, which could have influenced the outcomes. Furthermore, while the study effectively compared pain relief between the two groups, it did not evaluate patient satisfaction comprehensively, which is a crucial component of postoperative care. Future studies with larger sample sizes, multicenter designs, and extended follow-up periods are needed to validate these findings and explore additional clinical outcomes.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Salman Athar Qureshi
Drafting or Revising Critically:	Faiqa Qurban, Muhammad Usman Ilyas
Final Approval of version:	All the above authors
Agreement to accountable for all aspects of work:	All the above authors

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Original Article

Comparison of Outcome of Median and Paramedian Spinal Anaesthesia in Patients Undergoing Elective Lower Abdominal General

Zain Fatima, Salman Athar Qureshi and Faiqa Qurban

ABSTRACT

Objective: To evaluate the risk of postdural hypotension and postdural pulsus paralysis (PDPH and PDPB, respectively) in patients following elective lower abdomen general operations under spinal anesthesia.

Study Design: Randomized Controlled Trial study

Place and Duration of Study: This study was conducted at the Department of Anesthesia DHQ, Gujranwala from December 27, 2021 to June 27, 2022

Methods: After approval of hospital ethical committee a total of 216 cases (108 cases in each group) were enrolled after taking informed consent. Their basic demographical details, contact details and type of surgery was noted. All procedures were done by single anesthesiologist to ensure the no bias. Patients were randomly divided into 2 groups using lottery method.

Results: The mean age of patients in median and para median groups were 37.20 ± 12.31 years and 38.38 ± 11.59 years. In Median group, there were 37(34.26%) male and 71(65.74%) female cases while in Para median group there were 44(40.74%) male and 64(59.26%) female cases. The frequency of PDPH was statistically lower in Para medina group (3.7%) as compared to Median group (18.5%), p-value < 0.05. The frequency of PDPB was also statistically lower in Para median group (4.6%) as compared to Median group (13.9%), p-value < 0.05.

Conclusion: The incidence of PDPH and PDPB was found less in para median group as compared to median spinal anesthesia in patients undergoing elective lower abdominal general surgeries.

Key Words: General surgery, spinal anesthesia, median, para median approach, pain

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INTRODUCTION

Isolating local anesthetics like cocaine (the only naturally occurring local anesthetic) was the initial step in developing regional anesthesia. In 1898, in Germany, August Bier conducted the first surgery using spinal anaesthetic, making it the first regional anesthetic procedure to be used. Surgery involving the lower extremities, the genitourinary tract, the reproductive organs, or the abdominal cavity are among the most frequent surgical procedures for which spinal anesthetic is employed.[1]

Up to 25% of patients undergoing a lumbar puncture report experiencing symptoms of postdural puncture headache (PDPH), which are thought to be caused by intracranial hypotension due to decreased cerebrospinal fluid (CSF) pressure.[2]

The pain usually subsides on its own, but it may become highly bothersome for the patient and the anesthesiologists if it persists for too long.[2] The headache is typical changes with position and in a throbbing pattern also accompanied by photophobia and vision blurring. Unfortunately, the incidence of PDPH is higher in parturients compared to other patients.[3,4]

The paramedian approach involves inserting the needle 1 centimeter laterally and 1 centimeter caudally from the caudal margin of the superior spinous process in the sagittal plane.[4] When using this method, the needle will initially make contact with the ligamentum flavum rather than the interspinous or supraspinous ligaments.[4]

A study was done on different surgical procedure, and reported that in paramedian approach, 48 (4%) of the patients complained headache while in median approach, 20% cases reported spinal headache. In median approach, 10% patients complained of back pain while in paramedian approach, 2% patients complained of back pain. One more study was done on different surgical procedures and reported that the overall incidence of Postdural puncture

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backache (PDPB) was higher in the median Group (18/50, 36%) than in the Paramedian Group (8/50, 16%) (P = 0.023).[4]

The current study is designed with a rationale to compare outcome of median and paramedian spinal anesthesiain patients undergoing elective lower abdominal general surgeries in our setup. Although local and global data is available on these techniques but back pain is different in reported studies for both techniques.[2,4] Local studies were also done but they had different outcome[5] and studied population was also different, was done on C-section or elderly population was taken[6-7].

Hence this study focused on elective lower abdominal general surgeries in adult cases. After the results of this study appropriate preoperative prophylactic preventive (medication, needle preference, needle bevel direction, etc.) and therapeutic options may done to reduce the related discomfort and complications.

METHODS

The study aimed to evaluate the risk of postdural hypotension and postdural pulsus paralysis (PDPH and PDPB, respectively) in patients undergoing elective lower abdomen general surgeries under spinal anesthesia.

This randomized controlled trial was conducted in the Department of Anesthesia at DHQ, Gujranwala, over six months from December 27, 2021, to June 27, 2022. A total of 216 cases were included, with 108 patients in each group. The sample size was estimated based on the percentages of back pain in the median group (10%) and in the paramedian group (2%), with 80% power of the test and a 5% level of confidence. Patients were selected using a non-probability consecutive sampling technique.

Patients aged 18–59 years, of both genders, with an American Society of Anesthesiologists (ASA) physical status of Class I or II, who were undergoing elective lower abdominal general surgeries, were included in the study. Patients with a preoperative diagnosis of cluster headache, migraine, stress headache, or tension headache, a history of bleeding diatheses, traumatic deformity or congenital abnormalities of the lumbar spine, refusal of spinal anesthesia, or pregnancy were excluded.

Following approval from the hospital's ethical committee, all eligible patients were recruited from the Department of Anesthesia at DHQ, Gujranwala, after obtaining informed consent. Demographic details, contact information, and type of surgery were recorded. To minimize bias, all procedures were performed by a single anesthesiologist. Patients were randomly assigned to two groups using the lottery method.

Before the procedure, all patients were equipped with a wide-bore IV catheter and standardized monitoring. Spinal anesthesia was administered in the sitting position using a 25-gauge Quinke needle. Surgery was initiated after successful anesthesia administration. Postoperatively, patients received 100ml of Provas IV every 8 hours and 4mg of Nelbine IV as needed.

Follow-up visits were scheduled at 12-hour intervals. Some patients experienced no pain, while others had mild, moderate, or severe pain. Patients with pain were reassured and advised to increase fluid and caffeine intake. They were also prescribed 3 liters of Ringer's lactate per day and 2 tablets of Panadol Extra three times a day. Patients who did not recover were advised to undergo an epidural patch or sphenopalatine block.

Patients were monitored for postdural puncture backache (PDPB) for one month and postdural puncture headache (PDPH) for 24 hours. PDPH was measured using a visual analogue scale (VAS) ranging from 0 to 10, where 0 indicated no pain and 10 represented the worst pain. PDPH was considered significant if the pain score was ≥4/10 within 24 hours post-procedure. PDPB was also measured using the VAS after one month, and it was recorded if the pain score was ≥4/10.

Data collected during the study were entered and analyzed using SPSS version 24. The Chi-square test was applied to compare the occurrence of PDPH and PDPB between the two groups. All results were recorded on an attached proforma.

RESULTS

The mean age of patients in median and para median groups were 37.20 ± 12.31 years and 38.38 ± 11.59 years. The mean weight of all cases was 77.32 ± 15.67 kg, the mean height was 1.69 ± 0.10 m and mean BMI was 27.17 ± 5.71. In Median group, there were 37(34.26%) male and 71(65.74%) female cases while in Para median group there were 44(40.74%) male and 64(59.26%) female cases. According to ASA classification, in median group there were 66(61.11%) cases who had ASA-I and 42(38.89%) cases had ASA-II while in Para median group, there were 58(53.70%) cases who had ASA-I and 50(46.30%) cases had ASA-II.

Table No. 1: Demographics of patients at enrollment

	Study group	
	Median	Para median
n	108	108
Age (years)	37.20 ± 12.31	38.38 ± 11.59
Gender		
Male	37 (34.3%)	44 (40.7%)
Female	71 (65.7%)	64 (59.3%)
Weight (kg)	75.53 ± 14.99	79.11 ± 16.19
Height (m)	1.68 ± 0.10	1.70 ± 0.09
BMI	26.78 ± 5.56	27.56 ± 5.85
ASA		
I	66 (61.1%)	58 (53.7%)
II	42 (38.9%)	50 (46.3%)

Table No.2: Comparison of outcome in both study group

		Groups		Total	P-value
		Median	Para median		
N		108	108	216	
Post dural puncture Headache	Yes	20(18.5%)	4(3.7%)	24(11.1%)	0.001
	No	88(81.5%)	104(96.3%)	192(88.9%)	
Post dural puncture Backache	Yes	15(13.9%)	5(4.6%)	20(9.3%)	0.019
	No	93(86.1%)	103(95.4%)	196(90.7%)	

The frequency of post dural puncture headache was statistically lower in Para medina group (3.7%) as compared to Median group (18.5%), p-value < 0.05. The frequency of post dural puncture backache was also statistically lower in Para median group (4.6%) as compared to Median group (13.9%), p-value < 0.05.

