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EDITORIAL

Revolutionizing Medical Education Through Digital Technologies

Muhammad Nadim Akbar Khan[1], Saadia Sultana[2], Noor-Mah Khan[3]

Digital technologies are electronic tools, systems, processes, devices, and resources that generate, store, or process data. Common examples are websites, video streaming, e- books, blogs, virtual patients, social media platforms (Facebook, Twitter, and Instagram), tools (personal computers, smart phones, tablets) and education-specific devices (data projectors, multimedia, simulators, digital cameras, digital stethoscopes, and laparoscopic simulators).

As a matter of fact, it is critical for medical educationists to have a basic understanding of these dependencies to make the best use of these technologies in their teaching. A wide range of available digital technologies support today's medical teaching, including content, tools, devices, systems, and processes, all of which are mutually dependent, and in turn, all rely on infrastructure. Furthermore, it is important to choose and use appropriate digital tools and processes that best meet their needs.

The effective implementation of technology-enhanced learning in medical education hinges upon the awareness and apt utilization of these technologies by medical educators. The significance and crucial role of digital technology in medical education became particularly evident and underscored during the Covid-19 pandemic. With the closure of medical schools, instructors transitioned to remote work, and students were compelled to participate in online classes, magnifying the importance of integrating digital technology in medical education. We discuss the utilization and integration of digital technology in medical education as follows:

- Significance and Advantages of Incorporating Digital Technology into Medical Education
- Guideline for Appropriate Timing and Methods for Utilizing Digital Technology in Teaching
- Addressing Challenges Associated with the Use of Digital Technology and Strategies to Overcome Them
- Involvement and Oversight of Institutions and Regulatory Bodies in Facilitating Digital Technology Integration

Significance and Advantages of Incorporating Digital Technology into Medical Education:

The incorporation of technology into medical teaching and learning is prompted by various compelling reasons. Digital technology has fundamentally transformed the accessibility, storage, and sharing of medical knowledge. The utilization of high-quality educational materials such as online courses, e-learning modules, and simulations has significantly elevated the standard of medical education, enabling instructors to remain abreast of the latest medical advances. While acknowledging the irreplaceable value of face-to-face teaching, especially in imparting clinical skills, it is imperative to recognize the indispensable role that technology plays in the contemporary era.

Internet technology, e.g. platforms like Moodle, contributes to enhancing connectivity and communication among all stakeholders within the teaching and learning system. Moreover, digital technologies enable the teaching of clinical knowledge and skills by connecting students across different locations with physicians and patients through telehealth networks, addressing the challenges associated with limited clinical learning opportunities. Additionally, technology-based teaching introduces the flexibility of asynchronous learning, empowering students to engage with the material at their own pace within specified timeframes.

Furthermore, the integration of technology facilitates innovative teaching and learning methods that foster critical thinking and problem-solving abilities in students. In a "blended learning

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environment," for instance, reading content is delivered in the form of text or online prerecorded lectures, allowing students to come prepared for classroom discussions and problem-solving activities. This dynamic approach to education opens avenues for creativity and adaptability in the pursuit of effective medical teaching.

Guidelines for Appropriate Timing and Methods for Utilizing Digital Technology in Teaching

Medical teachers should not only be aware of different available digital technologies but should also be mindful of when and how to use digital technologies in their teaching. *According to R. H. Ellaway, "we are currently training the last generation of doctors who can remember a time before the Internet, the first who will learn in an environment dominated by digital technologies and the first who will practice in a predominantly e-health environment. Medical teachers need to be attentive, reflective, and considerate in how they both use and respond to digital technologies.*"

When deciding on when to use digital technology in medical teaching, it's important to consider the goals and objectives of the course or program, as well as the skills and knowledge that the students require. Digital technology should be used to complement and enhance traditional teaching methods, rather than replace them. It is also important to ensure that students are equipped with the digital skills and literacy required to make the most of these technologies. This may include providing training and support in using virtual learning platforms, virtual-reality simulations, and mobile apps.

Different strategies can be used to adopt digital technologies in medical teaching. Teachers in the medical institutions should plan a strategy for the use of different technologies in their day-to-day teaching. They must consider different factors like, infrastructure and equipment - availability of PCs, laptop computers and connections to the internet, capabilities, aptitude and preferences of their students and the type of content to be included such as slide presentations, hand-outs, reading materials, audio and video, and resources for practical work, before incorporating these technologies into their teachings. Multimedia, overhead projectors and videos should be used for classroom teaching. Virtual patients for online teaching the clinical skills can be employed, and webinars may be arranged with MS teams and zoom. Instructors can share teaching materials and communicate with the students on educational projects through social media like WhatsApp, Twitter, Wikis etc. Teachers can also use these platforms to facilitate online discussions and debates. Work can be shared through blogs and educational videos on YouTube. Nowadays, technology is widely used for online assessment with quizzes or regular computer-based exams. Furthermore, post-hoc assessment analysis is now possible with the help of multiple software's.

Challenges Associated with the Use of Digital Technology and Strategies to Overcome Them:

The integration of digital technology into medical education offers numerous advantages, yet it is imperative to acknowledge and address certain drawbacks associated with its implementation. Cost stands out as a significant barrier, encompassing expenses related to acquiring computers, tablets, and educational software, potentially limiting access for both educational institutions and students. Moreover, issues of accessibility arise, as not all students may have equal access to the latest medical technology, potentially creating disparities in the learning environment.

Technical challenges, such as internet connectivity issues, hardware malfunctions, and software problems, pose potential disruptions to learning experiences and can impact student engagement. Another drawback is the potential lack of face-to-face interaction and collaboration intrinsic to traditional medical education, as technology-based learning can be isolated. Furthermore, while technology can enhance hands-on experiences in medical education, it cannot fully replace the indispensable practical exposure with patients, procedures, and equipment.

The assessment of practical skills, such as surgical procedures, through technology-based evaluations can be challenging, leading to potential limitations in accurately gauging students' abilities. Additionally, the risk of distraction, privacy concerns, and the potential for over-reliance on technology, to the detriment of problem-solving and critical thinking skills, further underscore the need for careful consideration.

In conclusion, while digital technology holds

significant promise for medical education, a balanced approach is crucial. It is essential to navigate these drawbacks judiciously and strive for a harmonious integration of technology-based learning with hands-on experiences to ensure a comprehensive and effective medical education.

Involvement of Institutions and Regulatory Bodies in Facilitating Digital Technology Integration:

Medical institutions play a pivotal role in the integration of digital technologies into medical education, shaping an environment that facilitates the effective use of these tools. This ensures that future healthcare professionals are adequately equipped to navigate the evolving digital landscape within modern medicine. To achieve this, institutions should integrate digital technology education into the curriculum, creating modules or courses focused on instructing students in the utilization of digital tools such as virtual reality simulations, telemedicine platforms, and AI-based diagnostic systems.

Facilitating training programs and workshops for both faculty and students is essential, enhancing their familiarity with emerging technologies and enabling faculty members to seamlessly incorporate digital tools into their teaching methodologies. Continuous support and professional development initiatives are critical to keeping educators up to date with the latest advancements. Establishing an assessment plan to evaluate students' competency in using digital tools ensures they acquire the necessary skills for contemporary medical practice.

Encouraging research initiatives in digital health education can drive innovations and improvements in teaching methodologies. The development of ethical guidelines for digital professionalism, encompassing issues related to patient privacy, data security, and the ethical use of AI and machine learning in healthcare, is imperative. Moreover, institutions must allocate budgets and resources to establish digital infrastructure, providing essential components such as computers, software, high-speed internet access, and devices conducive to digital learning.

In parallel, regulatory bodies can contribute by formulating guidelines and standards to evaluate the effectiveness and safety of digital tools employed in medical education. This proactive approach helps uphold educational standards while ensuring the reliability of technology-driven learning experiences.

