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Editorial

Use of Tobacco and its Health Hazards

Mohsin Masud Jan
Editor

Tobacco use still remains one of the biggest challenges our world faces in public health. One in 10 deaths around the world is caused by tobacco use. Tobacco is the single greatest preventable cause of death in the world today. It kills over 7 million people every year.

In 2022, an estimated 25.4 million people (20.7 million males and 4.6 million females) aged 15 years and older were tobacco product users in Pakistan. This positions the country as the 7th globally and the 1st in the WHO Eastern Mediterranean Region in terms of number of tobacco users.[1,2]

Tobacco use jeopardizes human health and is one of the major sources for non-communicable diseases including chronic obstructive pulmonary diseases (COPD), cardiovascular diseases, diabetes and cancers.[3] Tobacco related diseases are a major cause and consequence of poverty in low- and middle-income countries.[4]

Globally, 942 million men and 175 million women ages 15 or older smoke tobacco.[5] It is responsible for death of about seven million people each year; many are premature deaths reported by World Health Organization's (WHO) new Global Report on Trends in Prevalence of Tobacco Smoking 2000-2025.[6] In a recent study, overall prevalence of tobacco use in Pakistan are found less common compared to its neighboring countries (19.1% vs. >25%).[7]

Generally, use of tobacco start around adolescence.[8] In developing countries, more than half of the adolescents start smoking at an early age and become regular tobacco users subsequently.[9] Male gender, old age, less education, high coffee or tea consumption, sharing a household with smoker are the most common risk factors for using tobacco.[10]

According to a study, aimed to assess the age standardized prevalence of tobacco use in urban and rural areas of four provinces of Pakistan amongst people aged 20 years or more.

The age-standardized prevalence of tobacco use in Pakistan was found to be 13.4%. Tobacco use in urban areas was 16.3% and rural areas was 11.7%. Tobacco use in urban and rural males was 26.1% and 24.1%, while in females was 7.7% and 3.1%, respectively. The age-standardized prevalence of ex-tobacco use in Pakistan was found to be 2.3%. Ex-tobacco use in urban areas was 2.6% and rural areas was 2.3%. Similarly, ex-tobacco use in urban and rural males was 4.6% and 4.6%, while in females was 0.7% and 0.5%, respectively.

In 2021, it was estimated that tobacco was the 5th highest risk factor driving the most deaths and disability combined in Pakistan. In 2021, the top 10 causes of the most deaths in Pakistan included Ischemic Heart Disease (IHD) ranking 3rd, Stroke ranking 4th, and Chronic Obstructive Pulmonary Disease (COPD) ranking 6th. Tobacco was responsible for an estimated 37.6 thousand or 20.5% of all IHD deaths, 13.7 thousand or 15.7% of all Stroke deaths, 9.8 thousand or 75.6% of all Lung Cancer deaths, and 26.8 thousand or 48.3% of all COPD deaths.

In 2019, tobacco use caused an estimated loss of 4.3 million disability-adjusted life years, which was about 9.3% of total disability-adjusted life years. Tobacco accounted for 1.2 million for IHD, 422.6 thousand for Stroke, 265.5 thousand for Lung Cancer, and 644.9 thousand for COPD.

According to Global Adult Tobacco Survey (GATS 2014), almost 24 million (19.1%) adults currently use tobacco in any form. That accounts for 15.6 million (12.4%) adults who currently smoke tobacco, including 3.7 million adults using water pipe, hookah or shisha, and another 9.6 million (7.7%) adults who use smokeless tobacco.

As per Global Youth Tobacco Survey (GYTS 2013), 13.3% boys and 6.6% girls are current tobacco users. Point of concern is the narrowing of ratio between male and female tobacco users among youth.

Another cause of concern is shisha smoking which is as dangerous as cigarette smoking.

The GATS and GYTS data provide critical information to stakeholders and decision-makers in Pakistan to protect the public's health and well-being. Addressing tobacco use as a contributing factor for morbidity and mortality in Pakistan will require strong commitment to high-level achievement, including implementation and enforcement of the WHO MPOWER measures.

WHO's MPOWER is a package of strategies and interventions to reverse the tobacco epidemic while using 6 strategies:

- Monitor tobacco use and prevention policies
- Protect people from tobacco smoke
- Offer help to quit tobacco use
- Warn about the dangers of tobacco
- Enforce bans on tobacco advertising, promotion and sponsorship
- Raise taxes on tobacco

Fighting tobacco in Pakistan will require a strong commitment to the WHO's Framework Convention on Tobacco Control (WHO FCTC) and the related MPOWER strategies. These are proven strategies that can help avert unnecessary illness and death.

WHO works closely with the Government of Pakistan to curb the use of tobacco in the country. Despite

powerful presence of the tobacco industry, 2 major mile stones were achieved in the country:

- Prohibition of Smoking and Protection of Non-smokers Health Ordinance 2002.
- Ratification of WHO Framework Convention on Tobacco Control (FCTC).

It is now time for Pakistan to fully implement MPOWER Strategies particularly the tobacco control "best buys": strict implementation of smoke-free laws; a comprehensive ban on tobacco advertisement, promotion and sponsorship; implementing large-sized graphic health warnings on cigarette packs; introducing plain packaging; and raising tobacco taxation.

WHO looks forward to the development of an evidence-based multisectoral plan of action for tobacco control in Pakistan that will pave the way to accelerating implementation of the WHO FCTC and achieving the global target of a 30% relative reduction in prevalence of current tobacco use in persons aged 15 years and over.

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Original Article

Polymorphism of Interleukin -17 Gene in Scabies

A Serum Level and Polymorphism of Interleukin -17 Gene (RS 8193036, RS 2275913) in Scabies Patients

Noora D. Abd[1], Nagham Y. Albayati[1] and Ali H. Abbas[2]

ABSTRACT

Objective: To assess how genotyping affects an individual's likelihood of developing scabies.
Study Design: Cross-sectional study.
Place and Duration of Study: This study was conducted at the Baquba Teaching Hospital- Consultation Clinic-Dermatology Unit/ Diyala Governorate from 4th of December, 2022 to 10th June, 2023.
Methods: Seventy-five male and female volunteer patients who clinically diagnosed with scabies and 75 non-infected individuals as a control were enrolled.
Results: There was an increase in IL-17 concentration of the patients' serum compared with control and there was genotype variation in both studied single nucleotide polymorphisms.
Conclusion: The serum level of IL-17 was increased in scabies group, the GA genotype and G allele of IL-17 SNPs rs 8193036 and the TT,CT genotypes and T allele of rs 2275913 were increased too with high OR value, the genotypes and alleles might be a risk factors from scabies infestation.
Key Words: Scabies, Genetic polymorphism, IL-17, Allele-specific, Serum levels

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INTRODUCTION

Scabies is one of cutaneous disease mediated by inflammatory and allergic reaction caused by a skin parasitic infection with parasite named Sarcoptes scabieivarhominis.[1] The disease is cosmopolitan in distribution as it affects millions (more than 300 million people) It is endemic in many countries and it although infects all age groups in both sexes , it is more frequent in children and elderly in low economic countries.[2] It is easily transmits by direct skin contact, in addition to indirectly methods using clothing, blankets, and towels.[3] Severe nocturnal itching occurs as a result of the females burrows digging skin tunnels to lay their eggs inside them, as well as result of the parasite's secretions and remains which is the most important symptom of the disease.[4]

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Burrows and papules are frequently signs in patients.[5] Skin scratching may leads to worsen the disease as a result of Secondary infection.[6] There are three clinical forms of scabies including classic scabies, Norwegian scabies and Nodular scabies.[7] Symptoms of the disease appear 2-4 weeks after infection.[8]

Mite infestation was stated to induce allergic and inflammatory immune response as a parasite-host relationship.[8] The Interleukin-17(IL-17) is a cytokine that was noticed after expose to allergens and it is involved in skin allergic reaction. It is a cytokine secreted by (Th-17) T cells and is a glycoprotein with a molecular weight of 20 kilo Daltons.[9] IL-17 stimulates immune cells fibroblasts, macrophages, neutrophils, and endothelial cells to produce pro-inflammatory mediators such as IL-1, TNF-a, and IL-6.[10] IL-17 has a role in protecting against bacterial and parasitic infections and has a role in recruiting neutrophils and producing antimicrobial peptides.[11,12]

Association between the polymorphism of IL-17 and inflammatory and infectious dermal disease such as psoriasis, basal cell carcinoma, lichen planus and cutaneous leishmaniasis was previously recorded.[13-14] The current study was designed to evaluate the role of serum and IL-17 genotyping in susceptibility to scabies in humans.

METHODS

The study conducted at Baquba Teaching Hospital, Consultation Clinic, Dermatology Unit/Diyala Governorate from December 2022 to June 2023, and

the policies and ethics followed by the Ministry of Health were taken into consideration. Seventy-five samples (41 males and 34 females) were collected from patients infected with scabies after they were diagnosed by Dermatologist and confirmed the diagnosis by a dermoscope as well as to 75 samples were collected from healthy people (45 males and 30 females), and after ensuring that they were free of all infectious and chronic diseases they underwent a CBC test (control group). Five ml of blood was drawn and divided into two parts. Three ml was used to serological test, and 2 ml was placed in an EDTA tube to detect polymorphisms of the IL-17 gene, SNP rs 8193036 and rs 2275913. The purity and concentration of the DNA were estimated using Nanodrop. The primers used in the study were designed according the NCBI-Blast online website by the authors and were proceeded according to the instructions of Alpha-DNA (Canada), as shown in (Table No. 1).

Table No. 1: IL-17 SNP of rs 8193036 and rs 2275913 Primers Information

rs 8193036	**Sequence(5´>3´)**	**Product length**
Forward primer	ACTGGCCCTTCCTTGTCCTA	
Reverse 1 primer	GATAGAGACTGGACAAAGGTGATGG	217bp
Reverse 2 primer	GATAGAGACTGGACAAAGGTGATGA	
rs 2275913	**Sequence(5´>3´)**	
Forward primer	AACACCTGGCCAAGGAATC	
Reverse1 primer	CAATGAGGTCATAGAAGAATCTCTC	298bp
Reverse2 primer	CAATGAGGTCATAGAAGAATCTCTT	

The polymerase chain reaction/allele-specific primer (ASP-PCR) technique was used to detect single nucleotide polymorphisms (SNPs) of the IL-17 rs 8193036, rs 2275913 gene. Amplicons product was visualized by ultraviolet transilluminator. IBM SPSS version 26.0 was used for statistical analysis, with the Duncan test, student's t-test, and ANOVA table utilized to compute probability at the $p<0.05$ level.

RESULTS

A significant increase in the mean concentration of IL-17 was seen among patients in comparison with control 759.63±172.27 and 20.95±0.93 pg/ml. There was also a insignificant raise in the IL-17 mean serum concentration of males infected with scabies compared to females, 948.95±247.62 and 531.33±233.01 pg/ml respectively, while insignificant reduction in the level in the level of IL-17 concentration in the sera of males compared to females in the control group 20.08±1.18, 22.34±1.50 pg/ml respectively (Table No. 2).

The IL-17 gene (SNPs) rs8193036 and rs2275913 were the two genetic variants that were examined in both studied groups. The study examined the genetic variation of (SNP)rs 8193036 in two alleles, G and A, which corresponded to three genotypes: AA, GA, and GG. When the well on the agarose gel was loaded with Reverse 2 primer in this technique, the homozygote AA showed up as a single band. The homozygote GG genotype emerged as a single band loaded with Reverse 1 primer on an agarose gel, but the heterozygote GA genotype presented as two bands, the first loaded with Reverse 1 primer and the second band with Reverse 2 primer (Fig.1).

The frequencies of genotypes and alleles of IL-17 rs8193036 SNPs for the patient group are incompatible with Hardy Weinberg equilibrium while it is compatible with a control group $1.0x10^{-12}$ and 0.1258 respectively (Table 3).

A non-significantly decreased frequency percentage of the GG genotyping in the scabies patient group compared to the control (9.3 vs. 13.3, OR:0.67, Pc value: 0.452) respectively (Table.4). There was a significant decrease in the frequency of the AA genotyping and the A allele in the patient group compared to the control (0 vs. 29.3, OR: 0.02, Pc value $3.3x10^{-8}$) (45.0 vs. 58.0, OR:0.06, Pc value: 0.029) respectively. It also showed a significant increase in genotyping frequencies percentage GA and G allele in the scabies patients group compared to the control (90.7 vs. 57.3, OR:7.23, Pc value: $2.2x10^{-6}$) and (55.0 vs. 42.0, OR:1.67, Pc value: 0.029) respectively. According to the results the high OR value of GA genotype and G allele referred to this genotype and allele may be risk factors for scabies, while GG, AA, and A allele may be protective agents from the disease development. The significant increase in the proportions of people carrying the GG and AG genotyping in the patient group compared to the control when measuring the serum levels of the IL-17 gene SNPs rs 8193036 among the study groups (456.57±278.67 vs. $20.56±9.91^{A}$ pg/ml and (790.83±187.83vs. $21.25±826^{A}$ pg/ml respectively (Table 5).

When the genotype is homozygote, CC, and TT, the genotype appears loaded in the first primer, Reverse 1 or 2 respectively when loaded in the agarose gel. If the genotype has heterozygote CT appears in two bands, one of them loaded in the first primer reverse1 and the other with the well loaded with Reverse 2 (Fig. 2).

In addition, the genotyping and allele frequencies for IL-17 rs 2275913 showed incompatible genotypes for both groups with Hardy-Weinberg equilibrium (Table 6). The TT, CT genotypes and T allele were non

significantly increased frequency percentage in scabies patients compared with control groups (1.3 vs. 0, OR:3.04, Pc value:0.75) and (12.0 vs. 8.0, OR:1.57, Pc value:0.429) respectively, and the T allele (7.0 vs.4.0, OR:1.90, Pc value:0.223) (Table 7).

The CC genotyping and C allele appeared non significantly decrease frequency percentage in the scabies patients group compared to a control group (86.7 vs. 92.0 OR: 0.57, Pc value:0.303) (93.0 vs. 96.0, OR:0.53, Pc value:0.223) respectively. The high OR value of TT, CT, genotypes, and T allele referred to this genotyping and allele might be risk factors for scabies, also the low OR value of CC genotype and C allele in patients group compared to control group might be a protective role from scabies disease. The significant increase in the level of IL-17 for the CC genotype in the patient group compared to the control group 866.73 ± 159.49^{A} and 20.95±8.15pg/ml respectively while there was a non-significant increase in the level of the CT genotype in the patient group compared with the control group,23.14 ± 12.49^{B} and 20.96±7.48 pg/ml (Table 8).

Table No. 2: The serum level of IL-17 between the study groups

Gender	IL-17 concentration (pg/ml)		Probability
	Scabies Patients (n=75)	Control (n=75)	
Males	948.95±247.62	20.08±1.18	0.000065
Females	531.33±233.01	22.34±1.50	0.057
Total	759.63±172.27	20.95±0.93	0.000032
Probability	0.089	0.993	

Table No. 3:The IL-17 SNPs rs8193036 genotyping frequencies and Hardy Weinberg compatibility in the patients' group compared to controls

Genotyping frequencies of IL-17	Patients group (n=75)		Control group (n=75)	
	Observed	Expected	Observed	Expected
GG	7 (9.3%)	22.4 (29.9%)	10 (13.3%)	13.2 (17.6%)
GA	68 (90.7%)	37.2 (49.6%)	43 (57.3%)	36.5 (48.7%)
AA	-	15.4 (20.6%)	22 (29.3%)	25.2 (33.6%)
P-HWE	1.0×10^{-12}		0.1258	

P-HWE: probability of Hardy-Weinberg equilibrium

Table No. 4: The IL-17 SNPs rs8193036 genotypes and alleles frequencies in the patients' group compared to controls

Genotyping and alleles frequencies of IL-17 rs8193036	Patients group (n=75)	Control group (n=75)	OR (95% CI)	P-value	Pc-value
G	82 (55.0)	63 (42.0)	1.67 (1.06-2.62)	0.037	0.029
A	68 (45.0)	87 (58.0)	0.06 (0.38-0.95)	0.037	0.029
GG	7 (9.3)	10 (13.3)	0.67 (0.24-1.85)	0.608	0.452
GA	68 (90.7)	43 (57.3)	7.23 (2.95-17.72)	4.5×10^{-6}	2.2×10^{-6}
AA	0 (0.0)	22 (29.3)	0.02 (0.0-0.26)	7.8×10^{-8}	3.3×10^{-8}

OR: odd ratio, 95% CI: 95% confidence intervals, P-value: Fisher's exact probability value, Pc-value: Bonferroni corrected probability value

Table No. 5: IL-17 serum levels according to the IL-17 SNPs rs8193036 of the studied groups

Genotyping frequencies of IL-17 rs8193036	IL-17 serum level (pg/ml)		Probability
	Patient Group	Control Group	
GG	456.57±278.67	20.56 ± 9.91^{A}	0.004
GA	790.83±187.83	21.25 ± 8.26^{A}	0.000290
AA		20.55 ± 7.04^{A}	
Probability	0.576		

Duncan test: The similar letters referred to non-significant differences (P > 0.05) between the genotyping of the control group

Table No. 6: The IL-17 SNPs rs 2275913 genotyping frequencies and Hardy Weinberg compatibility in the patients' group compared to controls

Genotyping frequencies of IL-17 rs2275913	Patients group (n=75)		Control group (n=75)	
	Observed	Expected	Observed	Expected
CC	65 (86.7%)	64.4 (85.9%)	69 (92%)	69.1 (92.2%)
CT	9 (12%)	10.2 (13.6%)	6 (8%)	5.8 (7.7%)
TT	1 (1.3%)	0.4 (0.5%)	-	0.1 (0.2%)
P-HWE	0.3107		0.7182	

P-HWE: Probability of Hardy-Weinberg equilibrium

Table No. 7: The IL-17 SNPs rs2275913 genotypes and alleles frequencies in the patients' group compared to controls

Genotyping and alleles frequencies of IL-17 rs2275913	Patients group (n=75)	Control group (n=75)	OR (95% CI)	P-value	Pc-value
C	139 (93%)	144 (96%)	0.53 (0.19-1.46)	0.318	0.223
T	11 (7%)	6 (4%)	1.90 (0.69-5.26)	0.318	0.223
CC	65 (86.7%)	69 (92%)	0.57 (0.20-1.63)	0.428	0.303
CT	9 (12%)	6 (8%)	1.57 (0.53-4.62)	0.558	0.429
TT	1 (1.3%)	-	3.04 (0.12-74.24)	1.0	0.750

OR: odd ratio, 95% CI: 95% confidence intervals, P-value: Fisher's exact probability value, Pc-value: Bonferroni corrected probability value

Table No. 8: IL-17 serum levels according to the IL-17 SNPs rs2275913 of the studied groups

Genotyping frequencies of IL-17 rs8193036	IL-17 serum level (pg/ml)		Probability
	Patient Group	Control Group	
CC	866.73±195.49 ^{A}	20.95±8.15	0.000017
CT	23.14±12.49 ^{B}	20.96±7.48	0.708
TT	426.40^{A}		
Probability		0.999	

Duncan test: The similar letters referred to non-significant differences (P > 0.05) between the genotyping of the control group

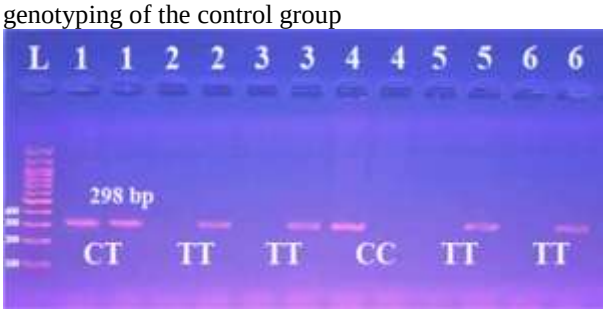

Figure No. 1: Electrophoresis of the IL-17 SNP rs8193036 gene resulting from PCR-ASP

DISCUSSION

Scabies is a parasitic skin disease brought by the mite Sarcoptes scabies var hominis.[15,15] The study indicated higher levels of IL-17 in the sera of scabies patients compared to the control group, and this agreed with previous studies.[5,17] IL-17 is a proinflammatory cytokine that is associated with allergic and inflammatory diseases, and it works to increase the secretion of IL-2, TNF-a, and IL-8, which have a major role in exacerbating the disease and amplifying the immune response.[18]

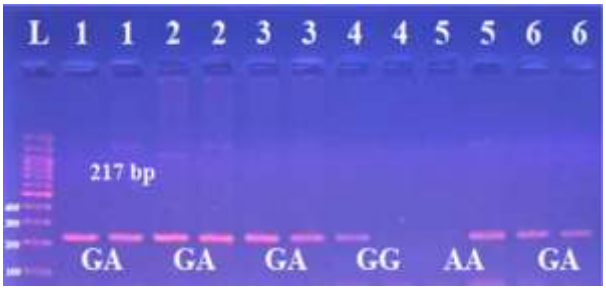

Figure No. 2: Electrophoresis of the IL-17SNP rs2275913 gene resulting from PCR-ASP

IL-17 also works to stimulate keratinocytes and many inflammatory cells near the sites of the parasite in the skin infected with the disease and thus works to induce an inflammatory response as the disease progresses.[19] The current study may be the first to study the polymorphism of the IL-17 gene, SNPs rs 8193036 and

rs 2275913, among scabies patients. Both SNPs were related with some disease,

IL-17A increased in sera of Iraqi patients with asthma. As well as to the rs2275913 variant was associated with a higher risk of pathogenesis of asthma, while the rs8193036 variant was possibly associated with protection from asthma in Iraqi patients.[20] A meta-analysis showed that there was significantly increase in circulating IL-17in patient with rheumatoid arthritis and there was evidence of associations between IL-17A rs2275913 polymorphism and the pathogenesis.[21] A study was reported on Erysipelas disease that the CT genotypes and the T allele have an important role as a risk factor for the disease.[22] Another study was also recorded on COVID-19 disease, indicating the active role of the AA genotype and the A allele as risk factors in the development of the disease.[21] Xie et al[23] reported that genetic variation of the IL-17 gene rs 2275913 for endometrial cancer in women. The AA genotype and the A allele are risk factors in the development of the disease, and a high level of this genotype is associated with a higher risk of developing uterine cancer.

CONCLUSION

IL-17 levels were high among scabies patients, as polymorphisms genotyping rs 8193036, according to the results based on the OR value the high OR value of GA genotype and G allele referred to this genotype and allele may be risk factors for scabies, while GG, AA genotypes, and A allele may be protective agents from the disease development. while the genotyping of rs 2275913 the high OR value of TT, CT, genotypes, and T allele referred to this genotyping and allele might be risk factors for scabies, also the low OR value of CC genotype and C allele in the patients group compared to control group might be a protective role from scabies disease.

Author's Contribution:

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Final Approval of version:	By all above authors

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Original Article

Effectiveness of an Instructional Program on Practice of Patients' Safe Measures Post Implantable Cardioverter Defibrillator

Mohammed Kadhum Sadiq[1] and Wafaa Abed Ali Hattab[2]

ABSTRACT

Objective: To ascertain the effectiveness of the instruction program on patients' practices about safe measures post implantable cardioverter defibrillator.

Study Design: A quasi-experimental study

Place and Duration of Study: This study was conducted at the Ibn–Al-Bitar Specialized Center, Baghdad city from 19th May 2023 to 16th February 2024.

Methods: Pre-test and post-test approaches are used for the groups (control and study). Sixty patients participated (30) in each group. Date was collected through the use of constructed program and instruments for the safe measures after ICD implantation, the study instrument included three sections: socio-demographic characteristics, medical information, and patients' practices regarding safe measures post-ICD implantation.

Results: The study group demonstrated a fair level of practice in safe activity and a good level of electrical devices, and magnetic devices domains, while in the control group, the domains were within fair level except the electrical devices were at poor level at pre-program. However, after the program implementation, the majority of study group had adequate total practice scores on the contrary the control group remained at a fair level.

Conclusion: The practices of patients regarding safe measures post ICD was fair level for both groups. After implementing the instructional program, the study members' practices increased to a respectable level. While the practices of the control group remained unchanged over the testing period.

Key Words: Instruction program, Safe measures, Implementable cardioverter defibrillator.