DISCUSSION

Karl August bier is widely regarded as the forefather of spinal anesthesia. After seeing patients with postspinal headache, he theorized that the leakage of cerebrospinal fluid (CSF) caused by the use of large bore needles was to blame. The onset is usually within 2 days, and the regression is usually complete within a few days. The pain in the bifrontal and occipital regions, as well as the accompanying nausea, vomiting, neck stiffness, tinnitus, diplopia, dizziness, and severe headache, seem to worsen while the sufferer is seated or standing.[8] Excessive CSF leakage from the dural hole can lower intracranial pressure, causing tension on the pain-sensitive dura and compensatory venodilation. Using small-gauge (25–29) and noncutting bevel needles may reduce postspinal headache and low backache, but they have drawbacks such as high failure rates, cost, limited availability, and the need for an introducer.[9]

In addition, a paramedian strategy to administering a subarachnoid block has been shown to reduce the incidence of postspinal headache compared to a median approach in a trial of pregnant women undergoing spinal anesthetic for a cesarean delivery.[10] This is because the paramedian method involves a valve mechanism that prevents cerebrospinal fluid (CSF) from leaking out of the dura and into the epidural area. Low back pain is a typical post-spinal-anesthesia-in-the-median-approach complaint. The length of this discomfort ranges from three days to a week, but it may also be chronic and continue more than three months. Inflammation, reflex spasm of the paraspinous muscles, and myalgia may occur when a needle penetration causes stress to the ligaments.[11]

There is a wide variation in reported PDPB rates, from 2% to 29%. Paraspinal muscle relaxation and/or localized tissue damage are hypothesized to have a role in the pathophysiology of PDPB by excessively stretching the spinal ligaments. Local anesthetics are injected into the lumbar subarachnoid space to achieve spinal anesthesia.[12]

The subarachnoid space may be reached from a seated or lateral posture by median or paramedian methods. To perform the median approach, a needle is placed below the spinous process of the chosen upper vertebrae.[13] Patients receiving spinal anesthetic using a large-bore spinal needle may be at a higher risk for postdural puncture brain damage (PDPB), according to a review of the available literature. No studies have looked at whether or not the method of anesthesia has an influence on PDPB. It is possible that the median approach method contributes to PDPB by further straining the spinal ligaments.[14]

In the present research, participants in the Para medina group had significantly less headaches (3.7% vs 18.5%, $p < 0.05$) after undergoing a dural puncture. The Para median group also had a significantly decreased incidence of back pain after dural puncture (4.6% vs 13.9%, $p < 0.05$). A recent research compared the frequency and severity of PDPB in operations performed using median and paramedian approaches. Group M had a greater overall incidence of PDPB (18/50, 36%) than Group P (8/50, 16%) ($P = 0.023$). Eight patients in Group M and six individuals in Group P reported back discomfort twenty-four hours following surgery. Sixteen Group M patients and five Group P patients reported discomfort seven days after surgery ($P = 0.007$). After one month, five Group M patients and one Group P patient reported discomfort. After three months, just one person in each group had reported feeling any discomfort. During the course of the investigation, there were no discernible variations in NRSs across the groups. Thus, the findings of this investigation support the hypothesis that paramedian spinal anesthesia decreases the occurrence of PDPB in the immediate postoperative phase.[4]

Another research evaluated low back discomfort following lithotomy with and without spinal anesthesia using a midline or paramedian route. The specialist who administered the spinal anesthetic used both the midline and paramedian methods. Needle type Quincke 25G, inserted at 1 cm inferior and 1 cm lateral to the spinous process (midline and paramedian, respectively). An anesthesiology assistant assessed patients' levels of back pain 24 hours, 72 hours, and 7 days following

surgery using a numeric rating scale. A total of 139 participants were analyzed, and the results show that... Back discomfort was experienced by 21% of the midline group and 25.4% of the paramedian group after 24 hours. The variations between them were negligible. Within the first twenty-four hours, just the total number of attempts mattered. Patients who had spinal anesthesia more than twice had a 4.7-fold increased risk of experiencing back discomfort compared to those who underwent spinal anesthesia just once (OR 4.70, CI 1.79-10.18; p = 0.001). Therefore, the incidence of back discomfort after spinal anesthetic did not vary significantly between the midline and paramedian techniques. However, the chance of developing low back discomfort was higher for those who tried it twice or more than once[15].

Another research looked at the frequency of postoperative headache and low back pain after spinal anesthesia for lower abdominal surgery. Post-spinal headache was seen in 4% of patients after a paramedian approach, but in 20% of patients after a median one. There was a 2% and 10% backache occurrence in both groups. Both the incidence of postspinal headache and backache were shown to be statistically significantly lower in patients treated with the paramedian method (P value < 0.05). This means that the paramedian technique results in a lower rate of low back pain and headaches after spine surgery than the median approach.[8]

Another investigation into the relative risks of paramedian and median approaches to spinal anesthesia was conducted in 2016. Group M (median) and Group P (paramedian) are the two groups into which eighty patients with ASA I-III were divided. The results indicated that Group P had significantly more applications of spinal anaesthetic and longer periods of anesthesia than Group M did (p < 0.05). There were 52 immediate problems and 23 delayed complications. Both groups had similar rates of hypotension (21%), the most frequent early consequence, and post-spinal headache (8.7%; Group P, six patients; Group M, one patient). Therefore, it can be concluded that short-continuation surgical cases requiring spinal anesthetic did not vary significantly in terms of complication rates across technical techniques[16].

CONCLUSION

It is concluded that incidence of PDPH and PDPB was found less in para median group as compared to median spinal anesthesia in patients undergoing elective lower abdominal general surgeries. Hence, para median may be useful in future for lessen in pain and reduction of analgesia consumption.

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Original Article

Nurses' Practice to Prevent Complications after Ischemic Stroke and Improve Patient Outcomes

Khadija Mohammed Jassim and Widad K. Mohammed

ABSTRACT

Objective: To determine the nurses' practices about the prevention of complications after ischemic stroke.
Study Design: Pre-experimental study
Place and Duration of Study: This study was conducted at the AL-Basrah Teaching Hospitals, AL-Basrah Governorate from 16th April 2024 to 30th October 2024.
Methods: Twenty nurses, both male and female, who cared for stroke patients made up a non-probability sample.
Results: The nurses' practices do not appear to have a statistically significant effect on the clinical outcome of stroke patients, none of which are statistically significant (p-values of 0.782).
Conclusion: The nurses' practices do not appear to have a statistically significant effect on the clinical outcome of patients' strokes.

Key Words: Nurses, Practice, Complications, Ischemic Stroke

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INTRODUCTION

With an estimated cost of more than $721 billion, cerebrovascular accidents (CVAs), sometimes referred to as strokes, continue to rank as the second leading cause of mortality and the third leading cause of disability globally. The World Health Organization reports that 20,793 CVA-related deaths occurred in Iraq, accounting for 14.19 percent of all fatalities.[1]

One of the main causes of death and disability in the globe is stroke. Acute ischemic stroke (AIS) affected 77.2 million of the 101.5 million stroke victims worldwide in 2019. In the US, ischemic strokes make up 87% of all strokes, but subarachnoid hemorrhage (SAH) and intracranial hemorrhage (ICH) make up 3% and 10% of all strokes, respectively. By the age of 80, the chance of having a silent stroke is about 100%, although the lifetime risk of having an apparent stroke is roughly one in four.[2]

Several elements have been established as stroke risk factors. These factors are separated into two categories: modifiable and non-modifiable. Diabetes, asymptomatic carotid artery stenosis, hypertension (HTN), age, cholesterol, smoking, and non-valvar atrial fibrillation are among the risk factors for ischemic stroke that have been discovered.[3]

In the Middle Eastern nation of Iraq, coronary heart disease and stroke are common conditions seen in clinical settings. In the Stroke Collaborators' 2019 Global Burden of Disease Report, the incidence rates of stroke in Iraq varied from 196.2 to 218.3 per 100,000. Additionally, it is projected that over 30% of Iraqis are obese, 38% smoke, 14% have diabetes, and 35.8% have hypertension. Additionally, a lot of Iraqis report leading unhealthy lives that include eating a lot of high-calorie meals and not exercising.[4]

Choosing the right kind and degree of rehabilitation for both ischemic and hemorrhagic strokes is a top consideration for stroke patients while they are in the hospital. In addition to treatment, secondary prevention aids in the management of neurological disability-related consequences.[5]

Infection is a significant clinical consequence that stroke survivors face. Thirty percent have been reported to suffer post-stroke sequelae, with urinary tract infections accounting for one-third and pneumonia for one-third. Despite having comparatively comparable incidence rates, the two illnesses show quite different clinical pathways.[6]

An indwelling urinary catheter raises the risk of infection by 3% to 7% every day. About 25% of all hospitalized patients experience indwelling at least once a year, and 10% get a urinary tract infection. Chronic UTIs are widespread, dangerous, and expensive.[7]

To deliver excellent, patient-centered care, nurses who care for stroke patients need continual specialized training. Since they are essential members of the stroke

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neurology team, they must receive educational training. Enhancing the abilities needed for effective administration is essential.[5]

METHODS

This pre-experimental study design was used to guide this study, with the application of nursing care practices for all study participants, and performed post-test for the same participants after the researcher applied the nursing care practices to evaluate the effect of nursing care practices to prevent complications 3 months after ischemic stroke and improve patient outcomes in AL-Basrah teaching hospitals in AL-Basrah governorate from AL-Basrah teaching hospitals in the AL-Basrah Governorate from 16th April 2024 to 30th October 2024. AL-Basrah Teaching, AL-Sader Teaching, and AL-Mawani Teaching Hospital were the three hospitals where the AL-Basrah government conducted the study. Twenty nurses, both male and female, who cared for stroke patients made up a non-probability sample was enrolled. Every member of the research sample was exposed to the use of nursing care practices. Nurses who work in the neurology ward, Nurses who provide care for patients with stroke, all levels of education, and staff members who consented to participate in the research were included. All nurses who declined to be involved in the study and nurses who don't work in the neurology ward were excluded. The training was implemented in two lectures given to the nurses; the first lecture was given on the first day, and the second lecture was given on the second day, over two weeks for three days (Tuesday, Wednesday, and Thursday). The instrument of the present study was an observational checklist that used the Modified Rankin Scale (mRS), the Center for Disease Control and Prevention, and the Braden scale; the observational checklist consists of (3) parts. The gathering of demographic information from the nurses is the focus of this section. It includes (5) items relative to age, sex, educational level, years of experience, and working hospital. The observational checklist related to assessing the extent of improvement or deterioration over time of stroke consisted of (6) responses. These are scoring and rating (poor= 1 – 1.33, Fair= 1.34 – 1.66, Good= 1.67 – 2) according to Apply (2) and Not Apply (1).