The future of digital technologies in medical education holds great promise, with ongoing advancements paving the way for increasingly sophisticated virtual simulations, interactive online learning platforms, and augmented reality applications. The integration of artificial intelligence (AI) and machine learning has the potential to personalize learning experiences, offering adaptive feedback to students. Further enhancements, such as wearable devices, virtual reality, and haptic feedback, contribute to a more immersive and effective learning environment. However, ethical considerations, including data privacy and inclusivity, must be diligently addressed as these technologies evolve within medical education. It is a collective responsibility, encompassing teachers, students, medical institutions, and regulatory bodies, to champion and ensure the ethical and effective integration of digital technologies into medical education.

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CONFLICT OF INTEREST

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Risk Stratification of Adnexal Masses Using MRI Ovarian-Adnexal Reporting and Data System (O-RADS) In Comparison to Sonographic Evaluation

Saerah Iffat Zafar, Syeda Tatheer Fatima

ABSTRACT

Objective: To assess the improvement in MRI categorization of adnexal lesions in females by adoption of standardized ovarian and adnexal reporting and data system (O-RADS) for differentiation between benign and malignant masses, in comparison to sonographic findings.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: Radiology department of CMH Abbottabad for a period of 12 months from 01 September 2021 to 31 August 2022.

Materials and Methods: A total of 26 adult female patients with pelvic masses referred to CMH Abbottabad between September 2021 to August 2022 for MRI pelvis were included in the study with the prerequisite of prior ultrasound examination. Signal characteristics of adnexal masses, presence of septae, papillary projections, degree of enhancement, diffusion restriction, and ancillary findings were identified. Grading of the lesions was performed according to O-RADS following the American College of Radiologists (ACR) criteria- from 1-5 in order of potential of malignancy; findings were compared with sonographic results. Clinico-lab correlation and management outcomes of these patients were followed for final diagnosis.

Results: Out of 26 patients included in the study, majority were benign on MRI - 84.6% (n=22/26), falling in O-RADS 2/3 categories. Only 2 out of 11 complex cysts (18.2%) turned out to be definitely malignant (O-RADS 5) on MRI, while rest were benign (O-RADS 3) showing varying stages of bleed (9 out of 11 at 81.8%). All sonographically malignant lesions -15.3% of adnexal masses (n=4/26) were confirmed on MRI (O-RADS 5) and histopathology.

Conclusion: Risk stratification scoring through MRI O-RADS aids in accurate differentiation of malignant from benign lesions, particularly in sonographically indeterminate lesions, aiding gynaecologists in timely management and referral of these patients.

Key Words: *Adnexal, Malignancy, MRI, Risk, Stratification.*

Introduction

Pelvic adnexal masses are a common gynaecological finding. However, they are also a diagnostic and management dilemma. Usually, adnexal masses present incidentally or during a physical examination.[1] However females may present with gynaecological symptoms like irregular or post-menopausal per vaginal bleeding, palpable masses or feeling of lower abdominal heaviness/ pain. At times, these masses may present in asymptomatic women, discovered incidentally on ultrasound done for other reasons. Initial categorisation of these is done by ultrasound which may prove diagnostic; in borderline findings however, decision has to be made on magnetic resonance imaging (MRI).

Pelvic adnexal masses form a large proportion of referrals to Radiology department in women of all ages. Ultrasound is a safe, hazard-free, and sufficiently reliable first investigation for gynaecological assessment of pelvic lesions.[2] In cases however, which lack definitive sonographic benign and malignant features, further investigation becomes mandatory for optimal management. American College of Radiologists (ACR) approved Ovarian and Adnexal Reporting and Data System (O-RADS) was devised for MRI assessment of adnexal masses for risk stratification.[2] MRI with its unique ability to identify the nature of lesion contents - in particular haemorrhage- enhancement pattern, and ancillary findings can provide characterization of

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these lesions with considerable accuracy. A sensitivity of 85% has been reported for detecting malignant masses on MRI, even without the use of O-RADS.[3] It is imperative to draw a line between benign and malignant etiology in adnexal masses for appropriate management; however, ultrasound and even serological tumor markers at times are inadequate to characterize these lesions reliably.[1] To avoid misdiagnosis MRI O-RADS provides a considerably accurate identification of malignant features with sensitivity and specificity reaching up to 91% in some studies.[3] The assignment of a scoring system for evaluation of an adnexal lesion has optimised the management in females with adnexal/ovarian lesions, leading to timely referral to oncologists in suspected malignancy and avoidance of unnecessary surgeries in benign masses.[4]

The presence of solid tissue within adnexal lesions and its enhancement is one of the most important determinants of malignancy, hence MRI remains the gold standard for imaging of borderline sonographic lesions. MRI O-RADS considers the presence or absence of locules, septae, papillary projections, evaluation of internal components, and their enhancement characteristics. Papillary projections are defined as solid protuberance from the wall or septae of the lesion with a branching configuration.[3] MR pelvis with dynamic contrast enhancement (DCE) is preferred for O-RADS, however in its absence, contrast uptake at 40 seconds relative to uterine myometrium is documented.[5] In fact, in ACR recommendation even the visual assessment of contrast uptake in a routine contrast enhanced pelvic MRI is approved.[6] This study aimed to evaluate adnexal lesions on MRI O-RADS for their characterization by application of a uniform system of reporting without any ambiguity, keeping the radiologists and gynaecologists on the same page; this would also in turn allow facilitation of speedy oncological referrals for patients with high MRI O-RADS grade.

Materials and Methods

Design of this study was cross sectional observational; it was conducted on 26 adult females suspected of having an adnexal mass and referred to Radiology department of CMH Abbottabad for MRI pelvis over a period of 12 months from September 2021 to August 2022. Non-probability consecutive sampling technique was used. Prior approval was taken from the Institutional Review Board (IRB) of the hospital No: CMHAtd/ETH-58-Radio-22, dated 31st August 2021. Inclusion criteria were age above 18 years, known adnexal lesion previously assessed by pelvic ultrasound, and normal renal function tests for administration of contrast. The exclusion criteria included females younger than 18 years, non-adnexal pelvic lesions, or patients whose diagnosis could not be followed up. MRI was performed on 1.5 Tesla GE machine and images were acquired in following sequences: T2-weighted, T1-weighted-with and without fat suppression, and T1-weighted after gadolinium injection with inclusion of diffusion-weighted functional sequence. The scans were interpreted by a senior Radiologist with experience of more than 15 years. Age, laterality, signal characteristics of lesion (soft tissue, fat, haemorrhage, calcification), papillary projection, septations, enhancement pattern and any ancillary findings such as omental deposits or ascites were recorded for each patient. Based on these findings, O-RADS was assigned to each lesion and findings were compared with sonographic results; follow up was done by serum tumor markers, surgery, or clinical outcome. Statistical Package for Social Sciences (SPSS v. 25.0) was used, and chi square was applied to compare the sonographic and MR O-RADS findings in keeping with the final diagnosis of the patient. In cases where the expected frequency of at least one cell was less than five, Fisher's exact test was applied. A *p* value of less than 0.05 with confidence interval (CI) of 95% was statistically significant.