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INTRODUCTION

Sudden cardiac arrest (SCA) predominantly affects adult patients, particularly men over the age of 35. The associated risk factors can be categorized into four groups: clinical, societal, genetic, and psychological. To reduce the incidence of SCA, various therapeutic modalities, including antiarrhythmic medications and implanted cardioverter-defibrillators (ICDs), are utilized.[1]

The implanted cardioverter-defibrillator (ICD) monitors heart rhythms for potentially life-threatening arrhythmias characterized by excessive rates or irregular rhythms. It provides diagnostic information and treatment responses through low-energy pacing or high-energy shocks to terminate arrhythmias, known as appropriate shocks.[2] Although patients with ICDs receive routine information about their condition, they often feel that their concerns are not fully addressed. Many report that their doctors focus primarily on clinical and device-related issues, neglecting the social and psychological implications of living with an ICD and the availability of psychological support. Engaging in face-to-face conversations with patients prior to device implantation allows physicians to assess their emotional state and address any concerns.[3] Many patients had inadequate (knowledge and practice) regarding ICD and pacemaker education program performance (knowledge and practice) with improved knowledge regarding ICD implantation.[5,6] Managing cardiac devices with nursing tracking and avoiding common problems, avoiding dislocation, and educating patients about device use and maintenance.[6] Also, some patients restrict activities, including sex, driving, and socializing.[7] Understanding the potential implications and implementing an appropriate care program can greatly enhance patients' ability to adapt to their

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condition following device implantation.[8] Various factors, including mental health and comorbid conditions, can affect patients' ability to cope with and accept their cardiac devices. However, the quality and extent of education provided prior to the implantation procedure significantly influence patient outcomes and overall acceptance.[9,10] A significant gap in clinical practice exists that could be addressed to better support individuals with ICDs. Leveraging the knowledge and perspectives of patient partners can facilitate this improvement. The goal of this project was to develop and evaluate a teaching program designed to educate patients and assist them in adjusting to life with an ICD.

METHODS

A quasi-experimental design was performed from 19th May 2023 to 16th February 2024 at Ibn–Al-Bitar Specialized Center for Cardiac Surgery. pre-test and post-test approaches were used for the group (control and study group). Sixty patients were participated (30 patients) in each group. The instrument was composed of 3 sections; first portion covers socio-demographics, second part covers clinical characteristics of patients, and third part covers the patients' practices about safe measures post ICD, concerning safe measures instrument consists of three domains; the first domain is concerned with the patients' safety of daily activities: consists of 15 items, and the second was concerned with patients' safety of usage of various household and work-related devices: consisting of 8 items, last part ask patients about harmful equipment with strong electromagnetic fields with ICD devices: consist of 6 items. Each item scored on a 3-point Likert scale, according to the following: the total scores of the practice ranged from 0 – 69. One mark for each never answer, two for some time and three mark for the always answer. Poor practice level <50% of the total score (score 0 to less than 35). Fair practice level 50-75% of total scores (score 36-52). A good practice level is >75% of total scores (scores 53 to 69).[11] All the participants of the study in both groups were subjected to a pre-test. The participants of the study group were exposed to the instructional program after the pre-test immediately. The program was delivered by face-to-face as used previously based on previous educational and instructional interventions. Finally, after 4 weeks all the participants of both groups were exposed to the post-test. The program application takes 2 sessions each session scheduled to be for 20 minutes.

The questionnaire's validity was assessed by content validity index approach the result of the study (0.85) that the questionnaire is valid. Also, the program applies to 16 experts. The study tool was tested-retested for reliability. The patient's knowledge reliability coefficient was 81. SPSS 26 utilized for analyzing study data.

RESULTS

83.3% of participants in the study group were male, compared to 66.7% in the control group. 33.3% of the study group were under 54 years old, while 36.7% of the control group fell within the 54-66 age. Freelancers constituted 33.3% of the study group, whereas 43.3% of the control group were unemployed. 50% of the study group had completed primary education, with only 10% being illiterate, while 26.7% of the control group were secondary graduates. Marital status indicated that 83.3% of the study group and 80% of the control group were married.

Table No. 1: Distribution patients according to socio-demographic characteristics

Variable	Study Group (N=30)	Control Group (N=30)
Gender		
Male	25 (83.3%)	20 (66.7%)
Female	5 (16.7%)	10 (33.3%)
Age Groups		
18- less than 30	5 (16.7%)	3 (10%)
30- less than 42	2 (6.7%)	4 (13.3%)
42- less than 54	10 (33.3%)	8 (26.7%)
54- less than 66	7 (23.3%)	11 (36.7%)
66 & above	6 (20%)	4 (13.3%)
Occupation		
Employed	8 (26.7%)	4 (13.3%)
Retired	5 (16.7%)	8 (26.7%)
Freelancers	10 (33.3%)	5 (16.7%)
Unemployed	7 (23.3%)	13 (43.3%)
Education level		
Iilliterate	3 (10%)	3 (10%)
Read and write	1 (3.3%)	4 (13.3%)
Primary graduate	15 (50%)	6 (20%)
Medium graduate	2 (6.7%)	3 (10%)
Secondary graduate	2 (6.7%)	8 (26.7%)
Institute/College graduate	7 (23.3%)	6 (20%)
Marital status		
Single	2 (6.7%)	4 (13.3%)
Married	25 (83.3%)	24 (80%)
Widowed	2 (6.7%)	2 (6.7%)
Divorced	1 (3.3%)	-
Socio-economic level		
Low	7 (23.3%)	6 (20%)
Mild	18 (60%)	19 (63.3%)
High	5 (16.7%)	5 (16.7%)

A significant portion of both groups reported median income, with 60% in the study group and 63.3% in the control group. In terms of implantation duration, 30% of the study group had devices implanted for five years or longer, while 26.7% of the control group had implants for between six months and one year or for five years and above. 60% of the study group and

56.6% of the control group did not have chronic diseases. Among those with chronic conditions, 90% of the study group and 63.3% of the control group were on medication for those diseases.

Table No. 2: Distribution of patient's medical information who has an ICD device

Variable	Study Group (N=30)	Control Group (N=30)
Duration of implantation		
less than 3 month	6 (20%)	7 (23.3%)
3- less 6 month	2 (6.7%)	1 (3.3%)
6- less one year	6 (20%)	8 (26.7%)
1- less 5 years	7 (23.3%)	6 (20%)
5 years &above	9 (30%)	8 (26.7%)
Chronic disease		
Non	18 (60%)	17 (56.6%)
Diabetic mellitus	0	6 (20%)
Hypertension	5 (16.7%)	5 (16.7%)
Others	7 (23.3%)	2 (6.7%)
Take drugs to the chronic diseases		
Yes	27 (90%)	19 (63.3%)
No	3 (10%)	11 (36.7%)
Smoking		
Yes	5 (16.7%)	2 (6.7%)
No	25 (83.3%)	28(93.3%)

Additionally, 83.3% of the study group and 93.3% of the control group were non-smokers. The study group demonstrated a fair level of safe activities and a good level for both electrical and magnetic devices, with mean scores of 18.37, 18.40, and 15.10, respectively. In contrast, the control group exhibited fair levels across most domains, except for electrical devices, which fell into the poor level, with mean scores of 18.03, 15.63, and 17.97, respectively. After the program was applied, the study group reflected a good level across all practice domains, with mean scores of 20.40, 19.70, and 16.80, respectively. Meanwhile, the control group maintained a fair level in all domains except good level in magnetic devices domain, yielding mean scores of 18.53, 18.20, and 15.83, respectively (Table 3).

Figure 1 revealed a comparison of descriptive analysis of total patients' level of practice for both study groups, in the pre-and post-test. The finding indicated that (60%) of the study group population had a fair level before receiving the instructional program and an additional (40%) had a good level. Large effects and changes have been found after conducting the program the majority of patients (90%) had a good level of practice with the device, while (56.7%) of the control population had a fair level of practice at the pre-test and improved (60 %) in post-test and (40%) were good level of practices about the device.

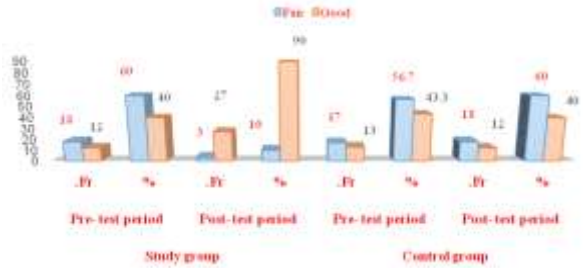

Figure No. 1: Evaluation of total patients' practices about the safe measures

Table No. 3: Descriptive analysis of patients' specific practice of safe measure for study and control groups before and after applying program

Specific knowledge of safe measure	Max score	Pre- test period				Post test period			
		Study group		Control group		Study group		Control group	
		M.S (SD)	Ass	M.S (SD)	Ass	M.S (SD)	Ass	M.S (SD)	Ass
Safe activity	27	18.37 (2.883)	Fair	18.03 (2.785)	Fair	20.40 (2.724)	Good	18.53 (2.501)	Fair
Electrical devices	24	18.40 (2.191)	Good	17.97 (2.671)	Poor	19.70 (2.380)	Good	18.20 (2.605)	Fair
Magnetic devices	18	15.10 (2.721)	Good	15.63 (2.470)	Good	16.80 (1.375)	Good	15.83 (1.877)	Good

DISCUSSION

The current study demonstrates that higher percentage of males in both the study and control groups align with findings from previous studies. Hussein & Mohammed[12] which found that largest percentage were males. The higher percentage of individuals aged 54-65 in the control group compared to the study group is consistent with the findings of a Mousa & Mansour[13] which reported that most of the age range was 48-55 years. Concerning the occupational status of the patients a study agree with present result which found (43.3%) of the sample had unemployed.[14] Half percent of the samples in the study group had a primary education level and twenty-six percent of the patients were secondary graduates for the control group, these findings supported a research that indicated 25.9% of patients were secondary school.[15] Also agree with a study which indicated that the most patients had ranged between high school and middle school 30% for each level.[16]

Sixty, and sixty-three percent of the samples in the both groups, were median income level, this data matches with a study that stated that 63.3% and 73.3% of study and control group patients, respectively, were median income level.[17] The result also shows that the mean duration of implantation of the ICD device was (33±3.103 months for the study group and 40±3.511 months for the control group). These findings align with Curtis et al[18] reported that the time since ICD implantation was 3.61±3.14 years. The majority of groups did not have a chronic disease. This indicates that the two groups were fairly similar in terms of their overall health status. In terms of specific chronic diseases, the prevalence of diabetes mellitus was 20% in the control group, had higher value compared to study group. This could suggest that there may be a higher risk of diabetes among the control group population, or other factors specific to the study group. The prevalence of hypertension was same in both groups, suggesting that groups are typical of the general population or that both groups have similar risk factor. This result is consistent with Ichikura et al[19] reported 16% of the samples had diabetes and 22.7% of the samples had hypertension. The individuals with ICD devices may have a higher prevalence of certain cardiac conditions, which could impact the overall health profile of study and control groups. The majority sample in both groups doesn't smoke. These results were supported by Iraqi studies, which found that the largest of his sample didn't smoking.[20,21]

Abd El-Aziz et al[22] reported that the home care management program improves knowledge and practices for patients with permanent pacemakers where 40.4% of participants exhibited satisfactory practices before the program, while 59.6% demonstrated satisfactory practices after the program. As well, a recent study agrees with our finding which found that patients' practice improved significantly both instantly and after 4 weeks, in comparison to the starting point, there were noticeable changes. Initially, the majority of patients had unsatisfactory overall practice but after post-educational intervention, 65.7% had satisfactory practice and 77.1% post 4 weeks of applying to the program, this result supported by Khalil et al[23] and Ahmed[24] discovered that the education program significantly improved patients' practice. As well, another study agrees with our finding and mentioned the high statistical significance of post-education patient performance and follow-up. Also, they reported that most of the sample scored well on all home environment categories except the magnetic field. Due to modern life, all patients have magnetic fields in their homes from TVs, mobile phones, recorders, computers, and hairdryers, so they must keep them at least 6 inches to 15 centimeters away.[25] The large number of patients expressed concerns regarding the high side effects of the ICD and, the limited use of microwaves. This result goes in the same line as our result in table 3 the result found poor practice in using microwave ovens.[1] In this regard, Mohamed et al[26] stated that a greater number of patients exhibited insufficient practice related to the pre-implementation education program for pacemaker placement, despite an improvement in their knowledge regarding permanent pacemaker implantation.

Recommendation: Comprehensive training programs that start in the pre-implantation period and continue into the post-implantation period should be organized, and focused on safe and unsafe activities after ICD.

CONCLUSION

The results revealed a fair level for both groups related patients' practice to safe measures post-ICD. After implementing the instructional program for the study group, members' practices had increased to a good level while the practices of the control group remained unchanged over the post-testing period.

Author's Contribution:

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Final Approval of version:	By all above authors

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Original Article

Methicillin-Resistant Staphylococcus Aureus Conundrum: Elucidating the Spectrum of Antibiotic Resistance

Awadh Alanazi

ABSTRACT

Objective: To assess MRSA's impact and the latest treatment strategies, seeking to improve management and containment efforts.

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Department of Clinical Laboratory Sciences, College of Applied Medical Sciences, Jouf University, Sakaka, Saudi Arabia, from March 2023 to February 2024.

Methods: S. aureus isolates from various clinical sources were identified using culture, biochemical, and phenotypic tests. MRSA isolates were identified using the cefoxitin (30 µg) disc as a surrogate marker. Antimicrobial susceptibility testing was performed using the Kirby-Bauer disc diffusion method to report antimicrobial resistance.

Results: Forty-eight S. aureus isolates, comprising 32 MRSA and 16 methicillin-sensitive S. aureus (MSSA) infections. Nasal swabs exhibited 100% MRSA occurrence, with high prevalence in wound swabs and blood cultures. MRSA isolates demonstrated multidrug resistance to various classes of antibiotics. In contrast, these isolates exhibited no or less resistance to fewer antibiotics such as vancomycin (0%), teicoplanin (0%), rifampin (0%), tetracycline (0%), linezolid (3%), and quinupristin/dalfopristin (3%).

Conclusion: The spectrum of antibiotic resistance in MRSA, emphasizing the need for tailored antibiotic treatment strategies and ongoing efforts to combat the spread of multidrug-resistant pathogens in healthcare settings.

Key Words: Staphylococcus aureus, Gram-positive infections, MRSA, antibiotic resistance, multidrug resistance

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INTRODUCTION

Staphylococcus aureus is a gram-positive bacterium belonging to the genus Staphylococcus. Several species and subspecies have been identified. S. aureus is part of the human microbiome, with 20% to 40% of humans carrying this organism as part of their normal flora.[1] However, S. aureus is the most commonly isolated organism in hospitals, community settings, and food sources, causing severe complications for patients and the hospital environment.[2,3] It causes many human diseases, including bacteremia, endocarditis, wound infections, and lung infections. The pathogenicity of S. aureus has been reported worldwide to be problematic in both community and hospital settings.[4]

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S. aureus infections rely on the evasion of the host's immune response, invasion of host tissues, and initiation of infection by producing enzymes and extracellular toxins that destroy host tissue and cells.[5] Clinically, the main issue with S. aureus is its ability to develop resistance to multiple drugs, leading to treatment complications. Traditionally, infections were treated with penicillin, which interferes with peptidoglycan assembly - the major component of the bacterial cell wall. This interference makes the bacterial cell wall fragile and deficient. Unfortunately, overexposure to penicillin led to the emergence of globally resistant strains, primarily through the deactivation and hydrolysis of the antibiotic's β-lactam ring by plasmid-encoded β-lactamase. A few years later, penicillin-resistant S. aureus rapidly became the predominant strain worldwide, causing severe infections. In 1959, methicillin was introduced as a treatment for β-lactamase-resistant penicillin. However, within a year of methicillin's introduction, the bacteria acquired the mecA gene, which encodes an alternative penicillin-binding protein. This gene conferred resistance to most β-lactam antibiotics.[6]

The rapid acquisition of resistance to penicillin and methicillin has been recognized as a global issue, making it increasingly challenging to treat S. aureus infections. In hospital settings, vancomycin, a late-stage

peptidoglycan synthesis inhibitor, is the preferred treatment for methicillin-resistant S. aureus (MRSA). However, vancomycin-resistant strains have been reported worldwide.[7] S. aureus can develop resistance to all classes of antibiotics available in clinical settings through various mechanisms, thereby limiting treatment options.[8]

Globally, MRSA is a life-threatening problem, leading to severe complications and a high risk of mortality, high therapeutic costs, and prolonged hospital stays.[9-11] In 2019, a study reported approximately 4.95 million deaths worldwide from multidrug-resistant infections, with around 100,000 associated with MRSA.[12] In Saudi Arabia, the number of MRSA cases has increased, with a prevalence rate of 35.6% derived from a pooled estimate of 22,793 infections with S. aureus.[13] Therefore, considering the significance of MRSA infections and the disease burden, the current study aimed to report the MRSA isolates and empirical therapeutic options for treating MRSA-associated infections.

METHODS

This cross-sectional study was conducted at the Department of Clinical Laboratory Sciences from March 2023 to February 2024. Leftover bacterial cultures from various clinical sources and wards of a tertiary care hospital were processed following the ethical considerations outlined in the WMA Declaration of Helsinki[14]. The study did not involve any animal or human participants.

The study specifically targeted S. aureus and excluded other bacterial isolates. S. aureus cultures were incubated aerobically on blood, chocolate, and mannitol salt agar overnight at 35–37°C. Identification of S. aureus was based on morphological characteristics, mannitol fermentation, catalase, coagulase, and DNase tests. Confirmed S. aureus isolates were screened to differentiate between MRSA and methicillin-sensitive S. aureus (MSSA) using a cefoxitin (30 µg) disc on Mueller-Hinton (MH) agar, following guidelines outlined in the CLSI manual.[15]

The antimicrobial sensitivity testing (AST) was performed according to CLSI guidelines using various antibiotic discs representing different classes of antibiotics, including amoxicillin/clavulanic acid, ampicillin, cephalothin, chloramphenicol, ciprofloxacin, clarithromycin, clindamycin, daptomycin, erythromycin, fosfomycin, fusidic acid, gentamicin, imipenem, levofloxacin, linezolid, moxifloxacin, mupirocin, penicillin, rifampin, quinupristin/dalfopristin, teicoplanin, tetracycline, trimethoprim/sulfamethoxazole, and vancomycin. The inoculum size of S. aureus was adjusted in sterile saline using 0.5 McFarland standard and all MRSA and MSSA isolates were streaked on MH agar plates using sterile cotton swabs. Antibiotic discs were then placed on the MH agar using the Kirby-Bauer disc diffusion method, and cultures were incubated at 35–37°C overnight. The susceptibility results were interpreted as resistant, intermediate, or sensitive based on predefined criteria.[15]

Data analysis was conducted using SPSS-27.0. A Chi-square test was utilized to investigate the significant association between antimicrobial resistance (AMR) and MRSA, with the significance threshold set at p-values lower than 0.05.

RESULTS

This study examined 48 bacterial isolates of S. aureus, comprising samples from 32 MRSA and 16 with MSSA. The distribution of MRSA and MSSA across different clinical specimens was investigated. Nasal swabs exhibited a 100% occurrence of MRSA, with no MSSA detected. A high prevalence of MRSA was also observed in wound swabs and blood cultures (66.67%), as well as in urine samples (60%). Conversely, sputum samples predominantly yielded MSSA, accounting for 66.7% of the isolates compared to 33.3% for MRSA. Ear swabs showed an equal distribution, with MRSA and MSSA each constituting 50% of the isolates. However, no significant difference ($p = 0.84$) was observed in the isolation rate of MRSA from various clinical sources (Fig. 1).

The results revealed that, for most antibiotics tested, a significantly higher proportion of MRSA strains were resistant than MSSA. Notably, amoxicillin/clavulanic acid and imipenem both demonstrated 100% resistance in MRSA strains, with highly significant p-values ($p< 0.001$). Additionally, resistance to ampicillin was observed in 100% of MRSA strains, with a p-value of 0.05. Resistance to ciprofloxacin and levofloxacin was also significantly higher in MRSA, at 78% for both antibiotics, with p-values of 0.001 and 0.003, respectively. In contrast, MSSA strains exhibited lesser resistance to most antibiotics, with no resistance (0%) noted for cefoxitin, imipenem, penicillin, and vancomycin (Table 1).

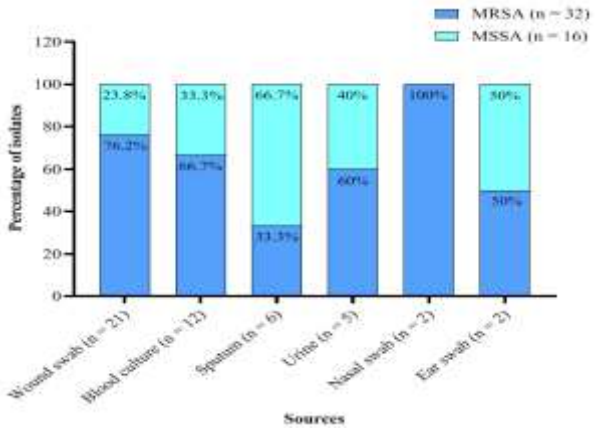

Figure No. 1: Comparative prevalence of MRSA and MSSA in clinical sources

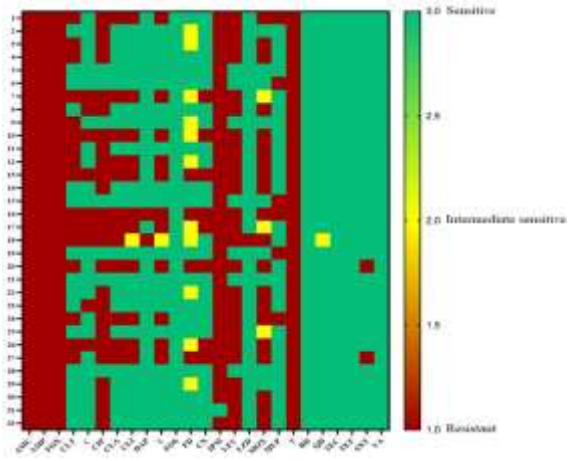

Figure No. 2: Antimicrobial spectrum in MRSA isolates

The variability in antibiotic response was evident among the MRSA isolates. A considerable number of these isolates were resistant to antibiotics such as amoxicillin/clavulanic acid, ampicillin, cefoxitin, penicillin, imipenem, and ciprofloxacin. Conversely, a few organisms exhibited resistance towards vancomycin, rifampin, teicoplanin, tetracycline, linezolid, and quinupristin/dalfopristin. These observed resistance patterns in the MRSA isolates underscore the evolving nature of bacterial resistance, highlighting the imperative for tailored antibiotic treatments in clinical practice (Fig. 2).

Antimicrobial response spectrum of MRSA isolates using a color-coded system: red indicates resistance (represented by a value of 1), yellow signifies intermediate sensitivity (value of 2), and green denotes sensitivity (value of 3). Amoxicillin/clavulanic acid (AMC), Ampicillin (AMP), Cefoxitin (FOX), Cephalothin (CLT), Chloramphenicol (C), Ciprofloxacin (CIP), Clarithromycin (CLA), Clindamycin (CLI), Daptomycin (DAP), Erythromycin (E), Fosfomycin (FOS), Fusidic Acid (FD), Gentamicin (CN), Imipenem (IPM), Levofloxacin (LEV), Linezolid (LZD), Moxifloxacin (MOX), Mupirocin (MUP), Penicillin (P), Rifampin RD, Quinupristin/dalfopristin (QD), Teicoplanin (TEC), Tetracycline (TET), Trimethoprim/sulfamethoxazole (SXT), Vancomycin (VA)

Table No. 1: Comparative analysis of antibacterial activity against MRSA (n = 16) and MSSA (n = 32).