RESULTS

The mean age was 32.7±8.7 years and the largest proportion of nurses 45% between 20–29 years. 45% of nurses were females and 55% were males. Half of the nurses 50% hold a diploma, while 40% have completed preparatory school education. Only 10% have a bachelor's degree in nursing. Nurses who have 11 years of experience constitute the largest group 40%, followed by those with 1–5 years 35%. Nurses belonged to Basrah Teaching Hospital 35% and Al-Sader Teaching Hospital 35%, while Mawani Teaching Hospital has a slightly smaller proportion 30% (Table 1).

Table No. 1: Distribution of nurses according to their socio-demographic characteristics (n=20)

Characteristics		No.	%
Age (years)	20 – 29	9	45
	30 – 39	5	25
	40 – 49	5	25
	50 and more	1	5
Gender	Male	11	55
	Female	9	45
Level of education	Preparatory school	8	40
	Diploma	10	50
	Bachelor	2	10
Years of experience	1 – 5	7	35
	6 – 10	5	25
	11 and more	8	40
Working Hospital	AL-Basra Teaching Hospital	7	35
	AL-Sader Teaching Hospital	7	35
	AL-Mawani Teaching Hospital	6	30

Nurses demonstrate strong adherence to practices related to the nursing care of aspiration pneumonia in stroke patients, with a high percentage applying most of the recommended observations. Key practices, such as monitoring for fever over 38.0°C, leukopenia or leukocytosis, new purulent sputum, increased respiratory secretions, shortness of breath, and changes in phlegm color, all show 75-85% compliance, leading to "Good" evaluation scores ranging from 1.75 to 1.85. Additionally, practices like assessing deterioration in gas exchange, conducting blood cultures, and monitoring for worsening cough also exhibit good compliance. However, the assessment of crackles or bronchial breathing sounds showed a lower compliance rate, with only 65% of nurses applying this observation, resulting in a "Fair" evaluation score (1.65). The highest level of compliance was observed for chest X-ray, with 90% of nurses applying this practice, earning the highest score of 1.90 ("Good") [Table 2].

Nurses are generally applying good practices related to the nursing care of pressure ulcer in stroke patients. High compliance is observed in key areas, including nutrition (90% adherence, resulting in the highest score of 1.90, "Good") and sensory perception, movement, and humidity (all showing 80-85% compliance, with scores ranging from 1.80 to 1.85, "Good"). Friction and shear, while still demonstrating a relatively high level of adherence (75%), receive a slightly lower score (1.75, "Good"). The assessment of activity showed the lowest compliance, with only 75% of nurses applying

this practice, also resulting in a "Good" evaluation (1.75) [Table 3].

Mixed adherence to nursing practices for the identification and care of urinary tract infections (UTIs) in stroke patients showed. Several observations, such as fever over 38.0°C, suprapubic tenderness, purulent drainage, and imaging tests (e.g., CT scan, ultrasound, MRI), show good compliance, with 70-90% of nurses applying these practices, resulting in "Good" evaluation scores (ranging from 1.70 to 1.90). Notably, the urine culture test to identify bacterial presence with a threshold of ≥105 CFU/ml received the highest compliance (90%), earning a "Good" score of 1.90. However, other indicators, such as cost overtebral angle pain, urinary frequency, urinary urgency, dysuria, lethargy, and vomiting, show more moderate adherence, with compliance rates ranging from 45% to 60%. These practices received "Fair" evaluations, with scores ranging from 1.45 to 1.60. The presence of urinary urgency (45% compliance) received the lowest adherence, reflecting an area that may require more focused attention (Table 4).

Nurses demonstrate strong adherence to the assessment of clinical outcome of patients, as measured by the modified Ranking Scale (mRS), for stroke patients. All nurses applied the mRS practices with 80%, with a mean score of 1.80, this reflect good nurses' practices and good clinical outcome in patients with stroke (Table 5). The nurses' practices do not appear to have a statistically significant effect on the clinical outcome of stroke patients, none of which are statistically significant (p=0.524) [Table 6). The practices of nurses and their age group do not significantly (p = 0.704) correlate (Table 7). There is no discernible correlation between nurses' practices and their sex as indicated by insignificant statistical p-values among nursing practices scores (Table 8). Nurses' practices are not significantly associated with their nursing educational level as indicated by insignificant (p=0.567) differences among nurses' practices (Table 9). The years of experience of nurses and their practices do not significantly (p=.784) correlate with nursing practices (Table 10).

Table No. 2: Evaluation of nurses' practices related to "identifies aspiration pneumonia" for patients with stroke (N=20)

The nurse observes	Scale	No. (%)	Mean	Evaluation
Presence of fever of more than 38.0 degrees	Not apply	4 (20%)	1.80	Good
	Apply	16 (80%)		
Leukopenia (≥ 4000 WBC/mm^3) or leukocytosis (≥ 12000 WBC/mm^3)	Not apply	5 (25%)	1.75	Good
	Apply	15 (75%)		
New presence of purulent sputum	Not apply	4(20)	1.80	Good
	Apply	16(80)		
Change in phlegm color	Not apply	5(25)	1.75	Good
	Apply	15(75)		
Increased respiratory secretions or increased suction requirements	Not apply	4(20)	1.80	Good
	Apply	16(80)		
Shortness of breath, or tachypnea	Not apply	3(15)	1.85	Good
	Apply	17(85)		
Presence or worsening of cough	Not apply	5(25)	1.75	Good
	Apply	15(75)		
Crackles or bronchial breathing sounds	Not apply	7(35)	1.65	Fair
Deterioration of gas exchange (increased oxygen requirements, or demand on oxygen saturation devices)	Not apply	3(15)	1.85	Good
	Apply	17(85)		
Blood culture to identify bacteria	Not apply	3(15)	1.85	Good
	Apply	17(85)		
Pleural fluid to identify bacteria	Not apply	5(25)	1.75	Good
	Apply	15(75)		
Chest X-ray	Not apply	2(10)	1.90	Good
	Apply	18(90)		

Table No. 3: Evaluation of nurses' practices related to "identifies pressure ulcer" for patients with stroke (N=20)

The nurse observes	Scale	No. (%)	Mean	Evaluation
Sensory perception	Not apply	3 (15%)	1.85	Good
	Apply	17 (85%)		
Humidity	Not apply	4 (20%)	1.80	Good
	Apply	16 (80%)		

Activity	Not apply	5 (25%)	1.75	Good
	Apply	15 (75%)		
Movement	Not apply	3 (15%)	1.85	Good
	Apply	17 (85%)		
Nutrition	Not apply	2 (10%)	1.90	Good
	Apply	18 (90%)		
Friction and shear	Not apply	5 (25%)	1.75	Good
	Apply	15 (75%)		

Table No. 4: Evaluation of Nurses' Practices related to "identifies urinary tract infection" for Patients with Stroke (N=20)

The nurse observes	Scale	No. (%)	Mean	Evaluation
Presence of fever of more than 38.0 degrees	Not apply	5 (25%)	1.75	Good
	Apply	15 (75%)		
Suprapubic tenderness	Not apply	6 (30%)	1.70	Good
	Apply	14 (70%)		
Costovertebral angle pain	Not apply	8 (40%)	1.60	Fair
	Apply	12 (60%)		
Urinary frequency	Not apply	8 (40%)	1.60	Fair
	Apply	12 (60%)		
Urinary urgency	Not apply	11 (55%)	1.45	Fair
	Apply	9 (45%)		
Dysuria	Not apply	7 (35%)	1.65	Fair
	Apply	13 (65%)		
Purulent drainage	Not apply	6 (30%)	1.70	Good
	Apply	14 (70%)		
Lethargy	Not apply	6 (305)	1.50	Fair
	Apply	14 (70%)		
Vomiting	Not apply	8 (40%)	1.60	Fair
	Apply	12 (60%)		
Urine culture to identify bacteria with a volume of ≥105 CFU/ml	Not apply	2 (10%)	1.90	Good
	Apply	18 (90%)		
Blood culture for bacterial identification (ASC/AST) Active Surveillance Culture/Testing	Not apply	3 (15%)	1.85	Good
	Apply	17 (85%)		
Imaging test evidence suggestive of infection. (CT scan, ultrasound, MRI)	Not apply	4 (20%)	1.80	Good
	Apply	16 (80%)		