Results

Age of the female patients recruited in this study ranged from 21-70 years with mean of 36.9 $\pm$ 11.1 years. Maximum referral (61.5%; n=16/26) was for the age group between 26-40 years; in this age group predominant O-RADS category fell between 2/3, while all malignant lesions (O-RADS 5) except for one occurred in ages more than 40 - Figure 1. Most of the pelvic lesions were unilateral in 57.7% patients (n=15/26); while maximum belonged to O-RADS category 3 (likely benign with very low probability of malignancy) in 69.2% (n=18/26) – Figure 2 (a/b). Malignant lesions (O-RADS 5) were detected in four patients; diagnosis in these patients was aided by

serum tumor markers/ follow up. Final diagnosis of these lesions among the patients on both ultrasound and MRI O-RADS is depicted in Figure 3. The discrepancy between sonographic grading of the lesions with MRI findings was found in lesions labelled as borderline/ suspicious for malignancy on ultrasound with MRI being definitive in comparison to ultrasound findings (p value *0.004). Benign findings and definitive malignant lesions on ultrasound were in keeping with MRI (confirmed through laboratory findings, treatment response or surgery). All lesions demonstrating haemorrhage on ultrasound were found to be O-RADS 2/3 on MRI (benign). Out of 11 complex lesions on ultrasound, only 2 (18.2%) turned out to be malignant (O-RADS 5) while rest were endometriomas/ hemorrhagic cysts (O-RADS 3)- with varying stages of bleed (9 out of 11 at 81.8%) In lesions having definite sonographic malignant components together with ancillary findings of ascites, omental thickening etc (2/23), MRI was confirmatory.

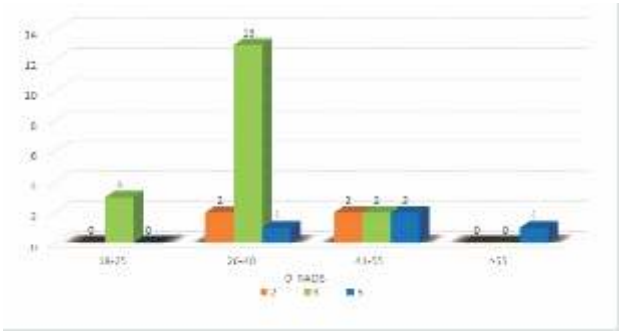
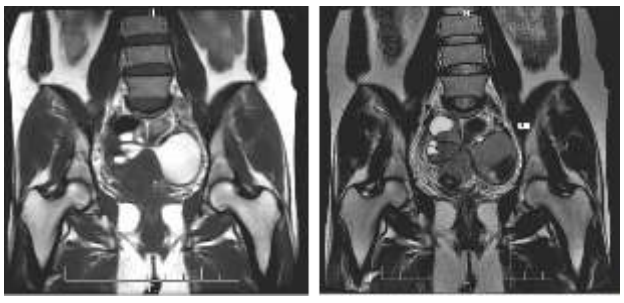


Figure 1: **Distribution of O-RADS within Age Groups- Predominantly Benign Lesions (O-RADS 2/3) Identified in Younger Age Group; Malignant Lesions (O-RADS 5) in Patients >40 yrs**



(a) **(b)**

Figure 2: (a)- T1 W Coronal Image of a 35-Year-Old Female Demonstrating High Signal in Adnexal Masses Representing Bilateral Endometrial Cysts; (b)- Corresponding Coronal T2W Images in the Same Patient Representing Varying Degrees of Haemorrhage.

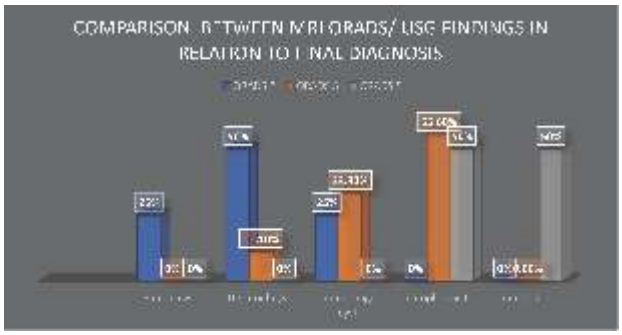


Figure 3: Final Diagnosis in Comparison to MRI O-RADS and USG Findings (% frequency)

Discussion

MRI O-RADS for pelvic masses has enabled the accurate characterization of lesions, particularly those which are found to be ambiguous on sonographic assessment resulting in timely referral and management of the patients. Although laboratory investigations such as serum tumor markers (CA-125) form part of the diagnostic protocol, there are a several shortcomings associated with these. In premenopausal women CA-125 can be raised in benign conditions such as endometriosis.[7] Moreover, it is raised only in 50% of cases in Stage I ovarian tumors hence is unreliable in initial diagnostic workup. Additionally, it is more commonly associated with serous than mucinous tumors.[8] These factors limit the diagnostic capability of this tumor marker. In post-menopausal women however, raised CA-125 is indicative of a malignant lesion and also used as a suitable marker for determining therapeutic efficacy post treatment.[9] MRI remains the gold standard for ascertaining the origin of pelvic lesions and for differentiation of benign from malignant etiology in sonographically indeterminate masses. In some studies, the incidence of indeterminate lesions has been found to be lowered from 18-31% on ultrasound to 10.8-12.5% on MR.[10] CT forms an important diagnostic tool in staging of the ovarian carcinoma and for assessment of associated abdominal complications.[11] PET CT is the gold standard for detecting recurrence of ovarian tumors post treatment however has no role in its initial management.[12]

Contrast enhanced MRI pelvis technique for evaluation of adnexal lesions has been modified to acquire the post contrast images in multiphase

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dynamic sequences for better characterization by plotting signal intensity curves,[13] however this is not widely available in all set ups. In our study, due to unavailability of dynamic enhancement technique, conventional contrast images were acquired. There are six risk score categories in the O-RADS MRI risk stratification system: O-RADS MRI 0 (incomplete examination), O-RADS MRI 1 (normal ovaries), O-RADS MRI 2 (almost certainly benign), O-RADS MRI 3 (low risk), O-RADS MRI 4 (intermediate risk), and O-RADS MRI 5 (high risk).[14]

Varwatte et al. compared ultrasound and MRI findings in adnexal lesions as a diagnostic tool; although no significant difference in accuracy was found between the two methods, the extent and epicentre were better determined using MRI.[15] This conformed to our study as well where no significant difference in accuracy was appreciated between USG and MRI pelvic findings.

Among benign lesions, endometriomas versus hemorrhagic cysts have been a diagnostic dilemma on ultrasound. 'T2 shading sign' previously thought to be specific for endometriomas has been assigned less diagnostic, as evidenced by a study by Lupean et al (68–93% sensitivity, 45–93% specificity).[16] In our study, 'T2 shading sign' was not reliable in differentiation of hemorrhage containing cysts (endometriomas versus hemorrhagic cysts) based solely on this sign- conforming to the international studies. The most important application of MRI O-RADS remained in the borderline cases on ultrasound, which improved the characterisation of such lesions aiding in their management, whereas MRI was found to have more specificity in lesion characterisation. MRI O-RADS provided adequate characterization of the lesions in all malignant cases which were confirmed on serology/ surgery. All of the O-RADS 5 cases had solid enhancing component, thick enhancing septae and had ancillary findings including ascites and/or omental thickening.

The limitations of this study include the small number of subjects. Also, some of the patients who were either lost to follow-up or whose definitive diagnosis could not be confirmed had to be excluded. Ultrasound O-RADS was not used in this study. A larger sample size and application of both MRI and USG O-RADS should be done in conjunction for better results.

Conclusion

Consistent application of MRI O-RADS in patients with adnexal lesions provides reliable and reproducible results in a standardized manner. MRI O-RADS is specifically important in characterizing sonographically indeterminate pelvic lesions to optimise patient referrals of malignant masses to oncologist and for prevention of unnecessary surgery and investigations in benign entities.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Difficult Laparoscopic Cholecystectomy and Its Conversion to Open Cholecystectomy Using Intra-Operative Scoring System

Syed Shams ud Din[1], Waleed Akbar[2], Inayat ullah Baig[3], Mirza Tassawar Hussain[4], Abdullah Sadiq[5], Talha Humayun[6], Tayyaba Ghulam[7], Aqsa Syed[8]

ABSTRACT

Objective: To determine the frequency of conversion of laparoscopic cholecystectomy to open cholecystectomy using proposed intra-operative scoring system and to check the validity of the scoring system.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: The study was conducted in the Department of Surgery, Federal Government Polyclinic Hospital (FGPC) Islamabad from 1st February 2019 to 31st July, 2019.