Antibiotic	MRSA (n=32) Resistance		MSSA (n = 16) Resistance		p-value
Amoxicillin/clavulanic acid	32	100%	1	6%	<0.001*
Ampicillin	32	100%	13	81%	0.05*
Cefoxitin	32	100%	0	0%	-
Cephalothin	16	50%	6	38%	0.41
Chloramphenicol	9	28%	1	6%	0.07
Ciprofloxacin	25	78%	5	31%	0.001*
Clarithromycin	12	38%	1	6%	0.02*
Clindamycin	11	34%	2	13%	0.09
Daptomycin	2	6%	-	-	1
Erythromycin	10	31%	1	6%	0.04*
Fosfomycin	15	47%	-	-	0.004*
Fusidic Acid	4	13%	2	13%	0.71
Gentamicin	8	25%	1	6%	0.27
Imipenem	31	97%	-	-	<0.001*
Levofloxacin	25	78%	4	25%	0.003*
Linezolid	1	3%	-	-	0.6
Moxifloxacin	20	63%	5	31%	0.01*
Mupirocin	6	19%	1	6%	0.24
Penicillin	32	100%	-	-	-
Rifampin	-	-	-	-	-
Quinupristin/dalfopristin	1	3%	-	-	0.8
Teicoplanin	-	-	-	-	-
Tetracycline	-	-	-	-	-
Trimethoprim/sulfamethoxazole	2	6%	1	6%	0.9
Vancomycin	-	-	-	-	-

*Significant p-value**.**

DISCUSSION

Despite improvements in healthcare facilities, S. aureus remains the primary cause of hospital infections worldwide, with a broad spectrum of clinical diseases ranging from superficial infections (such as folliculitis) to life-threatening.[16] This study focused on the characterization of S. aureus antibiotic resistance, mainly methicillin resistance. It has been reported that MRSA cases are frequently distributed in surgical

areas.[17] A study found that the prevalence of MRSA is more likely in males than in females.[18] This elucidates the variation in gender distribution based on geographic area and host factors such as age and general health status. The prevalence of MRSA fluctuated over various periods. A study from Pakistan in 2011 revealed a 35.8% incidence of MRSA in clinical environments.[19] There has been a notable variation in the prevalence of MRSA in Saudi Arabia, with a significant increasing trend reaching 14.5% in 2019 compared to 5.2% in 2009.[20]

According to the Centers for Disease Control and Prevention (CDC), in 2019, about 33% of healthy individuals carried MRSA in their noses without developing any severe MRSA infections. Although many people are considered carriers of MRSA, several studies have reported that these carriers are considered a source of infection in hemodialysis and surgical wards. In this study, despite the limited number of nasal samples, 2 out of 2 (100%) were found to be MRSA carriers, consistent with the findings reported by the CDC. In this study, bloodstream infections and skin infections were the most common sites of MRSA infection, in line with findings from other studies.[21]

Treating isolates resistant to multiple drugs, whether gram-negative or gram-positive, from clinical and non-clinical origins presents enduring challenges, with MRSA distinguishing itself as a particularly significant concern.[11,22,23] In 2014, the World Health Organization (WHO) Global Report on Surveillance reported that the treatment of verified or suspected cases of MRSA worldwide must rely on second-line treatments, which are costlier and have more side effects, since first-line treatments for severe MRSA have limited efficacy. Treatment of S. aureus infections is available based on different antimicrobial therapies; however, several reports have confirmed the limitations of treating the infection since the organism has become resistant to first-line drugs[24]. In this study, vancomycin, teicoplanin, and linezolid showed no resistance to MRSA and are considered excellent therapeutic options for MRSA infections.[25] Another study presented similar findings regarding vancomycin sensitivity, teicoplanin, and linezolid as treatment options for MRSA infections.[25,26] All MRSA strains showed resistance to amoxicillin/clavulanic acid, ampicillin, cefoxitin, and penicillin as therapeutic options against MRSA infection. These findings are consistent with various reports from around the world.[27,28]

In this study, ciprofloxacin showed poor therapeutic activity against the MRSA strain, exhibiting resistance in 78% of cases. A variable degree of ciprofloxacin resistance to MRSA infection has been reported in different Gulf Cooperation Council countries.[29] Fusidic acid has been used clinically to treat MRSA infections in various parts of the world and is considered a drug of choice for treating MRSA.[30] In this study, fusidic acid showed meager resistance (13%) to the MRSA strain, which is lower than what was reported in Riyadh in 2006[31] and similar to findings in the UK.[32] The risk factors for acquiring MRSA, continuous reporting of new cases, and monitoring of colonized individuals should be considered to control and reduce the spread of this disease. The current study has limitations due to its inability to explore the clinical data and the molecular basis of mecA genes involved in the emergence of MRSA.

CONCLUSION

The emergence of MRSA presents a significant challenge in healthcare settings due to its diverse antibiotic resistance patterns. MRSA exhibited high resistance to commonly used antibiotics, whereas MSSA strains demonstrated greater sensitivity. Although therapeutic options for MRSA infections are limited by resistance to first-line antibiotics, vancomycin, teicoplanin, and linezolid continue to be effective treatments. Continuous surveillance and identification of risk factors are essential for controlling the spread of MRSA despite limitations in investigating the molecular mechanisms underlying its emergence. This resistance extends the duration of illness and escalates the financial burden of treatment.

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Author's Contribution:

Concept & Design of Study:	Awadh Alanazi
Drafting:	Awadh Alanazi
Data Analysis:	Awadh Alanazi
Revisiting Critically:	Awadh Alanazi
Final Approval of version:	Awadh Alanazi

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Original Article

Effect of Two Different Impression Materials in Recording Mean Retention Bases on Heat Cure Acrylic Resins

Shahnila Sharif[1], Hina Memon[1], Nizam uddin Buriro[1], Naseem Shaikh[1], Uzma Bashir[2] and Muhammad Rizwan Memon[2]

ABSTRACT

Objective: This study was undertaken to compare the forces of retention for maxillary polymethyl methacrylate denture bases fabricated by using single step low fusing green stick compound (Group 1) and single step border moulding using addition silicone (putty) impression material (group 2).

Study Design: Randomised control trial study

Place and Duration of Study: This study was conducted at the Department of Prosthodontics, Institute of Dentistry Liaquat University of medical and health science Jamshoro from April to September 2021.

Methods: A sample of 90 edentulous patients, 45 in each group with age group 40-60 yrs, both genders were included in this study. Retention values of customised heat cure acrylic denture bases (Group 1 border moulded with green stick compound and Group II - border molded with addition silicone putty impression material) were recorded using digital force gauge machine company attached to wire loop at the center anterior part of each plate. Definitive wash impression were made with light body addition silicone for both groups.

Results: The average age of the patients was 51.27±5.4 years. There were 44(48.9%) male and 46(51.1%) female. Mean retention was found to be higher in group 2 (addition silicone : 32.75±6.78) as compared to group 1 (green stick compound : 29.94±10.89; p=0.0005].

Conclusion: It was concluded that the heavy bodied addition silicone is a better material for border moulding as compared to low fusing green stick impression compound.

Key Words: Complete dentures, addition silicone, green stick compound, border moulding materials

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INTRODUCTION

Edentulism is a debilitating and irreversible condition common amongst elderly population [1]. For years, the most often recommended course of treatment for edentulous patients has been the fabrication of complete dentures [2]. Thus, a complete denture needs to meet the three main goals of prosthodontics: support, stability, and retention[3]. The definition of retention is the ability of a prosthesis to resist forces of dislodgment along the path of insertion and the resistance of a denture to vertical movement away from tissues[4].

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There are certain factors that are more important than other in retention of complete dentures such as anatomical, physiological, physical, mechanical, muscular [5].

The most crucial clinical procedure in full denture construction—border moulding—is necessary to establish retention. Border moulding is the process of reshaping the imprint tray's border portions by manually or functionally manipulating the tissues next to the border to replicate the vestibule's size and shape. This will aid in forming the peripheral seal between the oral tissues and denture borders, preventing air from entering and causing the denture to loosen [6]. There are numerous materials available for recording peripheral seals, but the most often utilised ones are low-fusing green sticks due to their quick setting time, detail reproduction ability, affordability, reusability, and lack of noticeable dimensional changes after hardening.

Although addition silicon records all boundaries on a single placement, it is simple to handle, has a sufficient amount of working time, is free of undercuts, and is a time-saving method [7, 8]. These materials have been the subject of numerous research. In maxillary edentulous arches, single step border moulding (mean 8.26 kgf) and sectional border moulding (mean 9.05 kgf) utilising two distinct techniques differed significantly, according to a study by Qanungo A et al 7. Yarapatineni R et al.'s

subsequent investigation revealed no discernible difference between sectional border moulding (mean 3835.07) and single step border moulding (mean 4025.14)[8].

One common issue with people who have complete dentures is retention. Despite numerous studies, there is a lack of data and conflicting statements regarding retention. International data compares both materials, but the implementation of the results is not feasible in our population because of differences in genetics, anatomy, denture design, and skill. Additionally, a limited amount of local studies have been carried out, it has been noted. Therefore, the goal of this study is to compare the retention of border moulding materials composed of green stick compound and addition silicon for maxillary complete dentures. This study was beneficial for dental practitioners to use either green stick compound or addition silicon impression materials for recording accurate peripheral seal and it will also be beneficial for population in terms of improving quality of denture retention.

METHODS

The present study was conducted at department of Prosthodontics LUMHS Jamshoro for a period of 6 months from April to September 2021. Total 90 edentulous patients were selected using non probability consecutive sampling technique and divided into two groups randomly. The exclusion criteria included fibrous ridge, resorption of ridge, tissue undercuts to eliminate the effect of mechanical factors on dentures retention, bony exostoses, and tori. Informed consents were taken from all participants the procedure of methodology was explained in detailed before commencement of our data collection.

Metal stock impression trays were selected for each patient and initial impression were made using green stick impression compound material (Harvard). The primary cast were fabricated with (lab stone Gerecco) followed by custom tray fabrication using self cure acrylic resin (material name). After functional trimming of 2 mm of self cure acrylic resin trays, group-1 participants had their border mouldings done by addition silicone and group 2 had their border mouldings done by green stick compound impression material (Harvard) followed by final impressions made with a light body addition silicone material (Aquasil® Ultra Smart Wetting® Impression Material; Dentsply Sirona, York, USA) for both groups. All materials were used as outlined in the manufacturers' guidelines. The borders of denture bases were properly moulded by functional movements of surrounding musculature. The final cast were poured by using type 2 dental stone (material) for both groups. Final plates were fabricated using heat cure acrylic resin (material). Wire loop (0.7mm round stainless steel wire) were constructed and secured with the help of self cure acrylic resin (material name) at centre of anterior ridge portion of processed heat cure plate . Patients were asked to sit in upright position on dental chair with occlusal plane parallel to the floor. The heat cure acrylic denture plate for both groups were inserted in patient's mouth with uniform finger pressure. After a wait of one minute to allow the denture base plate to reach in stable position, the force gauge device was attached to the wire loops attached to plates to asses the forces of retention required to dislodge the denture base. The procedure of dislodgment by pulling force was repeated three times with each plate in same patient and the mean reading was noted down in proforma. Data was analysed using SPSS version 24. Mean value were calculated for quantitative variables like age of patients and dislodging force whereas frequency and percentage were calculated for qualitative variables like gender.

RESULTS

A total of 90 patients were randomly distributed in two groups, i-e group A, impressions were taken with green stick impression compound and group B with light body addition silicone. The forces of retention were assessed for both group (fig 1).The average age of the patients was 51.27±5.4 years (figure 2). There were 44 (48.9%) male and 46(51.1%) female. Gender distribution with respect to groups is shown in (figure 3). Comparison of mean retention pressure of maxillary complete denture between groups is presented in figure 4. Mean retention was significantly high in group B as compare to group A (32.75±6.78 vs. 29.94±10.89; p=0.0005).

Figure No.1: Retention Values for Different Patients

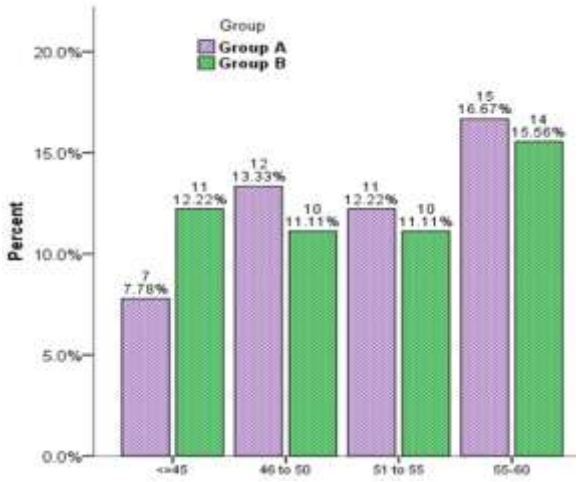

Figure No. 2: Age Distribution of the Patients With Respect to Groups

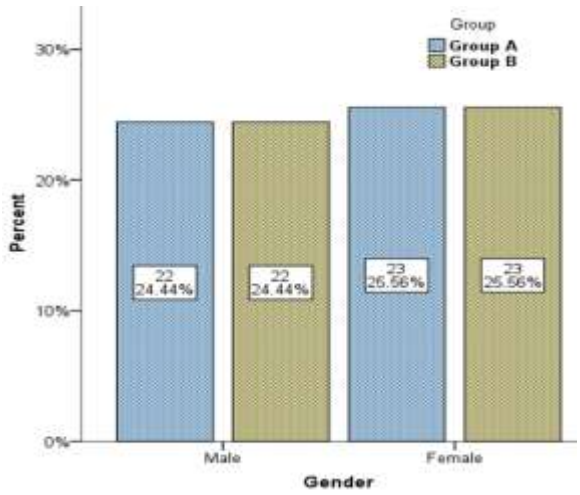

Figure No. 3: Gender Distribution of the Patients With Respect To Groups

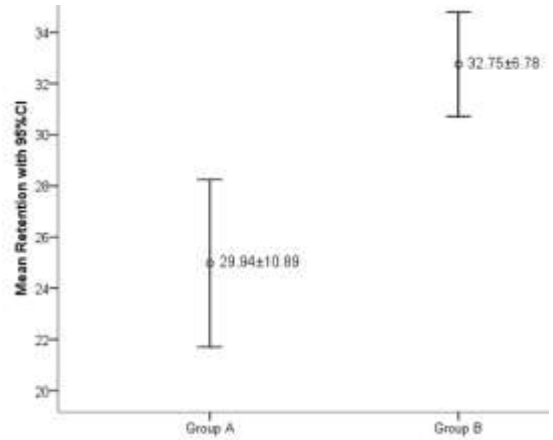

Figure No. 4: Comparison of mean retention pressure of maxillary complete denture between groups

Table No. 1: Descriptive Statistics of Age with Respect to Groups

	Group A	Group B
Mean	51,40	51,13
Std Deviation	5,41	5,44
Average age	51.27±5.4 years	

Table No. 2: Descriptive Statistics Of Gender

Gender	Total Number	Frequency
Males	44	48,9 %
Females	46	(51.1%)

Table No. 3: Mean Retention valies for both groups

Group 1	29.94±10.89
Group 2	32.75±6.78
P-value	0,005

DISCUSSION

One of the key components of removable prosthodontics is the construction of complete dentures[9], as dental restorations enhance both overall oral health and quality of life. However, precise replication of the oral foundation using impression techniques is essential for a complete denture to function as intended. To do this, records of the maximal coverage of denture-supporting areas within physiological bounds must be made[8,–10.] A polished and finished denture foundation should have optimal retention, and its boundaries should be in physiological balance with the surrounding soft tissues of the mouth[11]. Since border moulding concentrates on biological, physical, and mechanical aspects to help achieve retention through final impression method, it is regarded as a crucial step in the production of complete dentures[12]. The comparatively recent implications of new materials and devices have called into question the conventional wisdom, even though the traditional approaches to impression making in complete denture fabrication have served the profession well over the years. These approaches allow for the fabrication of accurate, pressure-controlled, definitive impressions without the need to develop custom impression trays. There are many viscosities of VPS impression material available, and a certain level of control over tissue placement can be achieved by applying these materials thoughtfully and varyingly at different points throughout impression procedures. To compare the mean retention pressure of maxillary complete denture, heat cure plates were made by using addition silicon and green stick compound border moulding materials.

A total of 90 patients of both genders were chosen at random. Two groups of patients were formed from this group. The patients who took part in the trial were chosen based on their age, which varied between 40 and 60 years old. The impression material's viscosity[13] and the tray's proximity of the oral tissues can both contribute to the pressure applied during an imprint technique.

When the maxillary complete denture's mean retention pressure was compared between the groups, group 2's mean retention was shown to be considerably higher than group 1's (32.75±6.78 vs. 29.94±10.89; p=0.0005). This demonstrates that silicone addition dominates impression compound as a superior material for border moulding.

Other studies corroborated our findings. In their investigation, Jassim et al. found that while using green stick composite material for the denture bases, the mean retention force was lowered when the final impression was created using zno eugenol. When a light-body final impression material and additional vinyl silicon border moulding material were used, the measured mean retention values increased noticeably [14]. In a different study, Gupta et al. used heavy body addition silicones for border moulding and found that the group using heavy bodied addition silicone had mean vestibular depths and widths of 12.31±1.29 mm and 6.44±0.76 mm, respectively. This suggests that heavy-bodied addition silicone produces dentures with more precise borders and better retention [15].

CONCLUSION

Based on the study it was concluded that the heavy bodied addition silicone is a better material for border moulding as compared to low fusing impression compound. In addition, single step done with heavy bodied addition silicone was found to be viable and advantageous alternative to conventional border moulding (sectional border moulding), as it results in reduction of chair side time, less discomfort for the patient and less efforts for the dentist.

Author's Contribution:

Concept & Design of Study:	Shahnila Sharif
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Data Analysis:	Nizam uddin Buriro, Naseem Shaikh, Uzma Bashir, Muhammad Rizwan Memon
Revisiting Critically:	Shahnila Sharif, Hina Memon
Final Approval of version:	By all above authors

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

Source of Funding: None

Ethical Approval: No.PR-058 dated 08.03.2021

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Original Article

Advancing Pterygium Surgery with the Reverse Striping Technique Using Locally Available Diamond Burr : A Prospective Cohort Study

Aurangzeb Shaikh[1], Mohammad Imran Sarwar Khan[1], Ali Zeb[2], Anjali Zeb[2], Raj Kumar[1] and Ummary Kalsoom[1]

ABSTRACT

Objective: This prospective study aims to evaluate the efficacy and safety of the reverse striping technique using a locally available diamond burr, comparing it with conventional surgical methods.

Study Design: A Prospective Cohort Study

Place and Duration of Study: This study was conducted at the Eye Department of Fazaia Ruth Pfau Medical College, Karachi from November 2022 to November 2023.

Methods: After ethics approval and informed consent, patients underwent thorough pre-operative assessments. They randomized to receive either conventional surgery or the reverse striping technique. Post-operative follow-ups conducted to evaluate visual acuity, corneal astigmatism, recurrence rates, and patient satisfaction.

Results: The study cohort comprised 15 females (41.6%) and 25 males (58.3%) with a median age of 47.22 years. The mean visual acuity for the entire cohort was 0.62134 LogMAR preoperatively. Postoperative mean visual acuity was 0.4467 LogMAR in Group 3 and 0.795 LogMAR in Group 4, with no significant difference between preoperative and postoperative outcomes. The mean k1 and k2 readings showed a reduction of 1.5D in cylindrical numbers postoperatively. Recurrence rates were 10% (RT1) and 90% (RT0).

Conclusion: The reverse striping technique using a locally available diamond burr offers a promising alternative for pterygium surgery, with moderate visual acuity improvements, significant reduction in corneal astigmatism, and a low recurrence rate. Future research should focus on standardizing surgical methods and exploring additional treatments to enhance visual outcomes and further reduce recurrence rates.

Key Words: Pterygium, recurrence, astigmatism, Visual Acuity

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INTRODUCTION

Pterygium is a common ocular surface disorder that can cause discomfort and vision impairment[1,2,3]. The abnormal tissue growth encroaching the cornea from the nasal side, a pterygium flattens the horizontal meridian of the cornea and consequently causes induced with the rule (WTR) astigmatism by mechanical traction [4,5].

Traditional surgical techniques for pterygium removal have been associated with a high rate of recurrence[7], leading to the development of innovative approaches such as the reverse striping technique using a locally available diamond burr. This prospective cohort study aims to examine the effectiveness and safety of this surgical method in comparison to conventional techniques[8]. By exploring the potential benefits of the reverse striping technique, we can contribute to the enhancement of pterygium surgery outcomes and ultimately improve the quality of patient care. The reverse striping technique using a locally available diamond burr offers a promising alternative for pterygium surgery augments with ant fibroblast drugs.

Through the rigorous collection and analysis of data, this prospective study aims to advance our understanding of pterygium surgery and contribute to the ongoing refinement of surgical techniques. By elucidating the potential benefits of the reverse striping technique using a locally available diamond burr, we aim to empower ophthalmologists with evidence-based insights to guide their clinical decision-making and ultimately enhance the standard of care for patients with pterygium.

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METHODS

This study was conducted at Eye department, Fazaia Ruth Pfau Medical College, Karachi from November 2022 to November 2023, on patients with primary pterygium after approval from Ethics and Research Committee (Ref no. IRB/03 dated 06.10.2020). After informed consent, a detailed history in relation to ocular and systemic disease was taken. A detailed ocular examination was recorded which includes visual acuity assessment (using Snellen's visual acuity chart later converted to the logarithm of the minimal angle of resolution), Pinhole testing if V/A less than 6/12, Retinoscopy (objective and subjective), Keratometry using autokeratometer, distant direct ophthalmoscopy to assess the cornea, cataract, slit lamp examination to rule out conjunctival pathology, corneal assessment, anterior chamber angle and depth, intraocular pressure measurement (Goldmann applanation tonometer), retinal examination (using Volk 90D lens) to record optic disc and macular changes. All patients with unilaterally or bilaterally nasal pterygium were included in the study and patients with secondary pterygium or temporal pterygium were excluded. The pterygium was classified according to the thickness of the pterygium in to three grades as described by the researcher Grade T1 (When episcleral vessels clearly visible through the pterygium body); Grade T2 (when episcleral vessels underlying the pterygium body were partially obscured); and Grade T3 (when episcleral vessels underlying the pterygium body).

For our study we categorized the pterygium according to the length of the pterygium in to four categorize(Group 1 pterygium growth confined at conjunctiva, Group 2 pterygium touches the nasal limbus, Group 3 pterygium remained ≤ 2mm away from the pupillary zone at nasal cornea , Group 4 pterygium encroaching ≥ 2mm on the corneal touching or crossing the nasal pupillary zone. Only patients with Group 3and Group 4 were included in the study.

After informed consent for surgical procedure, 0.2 ml of xylocaine was injected at the center of the pterygium to raise the conjunctiva. A peritomy was done with blunt scissors, tenon capsule was separated from conjunctiva, 2.5mm of tenon capsule was removed and gentle cautery was done to maintain hemostasis. The abnormal conjunctival tissue was lifted and cutdown with scissors. A superior rectus holding forceps was used to lift the pterygium and pull (strip) towards the corneal limbus, then using a diamond bur (a gentle touch on cornea) with continues irrigation was done to clear the attached remnant of pterygium debris from the cornea. Conjunctiva was secured using 8-0 absorbable sutures. At the end of the procedure, topical cyclopentolate drop installed to relieve the pain due to ciliary spasm along with a sub-conjunctival injection of antibiotic and steroid to reduce the inflammation.

Postoperatively, percentage of recurrent pterygium was the desired outcome. RT0 (no recurrent pterygium),RT1 (recurrent pterygium located only at sclera),RT2 (recurrent pterygium touches the limbus) and RT3(recurrent pterygium involving the cornea) . Statistically, we calculated our sample size keeping the following parameters in consideration, estimated efficiency rate of a standard treatment =60% P1, estimated efficiency rate of Pterygium removal using diamond burr was = 80% P2, Difference in efficiency of two treatments=20% P1-P2, Significant Level =5%, Power of the study= 90%, Sample size 40 subjects.

Table No. 1: Showing the Age, Sex, and Visual Acuity distributions of Study Participants.

Category 1 (Age)	Number of Patients
Group 1 - 20 to 30	19
Group 2 - 31 to 40	13
Group 3 - 41 to 45	8
Category 2 (Sex)	
Group 1 Male	25
Group 2 Female	15
Category 3 (VA)	
Group 1 - 6/9. to 6/12.	10
Group 2 - 6/18. to 6/24	13
Group 3 - 6/36 to 6/60.	17
Category 4 (Grade 3)	
Group 1 - 6/9. to 6/12.	10
Group 2 - 6/18. to 6/24	13
Group 3 - 6/36 to 6/60.	17

RESULTS

40 eyes of 35 patients (Five patients with bilateral pterygium) with primary pterygium were included in the study with a mean follow-up time of 12 months. The study population consisted of 15 females (41.6%) and 25 males (58.3%) with a median age of 47.22 years. The study cohort included 40 eyes with primary pterygium. Table 2 summarizes the baseline characteristics of our study sample.

Table No. 2: Descriptive Statistics of different variables

	Mean	Median	Mode	Standard Deviation
Age	47.23	48	40	4.90
Visual acuity Preoperative	0.63	0.60	1	0.33
Visual Acuity on Final Follow up	0.61	0.55	1	0.30
Group 3 K1/K2	43.35/45.85	42/46	43/46	0.13/0.26
Group 4 K1/K2	42.55/46.45	42/42	42/47	0.12/0.28

Visual Acuity: General (n=40): The mean visual acuity was 0.62134 Log MAR with 0.6020 Median, Mode1 and 0.30831SD.

Visual Acuity: Group 3(n=20) and 4(n=20): The mean visual acuity on final postoperative follow-up was 0.4467,0.795 Log MAR with 0.477,1 Median, Mode 0.477 , 1 and 0.2458SD and 0.2655 in group 3 and 4 respectively with no significant difference between Preoperative and postoperative visual outcome.

Corneal Astigmatism k1/k2: The mean k1 and k2 reading in group 3 sample unit with primary pterygium was k1=43.35,k2=45.85, mode k143,k246, median k142, k246,SDk1=0.1312891,SD k2=0.812727, range k1=2, k2=3. The mean k1 and k2 reading in group 4 sample unit with primary pterygium was k1=42.55,k2=46.45,mode k1=42,k2=47,median 42

Recurrence Rate: Out of 40 patients, 90% (36 patients) remained in RT0 (no recurrent) and 10% (4 patients) in RT1 (recurrent pterygium at sclera). On final postoperative follow up with one line impotent in Visual acuity on Snellen's chart (preoperative mean V/A 0.63 and postoperative 0.61) and reduction of 1.5D of Cylindrical number on K1/K2 readings.

DISCUSSION

Patient Demographics and Study Cohort: This study evaluated the outcomes of pterygium surgery in a cohort of 35 patients (40 eyes) with primary pterygium, including five patients with bilateral cases. With a mean follow-up period of 12 months, our study population comprised 15 females (41.6%) and 25 males (58.3%), with a median age of 47.22 years. This demographic distribution indicates a slightly higher prevalence of primary pterygium among males in our sample.