Table No. 5: Evaluation of nurses' practices related to "the extent of improvement or deterioration over time" for patients with stroke (N=20)

Assessment	Scale	No. (%)	Mean	Evaluation
Modified Ranking Scale	Not apply	4 (20%)	1.80	Good
	Apply	16 (80%)		

Table No. 6: Effect of nurses' practices on clinical outcome of patients with stroke (N=20)

mRS/Practices	Unstandardized Coefficients		Standardized Coefficients	T	Sig.
	B	Std. Error	Beta		
Nursing practices	-.214	.329	-.307	-.65	.524

				2	

Table No. 7: Association among nurses' practices and their age group (N=20)

Nursing	Age (year)	Mean±SD	r^s	Sig.
Nursing practices	20 – 29	2.78±0.44	-.091	.704
	30 – 39	2.40±0.89		
	40 – 49	2.60±0.54		
	50 and more	3.00±0.58		

r^s = Spearman correlation

Table No. 8: Association among nurses' practices and their sex (N=20)

Practices	Sex	No.	Mean Rank	Mann-Whitney	Z	Sig.
Nursing practices	Male	11	9.23	35.500	-1.065	.287
	Female	9	12.06			

z = z score

Table No. 9: Association among nurses' practices and their educational level in nursing (N=20)

Practices	Qualification	N	Mean Rank	Krusk al-Wallis	Df	Sig.
Nursing practices	Preparatory school	8	9.00	1.134	2	.567
	Diploma	10	11.10			
	Bachelor	2	13.50			

Table No. 10: Association among nurses' practices and their years of experience (N=20)

Nursing	Experience (year)	Mean±SD	r^s	Sig.
Nursing practices	1 – 5	2.71±0.48	-.065	.784
	6 – 10	2.60±0.89		
	11 and more	2.63±0.51		

r^s = Spearman correlation

DISCUSSION

The current study's findings show that, with a mean age of 32.7±8.7 years, the largest proportion of nurses (45%) in the 20–29 age range. The results of this study agree with numerous studies[8-11,] which mention that most of the study samples were between 20 and 29 years old. This result is incompatible with a study conducted by Baiez and Mohammed[12] on nurses; their studied results revealed that (41.7 %) of the sample was aged between (30-39 years). According to the study's findings, 45% of nurses were females and 55% were males. Mohammed[13] reported that 24.7% were males.

In terms of nursing education, 40% of nurses have finished middle school, and 50% of nurses have a diploma. Merely 10% possess a nursing bachelor's degree. Jaddoue[14] found that 50% of nurses had completed high nursing school, is contradictory with this study. These results disagree with numerous studies[15-18,] which mention that most of the study sample has secondary school graduates or less.

The results of the current study reveal that nurses with more than 11 years of experience constitute the largest group (40%), followed by those with 1 to 5 years (35%). This study is incongruent with a descriptive study by Na'el and Mohammed[19] that 76.7% of nurses had experience in a hospital from 1 to 5 years.

This study indicates that nurses demonstrate strong adherence to the assessment of clinical outcomes of patients, as measured by the modified Rankin Scale (mRS), for stroke patients. All nurses applied the mRS practices with 80%, with a mean score of 1.80, this reflects good nurses' practices and good clinical outcomes in patients with stroke. These results are consistent with a cross-sectional descriptive study conducted by Babkair et al[20], which found that 42% of nurses said they used the mRS or other measures more often in stroke units than in the intensive care unit to evaluate patients' physical disabilities.

The present study indicates that the nurses' practices do not appear to have a statistically significant effect on the clinical outcome of stroke patients, none of which are statistically significant (p-values of 0.782). These results contradict with Abd El-Hay et al[21], showed that nurses' understanding and practice of caring for stroke patients significantly improved after the training program ($p<0.01$).

The result of the study indicates that there is no significant association between nurses' practices and their age group. The overall practices show a slightly positive correlation ($r^s=0.171$) with age but with no statistically significant ($p=0.472$).These findings disagree with Atiyah and Khudhur[22], the results of the study showed a strong positive relationship between age and nurses' practices.

The current study showed that insignificant statistical p-values among the total practice scores show that there is no significant correlation between the sex of nurses and their practices. These results are consistent with Zheng et al[23] finding that gender did not significantly differ ($p>0.05$).

The current study indicates that nurses' practices are not significantly associated with their nursing educational level, as indicated by insignificant differences among overall practices. The findings are congruent with Niyongabo et al[24], that nursing practice ratings and knowledge of PU prevention and treatment were inversely correlated with educational attainment.

According to the current study, there is no discernible correlation between the number of years of experience a nurse has and their assessment, nursing care, or general practices. There are no discernible variations in general practices, according to the p-values. The finding is agreement with Kolankoh et al[25] and were substantially connected with the nurses' care management of patients with acute stroke and job experience.

CONCLUSION

The nurses' practices do not appear to have a statistically significant effect on the clinical outcome of patients with stroke.

Author's Contribution:

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Original Article

Prevalence of Diabetes Mellitus Over the Years in Iraqi Governorates

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ABSTRACT

Objective: To determine the prevalence of Diabetes Mellitus (DM) cases in Iraqi Governorates over the years and highlight the underlying factors.

Study Design: This descriptive cross-sectional study.

Place and Duration of Study: This study was conducted at the College of Nursing, University of Al-Kufa, Kufa, Iraq from 1st April 2018 to 30th March 2022.

Methods: All patients who visit Iraqi health directorates in the Ministry of Health with a confirmed diagnosis of diabetes Mellitus were included in the study. Eighteen Health Directorates in Iraq affiliated with the Iraqi Ministry of Health were included in the Study, Kurdistan region (North Iraq) was excluded from the study. Each Health Directorate includes a different number of hospitals.

Results: A significant increase in diabetes mellitus patients over the years among males and females, the overall number (males & females) 547149 in 2018 and rose to 710359 in 2022. The males recorded 280574 in 2018 and the number increased to 352382 in 2022 while the females recorded 266575 in 2018 and dramatically increased to 357977 in 2022.

Conclusion: All the Iraqi governorates reveal a high prevalence of diabetes mellitus and the number proceeded to increase over the years, the numerals grew in both sexes. It is expected that DM become a major health problem in Iraq.

Key Words: Epidemiology, Diabetes Mellitus, Over Years, Iraqi Governorates

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INTRODUCTION

Not only in Iraq, diabetes mellitus is considered a global health problem, and the numeral going to increase. Due to stressful life events, machine-based jobs, decreased physical activity, fast food etc. the number of diabetic people is increasing.[1] Even though the predisposing factors of DM are clearly defined, the Incidence is expected to increase from 30 Million in 2025 to 80 Million in 2030 in the South East Asia Region.[2] The Middle East region has shown an epidemic increase in DM, in Basrah, Iraq, The prevalence of DM is extremely high. About every 5 adults, at least one of them suffering from DM. There is a significant strain on the health care system and fiscal resources.[3] Poor knowledge, low educational level, bad healthcare provider practices, and inadequate policymaker role-play directly affect the prevalence of DM in Iraq.[4] In the Middle East, the Number increased approximately two-five percentages per year. A regimen that includes a balanced diet, consistent exercise, and the maintenance of a healthy body mass index can potentially prevent or postpone the onset of DM. the majority risk factor of DM is obesity, providing accurate and valid data of DM prevalence rate will initiates a primary prevention plans which considered a cornerstone to minimize the incidence rate.

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METHODS

This descriptive cross-sectional study was used to identify the prevalence of diabetes mellitus over the years in Iraqi governorates. Eighteen Health Directorates were included; a non-probability (convenience) sample was used to gather all patients in the Iraqi Governorates/Health Directorates/ Governmental Hospitals. Ethical considerations are the cornerstone of the research. Official approval was obtained from the supreme council in the College of Nursing / University of Baghdad and then submitted to the Iraqi Ministry of Health/Health Directorates across the Governorates, furthermore, each patient was informed that all the subjective data would be secured. Data were collected at Consultation Departments/ Governmental Hospitals of the following Health

Directorates: Ibn Sina Hospital, Baghdad Health Directorate/Al-Karkh, Baghdad Health Directorate/Al-Rusafa, Baghdad Health Directorate/Medical City, Basra Health Directorate, Nineveh Health Directorate, Maysan Health Directorate, Diwaniyah Health Directorate, Diyala Health Directorate, Anbar Health Directorate, Babylon Health Directorate, Karbala Health Directorate, Kirkuk Health Directorate, Wasit Health Directorate, DhiQar Health Directorate, Muthanna Health Directorate, Salah al-Din Health Directorate and Najaf Health Directorate. The data was analyzed through SPSS-24.