Materials and Methods: This study enrolled 197 patients of either gender with age ranging between 20-60 years planned for laparoscopic cholecystectomy (LC). All the recruits were assessed intraoperatively using proposed objective intraoperative scoring-system for difficult LC. The conversion rate of LC to open cholecystectomy was recorded in correlation with demographic data and co-morbidities. Data was entered and analyzed using SPSS version 25.0.

Results: Out of 197 enrolled patients, 64% were females. The mean age of study population was 42.7 ± 12.1 years. Forty six percent (46%) patients had co-morbidities with fifty-nine (n=59) being diagnosed as hypertensive and thirty-two (n=32) as diabetic. A total of 8.1% (n=16/197) patients underwent conversion to open cholecystectomy. The overall mean objective intra-operative score was 3.6 ± 1.73; which was significantly higher in patients who underwent conversion to open cholecystectomy compared to those who did not undergo conversion (7.19 ± 0.83 vs 3.28 ± 1.39; p-value = 0.001). Conversion rate was significantly more in the patients who were above 40 years, hypertensive, and diabetic. ($p<0.05$ in all cases).

Conclusion: The intra-operative scoring system can be used as a valuable predictor of difficult LC and conversion to open surgery to improve clinical outcome for the patients indicated for LC.

Key Words: *Cholelithiasis, Complications, Conversion to Open Surgery, Laparoscopic Cholecystectomy, Surgical Procedure.*

Introduction

Gallstone disease poses a widespread global concern, with an estimated prevalence of 10-15% worldwide.[1] Approximately 1-3% of the cases progress to acute calculus cholecystitis.[2] In Pakistan, gallstone disease extensiveness is no-exception with a reported prevalence of around 10.2%.[3] The way gall stone disease is managed has dramatically changed over time. One of the most frequent reasons for cholecystectomy is gallstone disease and laparoscopic cholecystectomy (LC) has gained the status of standard surgical intervention for symptomatic gallstone disease.[4,5] LC has significant advantage over traditional open cholecystectomy in terms of early and quick recovery, decreased postoperative pain, and a brief hospital stay.[6] The conversion of a LC, however, may occasionally be necessary because of access or dissection issues.[7,8] LC conversion is nothing more than a straightforward and secure procedure to prevent pointless difficulties and guarantee patient safety.[9]

In the early stages of laparoscopic technique development, a steep learning curve led to a notable occurrence of bile duct injuries and complications. Over time, the incidence of significant lesions decreased from 0.08% to 0.12%, accounting for 1.5% of all lesions. The challenges associated with cholecystectomy have been linked to these

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complications.[8] There are various preoperative grading methods that have been presented to predict difficult cholecystectomy to reduce complications associated with LC.[9] The authors pinpointed preoperative factors correlated with extended operative time and conversion rate, including gallbladder wall thickening, C-reactive protein levels, body temperature, age, BMI, history of previous abdominal surgery, and ultrasonographic findings.[8,10] The assessment of these factors may differ between the perception of a surgeon and another. Therefore, it is crucial to employ a unified intraoperative difficulty scale that describes the findings during the procedure. The chosen scale should be grounded in intraoperative observations to consistently define the complexity of LC, ensuring consistency regardless of the operating surgeon.[11] Considering the mentioned limitations in predicting challenging cholecystectomy through objective evaluation, Sugrue M *et al*., primed in conducting a study where they devised and validated a system based on intra-operative variables to anticipate the complexity of LC.[12] Ever-since then, several studies have been conducted in validating this intra-operative grading system and its outcome in predicting difficulty LC. Our research will contribute an additional milestone to validate the predictability of the proposed grading system which in turn will help in building local guidelines to further reduce the complication rate of LC and improve the patient healthcare outcome while improving cost effectiveness.

The aim of this study was to determine the reliability of the suggested intra-operative grading system and to forecast the conversion of LC to traditional open cholecystectomy.

Materials and Methods

A descriptive cross-sectional study was carried out at Department of Surgery, Federal Government Polyclinic Hospital (FGPC) for a period of 6 months from 1st February 2019 till 31st July 2019. The study was approved from the ethical and research review committee of Federal Government Polyclinic Hospital (Reg. No. 1/2017-E/C-64) on 4th June 2018. Before participating in the research study, informed written consents were obtained; anonymity and confidentiality were maintained throughout the study period. The study included patients with symptomatic gallstone disease between the ages of 20 and 60, of either gender, who were candidates for LC. Jaundice, malignancy, hepatitis B or C infected patients, LC with common bile duct (CBD) exploration, and pregnancy were the exclusion criteria. Using non-probability convenience sampling; a total of 197 patients meeting the selection criteria were recruited for the study (CI=95%, anticipated population proportion=6.7%, absolute precision=3.5%)[19]. Necessary pre-operative examinations and assessments were completed, and LC was performed using the traditional four port approach.

A structured questionnaire was used to capture pertinent medical history, including demographic information (such as age and gender), individual-level anthropometrical computations (such as weight, height, and BMI), and co-morbidities (such as hypertension and diabetes mellitus). Utilizing the proposed intraoperative grading method, all the patients who underwent LC were assessed. The gallbladder (GB) appearance and adhesions, gallbladder (GB) distention/contraction, access during the procedure, local or septic complications, and time needed to identify cystic duct and cystic artery are the five aspects that make up the operative grading system proposed by Sugrue M et al., described in Table I.[12] The interpretation of the grading scale is broken down into four categories: easy (scoring less than 2), moderate (score 2 to 4), very difficult (score 5-7), and extreme (score 8 to 10). Data was entered and analyzed with SPSS version 25.0. Age, body mass index, intraoperative scores, and other quantitative data were expressed by mean and standard deviation. Qualitative information including gender, age groups, the existence of diabetes and hypertension, conversion status, etc. was represented by frequency(n) and percentage. Using an independent t-test, the mean scores from the intraoperative grading system were compared between the conversion and non-conversion groups. The chi square test was used to compare the categorical variables between two groups. A p-value of 0.05 or lower was deemed significant.

Results

One hundred and ninety-seven patients who were scheduled for LC were enrolled in the current study. The study's participants' mean (SD) age was 42.7 ±

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12.1 years. Around 49% of the participants were above the age of 40 years. Also, a higher percentage of women (64%) were recruited for this study. Significantly, the study's enrolled individuals had higher body mass indices, with a mean ± SD of 30.1 ± 3.2 kg/m^2. Additionally, no comorbidity was recorded in more than half of the patients. Co-morbidities were detected in around 46% of individuals, with fifty-nine individuals (29.9%) being hypertensive and thirty-two individuals (16.2%) being diabetic as shown in Table II.

Sixteen (n=16) individuals (8.1%) of the total 197 participants in the research study underwent conversion to open surgery. The patient's age and co-morbidities (such as diabetes and hypertension) also made a substantial impact in whether the LC was later switched to open surgery. All the patients who underwent conversion to open surgery (n=16) were above the age of 40 years. Approximately twenty percent (n=12) of the total patients diagnosed with hypertension, and twenty eight percent (n=9) diagnosed with diabetes underwent conversion to open cholecystectomy. Table-III compares the intra-operative findings between recruits converted to open surgery with those who were not, using the new score system. The gall bladder's appearance was observed to differ significantly. In comparison to around 24.9% (n=45) of patients who were not converted to open, all 16 patients who underwent conversion; their gall bladders were buried due to adhesions (p-value=0.001). Additionally, a great percentage of participants had a distended or contracted gallbladder (100% Vs. 61.3%; p-value = 0.025), GB not been able to grasp (100% Vs. 53.6%; p-value = 0.009), had stones equal or larger than 1.00 cm in diameter lodged in Hartman's pouch (62.5% Vs. 23.2%; p-value = 0.027), had local complications (100% Vs. 24.3%; p-value < 0.001) and time needed for cystic duct and cystic artery identification greater than 90 minutes (75% Vs. 9.9%; p-value < 0.001).