Visual Acuity: Visual acuity is a vital measure of the success of pterygium surgery. In our study, the mean visual acuity for the entire cohort (n=40) was 0.62134 LogMAR, with a median of 0.6020 and a standard deviation of 0.30831. Analyzing the outcomes by group, the mean postoperative visual acuity in Group 3 (n=20) was 0.4467 LogMAR and 0.795 LogMAR in Group 4 (n=20), with medians of 0.477 and 1, respectively, and standard deviations of 0.2458 and 0.2655. Importantly, there was no significant difference between preoperative and postoperative visual outcomes. Our study results show a lesser degree of visual acuity improvement compared to these studies[9.] The discrepancy could be due to variations in surgical techniques, patient demographics, or the initial severity of the pterygium.

Corneal Astigmatism: Corneal astigmatism, assessed through k1 and k2 readings, provides additional insight into the impact of pterygium surgery on corneal shape. In Group 3, the mean k1 and k2 readings were 43.35 and 45.85, respectively, with standard deviations of 0.2655. Both groups showed a reduction of 1.5D in cylindrical number on k1/k2 readings postoperatively. Salih Sharif[10,11], Observed a significant reduction in corneal astigmatism postoperatively, with the mean k2 decreasing from 45.72 to 43.12 diopters[10,11] and Kheirkhah et al[14] reported significant improvements in corneal astigmatism, with mean k2 values decreasing from 46.00 preoperatively to 44.50 diopters postoperatively.

Our study demonstrates a notable reduction in corneal astigmatism, aligning with findings from other studies, although the degree of improvement varies. This variation may be attributed to differences in surgical techniques or patient selection criteria.

Recurrence Rate: Recurrence of pterygium is a crucial concern following surgery. In our study, 90% of patients (36 out of 40) showed no recurrence (RT0), while 10% (4 patients) had recurrence limited to the sclera (RT1). Despite these recurrences, there was only a slight improvement in visual acuity on the Snellen chart (preoperative mean V/A 0.63 to postoperative 0.61) and a reduction of 1.5D in cylindrical number on k1/k2 readings.

Researcher reported a lower recurrence rate of 15% at the one-year follow-up using conjunctival auto-graft transplantation.[14] Clearfield et al[15] found recurrence rates ranging from 5% to 39%, depending on the surgical technique used, with lower rates associated with the use of mitomycin C and conjunctival auto-graft.[16]

Our study's recurrence rate is comparatively lower, suggesting the effectiveness of our surgical approach in reducing recurrence. However, it still emphasizes the need for exploring adjunctive treatments or refined surgical techniques for further minimize recurrence.

CONCLUSION

In summary, our study indicates moderate improvements in visual acuity and corneal astigmatism following pterygium surgery, with a relatively low recurrence rate. Compared to other studies, our results show a lesser degree of improvement in visual acuity but a more favorable recurrence rate. These discrepancies highlight the variability in surgical outcomes and underscore the importance of optimizing surgical techniques and considering adjunctive therapies to enhance patient outcomes and reduce recurrence rates in the management of primary pterygium. Future research should focus on standardizing surgical methods and exploring additional treatments to improve visual outcomes and further reduce recurrence rates.

Author's Contribution:

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Final Approval of version:	By all above authors

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Original Article

Investigating the Rise in Pediatric Obesity Among Children Aged 1 to 5: The Impact of Nutritional Intake and Dietary Patterns

Shabnam Mahsood[1], Wagma Maqsood[1], Shahrukh Yar[2], Jahanzeb Khan Afridi[2], Mian Abdur Rehman[1] and Tanzeel Ur Rahman[1]

ABSTRACT

Objective: The purpose of study is to determine the effects of nutrient and dietary on the increasing prevalence of obesity amongst children of age 1 to 5 years.

Study Design: A Cross Sectional Study

Place and Duration of Study: This study was conducted at the Department of Pediatrics, HMC Peshawar, starting January 2023 to January 2024.

Methods: Consequently, the sample was selected from 300 children at the age of 1 to 5 years. Dietary consumption habits were captured using the parent's self-administered dietary forms, while the child's BMI was determined to categorise weight status. Information were also analyzed and compared with a view to identifying relationship between eating habits and obesity.

Results: The mean age of the children was 3. 2 years SD = 1. 4 years. Of the 300 participants, 28% of the participants were categorised as obese, 15% as overweight, and 57% as having normal weight. The study further showed that there was a difference in dietary behaviour between the Obese and non-Obese groups ($p < 0.05$). Boy and girl and boy child consuming a large number of calories were more likely to be obese.

Conclusion: The study therefore finds that unfavourable dietary practices are rapidly contributing to obesity among the 1 to 5 years old children in Peshawar. It is now important that giving proper information to parents and having healthcare providers' cooperation to make early prevention because this ascending public health problem.

Key Words: Child Obesity, Diet, Nutrient Profile, Child Health

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INTRODUCTION

Obesity in childhood has been described as a growing epidemic across the globe with numerous impacts in later life patterns of health. It is well noted that children between the age of 1-5 years are important, in shaping dietary patterns and setting future course of life. This age group of children has many health complications based on obesity; they are prone to develop other diseases such as type 2 diabetes, cardiovascular diseases as well as metabolic syndrome in their later years.

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The increasing incidence of childhood obesity is of great concern especially in developing countries such as Pakistan: A Review of Current Trends in Children's Nutrition, Urbanization and Other modifiable Factors[1]. In Pakistan pediatric obesity has been growing much faster and commonly seen in urban region like Peshawar due to increase in socio economic status and changes in life style which has resulted in direct intake of energy dense nutrient-poor foods. The original diet, which was plenty of fruits and vegetables, whole grain products and others were swapped by processed foods products containing high level of sugars, fats and calories. Adequate changes in dietary habits have been coupled with reduced activities that require physical exertion, thus children spend most of their time watching television or playing video games. These have escalated to form the perfect early childhood obesity storm since they all work cohesively. The etiology of pediatric obesity is not well understood but is mutually interactive with pathways such as genetic, environmental and behavioral factors. However, dietary intake is another influential factor; research indicate that improper diet in childhood increases the risk of obesity and weight gain[2]. Increased consumption of

calories, taking lots of sugars and fizzy drinks and the lack of portions control are largely responsible for obesity in young kids. Also, family factors with special emphasize on parents, have a significant impact in the determination of children's diet. The following long-term effects of pediatric obesity are evident; physical health: psychological and social. In addition, such children are vulnerable to developing poor self-esteem, depression, and social isolation which actually worsens their weight problem[3]. However, obesity also has its own drawbacks: people with this pathology often become the target of discrimination and bullying, which means that they develop a vicious circle that is very difficult to overcome. Hence, the best time to tackle obesity in the children is early in their ages and this requires putting into place good measures that can effectively prevent the condition. To this end, the purpose of the current research is to analyze the relationship between an increasing prevalence of obesity among children aged 1 to 5 years in Peshawar and their nutritional status and behavior. Thus, with reference to the aspect of the specified problem under investigation, namely the consumption of foods as a cause of obesity in young children this research aims at establishing the most appropriate factors that may be attributed to this age group of children. This knowledge assists in designing interventions that can help in preventing early childhood obesity and eventually decrease the cases of the condition. It is even more important in the case of Peshawar, where there is a dearth of literature on pediatric obesity and its antecedents. In conclusion, the results of this study will help to slightly open the veil over the identification of dietary patterns of young children in this region, and will contribute to the formation of the relevant concepts and further public health programs designed to prevent the increase in the rate of paediatric obesity.

METHODS

This research work was planned as cross-sectional at the Department of Pediatrics HMC Peshawar carried out for one year between January 2023 to January 2024. Two hundred and five of the respondent children were males while ninety-five were females The study children were selected through random sampling and they were 300 in number aged 1-5 years. Measures of nutrition and diet behaviour were assessed with structured questionnaires that involved the parents or guardians of these children. Anthropometric measurements included weight, height and body mass index (BMI) of the children were determined and the children were categorized by the WHO growth reference. For this purpose, the study planned to associate the dietary habits prevailing in this age group with receipt of obesity.

Data Collection: Demographic data was collected through structured dietary questionnaires completed by parents or carers which included information on the child's daily intakes of foods and beverages, portion sizes and frequency of foods groups. Height, weight and BMI data were obtained at times when the child was being taken for a routine pediatric check up.

Statistical Analysis: All statistical analyses of the data collected were done with SPSS version 22. 0 . To analyse the data conveniently the Descriptive statistics were used; and for analysing the significance of the differences in obesity with different washroom dietary groups, chi-square statistics were used. Data was analysed using descriptive statistics and chi square test; $p < 0 \bullet 05$ was used as the level of significance.

RESULTS

The mean age of the children in the study was 3 years and 2 months with standard deviation of 1year and 4months. Among 300 children 28 % children were come under the category of obesity, 15% of children come under over weighted children and 57% of children come under normal weighted children. The study confirmed the findings showing that children who took more calories on a regular basis and had a high tendency of taking processed foods were more likely to be obese than children who took their nutrition in the right balance ($p < 0.05$). They underscore the link between inadequate nutrition and on set of obesity in early childhood stage.

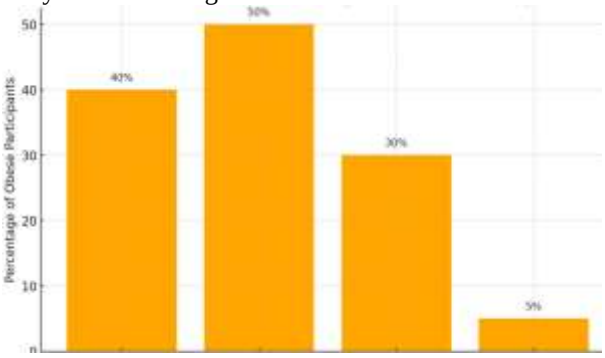

Figure No. 1: Correlation between Dietary Patterns and Obesity

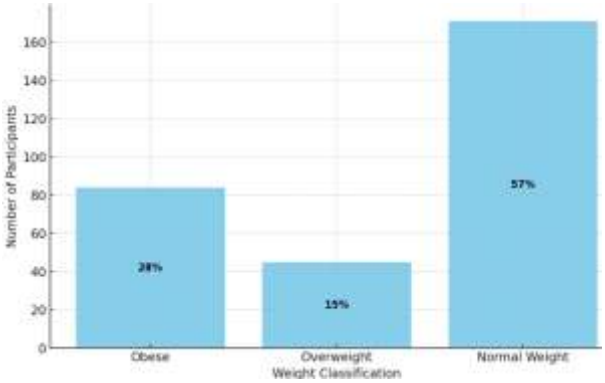

Figure No. 2: Weight Classification Distribution Among Participants

Table No. 1: Demographic Characteristics of Study Participants

Characteristic	Value
Total Number of Participants	300
Mean Age (Years)	3.2
Standard Deviation (Age)	1.4
Gender Distribution (Male)	52%
Gender Distribution (Female)	48%

Table No. 2: Nutritional Intake and Dietary Patterns

Dietary Pattern	Percentage of Participants
High-Calorie Diet	30%
Frequent Processed Food Consumption	35%
High Sugar Intake	25%
Balanced Diet	10%

Table No. 3: Weight Classification of Participants

Weight Classification	Number of Participants	Percentage of Participants
Obese	84	28%
Overweight	45	15%
Normal Weight	171	57%

Table No. 4: Correlation Between Dietary Patterns and Obesity

Dietary Pattern	Percentage of Obese Participants	p-value
High-Calorie Diet	40%	<0.05
Frequent Processed Food Consumption	50%	<0.05
High Sugar Intake	30%	<0.05
Balanced Diet	5%	>0.05

DISCUSSION

The presented current study supports the accumulating literature regarding the significance of dietary habits and nutritional consumption for pediatric obesity. Much of this research aimed at investigating the factors responsible for obesity among children aged 1 to 5 years in Peshawar; the findings confirm that high calorie diets, frequent consumption of processed foods, and obesity rates are generally on the rise among this age bracket. The effect of dietary habits during early childhood period has been proved in number of previous works concerning the estimation of the long-term health status. For instance, according to the study conducted by Kelishadi et al. (2007) underlined that the sacrifices of poor diet in childhood may transfer in adolescence and adulthood, causing the increased threats of chronic diseases including obesity, diabetes and cardiovascular diseases[4]. The results of the present work are in parallel with the studies conducted by Kelishadi et al as children in Peshawar who consumed calories and processed foods were much more prone to become obese or overweight[5] This change in the eating pattern, more so in the urban society, has been well captured in the literature. For instance, Popkin (2001) explained nutrition transition in many developing nations where fruits, vegetables and whole grain based diets are being replaced with energy intensive, nutrient sparse foods[6]. In line with these changes, different factors that have been known to promote the shift include; globalisation, urbanisation, and easy access to processed foods. The results of the current study are in line with this trend because a large number of children in Peshawar consumes non-traditional diets that increase their vulnerability to obesity[6]. Furthermore, lifestyle, including dietary behaviours and obesity has been associated with socioeconomic characteristics. Wang et al. observed that obese children are more common in the higher sensitive economic status due to increased affordability of unhealthily foods and reduced physical activity[7]. This finding supports the findings reflected in the present study, where children from the affluent families in Peshawar reported higher levels of obesity, because of their regular intake of processed food and soft drinks. These 'diets' were found to relate highly to obesity and this was confirmed by the statistical test results giving a $p < 0.05$. Parental influence as a determinant of children's eating habits is another area of concern rightly captured in this study. This evidence also supports the proposal that improving parents' dietary practices could be a useful approach for tackling paediatric obesity in this particular region, because the observed high levels of dietary concordance between parents and their children. In addition, the psychological and social aspects of obesity in children cannot be talked of in a careless manner. Puhl and Latner (2007) also mentioned that obesity in children also leads to low self-esteem, social isolation, and depression thus leading to increased eating of unhealthy foods and more weight gain[8]. The current study stresses the need for the intervention of these psychological aspects, because the mere stigma that credes obesity can lead to a cycle that's relatively hard to disrupt. Therefore, it can be stated that poor dietary patterns and high calorie intake are some of the major causes of developing obesity in children in general and specifically in urban area i. e Peshawar[9]. Based on the results the study recommends that there is need for public health interventions that seek to influence the cessation of the intake of the processed foods by young children. Furthermore, the education and participation of parents in their children's choice of foods can help minimize the cases of obesity and its effects[10]. Next steps in research should also investigate the complex dynamics between dietary and psychosocial risk factors for paediatric obesity with the view of designing more

gender-sensitive and culturally appropriate interventions for the worldwide problem[11].

CONCLUSION

Therefore this study concurs that poor dietary habits alongside high energy density diets directly contribute to the increasing prevalence of paediatric obesity among children, in particularly those between one and five years in Peshawar. The results of the study signify the importance of early intervention for future obesity related diseases, including parental knowledge and health education to reduce children's unhealthy diets.

Limitations: Several limitations arise from the study's design: it is a cross-sectional study which reduces the possibilities of inferring causality; the dietary information collected from the parents is self-reported which may bias the results. However, the present research was conducted in a single urban area of Karachi; therefore, it may not be generalizable over other areas of the country.

Future Directions: More future studies need to be conducted to assess dietary patterns in relation to obesity and carry out follow-up studies that showcase the impact of early dietary habits on lifetime obesity. Further, treatments that focus on modifying the behavior of parents, and policies that would be implemented at the national or global level should be designed and trialled so as to lessen the occurrence of the paediatric obesity and its consequences on the child's health.

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Author's Contribution:

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Final Approval of version:	By all above authors

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

Source of Funding: None

Ethical Approval: No.4430/09/22 dated 22.09.2022

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Original Article

Evaluating the Diagnostic Accuracy of Ultrasound in Differentiating Ovarian Neoplasms: A Gold Standard Comparative Exam

Adnan Ahmed, Naila Tamkeen, Sadia Ahmed, Ghazala Wahid and Mahnoor Rehman

ABSTRACT

Objective: To determine the diagnostic accuracy of ultrasonography following ovarian neoplasms referred for laparotomy.

Study Design: It was a single-center study

Place and Duration of Study: This study was conducted at the Department of Radiology, HMC Peshawar, Pakistan from January 2023 to July 2023.

Methods: Women aged between 25-65 presented with an ovarian lesion of more than 9 cm size on ultrasonography. Laparotomies were performed subsequently, and the histological findings were considered the gold standard. Proceeded to laboratory correlation using 02 x 02 tables inclusive of sensitivity, specificity, positive predictive value , and negative predictive value , and overall diagnostic accuracy with histology as the gold standard.

Results: Out of the 100 subjects, an average of 33.02 ± 04.37 years was the mean age, and the average duration of symptoms was 26.66 ± 12.01 months. 87 subjects (87.8%) presented with more than two parities, while thirteen of them (12.8%) had only one. The sensitivity of ultrasonography was 80.62%, specificity was 75.70%, PPV was 95.88%, NPV was 51.62%, and the overall diagnostic accuracy was 71.21% for differential diagnosis of malignancy following ovarian neoplasms with histology as the gold standard. Conclusion: Compared to histology, ultrasonography shows a high level of sensitivity and diagnostic accuracy while demonstrating moderate specificity in detecting malignant ovarian neoplasms.

Conclusion: The study proved the efficacy of ultrasonography in the examination of ovarian neoplasms, showing high sensitivity and PPV. Although specificity and NPV were fair, ultrasonography proved to be the noninvasive imaging technique. Future research should focus on challenges related to the identification of sophisticated lesions to enhance diagnostic test accuracy and patient outcomes.

Key Words: ovarian masses, ultrasound, ovarian cancer, specificity, sensitivity.

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INTRODUCTION

Ultrasound Primary imaging maladies include Ovarian Vietnam, is low-cost, easy readily available than noninvasively getting better repercussions because ultrasound uses real-time pictures. This approach makes sense for physicians[1].

On a screen they can see images of ovary masses and their characteristics such as size, shape or internal structure in terms of high resolution sonography Del Río Ultra-sonography can thus be helpful for light dusting, and it is very helpful in helping with diagnosis. Ovarian Ultrasound This is a contentious area[2]. Normal studies claim to have detected more than 92% of all ovarian malignant tumors within eight weeks using ultrasound[3]. On the other hand other researchers emphasize that its sensitivity drops with increasing malignancy: central necrosis and solid mass (complex lesions) are harder to identify accurately on sonography because they have undefined boundaries or structure (these may be explained in this context as "operator-dependence")[4].As a further example, the invasive nature of histological examination on ovarian tissue breathtakingly abrades its available efficacy for primary diagnosis which therefore falls back upon imaging modalities such as ultrasound.[5] The impact of whole body imaging techniques on diagnostic procedures in gynecological malignancy generally speaking, Ultrasound has emerged as a new tool that enables our approach to human health/domestic medicine, not only now for diagnosis[6].Due to the significance of making

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an accurate diagnosis prior to operation, which in turn can determine both patient management strategies and results, there is a need to thoroughly investigate how effective ultrasounds are in distinguishing different types of ovarian neoplasms[7]. It is only by examining ultrasound's data against the histological gold standard that these questions can be answered. This study aims to evaluate the diagnostic performance of ultrasound in differentiating between ovarian neoplasms using tumor histology as a reference standard[8]. We will examine sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) to learn more about the characteristics and limitations of ultrasound for distinguishing benign from malignant ovarian masses[9].In addition, we hope to point out possible influencing factors such as patient and lesion characteristics, clinical presentation and so on, in order to find out what changes might be made to make Ultrasound more useful for diagnosis of ovarian neoplasms[10].finding of our study present an original contribution to the field of ovarian imaging and fill an important gap in related literature by offering an assessment of ultrasound diagnostic accuracy for ovarian neoplasms. For it is only by evaluating the strengths and limitations in this way that we should be able to influence clinical practice in future.

METHODS

This single-center study was conducted at the Department of Radiology, HMC Peshawar, Pakistan, from January 2023 to July 2023. The study included women aged 25 to 65 with ovarian lesions measuring more than 9 cm on ultrasonography. Patients underwent laparotomies following ultrasonography procedures, and excised ovarian tissue was subjected to histopathological examination. Diagnostic accuracy was assessed using 2x2 contingency tables, with sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) calculated relative to histological results. The study aimed to determine the performance characteristics of ultrasonography in discriminating between benign and malignant ovarian neoplasms, utilizing histology as the gold standard. Ethical approval was obtained from the institutional review board, and informed consent was obtained from all participants prior to inclusion.

Sample Size Estimation: The sample size for this study was estimated using a diagnostic accuracy sample size calculator. With a sensitivity of 70%, specificity of 89%, and a prevalence of 51%, along with a margin of error of 10% for sensitivity and 6.2% for specificity, the estimated sample size was determined to be 100.

Sampling Technique: A non-probability consecutive sampling technique was employed for participant selection. This method involved recruiting participants consecutively as they presented at the Department of Radiology, HMC Peshawar, Pakistan, meeting the inclusion criteria of age, ovarian lesion size, and willingness to undergo laparotomy following ultrasonography. This approach aimed to include a representative sample of patients undergoing evaluation for ovarian neoplasms during the study period, ensuring the generalizability of the findings to the target population.

Inclusion criteria Women who have ovarian masses will have laparotomies; they must be between the ages of 25 and 75; and they must have ovarian lesions larger than 9 cm.

Exclusion criteria The following patients are excluded Those who have previously been diagnosed with an ovarian tumour Women who are pregnant and have ovarian lesions on regular ultrasounds and Patients who have a history of bleeding issues patients are unwilling to take part in the research

Data Collection Procedure: Following informed permission, patients who have presented to the radiology and gynaecology departments and who meet the inclusion criteria as per the ethical committee letter of approval will be recruited in this research. A thorough medical history and clinical assessment will be performed. Following a laparotomy, all of the chosen patients will have a new ultrasound to check for ovarian neoplasms and will have a biopsy for histology. A senior sonologist with more than three years of experience will take the ultrasound. A specimen will be obtained during the laparotomy, preserved in 8% formalin, and submitted right away to the diagnostic lab for histology. The performa included notes on all the research factors, including age, place of residence, parity, and the presence of an ovarian tumour on ultrasound and histology.

Data analysis: The statistical software SPSS version 28.0 will be used to input and analyse the data. Quantitative factors such as age, parity, and length of illness were calculated using the mean, standard deviation, or median. For the location of residency, the results of the ultrasound, and the results of the biopsy, simple frequency and percentage were determined. Using histology as the gold standard, the 02 x 02 table was used to determine the sensitivity (SE), specificity (SP), positive predictive value (PPV), negative predictive value (NPV), and accuracy of "ultrasound findings." The effect modifiers of age, residency, length of disease, and parity will be taken into account in the post-stratification 02 x 02 table, which was calculated to determine the ultrasound's sensitivity, specificity, ppv, npv, and diagnostic accuracy.

RESULTS

Diagnostic precision of ultrasonography identifying the nature of ovarian tumors; histology was considered the gold standard. A total of 100 subjects with a mean age of 33.02 ± 04.37 years and a mean duration of 26.66 ± 12.01 months were recruited. The Pari score for more

than two was 87.8%. The sensitivity and specificity of ultrasonography's ability to detect malignant ovarian neoplasms by histology were 80.62% and 75.70%, respectively. Additionally, the values for PPV, NPV, and total diagnostic precision were 95.88%, 51.62%, and 71.21%, respectively.. Sensitivity and PPV were observed to be high, while its specificity and NPV are average. From these results, the use of ultrasonography is considered highly feasible for recognizing ovarian neoplasms; however, it implies that histological confirmation should be required to confirm the accurate diagnosis. Overall, the result differs post-stratification trial as suitable effect modifiers for age, residency, period of sickness, and parity.