RESULTS

Iraq, Baghdad (Capital of Iraq) Health Directorates in the Ministry of Health recorded a significant increase in the number of patients with Diabetes Mellitus (DM) in both males and females. The Health Directorates in Baghdad recorded 911604 cases from 2018 to 2022 (Table1). The Health Directorates within the Ministry of Health, located in the northern region of Baghdad (Nineveh, Salah al-Din, and Kirkuk), have reported a significant increase in the prevalence of diabetes mellitus (DM). The recorded cases were 68979 in 2018 and have been raised to 96980 in 2022 (Table 2). On the other hand, the South Baghdad Provinces which include Basrah, Maysan, Diwaniyah, DhiQar, and Muthanna also demonstrated a remarkable increase in DM prevalence, 138773 in 2018 which increased over the years to 209352 in 2022 (Table 3). The highest increase in the prevalence of DM was in the Al-Furat Al-Awsat Provinces (Diyala, Anbar, Diyala, Karbala, Wasit, and Najaf), which was 139066 cases in 2018 and dramatically worsened to 2013080 cases in 2022 (Table 4). The results of the study demonstrate a significant increase in Diabetes Mellitus patients over years among male and female, the male record 280574 in 2018 and the number increased to 353781 in 2022 while the females record 266575 in 2018 and increased to 356578 in 22022 (Fig. 1). Baghdad records the highest prevalence of DM followed by Al-Furat Al-Awsat, Southern Baghdad, and Northern Baghdad health directorates as 911604, 830511, 813041, and 378241 respectively, the overall number was 2933397 (Table 5).

Table No. 1: Baghdad (Capital of Iraq) Health Directorates

Years	Medical City		Baghdad/Al-Rusafa		Baghdad/Al-Karkh		Ibn Sina Hospital		Total
	Male	Female	Male	Female	Male	Female	Male	Female	
2018	1999	2125	80946	67282	23872	23479	481	147	200331
2019	2112	2403	79789	74623	26869	27600	100	46	213542
2020	1003	938	51381	52394	21441	21185	74	37	148453
2021	3654	3664	51330	48983	25272	25188	134	106	158331
2022	6772	7104	60849	61461	28345	26126	207	83	190947
Total	15540	16234	324295	304743	125799	123578	996	419	911604

Table No. 2: North Baghdad Health Directorates

Years	Nineveh Health		Salah al-Din		Kirkuk		Total
	Male	Female	Male	Female	Male	Female	
2018	9406	8722	8896	9156	15048	17751	68979
2019	8646	9028	10428	10429	19016	19538	77085
2020	8123	8294	6652	6457	13886	16305	59717
2021	14052	14885	9133	9852	13443	14115	75480
2022	16853	17248	13587	13131	19293	16868	96980
Total	57080	58177	48696	49025	80686	84577	378241

Table No. 3: South Baghdad Health Directorates

Years	Basra		Maysan		Diwaniyah		DhiQar		Muthanna		Total
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	
2018	12741	12172	18298	18670	12234	11812	11273	12501	15567	13505	138773
2019	16638	17460	20917	21895	14150	13491	12838	14910	13060	12375	157734
2020	19593	21672	16888	17546	7971	7385	12740	13967	13005	11606	142373
2021	26507	28714	15108	16662	9089	9142	13177	14324	16550	15536	164809
2022	36007	37474	16484	18261	12454	11168	17764	18276	21084	20380	209352
Total	111486	117492	87695	93034	55898	52998	67792	73978	79266	73402	813041

Table No. 4: Al-Furat Al-Awsat Health Directorates

Years	Diyala		Anbar		Babylon		Karbala		Wasit		Najaf		Total
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female	
2018	3003	3336	11072	11359	13038	12227	16819	17257	13734	15170	12147	9904	1390

													66
2019	3447	3462	19143	18189	15486	14875	15384	17162	11948	13237	15407	14536	162276
2020	3132	3197	22116	18780	13465	12616	11719	15584	10257	11993	12586	12109	147554
2021	4188	4242	24635	23466	17294	19568	12345	14056	13199	15122	10136	10284	168535
2022	5213	5429	27783	25221	25617	26587	17585	20779	20244	23130	7640	7852	213080
Total	18983	19666	104749	97015	84900	85873	73852	84838	69382	78652	57916	54685	830511

Table No. 5: Overall Number of patients with DM in the Iraq Regions over the years

Years	Baghdad Health Directorates	North Baghdad Health Directorates	South Baghdad Health Directorates	Al-Furat Al-Awsat Health Directorates	Total
2018	200331	68979	138773	139066	547149
2019	213542	77085	157734	162276	610637
2020	148453	59717	142373	147554	498097
2021	158331	75480	164809	168535	567155
2022	190947	96980	209352	213080	710359
Total	911604	378241	813041	830511	2933397

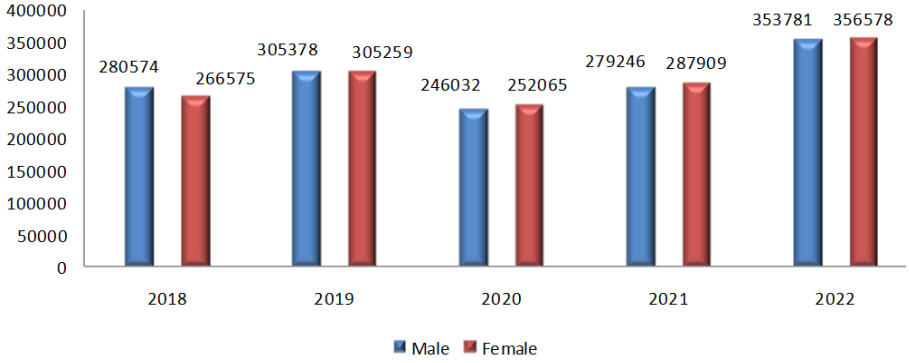

Figure No. 1: Distribution of DM patients by Sex over Years

DISCUSSION

The World Health Organization stated that the Iraqi Ministry of Health estimated that 14% of Iraqis have diabetes.[5] The incidence of type 1 Diabetes Mellitus (T1DM) has increased in the last three years in the Basrah, T1DM recorded a prevalence ratio of 87:100000 of adults <40 years old between January, 1st 2012, and December 31, 2016; the T1DM was 7.4: 100000 annual incidence rates.[6] The study results reveal that the overall number of cases in Iraqi provinces from 2018 to 2022 was 2,933,397 (Table 5), this comes along with the International Diabetes Federation (IDF) report which stated in 2021 that 9.4% of Iraqi adults have diabetes and estimates the total number of 2,011,400.[7]
Over the past three decades, there has been a consistent increase in the prevalence of diabetes worldwide, particularly in low- and middle-income countries, indicating rapid growth. This rise has also been observed in children, potentially attributed to the modernization of lifestyle. According to the International Diabetes Federation (IDF), the global prevalence of diabetes among the adult population in 2017 was estimated to be 8.8%, affecting approximately 425 million people. Among the IDF regions, the Middle East and North Africa (MENA) region recorded the second-highest rate of diabetes with a prevalence of 9.2%. Projections indicate that between 2017 and 2045, the prevalence of diabetes in the MENA region will surge by 110%, leading to an estimated 629 million cases worldwide by 2045.[8] In reference to Baghdad, the diabetes mellitus prevalence rate from 2018 to 2022 was 911604. The findings suggest a consistent increase in the prevalence over the years. This is corroborated by a cross-sectional study aimed at assessing the prevalence of pre-diabetes in Baghdad. The study, conducted on 735 Iraqi individuals, revealed that approximately 17% of the participants exhibited pre-diabetic conditions.[9] According to the 2006 national survey on risk factors for chronic non-communicable diseases in Iraq, it was found that the prevalence of diabetes mellitus (DM) is 10.4%. Notably, the survey revealed that women face a higher risk of developing type II DM, which could be linked to a greater susceptibility to adopting a Western lifestyle within specific Iraqi communities. While type II DM has traditionally been associated with adults,

there is a concerning trend of its diagnosis in children, reflecting the increasing rates of obesity.[10] Al-Rubaee Razzaq stated that in 2010 Nassiryah diabetic center estimated prevalence rate of DM was 10.2 % and this transcends the estimated prevalence rate of diabetes in the Middle East and North Africa region which was 9.3% and concluded the incidence rate had increased in the last five yrs in ALNassiryah city.[11]

Zalzala Sarah et al[12] conducted a study focusing on primary schools in the Al-Karkh region of Baghdad City, Iraq. The study encompassed 141 schools with an enrollment of 69,115 students, utilizing a multistage cluster sampling methodology. The research revealed a prevalence of type 1 diabetes mellitus at a rate of 159 per 100,000, aligning closely with prevalence rates in Saudi Arabia, lower than those in Al-Kuwait, but higher than those in Turkey. Additionally, the study observed a slightly higher proportion of female students compared to male students, with a female-to-male ratio of 1.3:1 among diabetic individuals.

Recommendation: Activate the role of the primary health care centers, the primary prevention programs are urgently required to control the expected burdens. Furthermore, conducting periodic assessments and including the private clinics to figure out the extent of the DM prevalence.

CONCLUSION

All the Iraqi governorates reveal a high prevalence of DM and the number proceeded to increase over the years, the numerals grew in both sexes. It is expected that DM become a major health problem in Iraq.

Author's Contribution:

Concept & Design or acquisition of analysis or interpretation of data:	Mohammed Abdulkareem Mustafa, Wafaa Abd Ali Hattab
Drafting or Revising Critically:	Wafaa Abd Ali Hattab, Sarah Abdulateef Kadhim, Musaab Majid Abdulwahhab
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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Original Article

Study of Biochemical Changes in Children with Autism Spectrum Disorder Aged 3-13 Years in Thi-Qarcetnter of Autism

Naeem Salih Yaser[1], Maha Fadhil Smaism[1] and Rebee Mohsin Hasani[2]

ABSTRACT

Objective: To find out the causes of autism spectrum disorder therefore some biochemical parameters were measured include serum lactate, pyruvate, lactate to pyruvate ratio, lactate dehydrogenase, ferritin and glutamate.