Table-IV provides specifics on the intra-operative scores assigned to the participants recruited using the new scoring system in a categorical way. The new intra-operative scoring classification's overall mean ± SD was 3.6 ± 1.73. Ninety-five individuals (48.2%) of the total fell into the moderate group, with very difficult (25.9%), mild (19.8%), and extreme (6.1%) following. The intraoperative scores showed a significant difference in participants who underwent conversion having a mean ± SD score of 7.19 ± 0.83 as opposed to those who did not convert who had a mean ± SD score of 3.28 ± 1.39. Moreover, a significantly large percentage of participants in the extreme-category underwent conversion to open surgery (62.5% Vs. 1.1%; p-value = 0.001).

Discussion

As surgical technology progresses, there is a growing demand and expectation from patients and their families to consider LC in most cases.[13] In our research, we employed an intraoperative scoring or grading system, based on the work of Sugrue et al., to assess the level of difficulty in LC.[12] However, alternative intraoperative scoring or grading systems for evaluating the difficulty of LC, such as the one introduced by Vivek et al., also exist.[14] Interestingly, certain operative predictors in Vivek et al.'s system were found to be similar to those in our present study. In our research, we found that the conversion rate was 8.1%. All patients who experienced a conversion to open surgery were above the age of 40 years. Approximately 20% of individuals diagnosed with hypertension and 28% diagnosed with diabetes underwent a conversion from LC to open surgery. When compared to other studies, the conversion rate from laparoscopic to open cholecystectomy varied between 7% and 35%.[13,15,16]

In our study, the primary factor leading to the conversion is the presence of densely adherent tissues or challenges in distinguishing anatomy. Similar reasons for converting from laparoscopic to open cholecystectomy are identified in other studies as well.[9,17]

In our research, the intraoperative grading system employed to assess the difficulty of LC included an operative predictor i.e. distended gallbladder/ unable to grasp. All the cases which underwent conversion had distended gallbladders which were difficult to grasp with atraumatic laparoscopic forceps (*p-value= 0.025).* Other studies have also highlighted this predictor as a significant factor contributing to heightened difficulty during LC.[18,19]

Another important operative predictor which significantly increased the chance of conversion from laparoscopic to open cholecystectomy is the stone ≥1 cm impacted at Hartman's pouch.

Approximately 63% of the cases with stone ≥1 cm impacted at Hartman's pouch were converted to open cholecystectomy (*p-value=0.027)*. Our results are consistent with other studies which have reported similar significance of the individual predictor.[20,21]

Another understated operative factor for prediction of difficulty and conversion is the time required for identification of Calot's triangle. In our study, approximately 75% of the cases which required more than 90 minutes to laparoscopically identify the cystic artery and duct ended up being converted to open surgery *(p-value=0.001).* The results are consistent with other independent studies identifying the same predictor as significant.[22,23]

Existing literature indicates that the conversion rate to open surgery falls within the range of 1% to 13%.[24] In our study, the conversion rate was 8.1%, aligning quite closely with the figures reported in the available literature. Among the sixteen cases that underwent conversion to open cholecystectomy in our study, 62.5% were classified as 'extreme difficulty', while 37.5% fell into the category of 'very difficult' intraoperative grade. The mean intraoperative conversion score was 7.19 ± 0.83. Notably, none of the patients in the mild and moderate intraoperative grade experienced a conversion to open cholecystectomy. Thus, the conversion rate to open cholecystectomy was significantly higher in cases classified as difficult according to intraoperative grade compared to those categorized as easy.

Conclusion

The intra-operative scoring system can be used as a valuable predictor of difficult LC and conversion to open surgery to improve clinical outcome for the patients indicated for laparoscopic cholecystectomy.

Limitations and Future Prospects:

Firstly, the percentage adhesion of gall bladder was subjectively assessed. Secondly, the study had limited sample size of only one hundred and ninety-seven patients being recruited from a single study site. Considering the smaller sample binary logistic regression with outcome as conversion to open (yes/no) was not performed. The results of the binary logistic regression would have provided valuable clinical information of independent role of each of the risk factors. Thus, in future multicenter study with adequate sample size should be conducted to identify the validity and predictive capability of intra-operative scoring system for conversion to open surgery.

Table I: Intra-Operative Scoring System for Laparoscopic Cholecystectomy

Operative Grading System	Score
Gallbladder appearance No Adhesions	0
Adhesions < 50% of GB	1
Adhesions burying GB	3
Maximum	3
Distension/Contraction Distended Gall bladder or	1
Contracted shrivelled GB Unable to grasp with atraumatic	1
laparoscopic forceps Stone ≥1 cm impacted in Hartman's Pouch	1
Access BMI >30	1
Adhesions previous surgery limiting access	1
Severe Sepsis/Complications Bile or Pus outside GB	1
Time to identify cystic artery	1
and duct >90 minutes Total Maximum	10

Table II: Demographic and other Parameters of the Study Individuals

Parameters	n (%) or Mean ± SD
Age (years)	42.7 ± 12.1
Age Categories ≤ 40 years	100 (50.8%)
> 40 years	97 (49.2%)
Gender Male	71 (36.0%)
Female	126 (64.0%)
Body Mass Index (Kg/m2)	30.1 ± 3.2
Co-morbidities No	106 (53.8)
Hypertension	59 (29.9)
Diabetes	32 (16.2)

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Table III: Comparison of Intraoperative Parameters Among Conversion and Non-Conversion Individuals

Intra Operative Parameters	Converted	Not Converted	Total	*p-value
	(n = 16)	(n = 181)	(n = 197)	
Gallbladder appearance No Adhesions	0 (0)	78 (43.1)	78 (39.6)	0.001
Adhesions < 50% of GB	0 (0)	58 (32.0)	58 (29.4)	
Adhesions burying GB	16 (100)	45 (24.9)	61 (31.0)	
Distension/Contraction **Distended/ Contracted GB** Yes	16 (100)	111 (61.3)	127 (64.5)	0.025
No	0 (0)	70 (38.7)	70 (35.5)	
Unable to Grasp Yes	16 (100)	97 (53.6)	113 (57.4)	0.009
No	0 (0)	84 (46.4)	84 (42.6)	
Stone ≥1 cm impacted in Hartman's Pouch Yes	10 (62.5)	42 (23.2)	52 (26.4)	0.027
No	6 (37.5)	139 (76.8)	145 (73.6)	
Access BMI >30 Yes	6 (37.5)	42 (23.2)	48 (24.4)	0.297
No	10 (62.5)	139 (76.8)	149 (75.6)	
Adhesions previous Surgery Yes	4 (25)	35 (19.3)	39 (19.8)	0.502
No	12 (75)	146 (80.7)	158 (80.2)	
Severe Sepsis/Complications **Bile or Pus outside GB** Yes	16 (100)	44 (24.3)	60 (30.5)	0.001
No	0 (0)	137 (75.7)	137 (69.5)	
Time to identify cystic artery and duct >90 minutes. Yes	12 (75)	18 (9.9)	30 (15.2)	0.001
No	4 (25)	163 (90.1)	167 (84.8)	

p ≤ 0.05 was considered statistically significant.

Table-IV: Comparison of Categories Based on Intra-Operative Parameters

Intra Operative Scores/ Categories	Converted	Not Converted	Total	*p-value
	(n = 16)	(n = 181)	(n = 197)	
Scores	7.19 ± 0.83	3.28 ± 1.39	3.6 ± 1.73	0.001
Categories Less than 2 (Mild)	0 (0)	39 (21.5)	39 (19.8)	0.001
2 – 4 (Moderate)	0 (0)	95 (52.5)	95 (48.2)	0.001
5 – 7 (Very difficult)	6 (37.5)	45 (24.9)	51 (25.9)	0.001
8 – 10 (Extreme)	10 (62.5)	2 (1.1)	12 (6.1)	0.001

p ≤ 0.05 was considered statistically significant.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

The Effect of Energy Drink on Histomorphological Changes in Skeletal Muscles of Wistar Albino Rats

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ABSTRACT

Objective: To observe the histomorphological alterations induced by consumption of energy drinks on skeletal muscles of Albino rats.