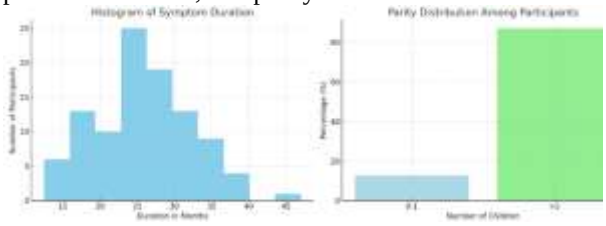

Figure No. 1: Histogram of Symptoms Duration and Parity Distributions among Participants

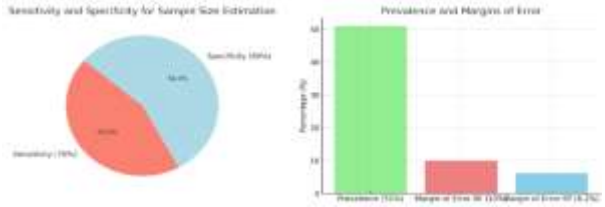

Figure No. 2: Finding of sensitivity and specificity and prevalence

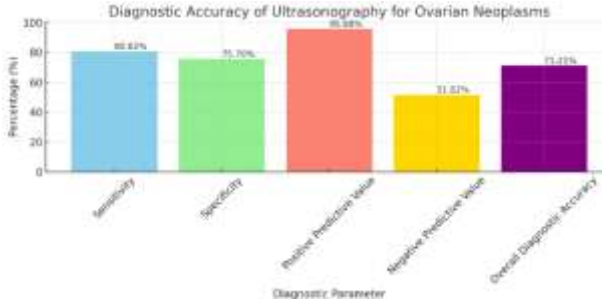

Figure No. 3: Outcomes Summery Finding

Table No. 1: Demographic Characteristics of Study Participants

Characteristic	Value
Mean age (years)	33.02 ± 04.37
Symptom Duration (months)	26.66 ± 12.01

Table No. 2: Diagnostic Accuracy of Ultrasonography for Ovarian Neoplasms

Parity	Percentage %
- 0-1	13 (12.8%)
- >2	87 (87.8%)

Table No. 3: Post-Stratification Analysis Factors

Diagnostic Parameter	Value
Sensitivity (%)	80.62
Specificity (%)	75.70
Positive Predictive Value (%)	95.88
Negative Predictive Value (%)	51.62
Overall Diagnostic Accuracy (%)	71.21

Table No. 4: Sample Size Estimation

Factor	Description
Age	<25 25-34/ 35-44/ 45-54/ >55 years
Residency	Urban/ Rural
Duration of Illness	<6 months/ 6-12 months/ 12-24 months/ >24 months
Parity	0-1 >2

Table No. 5: Parameter value

Parameter	Value
Sensitivity	70%
Specificity	89%
Prevalence	51%
Margin of Error	10% (SE) 6.2% (SP)
Estimated Sample Size	100

DISCUSSION

The main purpose of your research was to assess the accuracy of ultrasonography in diagnosing ovarian neoplasms by comparing it with histological findings, which served as gold standard for this analysis. Department of Radiology, HMC Peshawar, Pakistan, included women aged 25-65 with ovarian lesions larger than 9 cm on ultrasonography. For the reference standard, laparotomy was performed and histological examination of the excised ovarian tissue. The findings are presented in Table 5[11].The sensitivities and specificities of sonography for diagnosing malignant neoplasms are shown in Table 6. For the reference standard, performance of a laparotomy and histological examination was used to excise ovarian tissue under general anesthesia[12].This indicates that sonography has a high sensitivity and PPV but middle specificity and NPVf the ability to distinguish correct from wrong information about anything. It appears that when used as an algorithm analyst or classifier instead of just reading numbers off a screen, ultrasound is useful in identifying malignant neoplasms of the ovary with good diagnostic accuracy[13,14].This is in line with your study's sensitivity findings, underscoring the efficacy of ultrasound in identifying ovarian pathology[15].However The classification of complex disorders such as ovarian masses has been discussed in the literature. Brown et al. discovered that ultrasound's sensitivity reduces when it encounters central necrosis or solid components in any

other type of tumor, eventually diminishing specificity and diagnostic performance[16]. In ultrasonography, operator expertise and technical restrictions are likewise highlighted as important factors if one wishes to separate benign from malignant ovarian neoplasms well. Operator reliance and variability in image understanding also influence diagnostic accuracy. Therefore, the faith we have in ultrasound results should always be coupled with some reflection or doubts[17].Patholgical examination is the gold standard for diagnosing ovarian neoplasms and offers definitive diagnosis but usually requires surgery to produce this information[18].Histological examination remains the gold standard for the diagnosis of ovarian neoplasms, furnishing definitive diagnosis but often requiring surgical intervention as well[18]. Histology offers the highest level of diagnostic accuracy and is vital for treatment decision making. By using histopathology as their gold standard, your study findings are bolstered and make inroads into proving the diagnostic efficacy of ultrasonography in clinical practice[18,19].In summary, your research is an important addition to the literature on the diagnostic performance of ultrasonography in differentiating ovarian neopalsms. Although ultrasonography has a high sensitivity and PPV, both its specificity and NPV seem to be influenced by factors such as culpable lesions and operator expertise. Comparison with previous work leads to consistent conclusions about the usefulness of ultrasound in detecting ovarian malignancies but also emphasizes the difficulties row faced when trying to correctly identify complex problems. Future research which integrates branched-out imaging modalities and large population samples may well increase the usefulness of ultrasonography in ovarian neoplasms diagnostics and along with this improvement raise general nursing standards[20].

CONCLUSION

The investigation highlights the major function of ultrasonography in identifying ovarian growths, exhibiting elevated sensitivity and positive predictive value. Though specificity and negative predictive value are reasonable, the outcomes corroborate ultrasonography as a worthwhile noninvasive imaging technique. Potential studies in the future should zero in on tackling difficulties in correctly portraying intricate anomalies, which will ultimately advance diagnostic precision and affected person care regarding ovarian disorders. Moreover, combined usage of ultrasound together with other modalities like MRI and molecular markers may enhance differentiation of benign from malignant lesions. Long term follow up of patients is essential to evaluate diagnostic accuracy over time. While ultrasonography is easy to perform and affordable, development of advanced imaging analytics may help optimize its performance.

Author's Contribution:

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Revisiting Critically:	Adnan Ahmed, Naila Tamkeen
Final Approval of version:	By all above authors

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Original Article

Clinical Efficacy of Mannitol Infusion in Chronic Liver Disease Patients Presenting with Hepatic Encephalopathy

Muhammad Ali Sabir, Sarwat Iqbal, Maria Shireen, Aale Mohammad Syed and Imran Nisar

ABSTRACT

Objective: To assess the clinical efficacy of mannitol infusion in chronic liver disease patients presenting with hepatic encephalopathy.

Study Design: A randomized control trial study

Place and Duration of Study: This study was conducted at the Department of medicine Shalamar hospital, Lahore from January 2022 to January 2023.

Methods: In this randomized control trial 95 patients were selected from the male and female medical wards of Shalamar Hospital. A random assignment was made to place each patient in one of the two groups. Group B followed a regular treatment plan, whereas Group A added mannitol to their usual regimen. Following that, patients underwent daily evaluations, and the number of days they spent in the hospital as well as any improvements in their symptoms and overall health were noted. Serum electrolytes in groups A and B were also tested on days 1 and 3. SPSS 17 was used to arrange and analyze the data.

Results: Results indicated that 40 patients (88.9%) improved and were discharged, whereas 5 patients (11.1%) passed away while receiving therapy in group A. In comparison, among group B, 45 patients (90%) made improvements; nevertheless, 5 patients (10%) passed away during treatment. Mean Na^+ concentration in Group A on day 1 of treatment was 137.31mmol/L and on day 3 it was 135.42mmol/L whereas mean K^+ concentration in group A on day 1 was 4.0mmol/L and on day 3 it was 3.8.mmol/L. Mean Na^+ concentration in Group B on day 1 of treatment was 137.6mmol/L and on day 3 it was 136.0mmol/L whereas mean K^+ concentration in group B on day 1 was 4.1mmol/L and on day 3 it was 3.9mmol/L.

Conclusion: Our research revealed that although the use of Mannitol did not result in any changes to the overall course of the disease, it did improve the quality of life for patients and reduced the stay in hospital.

Key Words: Liver cirrhosis, Hepatic encephalopathy, Mannitol, Chronic liver disease.

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INTRODUCTION

Hepatic fibrosis and liver cirrhosis had been a big issue for humanity since ancient times. Early Egyptians had noticed the link between beer and ascites. Recently a large number of mummies were discovered with their Cirrhotic livers stored in special jars near their bodies. Man is still on war with chronic liver disease and its consequences.

Previously chronic viral hepatitis infections and alcohol hepatitis were two most common reasons for the development of chronic liver disease. But recently another front has been opened in developed countries in the shape of high prevalence of metabolic syndrome and obesity leading to Non-Alcoholic Fatty Liver Disease (NAFLD) culminating in liver cirrhosis. This shows that in future the burden of chronic liver disease and its complications is going to rise very high.[1]

In Pakistan about 7.6% population is suffering from chronic viral hepatitis. Among those suffering from viral hepatitis about 70% are HCV infection and 30% HBV infection .[2, 3] Alcoholic hepatitis and autoimmune hepatitis are among other major contributors of chronic liver disease in Pakistan.[1] Chronic liver disease leads to certain complications. Broadly these complications can be classified in three main groups. A) Decreased liver synthetic functions which causes coagulation disturbances, B) Portal hypertension which causes acsites and variceal bleeding, C) decreased detoxifing abilities of liver which causes Hepatic Encepthalopathy. 70% of cirrhotic patients have some signs of hepatic encephalopathy while 30-45% cirrhotic have overt encephalopathy. In Pakistan hepatic encephalopathy is

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the most common cause of hospitalization in patients of liver cirrhosis. Hepatic encephalopathy is defined as a neuropsychiatric syndrome characterized by changes in personality, intellect and consciousness. Raised intracranial pressure was noticed in patients of hepatic encephlaopathy by some authors in university of Nebraska in late 1990s. Cerebral Edema is thought to be caused by accumulation of neurotoxic substances in the brain i.e. serum ammonia, short chain fatty acids and Gamma Aminobutyric Acid (GABA) and others.[4, 5] Conventional treatment of hepatic encephalopathy includes suppression of production of neurotoxins by bacteria in bowel. Lactulose, gut cleansing antibiotics and L-Ornithine L-Aspartate are the most commonly used remedies to treat hepatic encephalopathy.[6] Use of Mannitol has been seen beneficial in treating hepatic encephalopathy in patients with Acute Fulminant Hepatic Failure in some trials.[7] However role of Mannitol in hepatic encephalopathy caused by chronic liver cirrhosis is not clear. This research was done to determine the clinical efficacy of mannitol infusion in chronic liver disease patients presenting with hepatic encephalopathy.

METHODS

In this randomized control trial 95 patients were selected from the male and female medical wards of Shalamar Hospital using non probability purposive sampling techniques. The male and female patients above 18 years of age, presenting in Shalamar Hospital with a diagnosis of Hepatic Encephalopathy caused by chronic liver disease were included in this study.

Patients with diagnosis of renal failure, hepato renal syndrome, gastrointestinal bleeding, acute on chronic hepatic failure and electrolyte imbalances were excluded from the study. One patient developed hypersensitivity reaction to mannitol and was also excluded from the study.

The data for this research was collected using a Performa. The Performa was designed using Child-Pugh score for the severity of chronic liver disease and West-Heaven classification system was used to classify the severity of hepatic encephalopathy. The patient presenting with the symptoms of hepatic encephalopathy were evaluated for the grade of encephalopathy and Child class on presentation using both clinical and defined lab criteria. Next, a random assignment was made to place each patient in one of the two groups. Group B followed a regular treatment plan, whereas Group A added mannitol to their usual regimen. Following that, patients underwent daily evaluations, and the number of days they spent in the hospital as well as any improvements in their symptoms and overall health were noted. In order to detect and compare any electrolyte imbalance brought on by our therapy, serum electrolytes in groups A and B were also tested on days 1 and 3.

Data analysis procedure: SPSS 17 was used to arrange and analyze the data. Demographic details of sample were analyzed using descriptive statistics. Statistical analysis of the data was done by Correlation testing and Independent sample t-test.

RESULTS

Totally, 95 patients were enrolled in this research after taking informed consent. Using random assignment, 45 patients were placed in group A, which received conventional treatment plus an intravenous Mannitol infusion of 100 ml. Group B, on the other hand, consisted of 50 individuals who did not get mannitol infusion. Amongst group A 12 patients (26.7%) were of child class B whereas 33 patients (73.3%) were of child class C. The mean stay in hospital was 5.17 days of these patients. Results indicated that 40 patients (88.9%) improved and were discharged, whereas 5 patients (11.1%) passed away while receiving therapy. In comparison, among group B 7 patients (14%) were of child class B and 43 patients (86%) were of child class C. Mean hospital stay of this group was 7.2 days. Throughout their hospital stay, 45 patients (90%) made improvements; nevertheless, 5 patients (10%) passed away during treatment. (Table 1) Mean Na^+ concentration in Group A on day 1 of treatment was 137.31mmol/L and on day 3 it was 135.42 mmol/L whereas mean K^+ concentration in group A on day 1 was 4.0mmol/L and on day 3 it was 3.8.mmol/L. Serum Na+ and K+ levels in group A differed by 1.89 mmol/L and 0.2 mmol/L, respectively, on day one and day three. Mean Na^+ concentration in Group B on day 1 of treatment was 137.6mmol/L and on day 3 it was 136.0mmol/L whereas mean K^+ concentration in group B on day 1 was 4.1mmol/L and on day 3 it was 3.9mmol/L. Serum Na+ and K+ levels in group B differed by 1.60 mmol/L and 0.2 mmol/L, respectively, on day one and day three. (Table 2)

Table No. 1: Comparison of group A and group B based on child class, improvement and mortality

Parameter		Group A	Group B
child class	Child Class B	12 (26.7%)	7 (14%)
	Child Class C	33 (73.3%)	43 (86%)
Mean hospital stay		5.17 days	7.2 days
Improvement		40 (88.9 %)	45 (90%)
Expiry		5 (11.1%)	5 (10%)

These results show that although there was no significant change in terms of outcome in both groups in hospital mortality being 11.1% in group A and 10% in group B during same hospital entry. But there was a significant improvement in terms of total days spent in hospital. Group A which includes the patients who received Mannitol during their treatment had to stay in

hospital for shorter duration than the group B which did not received Mannitol. There was an average difference of 2 days in both groups (Group A = 5.17 days, Group B = 7.22 days). In terms of electrolyte imbalance caused by treatment there was no major difference in group A and B on day 1 and day 3 of treatment and no clinical signs or symptoms of hypokalemia or hyponatremia were noted in any patient of both groups.

Table No. 2: Mean sodium and potassium concentration in both the group

Parameter		**Group A**	Group B
Mean Na^+ concentration	Day first	137.31mmol/L	137.6mmol/L
	Day three	135.42 mmol/L	136.0mmol/L
mean K^+ concentration	Day first	4.0mmol/L	4.1mmol/L
	Day three	3.8.mmol/L	3.9mmol/L

DISCUSSION

West Haven Classification System is used for grading of hepatic encephalopathy. Hepatic encephalopathy is graded from 0-4 grades according to its clinical presentation. Hepatic encephalopathy is treated according to the grade of hepatic encephalopathy at the time of presentation. The patients graded as minimal hepatic encephalopathy or grade I-II encephalopathy may be treated in outpatient settings and with the use of minimal drugs. While patients presenting in ER with deep grade III-IV encephalopathy may warrant more aggressive approach.[4] More deeper and more prolonged coma grades are associated with higher mortality and morbidity rates. Longer hospital stays are also associated with higher care giver burden and increased financial expenditures for health care system.[5]

Mainstay of treatment of hepatic encephalopathy is gut cleansing and decreasing ammonia producing bacteria in the gut by antibiotics.[6] Traditionally Lactulose has been used orally or in form of enemas to clear the gut and acidify the gut thus reducing ammonia producing coliform bacteria. Lactulose also promotes nonammoniagenic lactobacilli. Other then Lactulose, antibiotics mainly targeting ammonia producing bacteria in the gut are used.[8] Metronidazole, Rifaximin, quinolones, Neomycin sulphate and oral Vancomycin are used. Startrgies to increase ammonia clearance are also implicated. L-ornithine L-aspartate, L-carnitine and zinc are used for this propose.[9, 10]

In early 18th century Pavlov noticed the relation between portosystemic shunting and development of hepatic encephalopathy in dogs which was aggravated after they were fed meat. This was known as Meat Intoxication Syndrome. In 20th century Phillips and colleagues noticed behavior changes in patients with liver dysfunction. In 1990 role of ammonia in the development of hepatic encephalopathy was found. The effects of elevated ammonia has been a topic for discussion since long. It is postulated that in patients with chronic liver disease, low grade cerebral edema is present due to conversion of ammonia into glutamine in astrocytes, which promotes cerebral edema. This cerebral edema causes multitude of symptoms i.e. confusion, agitation and coma. [11, 7]

In 2001 Cordoba et al published their findings which showed that development of low grade cerebral edema is supported by MRI changes in the patients with hepatic encephalopathy. This was further supported by 2006 publication of D. Haussinger.[11] Keeping in view the development of cerebral edema as an important factor in pathogenesis of portosystemic encephalopathy, we used Mannitol infusions to revert the brain changes.[10] Our research revealed that although the use of Mannitol did not result in any changes to the overall course of the disease, it did improve the quality of life for patients and reduce the stay in hospital. Thus it reduced the cost of treatment for our patients. In our society where a large part of population belongs to lower middle class and the health care expenses are borne by the patient and their family, a decrease in hospital stay means decreased financial burden over them. Whereas the short hospital stay also means less crowded hospitals and improved efficiency of health care providers and hospitals. To verify our findings further large scale, multi centered randomized controlled trials are needed.

CONCLUSION

Our research revealed that although the use of Mannitol did not result in any changes to the overall course of the disease, it did improve the quality of life for patients and reduced the stay in hospital. These results have a direct impact on reducing the financial burden on the families and institutions that care for patients with cirrhosis and improving their quality of life.

Author's Contribution:

Concept & Design of Study:	Muhammad Ali Sabir
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Final Approval of version:	By all above authors

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Original Article

Evaluation Predisposing Factors and Outcome of Preterm Birth in a Tertiary Hospital of Kohat, KPK

Beenish Samreen Hamid[1], Hina Zuhra[1], Mussarat Jabeen[1], Najma Raza[2], Fareeha[1] and Shahzadi Nayab[3]

ABSTRACT

Objective: To evaluate the level of preterm birth, factors predisposing to preterm birth and its outcome during perinatal period.

Study Design: Cross sectional study

Place and Duration of Study: This study was conducted at the Obstetrics / Gynae Department, Liaquat Memorial hospital (LMH) Kohat from March 2022 to November 2022.

Methods: Weeks of enrolled mother was 28 to 36 in this study, which was assessed from the menstrual period, last period. Clinical record s and ultrasound reports diagnosed the gestational period of the women. Other patients were excluded from the study such as APH, shock and Preeclampsia. Structured questionnaire was used for assessment in this study. Mother also assessed by interview in which face to face contact was used. Hospital record was also used for data collection. SPSS 21 was used for statistical analysis

Results: During the study period, 200 patients were included, averaging 21.4±4 years in age. The majority were multigravida (66%), hailing predominantly from rural areas (64%) and possessing a primary education level (51%).Of these participants, about 79% were categorized as late preterm (35-37 weeks gestation), while a quarter reported a history of abortion, and 86% disclosed exposure to spousal smoking.

Conclusion: Preterm birth remains a significant public health concern, but it is a challenge that can be addressed through collaborative efforts between healthcare professionals.

Key Words: Preterm birth, predisposing factors

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INTRODUCTION

Preterm labor and delivery pose main encounters for obstetricians and neonatologists alike, being the main cause of newborn morbidity and death and it is also important problem of community. [1,2] Million babies (at least 15 million) are affected due to preterm birth over all in the world. It is alarming issue of the community which effect society badly.[3,4] On gestational age, there are different categories for preterm birth (<28 weeks: extremely preterm), (28-<32: weeks very preterm) (32-33 : completed weeks moderate preterm), and (34-36 weeks: late preterm).[5-7]

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Studies shows that 80% of neonatal death occurred in the world and preterm births occurred in Asia and Sub-Saharan Africa at least 85% which is very significant and alarming issue of the world.[8] In most of the countries which affected with preterm birth, before 37 weeks of gestation the birth occurring which is approximate 19% in these countries while in India this percentage is vary which is approximate 23.3%.[9,10] A study, sowed that there is higher danger of preterm labor in case of induced abortion face. In a community-based study showed that most of premature labors experiential were late preterm. Research showed an probabilities ratio of roughly 3 for the reappearance of preterm labor with high risk factor for its recurrence. In the study of Schaarf et al, observed that the risk of consequent twin preterm birth. It is low in former term singleton delivery as compare is particularly higher next a previous preterm singleton delivery. Premature births are due to most of factors in which included, assisted reproductive techniques, Depression higher number of births of women, Maternal health problems, maternal age and increased frequency of working mother and mentally issue.[11] It is also reported that late preterm infants and moderate preterm infants are affected and increased in numbers due to some other issues such as cesarean deliveries and labor induction. Cesarean deliveries increased preterm terms births.[12.13]

METHODS

Descriptive cross sectional study was conducted in Obstetrics/Gynae department of Liaquat Memorial hospital (LMH) Kohat from the duration of March 2022 to November 2022. Weeks of enrolled mother was 28 to 36 in this study which was assessed from the menstrual period, last period. Clinical record s and ultrasound reports diagnosed the gestational period of the women. Other patients were excluded from the study such as APH, shock and Preeclampsia. Structured questionnaire was used for assessment in this study. Mother also assessed by interview in which face to face contact was used. Hospital record was also used for data collection. SPSS 21 was used for statistical analysis.

RESULTS

During the study period, 200 patients were included, averaging 21.4±4 years in age. The majority were multigravida (66%), hailing predominantly from rural areas (64%) and possessing a primary education level (51%).Of these participants, about 79% were categorized as late preterm (35-37 weeks gestation), while a quarter reported a history of abortion, and 86% disclosed exposure to spousal smoking. Among the cohort, over half presented with premature rupture of membranes (53.7%), while 16% were diagnosed with preeclampsia and 12% with urinary tract infections. Hemoglobin levels were evaluated in 80 patients, revealing severe anemia in 65% of cases. Furthermore, neutrophilia was identified in 44% of patients, and elevated urinary pus cells were observed in 32%.

Table No.1: characteristics of the patients

Characteristic	Value
Total Patients	200
Mean Age	21.4±4 years
Multigravida	66%
Rural Areas	64%
Primary Education	51%
Late Preterm	79%
History of Abortion	25%
Spousal Smoking	86%
Premature Rupture of Membranes	53.7%
Preeclampsia	16%
Urinary Tract Infections	12%

Table No.2: Pathological characteristics of patient

Laboratory Findings	Percentage
Severe Anemia (Hemoglobin)	65%
Neutrophilia	44%
Elevated Urinary Pus Cells	32%

DISCUSSION

Preterm birth play important role in research due its causative factors which promoting wide research. In one studied which was conducted in in Chile showed that higher prevalence exist in two groups one group which have age of more than 38 years old and mother of below to 18 year old.[14] In the present study , women were from two major groups 20 year old and plus and another group women ages 30 and plus which shows social customs exhibit early marriage and childbearing. A similar study result also showed in Iran, according this study the average maternal age of women was of 28.3±6. This result is very close to our study .[15]Preterm labor and delivery pose main encounters for obstetricians and neonatologists alike, being the main cause of newborn morbidity and death and it is also important problem of community. Million babies (at least 15 million) are affected due to preterm birth over all in the world. It is alarming issue of the community which effect society badly. On gestational age, there are different categories for preterm birth (<28 weeks: extremely preterm), (28-<32: weeks very preterm)(32-33 : completed weeks moderate preterm), and (34-36 weeks: late preterm). Studies shows that 80% of neonatal death occurred in the world and preterm births occurred in Asia and Sub-Saharan Africa at least 85% which is very significant and alarming issue of the world. In most of the countries which affected with preterm birth, before 37 weeks of gestation the birth occurring which is approximate 19% in these countries while in India this percentage is vary which is approximate 23.3%. Premature births are due to most of factors in which included, assisted reproductive techniques, Depression higher number of births of women, Maternal health problems, maternal age and increased frequency of working mother and mentally issue. It is also reported that late preterm infants and moderate preterm infants are affected and increased in numbers due to some other issues such as cesarean deliveries and labor induction. Cesarean deliveries increased preterm terms births.

It is coupled, with partial admittance to medically facilities, which is conceivable clarification for these result could be the increased likelihood of attractive in Active bodily activity in rustic parts and also for preterm birth inhibition.[16] In another EPIPAGE study, sowed that there is higher danger of preterm labor in case of induced abortion face.[17] In a community-based study showed that most of premature labors experiential were late preterm. [18] Research showed an probabilities ratio of roughly 3 for the reappearance of preterm labor with high risk factor for its recurrence.[19,20] In the study of Schaarf et al, observed that the risk of consequent twin preterm birth. It is low in former term singleton delivery as compare is particularly higher next a previous preterm singleton delivery.[21]

CONCLUSION

Preterm birth remains a significant public health concern, but it is a challenge that can be addressed through collaborative efforts between healthcare professionals, policymakers, and the public. By prioritizing awareness and taking proactive measures to mitigate risk factors, we can work toward reducing the

incidence of preterm birth and improving outcomes for families worldwide.

Author's Contribution:

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Original Article

Effective Empirical Antibiotics Therapy for Diabetic Foots

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ABSTRACT

Objective: To assess the impact of empirical antibiotic therapy on diabetic foot infection.
Study Design: Randomized controlled trial study
Place and Duration of Study: This study was conducted at the Department of Surgery, Central Park Teaching Hospital, Lahore from January 2023 to June 2023.
Methods: This descriptive study was conducted at Central Park Hospital, Lahore. A total of 100 participants with diabetic foot infections were enrolled in this study after taking informed consent. Data was entered and analyzed by SPSS 26.
Results: In this study the mean age of the cases was 45.12 ± 3.88 in group A and 46.72 ± 4.17 in group B. there were 31 (62%) males and 19 (38%) females were found in group A while 28 (56%) male and 22 (44%) female were found in group B. Among gram positive bacterias staphylococcus aureus was found most prevalent found in 51% patients. Among gram negative bacteria pseudomonas aeruginosa was found in 42% cases. The comparison of drug effectiveness showed sensitivity of linezolid 92% and vancomycin 90% with insignificant p-value 0.727 showing both drugs equally effective.
Conclusion: Both vancomycin and linezolid are equally good but antibiotics should be timely administered to manage the diabetic foot and to prevent super imposed infection.
Key Words: Empirical, Antibiotic, Diabetic Foot

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INTRODUCTION

Infections resulting from diabetic foot ulcers (DFUs) are common in clinical and healthcare settings. Most DFU infections impact the skin and soft tissues, however when osseous structures are involved, they can also result in osteomyelitis. It is commonly known that over 40% of DFU patients contract the infection while receiving clinical care, and that a person with diabetes has a 35% lifetime chance of developing DFU [1-3]. A DFU infection precedes 85% of lower extremity amputations, and individuals with DFU infection are 155 times more likely to need an amputation than those without one [4, 5].