Study Design: Case-control study

Place and Duration of Study: This study was conducted at the Thi-Qar Autistic Center, Nasiriya City, Iraq from 1st September 2022 to 28th February 2023.

Methods: This study contained 192 children among which 96 patients were diagnosed as cases of ASD and age range was 3 to 13 years. The control group contained 96 children with ages range was 3-13 years. The Enzyme Linked Immunosorbent Assay method is applied in detection of parameters.

Results: there were significant statistical association between biochemical parameters and autism spectrum disorder in compare with control group except serum pyruvate in which there was no significant association

Conclusion: The cause of autisms spectrum disorder may be a defect in mitochondrial functions where there was elevation in serum lactate and lactate to pyruvate ratio.

Key Words: Autism spectrum disorder, Lactate, Pyruvate, Lactate dehydrogenase, Ferritin

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INTRODUCTION

Autism spectrum disorder (ASD) is a group of neurodevelopmental disorders that are characterized by early onset communication dysfunctions, limitations in social interaction, and repetitive and stereotyped movements with narrow interests.[1] The clinical picture of ASD often start to appear between 12 and 18 months and the diagnosis is typically made at two years of age.[2] Although the ASD is unknown etiology but it may be due to the interaction of multiple factors, include biological, environmental, and genetic factors.[3] The prevalence of ASD is approximately 1% in the pediatric age group worldwide. This prevalence has increased over time, and there are variations within and between sociodemographic groups.[4] The prevalence of ASD is about 2% in the pediatric age group in the United States.[5]

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The incidence is unaffected by race or ethnicity, and children from low socioeconomic status may delay diagnosis. The male to female ratio is about 4:1 and the recurrence rate among identical twins is high[6] and ASD is classified as a mild when individuals do not receive support, with visible disturbances in social communication while in moderate type, there is marked deficiencies in communication skills and unusual response to social activities while in severe type there are severe deficiencies in social communication skills.[7,8]

METHODS

It is a case-control study was performed at Thi-Qar Autistic Center, Nasiriya City, Iraq from 1st September 2022 to 28th February 2023. The collection of samples were performed for 192 children participate in this study included the patients group who include 96 children with ASD with ages range was 3 to 13 years. The control group consists of 96 apparently healthy children with ages range was 3-13 years. After collection of 3 ml of blood sample from all participant in serum separating gel tubes for biochemical tests and were allowed to clot for 15 minutes and then centrifuged at 1800 ×g for about 15 min, then separated into small aliquots and froze in a 20-ºC to be used for estimation of biochemical tests: serum lactate, pyruvate, ferritin, LDH, glutamate levels. The methods of measurement were enzyme linked immunosorbent assay kits from SunLong-biotech, China. This study

was approved based on the ethical principles that originated in the Declaration of Helsinki. It was conducted with patients' verbal and analytical approval before taking the sample. Children with schizophrenias, cerebral palsy and patient with iron supplement were included. The data was analyzed using Software Package for Social Science (SPSS-22.0 version). The t-test has been used to determine the significant difference between the groups. Significant difference if $p<0.05$, while very significant if $p<0.01$ and high significant if $p<0.001$.

RESULTS

There was a significant elevation in serum lactate in autistic patients subgroups (G1 and G2) in compared with control subgroups ($P<0.05$) and there were no significant difference in serum lactate and all other parameter in this study between patients sex subgroups of male and female ($p>0.05$) also between two patients age subgroups (G1 and G2) ($p>0.05$). The normal value of serum lactate is less than 22mg/dl (Table 1).

There was a no statistically significant difference between autistic patients age subgroups and apparently healthy control age subgroups in serum pyruvate ($P>0.05$), and the normal value of pediatric pyruvate is 0.3-1.5 mg/dl (Table 2). There was a significant statistically difference in serum lactate to pyruvate ratio between autistic patients age subgroups and control age subgroup ($P<0.05$) [Table 3].

There was significant statistical elevation in serum LDH in autistic patients subgroups in compare with healthy control subgroups ($P<0.01$). The normal value for LDH in 3-13 years is 120-300 U/L (Table 4).

There was a significant statistically difference in serum ferritin between patients subgroups and healthy control subgroups ($P<0.01$) and ($P<0.01$) also there were 10 cases with low serum ferritin or anemia who form 9.6% of total patients, considering the normal range of pediatric serum ferritin matching the age is 10-105 ng/ml (Table 5).

There was very significant statistically elevation of serum glutamate in autistic patients subgroups in compare with healthy control subgroup ($P<0.01$) and ($P<0.01$). The normal value of glutamate in this age group is 0.34-3.68 mg/dl (Table 6).

Table No.1: Serum lactate levels in patients and control groups

Parameter	Subgroups	No.	Mean±SD	Min.	Max.	P-value
Serum Lactate (mg/dl)	G1:Patients (3-8 yr)	72	16± 11	4	36	P<0.05
	G1:Control (3-8 yr)	72	11.7±3.8	8	20	
	G2:Patients (9-13 yr)	24	17± 8	5	35	P<0.05
	G2:Control (9-13 yr)	24	12.2 ± 4	6	18	
	Male	75	15.7± 8	4	36	p>0.05
	Female	21	17.3± 9	6	32	
	G1: Patients (3-8 yr)	72	16 ± 11	4	36	p>0.05
	G2:Patients (9-13 yr)	24	17±8	5	35	

Table No.2: Serum pyruvate levels in patients and control groups

Parameter	Subgroups	No.	Mean±SD	Min.	Max.	P-value
Serum pyruvate (mg/dl)	G1:Patients (3-8 yr)	72	1.10±0.23	1.40	0.6	P>0.05
	G1:Control (3-8 yr)	72	0.98±0.21	1.30	0.5	
	G2:Patients (9-13 yr)	24	1.20±0.23	1.35	0.4	P>0.05
	G2:Control (9-13 yr)	24	1.1±0.20	1.25	0.5	
	Male	75	1.09±0.21	1.40	0.5	p>0.05
	Female	21	1.13±0.25	1.35	0.6	
	G1: Patients (3-8 yr)	72	1.07±0.20	1.36	0.6	p>0.05
	G2:Patients (9-13 yr)	24	1.19± 0.17	1.40	0.8	

Table No.3: Serum lactate to pyruvate ratio in patients and control groups

Parameter	Subgroups	No.	Mean±SD	Min.	Max.	P-value
Serum lactate to pyruvate ratio	G1:Patients (3-8 yr)	72	14± 10	6	21	P<0.05
	G1:Control (3-8 yr)	72	11.93±3.8	7	14.6	
	G2:Patients (9-13 yr)	24	14.4± 8	4	23	P<0.05
	G2:Control (9-13 yr)	24	11.1± 4.3	5	13	
	Male	75	14.38± 8	4	30	p>0.05
	Female	21	12.61± 6	6	28	
	G1: Patients (3-8 yr)	72	14 ± 10	6	21	p>0.05
	G2:Patients (9-13 yr)	24	14.4 ± 8	4	23	

Table No.4: Serum lactate dehydrogenase in patients and control groups

Parameter	Subgroups	No.	Mean±SD	Min.	Max.	P-value
Serum lactate dehydrogenase (U/L)	G1:Patients (3-8 yr)	72	316±155	126	450	P<0.01
	G1:Control (3-8 yr)	72	254.4± 50.5	146	290	
	G2:Patients (9-13 yr)	24	304± 128	120	436	P<0.01
	G2:Control (9-13 yr)	24	240± 60	130	280	
	Male	75	311±140	140	480	P>0.05
	Female	21	314± 110	126	420	
	G1: Patients (3-8 yr)	72	316±155	146	480	p>0.05
	G2:Patients (9-13 yr)	24	304 ± 124	160	410	

Table No.5: Serum ferritin in patients and control groups

Parameter	Subgroups	No.	Mean±SD	Min.	Max.	P-value
Serum ferritin (ng/ml)	G1:Patients (3-8 yr)	72	35±20	4	100	P<0.01
	G1:Control (3-8 yr)	72	47± 21	16	102	
	G2:Patients (9-13 yr)	24	39.7±18	5	105	P<0.01
	G2:Control (9-13 yr)	24	48.8±26	14	106	
	Male	75	36 ±22	8	100	P>0.05
	Female	21	31±20	4	90	
	G1: Patients (3-8 yr)	72	35±20	4	100	p>0.05
	G2:Patients (9-13 yr)	24	39.7±18	5	96	

Table No.6: Serum glutamate in patients and control groups

Parameter	Subgroups	No.	Mean±SD	Min.	Max.	P-value
Serum glutamate (mg/dl)	G1:Patients (3-8 yr)	72	2.28 ±0.73	0.7	3.5	P<0.01
	G1:Control (3-8 yr)	72	1.55 ± 0.38	0.9	2.6	
	G2:Patients (9-13 yr)	24	2.1±0.61	0.6	3.6	P<0.01
	G2:Control (9-13 yr)	24	1.4± 0.48	0.4	2.2	
	Male	75	2.3 ± 0.77	0.8	3.5	P>0.05
	Female	21	2.1±0.90	0.7	3.3	
	G1: Patients (3-8 yr)	72	2.28± 0.73	0.7	3.5	P>0.05
	G2:Patients (9-13 yr)	24	2.1±0.61	0.6	3.6	

DISCUSSION

The possible cause of elevation of serum lactate and lactate/pyruvate ratio is one of several inherited metabolic disorder of gluconeogenesis, pyruvate oxidation, Krebs cycle or the respiratory chain disorder or production of glycolysis overwhelms the utilization of pyruvate in mitochondria[9] or harmful variants of nuclear genes encoding mitochondrial related proteins, lead to mitochondrial dysfunction.[10,11] There was a clear link between autism and mitochondrial dysfunctions which combined with biochemical alterations.[12] These results agree with most studies of Miae et al[13] and Shahjadi et al[14] in which there were high levels of serum lactate in autistic patient in compare with healthy control group and disagree with another study in which there was low serum lactate in ASD patient in compare with control group.