Study Design: An experimental study.

Place and Duration of Study: The study was conducted by the Department of Anatomy in collaboration with the animal house of Liaquat national hospital and medical college (LNH&MC), Karachi from November 2nd to December 1st 2020.

Materials and Methods: For the study, 30 adult male Wistar Albino rats weighing between 140 and 200 grammes were allocated evenly into 3 groups. Group A served as control, kept on a regular laboratory diet. Group B served as a low dose treated group receiving energy drink at a dose of 7.5ml/day while group C received a high dose of drink i-e 15ml/day via gastric tube. All the animals were sacrificed following completion of the experimental period and were subjected to microscopic examination for histo-morphological study. Data was analyzed by using SPSS version 25.

Results: The Hematoxylin and Eosin (H&E) stained sections revealed significant structural and parenchymal damage in skeletal muscle tissue. The regular parallel arrangement of skeletal muscle fibers was lost with the disappearance of nuclei. Dilated and congested blood vessels were observed in the treated tissues. Infiltration of mononuclear cells was also observed suggesting the inflammatory changes in the tissues of animals treated with caffeinated beverages in the present study.

Conclusion: The consumption of energy drinks produces a significant histo-morphological alteration in the skeletal muscles of Wistar Albino rats.

Key Words: *Congested Blood Vessels, Energy Drink, Loss of Nuclei, Mononuclear Cells, Skeletal Muscles.*

Introduction

Energy drinks (ED) are caffeinated beverages, consumed widely by athletes and sports-persons especially of younger age groups.[1] The basic purpose of their utilization is to gain instant energy for enhancing physical activity and cognitive performance. Other than caffeine, ED also contains taurine, ginko biloba, multivitamins, and a high content of glucose.[2] These beverages were first introduced in the market in the era of 1960 but a rapid boom in their production and consumption was seen in 1987 when they launched widely in Europe.[3]

The caffeinated beverages are marketed especially to attract the younger age groups.[4] They consume it to increase the attention span, augment the muscle strength, and as a source of mental stimulant .[5] With regular usage, the individual usually develops some degree of tolerance and needs to consume it at an even further higher quantity to acquire the desired effects. Similarly, its abrupt withdrawal leads to features like irritability, headaches, nervousness, and drowsiness.[6]

Caffeine is one of the major components of energy drinks. About 80 mg of caffeine is present in a 250 ml volume of energy drink.[7] Caffeine has got effects on many organ systems of the body. It has a stimulating effect on the nervous system, increases gastrointestinal motility, produces diuresis, and causes tachycardia with palpitation. Moreover, high content of sugar in it can cause obesity and increases

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the chances of type -2 diabetes if consumed excessively and for a longer period.[8] Literature has revealed that the use of ED prolongs the period of skeletal muscle contraction, increases endurance performance, and thus delays process of fatigability.[9] The musculoskeletal system is one of the major organ systems of the body, composed up of a bony framework with skeletal muscle attached to it.[10] The stimulant effect of caffeine has been shown to affect the voluntary skeletal tissues of the body. It increases the endurance while performing a physical activity by reducing the perceiving effect. This leads to sustained performance which can contribute to muscle fatigue and cramps.[11]

The risks of heavy consumption of ED among young individuals and especially athletes to improve their performance in various capacities have become a serious concern nowadays that can lead to significant health problems in the future. Still the damage to skeletal muscles at microscopic level caused by caffeinated beverages is yet to be discovered. The present study was therefore aimed to identify the histomorphological alterations induced by the intake of ED in the Wistar albino rats.

Materials and Methods

This laboratory-based experimental study was conducted in the department of Anatomy in alliance with the animal house of Liaquat National Hospital and Medical College (LNH&MC), Karachi from November 2nd to December 1st'2020. The ethical approval for the required experimentation was sought from the ethical committee of LNH&MC (App # 0529-2020-LNH-ERC).

In the current investigation, 30 mature male Wistar Albino rats weighing between 140 and 200 gramms were used. The institution's policies were followed while handling the animals. They were kept under close watch for a week prior to the commencement of the trial to gauge their health. They were given a laboratory animal diet and unlimited access to water ad libitum. General conditions and behavior of rats were noted throughout the study. The study utilised a popular energy drink that is sold in 250 ml cans in Pakistan. It was bought from a local supermarket of Karachi, Pakistan. A single serving of drink contained about 80mg of caffeine, 37g of sugar and 1000mg of Taurine, in addition to other constituents. The drink was administered orally via 22-guage plastic-made flexible feeding tube in addition to the normal feed of the animals.The rats were divided into three groups each having ten animals. Group A served as control group (CG). Group B served as Low-dose treated group (LDTG), received 7.5ml of ED[12], while group C served as High-dose treated group (HDTG), received 15 ml ED[12], which is the maximum tolerable dose for the experimental animals as mentioned in the literature[13] administered daily for four weeks.

All the animals were anesthetized and later dissected following the completion of the experimental period. The bodyweight of rats was measured before the start and at the end of the study by using the OHAUS pioneer model# PA214 (made in the USA). The process of dissection and sample collection was done in the dissection hall, Anatomy department, LNH&MC.

To see the effect of ED on the histo-morphological changes in skeletal muscles, the Achilles' tendons including the whole muscle belly were used in the current study. They were carefully dissected out bilaterally from lower limbs, rinsed with normal saline, and fixed in10% buffered formalin, and further processed to get paraffin blocks. Tissue sections of 4µm thickness were sliced with a microtome and stained with H& E to observe the morphology and cytoarchitecture of the muscle tissue. Each slide was observed under the light microscope (Olympus model # CX21FS1) at 100X and 400X magnifications at four non-overlapping randomly selected fields. All histopathological (HP) changes were analyzed by detailed microscopic examination which was graded as none, mild, moderate and severe. Based on the findings, if HP changes were noted in one field, they were labeled as mild, in two fields as moderate, and three or four fields as severe.[12]

Data were analyzed by using SPSS version 25. Paired T test was used to assess the comparison of initial and final body weight in different study groups. Fischer's exact T-test was applied to observe the comparison of histopathological changes within study groups P-value equal to or less than 0.05 was considered as statistically significant for all the variables of the current study. The statistical significance of microscopic observations of the data related to microscopic observations (HP chages in skeletal muscle) was sought by applying the Chi-

square test. Results were displayed in frequency tables.

Results

The results of the present study revealed that the mean value of the initial body weight control group was 168.75±8.53 while the mean value of final body weight was 173.50±4.93. There was no significant gain in body weight of the control group was recorded (P–value=0.095). The mean value of the initial body weight of low dose treated rats was found to be 161.50±10.85 while the final body weight's mean value was decreased to 152±11.05. Therefore the reduction in the bodyweight of rats was observed in low dose energy drink animals (p-value 0.001). This trend was also observed in the high dose treated group where the initial body weight's mean value was found to be 185.38±12.46 while the final body weight's mean value was 172.00±13.51 (p-value 0.012) (Table-I).

An in-depth qualitative analysis was performed on 4µm sections stained with Hematoxylin and Eosin (H&E) to look for the following pathological changes: vascular congestion, skeletal muscle disarray, and mononuclear infiltration. The tissues were graded as none, mild , moderate and severe on the basis of severity of the above mentioned histopathological parameters.