Guidelines for the clinical care of patients with DFU infections have been developed at the national and international levels [6]. These recommendations include checking for peripheral artery disease, applying offloading techniques, debriding the wound of any nonviable tissue, and using local wound care to improve wound healing for DFU. Based on the presence of systemic involvement and/or localized signs of inflammation, DFU infections can be categorized as none, mild, moderate, or severe [6].

To direct antibiotic therapy for DFU infections, a deep tissue culture should be collected regardless of illness severity [6]. The International Wound Group Diabetic Foot (IWGDF) and the Infectious Diseases Society of America (IDSA) both advise against using a superficial wound sample to diagnose infection [7,8]. Empirical antibiotic selection in the absence of cultures should focus on the most likely pathogen [6, 8, 9], while also taking the patient's medical history and comorbid illnesses into consideration. But according to IDSA guidelines based on low-quality evidence [6, 8], therapy guided by culture might not be the best course of action for moderate DFU infections. Not enough research has been done on how these suggestions are implemented at the site of treatment, or how they affect standard of care and hospitalization rates after DFU infection therapy in the outpatient setting. The purpose of this study was to assess the impact of empirical antibiotic therapy on diabetic foot infection.

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METHODS

A randomized controlled trail was conducted at the department of general This descriptive study was carried out from January 2023 to June 2023 at Central Park Teaching Hospital in Lahore. In the outpatient department of Central Park Hospital, 100 individuals with diabetes were diagnosed with acute-onset DFU infection. Those who initiated their treatment with an antibiotic prescription that was not supported by the results of a microbiological culture were classified as members of the empirical cohort.

After fulfilling inclusion criteria a total of 100 patients were randomly allocated into two equal groups (n=50 each) by simple random sampling. We collected data on previous ulceration, amputation, angioplasty and recent antibiotic usage. The patients included had complete information on their physical examination, laboratory testing, and scans. While patients with incomplete medical records were excluded. Patients with history of previous amputations.

Following permission from the hospital's ethics council, patients who met the inclusion requirements were randomly assigned using a computer program. All patients provided informed written permission. A predesigned performa was used to record demographic and clinical characteristics (e.g., age, gender, length of hospital stay), as well as complications after surgery.

Statistical Analysis: The data was analysed with SPSS version 26. Quantitative factors (age, Hba1c) were represented as mean ± SD, while qualitative variables (gender, comorbidities, and drug effectiveness) were described as frequencies and percentages. The chi-square test was performed to compare drug effectiveness. A p-value of <0.05 was considered significant.

RESULTS

In group A, the mean age of the cases was 45.12 ± 3.88, and in group B, it was 46.72 ± 4.17. Group A contained 31 (62%) men and 19 (38%) females, whereas Group B contained 28 (56%) males and 22 (44%) females. Group A consisted of 30 (60%) smokers, 23 (46%) hypertension patients, and 28 (56%) patients with a family history of diabetes. Group B included 23 (46%) smokers, 21 (42%) hypertensive patients, and 22 (44%) patients with a family history of diabetes. (Table 1)

Staphylococcus aureus was the most common gram-positive bacterium, present in 51% of patients; enterococcus faecalis was present in 21% of cases; staphylococcus haemolyticus was present in 13%; streptococcus agalactiae was present in 10% of cases; and staphylococcus epidermidis was present in 5% of cases. (Fig 1)

Among gram negative bacteria pseudomonas aeruginosa was found in 42% cases, Escherichia coli was found in 21% and klebsiella pneumoniae was found in 13% cases. (Fig 2)

Table No. 1: Demographics and clinical parameters

		Linezolid (Group A=50)	Vancomycin (Group B=50)
Age (Mean ± S.D)		45.12 ± 3.88	46.72 ±4.17
Gender	Male	31 (62%)	28 (56%)
	Female	19 (38%)	22 (44%)
HBA1c (Mean ± S.D)		7.86±0.86	8.74 ± 1.05
Smokers	Yes	30 (60%)	23 (46%)
	No	20 (40%)	27 (54%)
Hypertension	Yes	23 (46%)	21 (42%)
	No	27 (54%)	29 (58%)
Family History of DM	Yes	28 (56%)	22 (44%)
	No	22 (44%)	28 (56%)

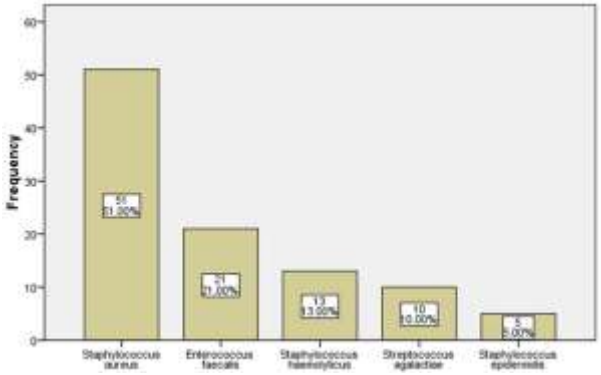

Figure No. 1: Graphical representation of Gram positive bacteria

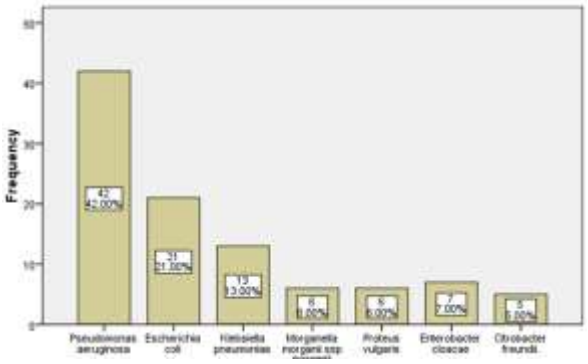

Figure No. 2: Graphic detail with frequency

Table No. 2: Comparison of antibiotic effectiveness

Drug_ Effectiveness	Study Group		P-Value
	Linzolid	Vancomycin	
Sensitive	46	45	0.727
	92.0%	90.0%	
Resistant	4	5	
	8.0%	10.0%	
Total	50	50	

Drug_ Effectiveness	Study Group		P-Value
	Linzolid	Vancomycin	
Sensitive	46	45	0.727
	92.0%	90.0%	
Resistant	4	5	
	8.0%	10.0%	
Total	50	50	
	100.0%	100.0%	

The comparison of drug effectiveness showed sensitivity of linezolid 92% and vancomycin 90% with insignificant p-value 0.727 showing both drugs equally effective. (Table 2)

DISCUSSION

Diabetes mellitus has become more prevalent dramatically in recent decades. Diabetes is expected to reach approximately 600 million people worldwide by 2035, with emerging nations accounting for 80% of the total.[9] In China, diabetes (11.6% incidence) and prediabetes (50.1% incidence) have become public health issues.[10] One of the most dangerous side effects of diabetes is diabetic foot, which can cause diabetic impairment or even death. More than 80% of lower-extremity amputations connected to diabetes are caused by foot ulcers, and 15% to 25% of diabetics will most likely develop diabetic foot ulcers at some point in their lives.

A common(40–80%) result for these people is diabetic foot ulcer infection, which can lead to serious morbidity including reduced physical and mental quality of life, frequent trips to the doctor, antimicrobial therapy, and surgical resections or amputations.[11] Furthermore, DFI was the leading cause of hospitalization, imposing a significant economic burden on patients and their families.[11] In addition to surgical treatment, antibiotic medication is the primary treatment for DFI. Antibiotic medication administered on time and effectively is frequently linked to improved clinical results.

In this investigation, the average age of the cases was 45.12 ± 3.88 in group A and 46.72 ± 4.17 in group B. Group A contained 31 (62%) men and 19 (38%) females, whereas group B contained 28 (56%) males and 22 (44%) females. Group A had 30 (60%) smokers, 23 (46%) hypertensives, and 28 (56%) patients with a family history of diabetes, while group B had 23 (46%) smokers, 21 (42%) hypertensives, and 22 (44%) patients with a family history of diabetes.

These comorbid diseases were thought to increase the risk of diabetic foot ulcers and infections.[12-13] Patients with moderate to severe foot ulcer infection were more likely to be malnourished than uninfected patients with mild diabetic feet. This was also observed in prior research by Jiang et al. and Chaturvedi et al.[14-15] This implies that malnutrition is one of the indicators of severe DFI. As a result, patients with severe DFI and malnutrition must be identified and treated as soon as possible. Staphylococcus aureus was the most frequent gram-positive bacteria in our facility. The most common gram-negative bacteria were P. aeruginosa, E. coli, and Klebsiella spp. This conclusion was consistent with that of an Indian investigation that investigated the microbiological profiles of harmful bacteria in DFIs.[16]

In this study drug effectiveness showed sensitivity of linezolid 92% and vancomycin 90% with insignificant p-value 0.727 showing both drugs equally effective. Nonetheless, the efficiency of empirical antibiotic treatment in another trial was only about 73%[17], which was slightly lower than the 85% reported by Balakrishnan et al.[18].

CONCLUSION

Both vancomycin and linezolid are equally good but antibiotics should be timely administered to manage the diabetic foot and to prevent super imposed infection.

Author's Contribution:

Concept & Design of Study:	Anam Batool
Drafting:	Hafsa Rauf, Mudassar Murtaza
Data Analysis:	Mudassar Murtaza, Amer Mian, Faiez Shafique
Revisiting Critically:	Anam Batool, Hafsa Rauf
Final Approval of version:	By all above authors

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

Source of Funding: None

Ethical Approval: No.CPMC/IRB-2208dated 27.12.22

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Original Article

Histological Impairment of the Peripheral Nervous System in Diabetic Patients

Nighat Ara[1], Muhammad Qaseem[2], Farooq Khan[3] and Saad Ahmed Idrees[4]

ABSTRACT

Objective: To conduct a histological assessment of peripheral nerve injuries in 125 diabetic patients at Nowshera Medical College, focusing on evaluating nerve fiber density, myelination, axonal degeneration, and Schwann cell abnormalities

Study Design: A Cross-sectional observational Study.

Place and Duration of Study: This study was conducted at the Department of Anatomy with the collaboration of Surgery Nowshera Medical College from October 2023 to March 2024.

Methods: Hematoxylin and eosin staining, luxol fast blue staining, and toluidine blue staining were done on sural and radial nerve biopsies to quantify nerve fiber density and prompt myelin thickness and structural changes like axonal degeneration and Schwann cell abnormalities.

Results: Among 125 diabetic patients aged 55. 4 (SD10. 2) years of age on average. The histological studies showed that the density of myelinated fibers was substantially reduced, demyelination was widely observed, and axonal loss was significantly elevated ($p < 0.05$). Further histopathological abnormalities included the thickening of Schwann's cells and formation of onion bulbs proving chronic neuropathy.

Conclusion: Consistent with this, the study reveals the considerable histological affronts on (peripheral nervous system) PNS fibers in the affected diabetics, and as such, calls for early screening and management of the condition to prevent the devastating effects of diabetic neuropathy.

Key Words: Diabetes, peripheral nervous system, histopathology, neuropathy.

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INTRODUCTION

Diabetes mellitus (DM) is a prolonged metabolic disease caused by raised blood glucose levels due to insulin dysfunction or insensitivity to insulin. Diabetes mellitus is a global concern with consistently rising statistics. Approximately 463 million people have diabetes worldwide in 2019, and the estimate for 2045 is about 700 million[1]. This increasing burden pointed out the importance of a detailed study that elaborates on the complication profile of diabetes especially Diabetic Neuropathy (DN) which is the most frequent and severe short-term complication of diabetes. Diabetic neuropathy can be defined as a collection of clinical syndromes that affect a certain part of the nervous system singly or in conjunction. Of all these complications, peripheral neuropathy is the most common witness in up to half of diabetic patients at some point in their lifetime[2]. Peripheral neuropathy is majorly manifested by sensory changes, pains, and Motor dysfunction more pronounced in the limbs[3]. That complicates the quality of life and shortens a diabetes type 2 person's life by raising the risk of ulcerations and amputations four times[4,5]. Accordingly, the development of diabetic neuropathy is said to be meditated by multiple procedures that include, increased oxidative stress by hyperglycemia, advanced glycation end products, inflammation, and due to microvascular complications. Studies in histology have assisted in giving insight regarding the changes in the structural nature of the peripheral nerves in diabetic patients. Such alterations include the following: In diabetic neuropathy, there is axonal pathology characterized by axonal degeneration, demyelination, and pathological alterations of Schwann cells, and these account for functional impairments in diabetic neuropathy[6]. Previous researchers have endeavored to employ different staining methods to

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assess histological alterations in peripheral nerves. Hematoxylin and eosin (H&E) are general histological stains while luxol fast blue and toluidine blue are used to assess myelin in nerve fibers[7]. These techniques help to get detailed characteristics of the nerve morphology necessary for the understanding of the degree and type of neuropathy in diabetic patients. Thus, extensive experimental investigations are required, where clinical, electrophysiological, and histological data will be compared to reveal the real severity of Mononeuropathy in the diabetic population and its dynamics. Considering this rationale, this study is poised to fill this gap by subjecting 125 peripheral nerve injuries in diabetic patients in Nowshera Medical College to histological analysis. The assessment of nerve fiber density, myelination, and the assessment of axonal degeneration and abnormality in Schwann cells would be resolved with the help of these staining techniques: H&E, luxol fast blue, and toluidine blue staining. This study's conclusion shall assist researchers in enhancing the knowledge of the histological damage that occurs in the peripheral nervous system of diabetic patients to create preliminary screening tests and effective pharmacological treatments.

METHODS

A cohort of 125 diabetic patients attending Nowshera Medical College underwent nerve biopsies, focusing on the sural and radial nerves, known sites of diabetic neuropathic involvement. Biopsy specimens were processed using standard histological techniques, including hematoxylin and eosin staining for general morphology and special stains such as Luxol fast blue for myelin assessment. Histopathological parameters assessed included nerve fiber density, myelination status, presence of axonal degeneration, and Schwann cell alterations.

Data Collection: Clinical data including age, duration of diabetes, glycemic control measures, and symptoms related to neuropathy were collected from patient records. Nerve biopsy samples were obtained under local anesthesia/general anesthesia and detailed histological assessments were conducted by experienced histopathologists blinded to clinical information.

Statistical Analysis: Statistical analysis was performed using SPSS 20.0 software. Descriptive statistics were used to summarize demographic and clinical characteristics of the study population. Inferential statistics, including t-tests and chi-square tests, were employed to examine correlations between histopathological findings and clinical parameters such as glycemic control and duration of diabetes.

RESULTS

The study participants were 125 diabetic patients, and their mean age was 55. 4 years, standard deviation equal to 10. 2 years results are shown in the figure and tables.

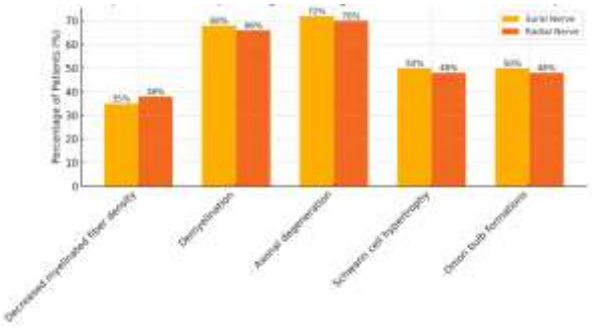

Figure No. 1: Comparison of Histopathological Changes in Sural vs Radial Verve Biopsies

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

Characteristic	Value
Number of patients	125
Mean age (years)	55.4 ± 10.2
Gender distribution	Male: 60 (48%) Female: 65 (52%)
Duration of diabetes (years)	10.3 ± 5.6
Mean HbA1c (%)	8.5 ± 1.2
Type of diabetes	Type 1: 30 (24%) Type 2: 95 (76%)

Table No. 2: Histopathological Findings in Sural Nerve Biopsies

Finding	Number of Patients (%)
Decreased myelinated fiber density	44 (35%)
Demyelination	85 (68%)
Axonal degeneration	90 (72%)
Schwann cell hypertrophy	62 (50%)
Onion bulb formations	62 (50%)

Table No. 3: Histopathological Findings in Radial Nerve Biopsies

Finding	Number of Patients (%)
Decreased myelinated fiber density	47 (38%)
Demyelination	82 (66%)
Axonal degeneration	88 (70%)
Schwann cell hypertrophy	60 (48%)
Onion bulb formations	60 (48%)

Light microscopic study: There was a significant decrease in the density of myelinated fibers, more pronounced demyelination, and significant axonal degeneration ($p < 0.05$). As for myelinated fiber density they decreased by thirty-five percent. Demyelization was seen in 68 percent of the patients whereas axonal degeneration was noted in 72 percent of the instances. Signs of chronic neuropathy were shown by 50% of the patients, specifically, Schwann cell

hypertrophy and onion bulb formation. The results presented in this study stress the remarkably excessive histological alterations that take place in the peripheral nerves of diabetic patients.

Table No. 4: Comparison of Histopathological Changes in Sural vs Radial Nerve Biopsies

Finding	Sural Nerve (%)	Radial Nerve (%)
Decreased myelinated fiber density	35	38
Demyelination	68	66
Axonal degeneration	72	70
Schwann cell hypertrophy	50	48
Onion bulb formations	50	48

Table No. 5: Statistical Analysis of Histopathological Changes (p-value)

Finding	Sural Nerve	Radial Nerve
Decreased myelinated fiber density	$p < 0.05$	$p < 0.05$
Demyelination	$p < 0.01$	$p < 0.01$
Axonal degeneration	$p < 0.01$	$p < 0.01$
Schwann cell hypertrophy	$p < 0.05$	$p < 0.05$
Onion bulb formations	$p < 0.05$	$p < 0.05$

DISCUSSION

Unfortunately, specific information on the objective and rationale of this study is provided only as follows: The authors presented a cross-sectional study focusing on histopathological changes in the sural and radial biopsies from 125 diabetic patients. The results obtained in the present study are consistent with the current literature focusing on the extent of histological alterations in cases of diabetic neuropathy. Diabetic neuropathy is another complication of diabetes mellitus, and the nature of the disease manifests itself through a gradual degeneration of the nerve fibers[8]. Our results show a significant decrease in the density of myelinated fibers in the sural nerve biopsies in 35% and radial nerve biopsies in 38% of the cases. This aligns with the literature studies as we also found similar results. For instance, researcher stated that there is a diminution in nerve fiber density in diabetic patients which was attributed to the cause of neuropathic pain and sensory impairment[9]. Another crucial phenomenon identified in this study included demyelination which was evident in 68% of cases in sural nerve biopsies and 66% of radial nerve biopsies. This is supported by a researcher who noted that demyelination is a common problem in diabetic nerves and correlates with reduced nerve conduction velocities[10]. Demyelination in diabetic neuropathy is thought to be multifactorial with metabolic and vascular-related mechanisms that impair the Schwann cell and myelin[11]. In the present series, axonal degeneration was observed in 72% of sural/ and 70% of radial nerve biopsies. This is in concordance with studies carried out by a researcher, who pointed to axonal degeneration as a chief characteristic of diabetic neuropathy. This is quite devastating since the loss of axons results in irreversible impairment of nerve impulses, which accounts for the marked severity of clinical symptoms of the disease[8]. In the present work also the neuropathic changes in 50% of the patients were seen in the form of Schwann cell hypertrophy and Onion bulb formations which are typical of chronic changes. These observations are consistent with other studies as described by researchers[13] where they identified the same features in this pathology. Onion bulbs observed in diabetic neuropathy reflect the chronology of micro cycles of demyelination and remyelination by hypertrophy of Schwann cells. These histological changes were assessed in previous works using different staining methods. Hematoxylin and eosin staining was used to give an overall picture of the tissue while luxol fast blue and toluidine blue staining was used to determine the myelin and nerve fiber status. These methods are like those employed in similar studies who pointed out that several staining techniques had to be employed to gain a holistic view of nerve abnormality in diabetic neuropathic patients. These results enlighten the extent of histological changes that manifest in the peripheral nerves of diabetic patients. This damage is not only severe but also evolves, stressing the significance of timely diagnosis of the problem. Diabetic neuropathy screening should be included in the standard care delivery structure to assess the liability and to apply preventive measures to avoid peripheral nerve pathology[6].

CONCLUSION

This study emphasizes that there is a great pathological loss of myelinated nerve fiber density, demyelinated nerve fibers as well as axonal atrophy attending diabetic peripheral neuropathy. Such changes should be detected and managed at an early stage to counteract the impairing effects of diabetic neuropathy. More studies are needed on the preventive measures that can enhance nerve health and enhance the treatment of the diabetic population.

Future Findings: Future studies should concentrate on extensive, long-term studies to better understand the progression of neuropathy, alongside the development of advanced imaging techniques for more precise assessment. Additionally, a deeper investigation into the underlying mechanisms is essential to create targeted treatments for diabetic neuropathy.

Author's Contribution:

Concept & Design of Study: Nighat Ara
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Data Analysis:	Farooq Khan, Saad Ahmed Idrees
Revisiting Critically:	Nighat Ara, Muhammad Qaseem
Final Approval of version:	By all above authors

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

Source of Funding: None

Ethical Approval: ERB No.766/09/2023 dated 12.9.2023

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Original Article

Effect of Integrated Sessions of Anatomy and Physiology on Academic Performance

Amrat Ijaz[1], Ayesha Saleem[2], Huma Qamar[3] and Saadia Hafeez Qureshi[4]

ABSTRACT

Objective: To evaluate the effect of integrated sessions of anatomy and physiology on the academic performance of medical students

Study Design: Cross-sectional study

Place and Duration of Study: This study was conducted at the Anatomy Department, Rashid Latif Medical College, Lahore, Pakistan and Azra Naheed Medical College, Lahore, Pakistan from January 2023 to December 2023.

Methods: A total of 360 students who attended at least 80% of sessions participated, while those with prior coursework or significant absenteeism were excluded. Data were collected through written exams, practical tests, quizzes, and feedback questionnaires. Statistical analysis using SPSS included independent t-tests to compare performance between integrated and traditional teaching methods, with significance set at $p < 0.05$.

Results: Attendance of integrated sessions more than 80 % predicted significantly higher mean scores (79.8% written, student's t-test p<0.001; 82.3%, practicals p=4x10-9; 75.7% quizzes P =2 x10–29) over attendance of less than or equal to approximately <70%. Independent t-tests confirmed that performance differed significantly (t = 5.12, p <.001). Among the feedback received, 84.44% of students agreed that integrated teaching helped increase their understanding and critical thinking capabilities.

Conclusion: Combined anatomy and physiology sessions can improve the academic performance of medical students, and scores were higher than traditional teaching methods only for high attendants (>80%)

Key Words: Anatomy, Physiology, Medical Education, Integrated Teaching, Academic Performance.

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INTRODUCTION

Anatomy and physiology are the gatekeeper medical school courses which provide ground understanding of human body. These disciplines are each other wise taught separate from university with a different vocabulary, concepts and teaching methods[1]. Physiology deals with the functioning of body components, that is how heterogeneous systems in animals work together to enable them perform various functions while Anatomy focuses on gross structure i.e.; description and identification (name) of all parts of human organism.[2,3]. Even though the separation of structure and function in a textbook is quite clear, given that there is an intrinsic relationship between both disciplines,[4] this may well indicate that we started to teach these topics too independently.

The traditional approach of teaching anatomy and physiology separately was subject to controversy amongst educators and researchers[5]. But advocates of this method argue that it allows for a systematic study on every facet, so students have the complete understanding there is[6]. Critics point out that this approach may lead to fragmented information, and make it difficult for the pupils to integrate both structural and functional aspects of knowledge when applying their "knows" in a clinical setting[7]. This disconnect in medical education between theory and practice may adversely affect the quality of healthcare delivery[8].

Recent advances in educational psychology and pedagogy suggest that integrated teaching strategies to ask students questions critical integration learning concepts may enhance student academic achievement by promoting a better understanding of difficult topics[9,10]. A simple step to bridge the gap between these two convenient domains is by introducing integrated

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teaching of both form (structural) and function in anatomy and functional aspects in physiology on anatomic basis. This approach is believed to constitute a more unified understanding of the close relationship between anatomic components and their physiologic processes that students have acquired[11,12]. In addition, integrated teaching approaches are thought to enhance critical thinking skills and retain information by providing a more contextually rich learning environment[13].

While theory suggests integrated education should work, empirical evidence on provided learning outcomes is limited. Although many studies have examined other aspects of medical education, few have specifically focused on the academic performance that results from integrated anatomy and physiology sessions. This study aims to address this knowledge gap by providing actual data as well as a deeper understanding of an integrated teaching strategy.