Pyruvate metabolism is crucial for energy homeostasis and mitochondrial fusion/fission. In this study, there was normal level of pyruvate with high level of serum lactate and high serum lactate dehydrogenase which responsible for conversion of serum pyruvate into serum lactate and this may reflect some mitochondrial dysfunction or difficulty in conversion of serum pyruvate to acetyl CoA and instead convert to serum lactate.[15] This results agree with Miae et al[13] in which there were no significant difference between patients and control groups and disagree with Giulivi C, et al[16] in which there were elevation of serum pyruvate in autistic children in compare with control groups.

The lactate to pyruvate ratio reflects the reduction-oxidation state of the cytosolic compartment and indicates the ratio of oxidized NAD^+ to reduced NADH and in patients with ASD may decrease NAD+/NADH ratio when high lactate to pyruvate ratio[17] and much higher oxidized redox state in ASD might promote anaerobic glycolytic more than oxidative phosphorylation for supply ATP.[12] These results agree with Dhillon S, et al[11] and Oliveira et al[10] in which there were a significant elevation in serum lactate to pyruvate ratio and disagree with another study in which there was no significant difference in serum lactate to pyruvate ratio between autistic subgroups and control subgroups.

Serum LDH activity has been found to be increased in ASD patients. LDH, are often used as a marker for mitochondrial dysfunction, as less pyruvate is

metabolized through the tricarboxylic acid cycle. Lactate interconvert with pyruvate by LDH.[17] One of the major pathways involve in developmental cognitive disorders is shift in energy production from mitochondrial oxidative phosphorylation to aerobic glycolysis despite the availability of oxygen.[18] These results agree with another studies conducted by a researchers, in all studies there were significant elevation in LDH level in patients group compare to control groups and there were not found any study in with low LDH in autistic patients.

Patient with ASD has been found to eat non food material from ground (pica) and eat only limited food groups, possible with low iron content and aggressive feeding behaviors. This supports iron deficiency and malnutrition in ASD. These results agree with Pakyurek M, et al[19] and Prakash P, et al[20] in studies there were significant decrease in serum ferritin in patients group and disagree with Çelik P, et al[21] and Gunes S, et al[22] in which were no significant difference in serum ferritin between patient and control groups.

CONCLUSION

The cause of autisms spectrum disorder may be related to dysfunctions of mitochondria where there was elevation in serum lactate and lactate to pyruvate ratio and high serum glutamate may be attributed to dysfunction of carrier protein gene of mitochondria wall. Low serum ferritin in patients may be related to bad food regime intake while high LDH may be response to high serum lactate.

Author's Contribution:

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Original Article

Growth Differentiation Factor-15 as a Marker for Assessment of Anemia in Chronic Kidney Disease Patients with Type II Diabetes Mellitus

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ABSTRACT

Objective: To assess the GDF-15 in conjunction with a number of biochemical markers in individuals with advanced chronic kidney disease and either type 2-diabetes or no diabetes at all.

Study Design: Case-control study

Place and Duration of Study: This study was conducted at the Al-Yarmouk and Baghdad Teaching Hospitals in Baghdad, Iraq from 1st January 2024 to 30th June of 2024.

Methods: One hundred and fifty participants were enrolled and they were divided into three groups. One group consisted of 50 individuals with late-stage chronic kidney disease (27 men and 23 women) who also had type 2 diabetes. There were three groups: one with fifty healthy people (28 men and 22 males) and another with fifty people who were in the last stages of chronic kidney disease (24 men and 26 females) but did not have type 2 diabetes.

Results: A significant difference was found in the age group of 50–59 years when comparing CKD patients (with and without T2DM) to the control group ($p < 0.05$), while gender distribution showed no significant variation ($p > 0.05$).In CKD patients with T2DM, GDF-15 correlated significantly with serum creatinine and glomerular filtration rate (GFR), whereas in CKD patients without T2DM, it was associated with iron levels ($p < 0.05$).ROC analysis showed that GDF-15 had a sensitivity of 97% and a specificity of 100%, highlighting its potential as a diagnostic biomarker.

Conclusion: Growth differentiation factor-15 as a key factor in the development of anaemia in patients with T2DM and chronic kidney disease.

Key Words: Chronic kidney disease (CKD), Type 2 diabetes mellitus (T2DM), Growth differentiation factor-15 (GDF-15), Glomerular filtration rate (GFR), Biochemical parameters

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INTRODUCTION

Chronic kidney disease (CKD) is a worldwide public health challenge and results in substantial morbidity, mortality, and health care costs in adults. CKD is diagnosed based on the presence of abnormalities of kidney structure or function (i.e. abnormal albuminuria or glomerular filtration rate [GFR] less than 60 mL/min per 1.73m^2) for more than 3 months, with implications for health.[1]

If untreated, the condition can progress to renal failure, making it a potentially lethal illness. The likelihood of effective therapy and the length of the patient's life are both enhanced by early and accurate predictions.

Poor clinical outcomes and a diminished quality of life have been associated with anaemia, a prevalent presenting feature in persons with chronic kidney disease (CKD). Decreased erythropoietin synthesis and reticuloendothelial iron blockage are two of the mechanisms that cause anaemia in chronic kidney sickness.[2]

A biomarker of anaemia as well as cardiovascular and chronic inflammatory illnesses, growth differentiation factor 15 (GDF-15) is an important protein in the human body. Growth differentiation factor-15, macrophage inhibitory cytokine-1, non-steroidal anti-inflammatory drug-inducible gene (NAG)-1, and MIC-

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1 are some of its alternate names. The GDF-15 super family includes transforming growth factor β and other divergent members which highly expressed in the heart, liver, kidney, intestine, lung, placenta and the prostate gland.[3-5]

GDF15 gene is located on chromosome 19p12-13.1 and consists of two exons separated by intron. The release of GDF-15 is stimulated by various growth factors and cytokines, including transforming growth factor beta (TGF-β), tumour necrosis factor-alpha (TNF-α), interleukin-1β (IL-1β), macrophage colony-stimulating factor (M-CSF), angiotensin II, and p53.[6,7]

It's mainly improves the function of kidneys in CKD and plays an important role in the prediction of CKD progression[8] so when it's level increased linked to an increased risk of incident chronic kidney disease. Under physiological conditions, the placenta is the only tissue that expresses high levels of this protein, with levels peaking during the third trimester of pregnancy.[4]

Also, the expression of this stress-responsive cytokine increases in many pathological conditions such as injury, ischemia, and other forms of oxidative and/or metabolic stress, sparking interest in its potential utility as a biomarker in human disorders cancer, cardiovascular disease, diabetes mellitus, chronic obstructive pulmonary disease.[6,9] Moreover, it is one of the regulators of hepcidin synthesis and thus participates in iron homeostasis. It has been shown that high concentration of GDF-15 is responsible for the reduced synthesis of hepcidin.[10,11]

METHODS

This case-control study was conducted at Al-Yarmouk and Baghdad Teaching Hospitals in Baghdad, Iraq from 1st January 2024 to 30thJune of 2024. Out of a total of 150 participants, the study separated them into three groups. One group consisted of 50 individuals with late-stage chronic kidney disease (27 men and 23 women) who also had type 2 diabetes. There were three groups: one with fifty healthy people (28 men and 22 males) and another with fifty people who were in the last stages of chronic kidney disease (24 men and 26 females) but did not have type 2 diabetes. The researchers used sterile disposable syringes to draw 8 mL of blood from the subjects using vein puncture. Separating serum for biochemical testing and haemoglobin measurement required dividing each sample in half, placing them in separate gel tubes, and then centrifuging the tubes. We determined haemoglobin using the automated CBC equipment (Human/Germany). The GDF-15 concentration (normal range = 494-654 pg/ml) was measured using the ELISA technique. The biochemical tests were also determined using the automated chemistry auto-analyzer (Cobas C311) and the Cobas e411 (Roche, Japan). The MDRD GFR equation was used to predict the glomerular filtration rate (GFR). This equation took creatinine and patient demographics like gender and age into account. The present data was analyzed using the SPSS-24. Receiver operating characteristic (ROC), Pearson's correlation, one-way analysis of variance (ANOVA), and independent T-tests were also utilized in our research. It was deemed significant when the significance criterion was less than 0.05.