The longitudinal section of the control group showed the regular pattern of skeletal muscle fibers arranged in parallel bundles with peripherally arranged nuclei separated by perimyseal connective tissue. Small blood vessels and capillaries were present in connective tissue lining surrounding muscle fibers with no sign of engorgement (Figure-1). However, in low dose treated animals moderate (60%) degree of vascular congestion was observed with dilatation and engorgement of the vessels. Moderate (20%) to severe (40%) congestion was observed in high-dose treated animals with some sections demonstrating Rouleaux formation and few diffusely present hemosiderin-laden histiocytes in perimysial connective tissue (Table-II, Figure-2).

It was determined by data in our study, a generalized feature of skeletal muscle fiber disarray was observed in most of the slides of low and high-dose treated animals however no skeletal muscle disarray was observed in any animal of the control group. Mild disarray was observed in the low dose treated group (40%) while half (50%) of the total number of high dose treated animals displayed severe loss of regular alignment of muscle fibers (Figure-3) . Splitting of the muscle fibers was also observed which appeared as a separation in the individual muscle fiber giving a patchy distribution. The nuclei were also completely absent at some fields of the microscopic sections (Figure-2). Mono-nuclear cell infiltration was also observed in both low and high-dose treated animals. None of the animals in the control group exhibited any inflammatory infiltrate while the moderate influx of inflammatory cells was revealed in 40% of the low dose treated group. The animals treated with a high dose of caffeinated beverages showed moderate (40%) to severe (20%) invasion of mononuclear cells predominantly lymphocytes (Table-II).

Table I: Comparison of Initial and Final Body Weight in Different Study Groups

	Initial body weight	Final body weight	P-value
Group A (control)	168.75±8.53	173.50±4.93	0.095**
Group B (LDTG)	161.50±10.85	152±11.05	<0.001*
Group C (HDTG)	185.38±12.46	172.00±13.51	0.012*

Paired t-test is applied.
*Significant at p-value ≤0.05
**Insignificant at p-value >0.05

Table II: Comparison of Histopathological Changes within Study Groups (A, B And C)

Histo-pathological Changes	Group A	Group B (LDTG)	Group C (HDTG)	P-value
Vascular Congestion				0.031*
None	10(100%)	2(20%)	1(10%)	
Mild	0(0%)	2(20%)	1(10%)	
Moderate	0(0%)	6(60%)	2(20%)	
Severe	0(0%)	0(0%)	4(40%)	
Skeletal Muscle Disarray				0.002*
None	10(100%)	4(40%)	0(0%)	
Mild	0(0%)	4(40%)	2(20%)	
Moderate	0(0%)	2(20%)	3(30%)	
Severe	0(0%)	0(0%)	5(50%)	
Mono nuclear infiltration				0.152**
None	10(100)	3(30%)	0(0%)	
Mild	0(0%)	3(30%)	4(40%)	
Moderate	0(0%)	4(40%)	4(40%)	
Severe	0(0%)	0(0%)	2(20%)	

Fisher Exact t-test is applied.
*Significant at p-value ≤0.05
**Insignificant at p-value >0.05

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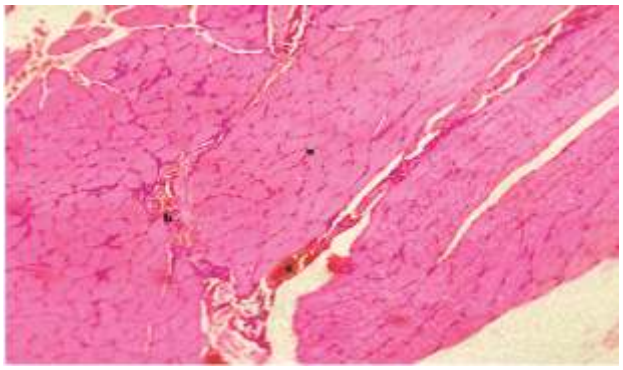

Figure 1: Group A (CG) at100x magnification a:in this H&E-stained, transverse (left field) and longitudinal (right field) sections of the skeletal muscle, numerous muscle fibers in the form of fascicles are seen in which dark stained basophilic nuclei are found to be peripherally arranged.b:the perimysium (loose connective tissue surrounding the bundles of muscle fibers) is also visible at this magnification.c:small capillaries are running in-between the muscle fibers.

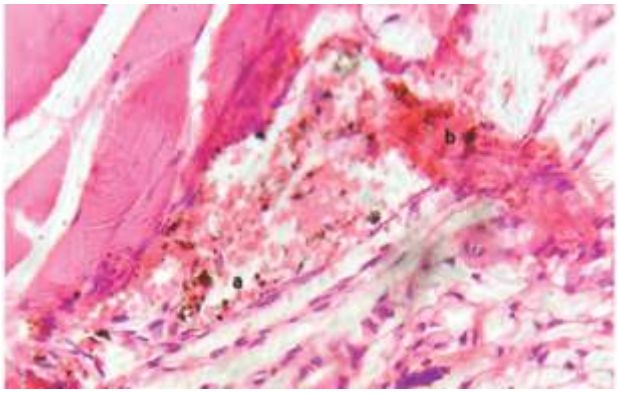

Figure 2: In Group C (HDTG) at 400 X magnification *a.* In this H&E stained-tissue, hemosiderin laden histiocytes with inflammatory infiltrates are seen *b.* an engorged and dilated blood vessel can also be be seen (left field)

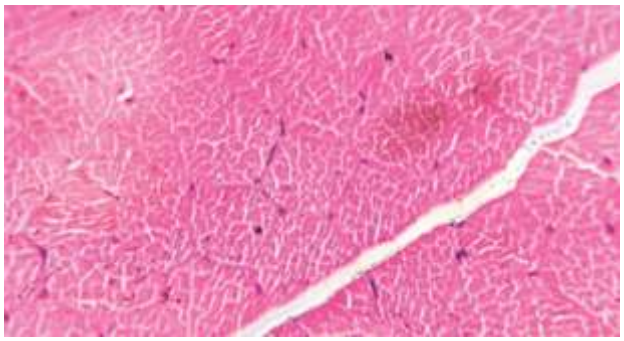

Figure 3: In Group B (LDTG) at 100 X magnification a. In this H&E stained-tissue section, muscle fiber disarray is noted. b: A loss of orientation and splitting in the regular parallel arrangement of skeletal muscle fibers were also observed. The fibers had a patchy distribution with the loss of cross-striations and peripheral nuclei.

Discussion

The present study was aimed to investigate the histo-morphological changes induced by energy drink consumption of Wistar Albino rats. Both heads of gastrocnemius along with soleus were identified and dissected from their point of origin till the insertion of the Achilles' tendon and were observed under the light microscope after processing of tissue.

A report titled “additional information on energy drink published by European Scientific Committee on food” in 2003[14] described the substantial reduction in body weight of experimental mice when they treat with energy drink (Red bull) to evaluate the oral toxicity of the drink. These findings are in agreement with the present study where a significant reduction in body weight was also observed in energy drink-treated animals. This outcome can be explained based on poor generalized well-being of the animals, impaired glucose tolerance, and thermogenic effect of caffeine.[15]

Skeletal muscle is a vital tissue needed for the maintenance of physical independence and quality of life across the lifespan. The preservation of normal cytoarchitecture of skeletal muscles is vital as its loss can contribute to the loss of functional capacity of an individual.[16]

At present, the consumption of caffeinated beverages among youngsters is increasing to boost up their stamina and attain vitality. Long-term consumption of energy drinks significantly decreases the fat content in the skeletal muscles stored in the form of triacylglycerols leading to a decrease in strength, metabolic rate, and aerobic capacity and thus, in functional capacity[17], which may affect the young generation producing musculoskeletal disorders at an early age.