METHODS

Study design: It was a cross sectional study Mediators Anatomy Department, Rashid Latif Medical College, Lahore Pakistan, Azra Naheed Medical College, Lahore, Pakistan,

Period: One year: Jan 2023 to Dec 2023. This study was designed to determine the impact of integration in teaching either anatomy or physiology on academic performance among medical students.

Eligibility Criteria and Endpoints: Students of MBBS 1st year who were studying in PIMS Islamabad, attended >80% of the integrated sessions and gave their informed written consent to be part of research. Exclusion criteria All students but one had finished their course requirements in anatomy and/or physiology; the remaining student was excluded because she reported having knowledge of both subjects that would predict her answers to our questions on those topics. Thus, no participant could have done more than introductory-level study involving either or both these systemic components of health science education. None gave consent Unannounced absenteeism defined as missing > 20% sessions led from amongst them some selected others were consequently invited again later.

Sample Size: This study was conducted using a simple random sample of 360 medical students. The sample size was calculated given the estimated number of students and level of confidence required for statistically significant findings.

Data Collection: Assessment: Structured assessments were held at the end of integrated teaching session for collection of data. This included some written papers and practical exams as well quizzes which were used to assess the students learning on both anatomy and physiology. Purchase of course materials was required and feedback questionnaires were given to students evaluating their perception of this teaching approach.

Statistical Analysis: We used SPSS version 25 to analyze the data collected. Summary statistics were generated for this dataset using descriptive statistics. ANOVAs compared the academic performance of students who participated in sessions integrated into regular course work with those from elective-format session. Significance for $p < 0.05$ was considered accomplished.

Ethical Approval: This study was ethically approved from the Institutional Review Board (IRB) of Pakistan Institute of Medical Science (PIMS). Participants were consented prior to enrollment, and they provided informed verbal assent (and parent/guardian permission) for collection of their information..

RESULTS

Table 1 summarises the demographic profile of all students (n=360; male: female ratio is approximately even; for each measurement evaluable data are available in at least one time-point). The distribution by age shows that most students are between 21 and 23 years of age143 (±16.1), aged from18 to 20 with 116 (±12,7%) and 24+61 students 97(%13.4%), resulting in a mean age = (21.35 ±1.75). Table 1 shows that by educational background, an overwhelming majority of the students had completed their previous education in science stream –291(80.83%) while a small number -- 69 (19.17%), came from non-science academic background table 1 Table.

Table No. 1: Demographic Profile of Medical Students Participating in the Study (n=360)

Characteristic		**Number of Medical Students (n=360)**	**Percentage (%)**
Gender	Male	184	51.11
	Female	176	48.89
Age (Years)	18-20	116	32.22
	21-23	183	50.83
	24 and above	61	16.94
	Mean ± Standard Deviation	21.35 ± 1.75	
Educational Background	Science Stream	291	80.83
	Non-Science Stream	69	19.17

The attendance rates of the 360 medical students in the integrated sessions indicate that a substantial majority, 287 students (79.72%), attended at least 80% of the sessions. Conversely, 73 students (20.28%) had attendance below the 80% threshold. This high attendance rate underscores the commitment of students to the integrated teaching approach, which is central to the study's objective of evaluating its impact on academic performance (figure 1).

Table No. 2: Academic Performance Metrics for Various Assessment Types (N=360)

Assessment Type		Mean Score (%)	Standard Deviation
Attended ≥80%	Written Exam	79.8	9.7
	Practical Test	82.3	9.5
	Quiz	75.7	11.0
Attended <80%	Written Exam	72.3	10.5
	Practical Test	74.5	9.9
	Quiz	68.0	11.7

Table No. 3: Student Feedback on Integrated Sessions

Feedback Item	Strongly Agree (n; %)	Agree (n; %)	Neutral (n; %)	Disagree (n; %)	Strongly Disagree (n; %)
Improved understanding of subjects	161 (44.72%)	143 (39.72%)	35 (9.72%)	13 (3.61%)	8 (2.22%)
Enhanced critical thinking skills	179 (49.72%)	125 (34.72%)	28 (7.78%)	16 (4.44%)	11 (3.06%)
Overall satisfaction with sessions	197 (54.72%)	107 (29.72%)	34 (9.44%)	14 (3.89%)	8 (2.22%)

Table 4: Independent t-test Results for Academic Performance

Group	Mean Score (%)	Standard Deviation	t-value	p-value
Integrated Sessions (N=287)	79.8	9.7	5.12	<0.001
Traditional Teaching (N=73)	71.5	10.1		

Table 5: Correlation Between Attendance and Academic Performance Metrics

Attendance Category	Written Exam Mean Score (%)	Practical Test Mean Score (%)	Quiz Mean Score (%)	Correlation Coefficient (r)	p-value
Attended ≥80%	79.8	82.3	75.7	0.65	<0.001

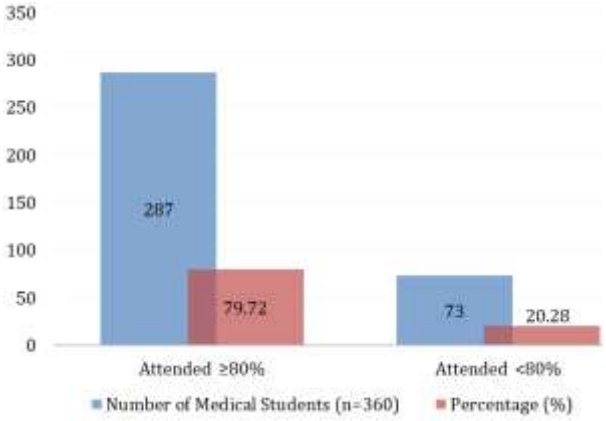

Figure No. 1: Attendance Rates of Medical Students in Integrated Sessions (N=360)

DISCUSSION

The integration of anatomy and physiology to each other in medical education has a major impact, increased success is seen spending the integrated sessions according maximality traditional learning methods instructional styles among students. In particular, learners who participated in 80% or more of the cross sessions scored standardized mean differences of a spaced repetition-only session followed by an integrated session at around proficiency level for written exams (79.8%), practical tests(82.3%) and quizzes (75.7%). These findings are supported by previous evidence that an integrated curriculum may help to deepen knowledge and foster retention of complicated subjects in medical education[14,15].

The feedback obtained from the students add more elastic support to these integrated teaching approaches. Nearly 44.72% of students unanimously agreed for improved understanding and about same percentage (49.72 %) claimed increased critical thinking skills due to integrated sessions This is in line with the previous findings, where integrated learning environments promote active participation and help students develop critical thinking skills — crucial for healthcare professionals of future[16,17]. The highest satisfaction levels with integrated sessions are possibly pointing towards a better pedagogical direction that would come under further support by research indicating how hand-in-glove is teaching more and achieving higher results, but also gaining of other attention regions.

Attendance rates were correlated with academic performance and the correlation coefficient for students who attended 80% or higher number of sessions is shown in fig. These findings are in support of Eagleton (2015) who suggests that attending co-taught class sessions on a frequent basis contributes significantly to improved academic[18,19]. Students who attended fewer than 80% performed substantially worse; mean scores

were 72.3% on written exams and 68.0% of quizzes, indicating that sustained engagement in the integrated sessions is necessary for optimal academic performance[19].

On the ground of pedagogical efficacy, t-test showed that there was a significant difference between integrated and traditional teaching kinds in which mean score70s89 theirs is 79.8% for integrated and 71.5% for trail method (p-value=0); accordingly we have proved to demonstrate Null hypothesis (Table 4) It reflects the notion that integrated teaching can help alleviate some knowledge division associated with traditional curricular training methods[20]. It seems that the structured connected format of integrated sessions may allow students to see anatomy and physiology from a more complete picture promoting linking structure (anatomy) with function(relevant physiology).

CONCLUSION

Impact of integrated sessions of anatomy and physiology the academic performance students at Pakistan Institute Medical Science That can mean students in integrated sessions scored an average of 79.8 percent on assessments — versus a nearly eight-point drop to just under 72 for those taught using traditional methods. In a study of ICM in first year students, there were subjective reports that they thought integrated teaching was beneficial for understanding and critical thinking skill[4]. The results of the correlation analysis that come from this study lend additional support to calls for improved classroom attendance, as regular attendees performed at a much higher level academically than those with lower levels of sessional presence. The findings of the present study give strength to implementing integrative curricula in medical education by indicating that teaching practices must incorporate pathways so as to elevate future healthcare professionals.

Limitations of the Study: This study, however, has several limitations. Conducted at a single institution, which could limit its generalizability. Data obtained via self-report may suffer from response bias, because the students might have overstated any perceived benefits of integrated sessions Moreover, similar to a sampling bias that may have resulted from excluding students with anatomy and physiology background. Finally, the influence of other confounders like different learning styles was missing in this study. Follow-up research is needed that includes more institutions and qualitative methodologies to gain a complete understanding.

Author's Contribution:

Concept & Design of Study:	Amrat Ijaz
Drafting:	Ayesha Saleem, Huma Qamar
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Final Approval of version:	By all above authors

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Original Article

Histological Changes in the Extracellular Matrix of the Human Placenta Complicated by Diabetes

Muhammad Qaseem[1], Nighat Ara[2], Farooq Khan[3] and Saad Ahmed Idrees[4]

ABSTRACT

Objective: To analyze the possible changes in placental histology and Altered deposition of ECM molecules and changes in the morphological organization of the spongiotrophoblast layer might alter the microenvironment of the placenta, leading to developmental abnormalities in the offspring of diabetic mothers.

Study Design: A case-control study

Place and Duration of Study: This study was conducted at the Department of Anatomy with the collaboration obstetric department Nowshera Medical College, Nowshera from 05 Jan 2023 to 05 March 2023.

Methods: A total of twenty pregnant women were included in this study, 13 in the diabetic group and 7 in the non-diabetic (control group) Placentas of full-term pregnancy were collected from the Labor Room and Gynecology operation theatre of QHAMC (Qazi Hussain Ahmed Medical Complex). Immunoperoxidase staining was used to determine the expression of ECM components proteoglycans (decorin and biglycan), fibronectin, and laminin.

Results: Twenty patients were included in this study, and the mean age of participants was 29.5 ±4.2 years Statistical analysis showed that maternal diabetes significantly influenced the localization of ECM proteins in placental tissues. Fibronectin deposition within the labyrinth layer was significantly greater in diabetic mothers at full-term gestational ages examined (Figure 1; $p < 0.01$). Disorganization of the ECM may have consequences for maternal-fetal nutrient exchange by abnormal fibronectin deposition. There were no significant differences in the distribution of decorin or biglycan between diabetic tissues compared with control tissues ($p > 0.05$). Laminin distribution was not changed in diabetic placentas but appeared decreased at term with the labyrinth nodular region near the umbilical cord where nutritional interchange occurs demonstrating simple regression ($p = 0.08$).

Conclusion: Our results indicate that the changes in ECM organization and fibronectin expression found that diabetes alters the microenvironment at the maternal-fetal interface, leading to developmental abnormalities in the offspring born from diabetic pregnancy. This insight is important to devise methods for the prevention of negative pregnancy outcomes due to diabetes. Future research should be conducted to examine the mechanisms underlying these associations and explore possible therapeutic interventions.

Key Words: Maternal diabetes, Placentation, ECM Fibronectin

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INTRODUCTION

Maternal diabetes, including pregestational and gestational diabetes, is a common condition associated with adverse maternal and fetal health outcomes[1].

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The increasing prevalence of diabetes in pregnancy has now escalated to the level of a public health problem with related risks for fetal macrosomia, preeclampsia, and an elevated rate of cesarean section[2]. The placenta is a vital organ for the fetus containing the exchange of nutrients, gases, and waste products between mother and fetus[3]. Macrocosmic fetuses following diabetic pregnancies may survive because of robust placental morphological and function adaptations, while in other circumstances competition for available fuels results in intrauterine growth retardation IUGR[4]. The different components of the ECM, which is a key factor in placental function that provides structural support and controls cellular behavior[5]. ECM is a component of extracellular proteins as linings in camaraderie with collagens, proteoglycans, and glycoproteins such as fibronectin while others[6]. They are critical in preserving the tissue integrity of the placenta and play a key role during pregnancy as they allow trophoblast invasion, and vascular remodeling[7]. Changes in the composition or distribution of ECM components can

disturb this delicate balance and may compromise nutrient and oxygen transfer from mother to fetus[8]. Increased expression of extracellular matrix (ECM) components has been detected in most of the tissue, including kidney and blood vessels triggered by diabetes[9]. As for pregnancy, diabetes-induced alterations in the ECM of the placenta can account for part of the pathophysiology observed on the maternal and fetal sides (i.e. diabetic fetopathy)[10]. An overaccumulation of specific ECM molecules (eg, fibronectin) has been implicated in disruptions to placental function and growth restriction[11]. Nevertheless, the outcomes of maternal diabetes on ECM in placenta distribution during various gestational levels continue to be further investigated[12]. Since the research of this protein family has been well supported in previous studies, we are not surprised to see a post-natal benefit resulting from these changes[13]. Given that ECM is due to its critical influences on placental development and function[14,15]. Intending to contribute to the body of knowledge in this field, the present study aimed to analyze the distribution of various ECM molecules (the proteoglycans decorin and biglycan; and the glycoproteins fibronectin and laminin) in the placentas of diabetic mothers. This research was carried out at the Department of Anatomy Nowshera Medical College with collaboration in the histopathology department to study placental ECM in diabetic pregnancies through a complete histological analysis. Understanding the distribution of these ECM components will provide information about specific targets and mechanisms by which maternal diabetes can alter the placental structure, thereby impairing function in diabetic conditions[16].

METHODS

Our case-control study consisted of 13 pregnant diabetic women compared to the control group of 7 non-diabetic pregnant women. Placental tissues were collected at 38 weeks in gestational age after parturition. This study was performed in the Department of Anatomy, with the collaboration of the obstetric department of Nowshera Medical College and Approved by IRB. Immunohistochemistry was used on proteoglycans (decorin and biglycan), fibronectin, and laminin. This was performed via immunostaining on paraffin-embedded placental sections with specific antibodies against each ECM component, followed by peroxidase-conjugated secondary antibody detection. This was followed by light microscopy of tissue sections stained to visualize ECM components.

Data Collection: Placental samples were obtained from diabetic and non-diabetic patients at the time of parturition or C sections. The tissue samples were fixed immediately in formalin, processed, and embedded for histological examination. Other clinical data, including maternal age, glycemic control, and pregnancy outcomes were recorded for statistical analysis.

Statistical Analysis: The analysis of the data was carried out with SPSS version 26. The continuous variables are provided as a mean with standard deviation and the categorical data is presented in frequencies (percentages). Independent Student t-tests were used to compare differences between groups, and a $p < 0.05$ was taken as statistically significant.

RESULTS

E (±SD) age of the subjects was 29.5 ± 4.2 years Objectives Statistical comparison demonstrated significant differences in ECM distribution between placentas from diabetic and non-diabetic patients. More specifically, there was a significant increase in fibronectin deposition within the labyrinth layer of the placenta from diabetic pregnancies tested ($p < 0.01$).

Immunoperoxidase staining, Placental morphology

Placentas harvested from diabetic mothers presented various morphological alterations throughout pregnancy, chief among which was an increase in the spongiotrophoblast layer. In addition, the classical pattern of trophoblast giant cell distribution was not observed in these placentas.

Decorin: Immunoreactivity for decorin was observed in the mesenchyme of the umbilical cord and fetal blood vessels of the labyrinth region. Immunoreactivity was present in the stroma of the metrial gland near decidual cells and surrounding the maternal blood vessels. Immunoreactive areas broadened only as the placenta grew. Throughout pregnancy, the presence and distribution of decorin immunoreactivity in the control group placentas was like that observed in the diabetic group placentas.

Biglycan: The immunoreactivity for biglycan had increased in the mesenchyme of the umbilical cord and surrounding the fetal blood vessels of the labyrinth but remained absent from the basal decidua and the stroma of the metrial gland. The immunoreactivity for Biglycan was not affected by the diabetic condition

Fibronectin: In placentas obtained from the control group on week 38, fibronectin was observed in the mesenchyme of the umbilical cord and the spongiotrophoblast layer. In the stroma of the metrial gland, immunoreactivity for fibronectin was primarily observed in the basal decidua and surrounding the maternal blood vessels. In placentas obtained from the diabetic group of mothers, fibronectin was observed in all regions previously described for the control group However, in contrast to the control placentas, diabetic placentas presented fibronectin expression in the labyrinth region.

Laminin: In term placentas, laminin immunoreactivity was once again seen to remain in the basement membrane of the fetal vessels present in the labyrinth in the vicinity of the spongiotrophoblast layer. Yet, this

immunoreactivity was not found in the labyrinth zone proximal to the umbilical cord. This peculiar pattern of laminin distribution in the labyrinth was observed in the placentas of both groups.

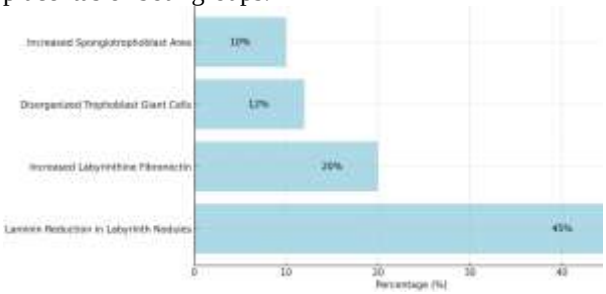

Figure No. 1: Placental Abnormalities in Control Group

Table No. 1: General Characteristics of the Study Population

Characteristics	Diabetic Group (n=13)	Control Group (n=07)	p-value
Mean Age (years)	29.5 ± 4.2	28.8 ± 4.5	0.18
Body Mass Index (BMI)	27.6 ± 3.8	26.9 ± 3.7	0.12
Gestational Age at Delivery (weeks)	38.2 ± 1.5	38.5 ± 1.3	0.24
Parity (median)	2 (1-3)	2 (1-3)	0.82
Fetal Weight (grams)	3250 ± 450	3400 ± 480	0.08

Table No. 2: Distribution of ECM Components in Placental Tissues

ECM Component	Diabetic Group (n=13)	Control Group (n=07)	p-value
Decorin	Similar distribution	Similar distribution	>0.05
Biglycan	Similar distribution	Similar distribution	>0.05
Fibronectin	High deposition in labyrinth	Low deposition, term only	<0.01
Laminin	Decrease at term, labyrinth	Decrease at term, labyrinth	0.08

Table No. 3: Fibronectin Deposition Across Gestational Ages

Gestational Age (weeks)	Diabetic Group: Fibronectin Deposition (AU)	Control Group: Fibronectin Deposition (AU)	p-value
38	75 ± 15	30 ± 10	<0.01
38	80 ± 18	35 ± 12	<0.01
38	85 ± 20	40 ± 15	<0.01

AU = Arbitrary Units for quantification of fibronectin deposition

Table No. 4: Summary of Placental Abnormalities Observed

Abnormality Observed	Diabetic Group (n=13)	Control Group (n=07)	p-value
Increased Spongiotrophoblast Area	42%	10%	<0.01
Disorganized Trophoblast Giant Cells	38%	12%	<0.01
Increased Labyrinthine Fibronectin	75%	20%	<0.01
Laminin Reduction in Labyrinth Nodules	60%	45%	0.08

DISCUSSION

It demonstrated how maternal diabetes changes the composition of the extracellular matrix (ECM) in the placenta, especially modifying fibronectin deposition within the labyrinth. These findings are consistent with other studies that have shown that abnormal shifts in ECM structure due to diabetic conditions drive pathology in preterm birth[17]. One of the most pronounced differences we found in this study was that fibronectin deposition was significantly increased throughout gestation within the placental labyrinth region from diabetic mothers[18]. These results are in agreement with previous reports that diabetes increases fibronectin expression in tissues such as the kidney and blood vessels[19]. Researcher reported an elevation of fibronectin levels in the placentas from term-diabetic rats indicating that this glycoprotein may have a significant role in diabetic placentation pathophysiology[20]. Over-deposition of fibronectin in the labyrinth layer might also alter matrix stability and could interfere with maternal-fetal nutrient exchange necessary for fetal growth and development. However, there were no differences in the distribution of decorin/biglycan between diabetic placentas and controls. This result indicates fibronectin is extremely sensitive to the hyperglycemic diabetic milieu, but other ECM components may show minimal alteration in this condition. Nevertheless, the exact mechanisms responsible for diabetic-induced changes in specific ECM components remain to be established. Strikingly, laminin distribution was not significantly modified by diabetes although an overall reduction in the levels of laminin occurred toward term within the labyrinth pericordal area.[21] The decrease in laminin expression we observed has been reported earlier in diabetic nephropathies and correlated with the integrity and function of tissue[22]. Changes in structural support within the labyrinthine regions could further add to impaired nutrient and gas exchange during diabetic

pregnancy by weakening laminin-dependent adhesion. The alteration in the spongiotrophoblast layer among diabetic pregnancies with enlargement, abnormal trophoblast giant cell arrangement, and reduction of the junctional zone is notable indicating that maternal diabetes has a significant effect on placental morphology. Evidence for such a phenomenon has been supported by histopathological examination of placentas from diabetic animals that display similar morphological alterations[23]. Collectively, our results continue to expand the spectrum of how maternal diabetes influences placental structure and function with an explicit role for fibronectin within the ECM. We have shown that changes in ECM composition due to diabetes may contribute significantly to determining fetal growth, so monitoring these important components will be crucial for a healthy outcome of diabetic pregnancies. Further studies are needed to understand the molecular pathways involved in such ECM alterations and to test potential therapeutic agents being developed targeting it as mechanisms by which diabetes has deleterious effects on placental function, leading to risk of inflammation-induced PTD[24].

CONCLUSION

This study provides evidence that maternal diabetes impacts extracellular matrix content within the placenta with a significant increase in fibronectin deposition specifically within the labyrinth layer. These changes could impair maternal-fetal nutrient transfer and contribute to adverse fetal outcomes that are associated with intrauterine group B Streptococcus Infection. Insight into these alterations can potentially be a key to understanding the biology of diabetes and pregnancy with opportunities for therapeutic interventions. I find it, readers will remember, only until much-needed research explains such phenomena (with mechanisms) and trials the appropriate intervention.

Limitations: It should also be noted that the very small sample size, although a good starting point to generate initial observations and questions around inferences, may impact generalizability. Larger human cohorts will be required to confirm these findings validate them and explore their clinical significance.

Future Directions: In future studies, molecular details responsible for selective changes of extracellular matrix components in diabetic placentas need to be addressed. Furthermore, studying the effects of various glycemic control regimes on ECM remodeling might also contribute to new therapeutic strategies. Future work from imaging methods such as MEG and EEG which have better temporal resolution, in addition to longitudinal studies, will help answer the question of when these changes take place.

Acknowledgment: We would like to thank the hospital administration and everyone who helped us complete this study.

Author's Contribution:

Concept & Design of Study:	Muhammad Qaseem
Drafting:	Nighat Ara, Farooq Khan
Data Analysis:	Farooq Khan, Saad Ahmed Idrees
Revisiting Critically:	Muhammad Qaseem, Nighat Ara
Final Approval of version:	By all above authors

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Original Article

Disrupting the Connection between Hospice Admission and the Cessation of Dialysis Treatment

Ghulam Mustafa[1] and Feras Almarshad[2]

ABSTRACT

Objective: To examine the latest trends and predictors utilization of hospice, ascertain the suitable hospice care duration, and investigate the discontinuation of dialysis without enrollment hospice among patients with end-stage renal disease.

Study Design A Prospective study

Place and Duration of Study: This study was conducted at the department of Medicine Nishtar hospital, Multan from January 2021 to December 2022.

Methods: A pre-designed questionnaire was utilized to gather comprehensive data on demographic characteristics, diagnoses, biochemical markers, clinical history, and claims patient's information with end-stage renal disease (ESRD). The final dataset consisted of 300 unique records for ESRD patients who had passed away during the study duration.

Results: The mean duration of hospice of enrolled hospice patients was greater than not enrolled hospice patients as 17.74±4.94 days and 12.39±4.58 days, respectively, ($p<0.001$). Whereas, most of the not enrolled hospice patients had <15 days of hospice care 75.9%.

Conclusion: Median hospice duration before death: 5 days; Elderly, and non-kidney transplant recipients more likely to enroll; Hospice duration increasing; Need for better coordination in ESRD and hospice care; Patients discontinuing dialysis without hospice likely need different interventions; Medicare barrier to hospice enrollment should dissolve post-dialysis cessation.

Key Words: Hospice, discontinuation of dialysis, End stage renal disease, Kidney transplant, Death

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INTRODUCTION

Hospice care for end-stage renal disease (ESRD) is an important aspect of managing the condition when curative treatments are no longer effective or desired. ESRD refers to the final stage of chronic kidney disease when the kidneys have lost most of their function[1]. Patients with ESRD typically require dialysis or a kidney transplant to survive. However, when individuals with ESRD reach a point where further aggressive treatments are not beneficial or desired, hospice care becomes an option[2]. Although inpatient palliative care utilization for addressing various needs in End-Stage Renal Disease (ESRD) and advanced kidney disease has been steadily increasing, the utilization of hospice care presents a more intricate scenario[3].