RESULTS

The gender distribution between the two CKD groups was not statistically significant. However, there was a significant difference in the age group (50-59 years) between the control group and CKD patients with or without T2DM (Table 1). The levels of serum FBS (mg/dl), urea (mg/dl), creatinine (mg/dl), ferritin (ng/ml), iron (µg/dl), and GDF-15 (pg/ml) were higher in CKD patients as compared to the healthy control group, as indicated in table (2). There was a significantly significant statistical difference between these two groups (P<0.01). (Table 2).

Based on the receiver operating characteristic (ROC) curve of the level between the patient groups and the control group, the cut-off value for GDF-15 was 684, indicating 100% specificity and 97% sensitivity. In addition, the AUC of 0.97 was extremely significant (P<0.0001) (Table 3, Fig. 1).

Results from CKD patients with type 2 diabetes show a robust relationship between GDF-15, serum creatinine, and glomerular filtration rate (GFR). Iron and GDF-15 were also significantly associated with CKD individuals who did not have type 2 diabetes (Table 4).

Table No.1: Distribution of study groups according to age and gender

Variable	CKD with diabetes mellitus (N=50)	Without diabetes mellitus (N=50)	Controls (N=50)	p-value
Age (years)				
30-39	5 (10%)	17 (34%)	5 (10%)	0.1NS
40-49	5 (10%)	-	17 (34%)	0.2NS
50-59	16 (32%)	22 (44%)	15 (30%)	0.01S
60-70	24 (48%)	11 (22%)	13 (26%)	0.06NS
Gender				
Females	23 (46.00%)	26 (52.00%)	22 (44.00%)	0.307 (NS)
Males	27 (54.00%)	24 (48.00%)	28 (56.00%)	0.294 (NS)

NS: Non-significant (P>0.05 P<0.05: Significant

Table No.2: Distribution of biomarkers among diabetic CKD patients, non-diabetic CKD patients and the control group (one-way ANOVA test)

Parameters	Control Group	CDK groups		P value
		WithT2DM	Without T2DM	
FBS (mg/dl)	85.52 ±1.87	212.30 ±7.70	87.68 ±1.30	0.0001
Urea(mg/dl)	20.16 ±0.44	153.54 ±7.87	150.88 ±5.14	0.0001
Creatinine(mg/dl)	0.674 ±0.02	9.09±0.32	8.06 ±0.27	0.0001
GFR(ml/min)	110.70 ±1.66	7.17 ±0.46	6.09 ±0.31	0.0001
Ferritin (ng/m)	124.38 ±9.57	788.16±34.60	737.58 ±37.91	0.0001
Hb(mg/dl)	12.83 ±0.10	8.69 ±0.22	8.94 ±0.17	0.0001
Iron(µg/dl)	63.90 ±2.06	53.08 ±2.12	57.20 ±2.18	0.0082
GDF-15(pg/ml)	539.76 ±7.52	1883.34±68.18	1196.04 ±34.04	0.0001

CKD: Chronic kidney disease, T2DM: Type 2 *Diabetes mellitus*, GDF-15: Growth differentiation factor-15, GFR: Glomerular filtration rate, Hb: Haemoglobin, FBS: fasting blood sugar, SD: standard deviation

Table No.3: ROC curve for GDF-15 (receiver operating characteristic curve test)

Markers	AUC	p-value	Cut-off Point	Sensitivity	Specificity
GDF-15(pg/ml)	0.97	<0.0001	684	97%	100%

ROC: receiver operating characteristic, AUC: area under the curve

Table No.4: Relationship between GDF-15 and some biomarkers in CKD patients with or without T2DM

Markers	GDF-15 in CKD patients with T2DM		GDF-15 in CKD patients without T2DM	
	Pearson's correlation	p-value	Pearson's correlation	p-value
Hemoglobin (g/dl)	-0.07	0.6 (NS)	-0.06	0.6 (NS)
Urea(mg/dl)	0.22	0.1 (NS)	0.03	0.8 (NS)
Creatinine(mg/dl)	0.39	0.004 (S)	0.19	0.1 (NS)
GFR(ml/min)	-0.51	0.000 (S)	-0.11	0.4 (NS)
FBS(mg/dl)	0.05	0.7 (NS)	-0.08	0.5 (NS)
Ferritin(ng/ml)	0.16	0.2 (NS)	0.01	0.9 (NS)
Iron(µg/dl)	-0.05	0.7 (NS)	-0.32	0.02 (S)

NS = Not significant

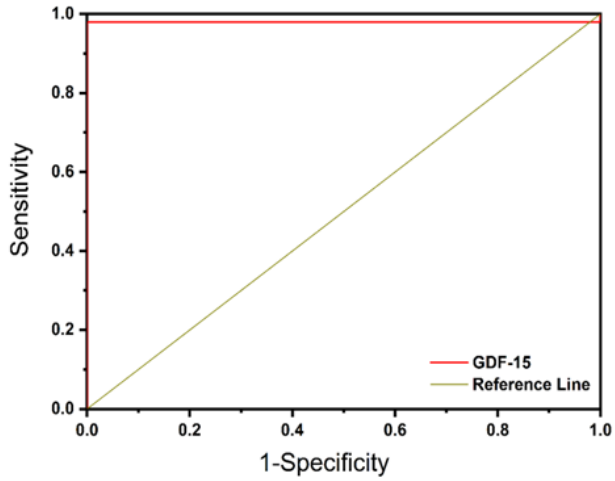

Figure No. 1: Receiver operating characteristic curve for GDF-15

DISCUSSION

One of the leading causes of death globally is chronic renal disease. This research has demonstrated a strong link between chronic renal disease and aging. The elevated occurrence of chronic kidney disease was attributed to decline in glomerular filtration associated with aging. Thus, a crucial strategy for improving results was to conduct screenings for chronic kidney disease in older adults, this result consistent with.[12] Researchers found no statistically significant difference in the gender distribution of the control group, diabetic CKD patients, or non-diabetic CKD patients. Findings from this investigation corroborated those of an earlier study by the same authors. Consistent with other studies, the results demonstrated that individuals with diabetic CKD had poorer renal outcomes and started dialysis earlier than CKD patients without diabetes.[13] Compared to healthy persons, CKD patients with or without T2DM had a much higher amount of urea. The findings aligned with those of another recent study.[14] Kidney function gradually declines during chronic kidney disease (CKD). Kidney function is compromised, making it harder for the kidneys to remove urea and other waste from the blood. These

waste products build up in the circulation when kidney function decreases, which causes blood levels to rise.

Creatinine levels rise above normal in diabetic individuals with chronic kidney disease (CKD) for a number of reasons, including reduced kidney function and the metabolic consequences of diabetes. These findings corroborated those of previous research.[15] Low glomerular filtration rate (GFR) is the primary reason for elevated creatinine in patients with chronic renal impairment. The kidneys' filtering capacity declines with the progression of chronic renal disease.[16,17]

Inflammation and disturbances in iron metabolism are common symptoms of chronic kidney disease (CKD), which may explain the dramatically elevated ferritin levels seen in this research. Ferritin is an acute-phase reactant, meaning that its levels increase in response to inflammation. Inflammation stimulates the liver to produce more ferritin, leading to higher blood ferritin levels.[18]

A significant drop in hemoglobin was discovered in the present investigation. Additionally, compared to non-diabetics, the prevalence of anaemia was greater in all CKD patients, especially diabetic patients. In individuals with chronic kidney disease (CKD), diabetes impacts iron utilization and erythropoiesis.[19,20]

In the past, chronic kidney disease (CKD) was often associated with anaemia because impaired kidney function lowered erythropoietin production.[21]

Malnutrition and inflammation are two of the many potential causes of the greater iron deficit seen in CKD diabetes patients compared to non-diabetic CKD patients in the research.[22]

Our findings corroborated those of previous research that found elevated GDF-15 levels in diabetic individuals with chronic kidney disease and were predictive of faster disease progression and higher mortality.[23,24]

In addition, GDF-15 demonstrated excellent sensitivity and specificity in ROC analysis. Due to its significance for disease progression, inflammation, and clinical outcomes, the link between GDF-15 and blood creatinine in CKD patients with diabetes was considered significant.[25] High GDF-15 implies higher renal damage and inflammation, which correlates with lower GFR and more severe CKD[26], further supporting the significance of the link between GDF-15 and GFR in diabetic individuals with chronic kidney disease. Faster development of chronic renal disease and impairment of kidney function are predicted by elevated GDF-15 levels. More thorough cardiovascular surveillance and care should be implemented for patients with high GDF-15 and low GFR since they are at a higher risk for cardiovascular events.[23]

The cytokine GDF-15 controls iron metabolism plays a role in the immune response, and regulates inflammation. When cellular stress and inflammation, both of which are prevalent in chronic kidney disease, are present, it rises. Elevated GDF-15 levels are linked to chronic illness anaemia and reduced iron utilization.[10] Since GDF-15 influences iron control, which contributes to the functional iron shortage, the association between GDF-15 and iron in non-diabetic CKD patients was substantial. Enhanced anaemia owing to impaired iron utilization was similarly linked to higher GDF-15 levels, according to prior research.[27]

CONCLUSION

The GDF-15 biomarker has strong relationships with other biochemical indicators. It has been linked to anaemia in chronic kidney disease (CKD) patients, whether or not they have diabetes. As a result, this biomarker can be utilized to diagnose anaemia in these individuals.

Author's Contribution:

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

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