Analysis spanning from 2000 to 2014 revealed a rise in utilization hospice among patients of ESRD; however, the use of hospice remained lower in ESRD as compare to chronic diseases, with many experiencing stays of less than three days[4]. Multiple barriers contribute to the shorter length of stay in hospice and lower rates of hospice utilization among ESRD patients compared to those with other serious illnesses[5], including the necessity to cease dialysis before hospice admission, limited provider awareness about benefits of hospice in dialysis patients, and cultural factors influencing patient preferences[6].

Structural impediments, such as Medicare policies prohibiting dialysis payment by Medicare for ESRD patients with a primary hospice diagnosis[7], absence of eligibility criteria for specific hospice for this population, and quality of dialysis care not prioritizing life's quality, further obstruct access to hospice care[8]. The predominant barrier lies in the policy-induced dilemma of choosing between hospice and dialysis care, complicating decision-making for ESRD patients, although the existence of a subgroup refraining from hospice even post-dialysis discontinuation suggests additional significant obstacles[9,10].

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The study underscores the importance of advance care planning discussions early in the disease trajectory. Patients with advanced kidney disease should have ongoing conversations with their healthcare providers about their treatment preferences, goals of care, and options for end-of-life care, including the possibility of concurrent dialysis and hospice services.

METHODS

Study was planned and preceded in the department of Medicine Nishtar hospital, Multan from January 2021 to December 2022 in two years time duration. Study approval was taken from institution and consent was obtained from patients and their family members. Contact numbers and addresses were taken. A pre-designed questionnaire was utilized to gather comprehensive data on diagnoses, demographic characteristics, clinical history, biochemical markers, and claims information of patients with end-stage renal disease (ESRD). The final dataset consisted of 300 unique records for ESRD patients who had passed away during the study duration. These records were meticulously compiled to provide a thorough understanding of the characteristics and circumstances surrounding the deaths of these individuals, allowing for detailed analysis and interpretation of the factors contributing to mortality in this population.

The study investigated several outcomes, hospice care duration, including hospice enrollment, and discontinuation of dialysis before death without enrollment in hospice. Hospice enrollment was determined using the variable "hospice admit date," while discontinuation of renal replacement therapy was defined by the variable "prior to death discontinuation of dialysis." Duration of hospice care was categorized as either adequate (15 days or more) or inadequate (less than 15 days), and hospice enrollment was categorized as 'yes' or 'no.' discontinuation of dialysis before death without enrollment in hospice was identified by combining the variables "hospice admit date" and "renal replacement therapy discontinued prior to death," resulting in a classification of 'yes' for those who discontinued renal replacement therapy without hospice enrollment and 'not applicable' for any other response combination.

The independent variables in the study encompassed age (categorized as 65 years or older versus younger than 65 years), gender (male versus female), hypertension (present versus absent), diabetes mellitus (present versus absent), cancer (present versus absent), COPD (present versus absent), alcohol dependence (present versus absent), drug dependence (present versus absent), absence of prior kidney transplant (present versus absent), and non-renal congenital abnormality (present versus absent). Additionally, newly devised variables included macrovascular disease microvascular disease, and debilitation.

SPSS version 27 was used and test of significant were chi square test and logistic regression. P value below or equal to 0.05 was taken as significant.

RESULTS

Overall, 300 patients were included in our study, both genders, with mean age 65.44±11.82 years. There were 170 (56.7%) males and 130 (43.3%) females. There were 11 (3.7%) patients, who received kidney transplant. In this study, 97 (32.3%) patients enrolled in hospice. The average duration of hospice care of all the patients was 14.12±5.32 days. Most of the patients had <15 days of hospice care. Dialysis discontinued prior to death without hospice enrollment was observed in 35 (11.7%) patients. Hypertension, diabetes mellitus, debilitated, cancer, COPD, microvascular disease and renal congenital abnormality was noted in 192 (64.0%), 177 (59.0%), 175 (58.3%), 135 (45.0%), 155 (51.7%), 179 (59.7%) and 119 (39.7%) patients, respectively. (Table 1).

The mean duration of hospice of enrolled hospice patients was greater than not enrolled hospice patients as 17.74±4.94 days and 12.39±4.58 days, respectively, ($p<0.001$). Whereas, most of the not enrolled hospice patients had <15 days of hospice care 154 (75.9%), ($p<0.001$). Further, hypertension, diabetes mellitus, debilitated, cancer, COPD, microvascular disease and renal congenital abnormality was high in not enrolled hospice patients than enrolled hospice patience, ($p<0.001$). (Table 2).

Debilitated, COPD, microvascular disease and renal congenital abnormality was in <15 days duration of hospice care patients than ≥15 days duration of hospice care patients, ($p<0.050$). (Table 3)

Table No. 1: Demographic and baseline characteristics of the study patients

Characteristic	Presence
Age (years)	65.44±11.82
≤65	160 (53.3)
>65	140 (46.7)
Gender	
Male	170 (56.7)
Female	130 (43.3)
Received a kidney transplant	
Yes	11 (3.7)
No	289 (96.3)
Enrolled in hospice	
Yes	97 (32.3)
No	203 (67.7)
Duration of hospice care(days)	
Mean±S.D	14.12±5.32
<15	194 (64.7)
≥15	106 (35.3)
Discontinuation of dialysis before death without enrollment in hospice	
Yes	35 (11.7)

No	265 (88.3)
Hypertension	
Yes	192 (64.0)
No	108 (36.0)
Diabetes mellitus	
Yes	177 (59.0)
No	123 (41.0)
Debilitated	
Yes	175 (58.3)
No	125 (41.7)
Cancer	
Yes	135 (45.0)
No	165 (55.0)
COPD	
Yes	155 (51.7)
No	145 (48.3)
Microvascular disease	
Yes	179 (59.7)
No	121 (40.3)
Renal congenital abnormality	
Yes	119 (39.7)
No	181 (60.3)
Mean±S.D, N (%)	

Table No. 2: Association of enrolled in hospice with demographic and baseline characteristics

	Enrolled in hospice		**p-value**
	Yes 97 (32.3%)	**No 203 (67.7%)**	
Age (years)	64.71±11.42	65.79±12.01	0.455
≤65	56 (57.7)	104 (51.2)	0.291
>65	41 (42.3)	99 (48.8)	
Gender			
Male	52 (53.6)	118 (58.1)	0.460
Female	45 (46.4)	85 (41.9)	
Received a kidney transplant			
Yes	4 (4.1)	7 (3.4)	0.711
No	93 (95.9)	196 (96.6)	
Duration of hospice care (days)			
Mean±S.D	17.74±4.94	12.39±4.58	<0.001
<15	40 (41.2)	154 (75.9)	<0.001
≥15	57 (58.8)	49 (24.1)	
Discontinuation of dialysis before death without enrollment in hospice			
Yes	11 (11.3)	24 (11.8)	0.903
No	86 (88.7)	179 (88.2)	
Hypertension			
Yes	37 (38.1)	155 (76.4)	<0.001
No	60 (61.9)	48 (23.6)	
Diabetes mellitus			
Yes	32 (33.0)	145 (71.4)	<0.001
No	65 (67.0)	58 (28.6)	
Debilitated			
Yes	30 (30.9)	145 (71.4)	<0.001
No	67 (69.1)	58 (28.6)	
Cancer			
Yes	16 (16.5)	119 (58.6)	<0.001
No	81 (83.5)	84 (41.4)	
COPD			
Yes	13 (13.4)	142 (70.0)	<0.001
No	84 (86.6)	61 (30.0)	
Microvascular disease			
Yes	14 (14.4)	165 (81.3)	<0.001
No	83 (85.6)	38 (18.7)	
Renal congenital abnormality			
Yes	9 (9.3)	110 (54.2)	<0.001
No	88 (90.7)	93 (45.8)	
Mean±S.D, N (%)			

Table No. 3: Association of duration of hospice care with demographic and baseline characteristics

	Duration of hospice care (days)		**p-value**
	<15 194 (64.7%)	≥15 106 (35.3%)	
Age (years)	65.29±11.68	65.71±12.13	0.772
≤65	105 (54.1)	55 (51.9)	
>65	89 (45.9)	51 (48.1)	
Gender			
Male	113 (58.2)	57 (53.8)	0.455
Female	81 (41.8)	49 (46.2)	
Received a kidney transplant			
Yes	5 (2.6)	6 (5.7)	0.174
No	189 (97.4)	100 (94.3)	
(days)			
Discontinuation of dialysis before death without enrollment in hospice			
Yes	26 (13.4)	9 (8.5)	0.205
No	168 (86.6)	97 (91.5)	
Hypertension			
Yes	130 (67.0)	62 (58.5)	0.142
No	64 (33.0)	44 (41.5)	
Diabetes mellitus			
Yes	122 (62.9)	55 (51.9)	0.064
No	72 (37.1)	51 (48.1)	
Debilitated			
Yes	126 (64.9)	49 (46.2)	0.002
No	68 (35.1)	57 (53.8)	
Cancer			
Yes	92 (47.4)	43 (40.6)	0.254
No	102 (52.6)	63 (59.4)	
COPD			
Yes	113 (58.2)	42 (39.6)	0.002
No	81 (41.8)	64 (60.4)	
Microvascular disease			
Yes	130 (67.0)	49 (46.2)	<0.001
No	64 (33.0)	57 (53.8)	
Renal congenital abnormality			

Yes	87 (44.8)	32 (30.2)	0.013
No	107 (55.2)	74 (69.8)	
Mean±S.D, N (%)			

DISCUSSION

The study examined clinical and sociodemographic factors associated with enrollment in hospice and duration of hospice care among ESRD patients in Pakistan between 2012 and 2013, revealing that while hospice enrollment was prevalent, a significant portion of patients opted for renal replacement therapy discontinuation without hospice care. Additionally, findings indicated a median hospice care duration of 5 days, with a standardized increase in hospice care duration observed over time, and identified elderly, White, and non-kidney transplant recipients as demographics more inclined to enroll in hospice.

According to Watcherman et al[11] study based on USRDS data, utilization of hospice among ESRD died was estimated to be 20%..This finding aligns with prior research indicating a consistent, albeit gradual, rise in hospice utilization among ESRD patients dating back to the year 2000[12].

Wetmore et al[13] and Hussain et al[14] have reported that several factors are associated with dialysis withdrawal. These include older age, female gender, white race, and originating from a rural setting. Additionally, factors crucial to physical independence, such as a history of cerebrovascular disease, have also been identified as significant contributors to the decision to withdraw from dialysis treatment.

Between 2012 and 2019, Soipe et al[15] found that about 1 in every 4 ESRD patients with history of hospice enrollment and died, while one in every twelve patients who discontinued dialysis prior death without enrollment in hospice, with an upward trend observed in the standardized duration of hospice care. Brown et al[16] reported that Medicaid patients exhibit less suitable track for the proxy of disability score and for acute medical events, while in the general population, conflicting literature exists regarding the association between lower socioeconomic status and end-of-life care, with some studies suggesting higher intensity of care and others paradoxically indicating increased utilization of palliative care consultative services.

Romero et al[17] found that patients receiving dialysis who enroll in hospice typically have shorter lengths of stay compared to the general Medicare population, with an average of 8 days versus 20 days, and nearly half of them are not enrolled in hospice until the last 3 days of life.In a study conducted by Schell et al[18] it was found that the median length of hospice care for dialysis patients is notably shorter at 5 days, in stark contrast to the 17.4 days observed for the general Medicare population. Additionally, nearly half of the dialysis patients receiving hospice services did so for 3 days or fewer, and they were just as likely to be hospitalized in the last month of life as those who did not utilize hospice care.

Holley et al[19] and Murphy et al[20] revealed that approximately one out of every twelve ESRD patients opted to discontinue renal replacement therapy prior to their demise without enrolling in hospice care. In the past, "withdrawal from dialysis" was recorded as a cause of death in ESRD patients' death notification forms, whereas "dialysis discontinuation" was not universally recognized as an interchangeable term by nephrologists.

CONCLUSION

Median hospice duration before death: 5 days; Elderly, and non-kidney transplant recipients more likely to enroll; Hospice duration increasing; Need for better coordination in ESRD and hospice care; Patients discontinuing dialysis without hospice likely need different interventions; Medicare barrier to hospice enrollment should dissolve post-dialysis cessation.

Author's Contribution:

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Drafting:	Feras Almarshad
Data Analysis:	Feras Almarshad
Revisiting Critically:	Ghulam Mustafa
Final Approval of version:	By all above authors

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Original Article

Benefits of Early Diagnosis and Early Management Helps in Speech and Language Development in Hearing Impaired Children

Ayub Musani[1], Faheem Ahmed Khan[1], Aqeel ur Rehman Hameed[2], Asif Uddin Abbasi[2], Syed Wadood ul Hasnain[2] and Farhat Jafri[3]

ABSTRACT

Objective: The objective of this study is to determine the age of diagnosis of hearing impairment in children and outcome of early management in linguistic acquisition in hearing impaired children.

Study Design: A descriptive cross-sectional study in cross section population.

Place and Duration of Study: This study was conducted at the Otorhinolaryngology department of Abbasi Shaheed Hospital. This study was conducted from January 2022 to June 2023.

Methods: Detail history and complete examination was done. Relevant investigations were performed. After fulfill the selection criteria, patients advised hearing amplification device and speech therapy. Patients called for follow-up and observe language development.

Results: Total number of patients selected for this study was 105 patients. Female were 57 (54%). Female male ratio was 1.18. 38 (36%) children were between the ages of 2-3 years came first time in ENT department with complaining of hearing impairment followed by 1-2 years 33 (31%). 59 (56%) patients showed improvement in speech and language development while 46 (43.8%) patients showed poor performance in development of speech and language. Highest frequency of improvement in language development was observed between ages of 0-1 years 15 (78.9%) patients out of 19 patients. Poor performance in development of speech and language was noted between 3-4 years 2 (13.3%) out of 15 patients.

Conclusion: Early diagnosis of hearing impairment and appropriate treatment observed good result in language development

Key Words: Hearing loss, hearing screening, hearing aid, rehabilitation, amplification device.

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INTRODUCTION

Globally, Childhood hearing impairment is a serious problem for children and families, about 34 million children present with hearing loss and most of the cases are preventable[1]. According to WHO, hearing impairment defines as inability to hear threshold of 20dB or loss of 35 dB in the better ear[2].

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All sense organs play an important role in life but vision and hearing have a vital in psychological growth and behavior. Hearing is one of the important senses of organ and helps in the development of language and speech. Hearing impaired child is at higher risk in speech – language development and weak in academic activities as compared to normal hearing child. Critical age in the development of speech and language till 3 years of age. Hearing problem is not only effects in academic activity but also effects in social and later in occupation[3]. Poor hearing threads to develop poor speech and language which affects the normal quality of life in long term[4]. Poor hearing child has poor Communication ability to maintain relationship in normal life[5]. In third world countries, about 10 infants with decreased hearing in every 1000 birth[5]. Hearing problem is one of the major problems of the third world countries. Local study shows, the incidence of hearing impairment in school going in Pakistan is 7.9%. The main reason for late diagnosis in third world countries is financial problem[6], due to financial constraints the proper facilities of neonatal screening is not present[7].

Most of the cases of mild cases of hearing impairment are missed which are treatable[8].

Proper newborn hearing screening procedure should be adopted in those cases where risk factors are present. Before the invention of Newborn screening, most of the minimal or moderate hearing loss was not identified till school age. In screening procedure include detail history of prenatal, perinatal and postnatal information, complete ear examination with nose and throat examination. If any suspicious found in history or child sleeps through loud noises or fails to startle to loud sounds or fails to develop speech at 1-2 years should do hearing assessment. There are subjective test and objective test are available to assess the hearing. Subjective test depends upon the response of the patient while in objective test, no need of patient response. Objective test includes, Otoacoustics emission (OAE) and brainstem evoked response audiometry (BERA). OAE usually advise on the second day of birth and BERA performed 28 days after the initial hearing assessment[9]. BERA usually advise for high-risk neonates[10].

Audiological rehabilitation considers one of the most effective way to improve hearing. Amplification device plays a vital role in aural rehabilitation. Residual hearing is required to use hearing aid. Now a day digital hearing aid is available to improve the quality of life. Hearing aids is a small electronic battery-operated device which amplify the sound. A hearing aid consist microphone which receives sound and convert it into electrical signals. Hearing aids are useful in hearing impaired child. It helps in improve hearing, speech, communications skill.

In developing countries like Pakistan proper screening protocol does not exist at the national level. The main reasons are lack of infrastructure, financial constraints, no proper patient data available, and limited access to health care units, parents and health workers are unaware for early referral benefits[11]. The main aim of this study is to determine the age of hearing impairment in children and benefits of early identification of hearing impairment in linguistic acquisition in children.

METHODS

This study was conducted in Otorhinolaryngology department of Abbasi Shaheed Hospital. This study was conducted from January 2022 to June 2023. After informed consent complete history was taken, which included pre-natal, peri-natal and post-natal problems. In history also asked about the age of detection of hearing loss and age of treatment start. Complete examination was done which included ENT examination and systemic examination. Relevant investigations were performed where required (Otoacoustic emissions, behavior observation, visual reinforcement audiometry, brain stem evoked response audiometry and auditory steady state responses).

RESULTS

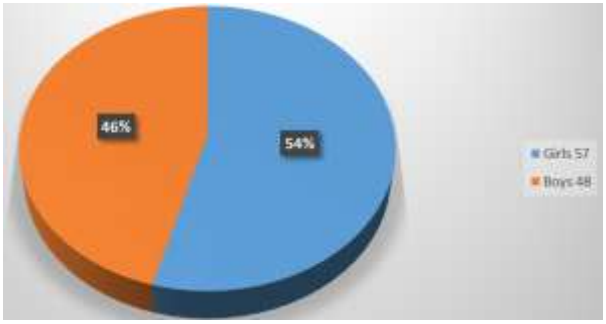

Figure No. 1: Pi Chart (Gender)

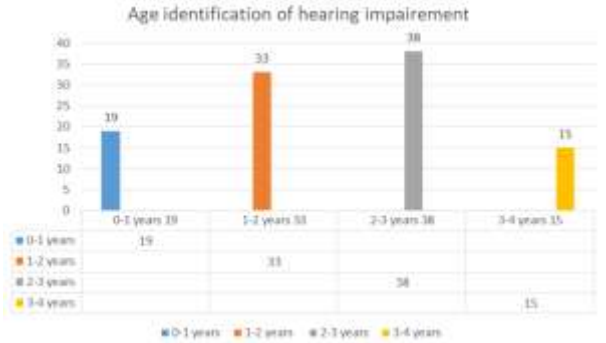

Figure No. 2: Bar Chart (Age)

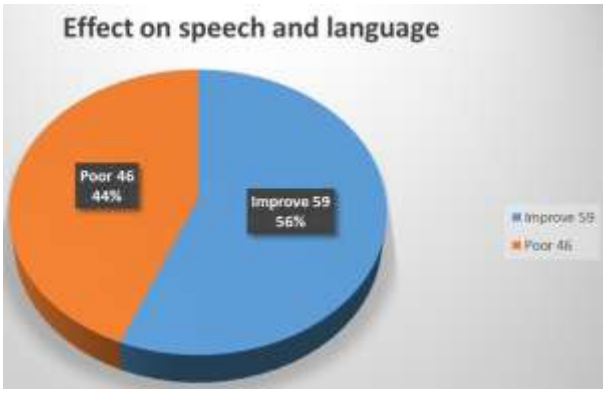

Figure No. 3: (Pi Chart) Speech and language development

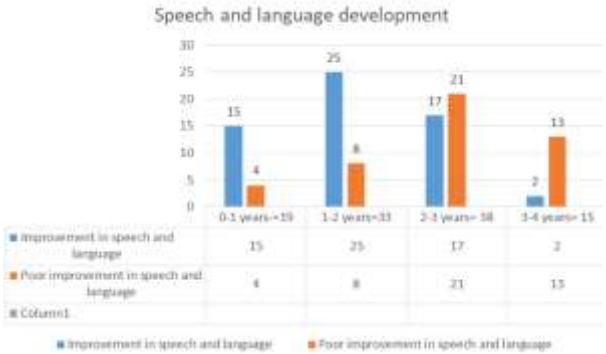

Figure No. 4: (Bar chart) Improve speech and language development vs poor speech and language development according to age groups

Children came with hearing loss were included in this study. Patients with history of previous ear surgery, children with intellectual deficit, above 4 years of age, not proper follow-up, not taken proper speech therapy session, in-consistent use of hearing aid, conductive hearing loss improve after treatment and profound hearing loss. After fulfilling the selection criteria, patients called for follow-up and noted speech and language development.

Total number of patients selected for this study was 105 patients. Male were 48 (45.7%) and female were 57 (54%). Female male ratio was 1.18. Bar chart 2 showed the age group in which hearing problem was noted. In 38 (36%) children hearing impairment was noted between the ages of 2-3 years followed by 1-2 years 33 (31%). Only 19 (18%) children were below the age of 1 year. 15 (14.2%) patients were between 3-4 years of age. 59 (56%) patients showed improvement in speech and language development while 46 (43.8%) patients showed poor performance in development of speech and language. Highest incidence of improvement in speech and language development was observed between 0-1 years of age, 15 (78.9%) patients out of 19 patients showed improvement. In 1-2 years of age, 25 (66.6%) patients out of 33 patients showed improvement in language development. Poor performance in speech and language development was noted between 3-4 years only 2 (13.3%) out of 15 patients showed better performance in speech and language development.

DISCUSSION

Hearing loss causes poor effects in the daily routine life[12]. Hearing impairment in school going children is a common problem which usually ignores by general practitioner. This affects the ability in spoken language[13,14]. Most of the causes of hearing loss are treatable if timely detect. Proper newborn hearing screening procedure should be adopted in those cases where risk factors are present.

This study is tried to determine the benefits of early detection and early management of hearing loss in children and its outcome in speech and language development. In the current study, frequency of hearing loss in female were more. 57 (54.2%) children were female while 48 (45.7%) children were male. Female male ratio was 1.18:1. In Preeti Chaudhary study, 51.83% children were female. In Milan Maharjan study, ratio of hearing loss in female is slightly more as compared to male[15]. In the current study, the most common age group in which hearing impairment was diagnosed between 2-3 years, 38 (36%) children came with hearing impairment were between the ages of 2-3 years followed by 1-2 years 33 (31%). Only 19 (18%) children were below the age 1 year. Study conducted in South Africa showed, median age of identification of hearing impairment was 28 months[16]. Similarly, two studies which were done in India and west Bengal showed the average age of confirmation of hearing impairment were 24.3 months and 2.4 years respectively[17]. There are multifactorial reasons for late diagnosis of hearing loss from both parents and professional. Mostly health professional is unaware about benefits of early detection of hearing loss in children, usually not advised any relevant test to assess the hearing and do not refer the case to otorhinolaryngologist. In developing countries, lack of facilities of rehabilitation center play important role in late diagnosis[18]. On the other hand, parents don't accept that child has hearing problem and they don't take any advice from relevant doctor. Both factors cause delay in diagnosis of hearing problem. Therefore, it is important to start awareness programme among health professional and parents for benefits of early detection of hearing impairment and early intervention[19].

In above study, 15 (78%) patients showed improvement in speech and language development were below 1-year of age while 4 (21%) showed poor performance in development of speech after proper use of hearing aid and speech therapy. Between 1-2 years, improvement observed in 25 (75.7%) children after proper use of hearing aid and speech therapy. The improvement in speech and language development drastically decreased with age. Between 2-3 years the percentage was decreased, out of 38 patients 17 (44.7%) children showed improvement while 21 (55%) showed poor performance in language development. The ratio of poor development of speech further decrease between 3-4 years of age, only 2 (13%) children improved in speech and language and 13 (86.6%) children showed poor performance in speech and language development. Overall improvement was observed in 59 (56%) patients while poor performance was noted in 46 (43.8%) patients. Early identification and intervention in rehabilitation of hearing-impaired child observed fundamental role in development of speech and language. Mostly parents are unaware regarding hearing problem of their child. Health professionals also fail to recognize the hearing problem in suspected cases which result delayed in diagnosis and fitting of amplification devices in the first 3 years of age[17]. One study compared phonological skills in two groups, one in early identified and intervention and other was late identified and intervention in hearing impaired children, showed early identified and intervention children showed positive effect in phonological skills as compared to late diagnosis and intervention[20].

First three years of age is crucial age of speech development, delay in diagnosis and interventions causes failure in speech and language development[20]. Early identification and intervention before the 6 months of age affects good result in development of language in hearing impaired children. The development of language is the same way as normal

hearing children and reduces the language defect in these children. According to Lisa study, more than 80% of children with hearing impaired found good in language levels with age-matched peers when diagnosed early and appropriate intervention[21]. Hearing loss children show poor performance in education, social and language development.

CONCLUSION

Early identification of hearing impairment in children and proper management play an important in speech and language development. Most of the parents and health professionals are unaware about this hearing impairment. Parents and health professional play a vital role in early identification of hearing impairment. Awareness programme should be improved specially among parents and health professional to prevent unnecessary delay in diagnosis of hearing impairment and management.

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Final Approval of version:	By all above authors

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