The microscopic observations in the present study were found to be more remarkable in animals treated with higher doses of caffeinated beverages as compared to low dose treated groups. Skeletal muscle disarray, mononuclear infiltration, and vasodilatation were served as a part of the examination. A loss of orientation and splitting in the regular parallel arrangement of skeletal muscle fibers were observed. The fibers had a patchy distribution with the loss of cross-striations and peripheral nuclei. These findings were concomitant

with the observations made by Alotaibi et al[18], who treated the skeletal muscles of rats with varying doses of caffeine and nicotine and found structural damage in the treated tissues as loss of striations, absence of nuclei with degenerative changes. These alterations could be a result of an adaptive response of the affected tissue due to a lack of oxygen and nutrient supply in response to inflammation.

Oxidative stress is a major attributing factor in producing the signs of inflammation. The generation of reactive oxygen species (ROS) induces a pro-oxidant environment which results in cellular dysfunction and tissue injury.[19] Scientific data has proved that consuming energy drinks leads to the generation of ROS in the body and thus results in pathological events.[20] Damage to the muscle tissue leads to leakage of inflammatory mediators in the parenchyma of tissue. The current study also revealed the presence of mononuclear infiltrates predominantly lymphocytes scattered in myofibrils of the treated tissues demonstrating the inflammatory changes.

Hyperemia is one of the earliest features of inflammation characterized by vasodilatation and congestion of vessels.[21] This outcome was also observed in the present study where a dose-dependent increase in the vascular congestion. These results are in agreement with the study conducted by Abd-El-Halim et al[22] when they observed the effect of acrylamide on tongue musculature of Albino rats and observed congested blood vessels with the fragmentation of myofibers. These findings can be an attribute of an inflammatory rection resulting in collagen deposition and vascular re-epithelialization.

Based on the findings of the present work, it can be stated that exposure to caffeinated beverages can lead to damage to skeletal muscle tissues, therefore its intake needs to be regulated. The present study was one of its kind in the fact that very limited work has yet been done on the effect of caffeinated drinks on skeletal muscles. Large scale studies should be planned in future in order to devise precautionary strategies against the harmful effects of these drinks.

Conclusion

In conclusion, data of the present study indicated the significant histo-morphological alterations were present on the microscopic examination of skeletal muscle tissue as a result of consuming the energy drinks. Caffeine was the most blamed element and aided by other ingredients of the drinks having a stimulating effect.

Future Recommendations

Further researches on a larger scale using different muscular tissues of the body should be encouraged to make a comparative analysis. Investigations regarding the optimal dosage of consumption of these beverages as well as the reversibility of the effects would also be essentially addressed on a large scale study in future.

Conflict of Interest

No conflict of interest has been declared by any author in the current study.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

GRANT SUPPORT AND FINANCIAL DISCLOSURE

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

To Determine the Relationship of Neutrophil/Lymphocyte Ratio (NLR) and Platelet/Lymphocyte Ratio (PLR) as Inflammatory Markers with Manic Episode of Bipolar Disorder Type I

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ABSTRACT

Objective: To investigate neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) as inflammatory markers in bipolar disorder type I patients with 1st episode and recurrent mania.

Study Design: An observational, cross-sectional study.

Place and Duration of Study: The study was conducted in HBS General Hospital, the tertiary care teaching hospital of HBS Medical & dental College, a private medical college located in Islamabad. The duration of study was from 01/11/2022 to 30/04/2023 for a period of 6 months.

Materials and Methods: Forty cases were recruited by consecutive sampling, comprising of 20 1st episode mania and 20 recurrent mania and these were compared to 20 healthy controls (HC). In the patients Young Mania Rating Scale was used to assess the severity of mania. Samples for blood counts were obtained from all the participants in the morning hours.

Results: Compared to HC, both 1st episode and recurrent mania patients had significantly higher neutrophil and NLR values, and lower lymphocyte counts. When the two patient groups were compared, first episode mania cases had significantly higher neutrophil counts and NLR than patients with recurrent mania.

Conclusion: The findings of the study showed a likely inflammatory pathophysiology in the manic phase of BD. Since 1st episode, drug naive mania patients had greater inflammation as compared to recurrent mania cases, it was conceivable that psychotropic medicines exerted an anti-inflammatory effect in the latter group.

Key Words: *Bipolar Disorder, First Episode Mania, Neutrophil/Lymphocyte Ratio, Platelet/Lymphocyte Ratio, Recurrent Mania.*

Introduction

Bipolar disorder (BD), a severe and common mood disorder effects about 4% of the population globally.[1] The current classification, as envisaged in DSM-5 and ICD-11 is a spectrum condition including bipolar disorder type I (at least 1 manic episode), bipolar disorder type II (recurrent major depressive episodes [MDE] plus at least 1 hypomanic episode), cyclothymic disorder (recurrent hypomanic episodes plus depressive episodes which do not meet criteria for MDE), and bipolar disorder not otherwise specified.[2] Importantly, a cumulative amount of research incriminates inflammatory mechanisms in the pathophysiology of BD.[3] This is particularly robust with regards to manic episodes; these epitomize a severe psychological disturbance represented by elevated mood, pressure of speech, flight of ideas, over activity, grandiosity, impulsivity and psychosis.[4] In BD several original studies, meta-analyses and systematic reviews have documented increased levels of pro-inflammatory factors like cytokines, chemokines and C-reactive protein in acute episodes, particularly manic exacerbations.[5] More recently studies have looked at blood cell indices as tools to investigate inflammatory mechanisms in BD.[6]

Complete blood count is an easily done and inexpensive test and cell indices like neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) are readily obtainable biomarkers. NLR and PLR are innovative and potential indicators of inflammation used in the management of several intractable systemic diseases. In this regard, some examples include coronary artery disease, cerebrovascular disease, chronic renal failure,

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inflammatory joint diseases like rheumatoid arthritis and ankylosing spondylitis.[7] In BD systemic inflammation can be measured by serum cytokine levels, but this is very expensive and requires well-equipped laboratories. Previous research has demonstrated higher NLR and PLR in BD subjects suffering from manic episodes, pointing towards intensified inflammatory processes in these patients. An important study was conducted in patients with different diagnoses, including schizophrenia, bipolar mania, bipolar depression, and major depressive disorder. It was shown that among all diagnostic categories NLR was greatest in BD type I, current episode manic signifying that inflammatory mechanisms were most activated in this group of patients.[8] However, it is not known for sure whether elevated NLR in mania actually represents a neuroinflammatory diathesis, such that specific mechanisms need to be elucidated that can relate this blood cell index with brain inflammation. Moreover, there is paucity of literature in the local population regarding the investigation of inflammatory mechanisms in psychiatric disorders.

In the current scenario, while the significance of finding reliable and easily obtainable markers of bipolar disorder is overwhelming there is a dearth of studies in our setting. Laboratory tests based on examination of peripheral blood samples can fulfill this purpose with the caveat that the purported biological markers are relatively inexpensive and within the technological reach of most laboratories. Our study which investigates NLR and PLR in manic patients is an endeavor to fill the gap in the local literature, while it is also likely to shed further light on the issue of inflammatory activation in bipolar disorder.

With this background we aimed to investigate neutrophil/lymphocyte ratio and platelet/lymphocyte ratio as inflammatory markers in bipolar disorder type I patients with 1st episode and recurrent mania.

Materials and Methods

Our study had an observational and cross-sectional design and was done in the department of psychiatry of a tertiary care hospital of a private medical college in Islamabad from 01/11/2022 to 30/04/2023 for the duration of 6 months. The Ethical Review Board of the institution gave approval of the study vide letter number Appl # EC, 3rd Sep '22. Subjects enrolled in the study included those of either gender, age 18 years or older and accepting to participate with proper consent. For 1st episode mania group and HC exclusion criteria were as following:

i) Prior history of psychiatric and chronic medical conditions,
ii) Presence of chronic inflammatory or autoimmune diseases,
iii) Systemic infection,
iv) Substance abuse,
v) Obesity defined as BMI ≥ 30 kg/m2,
vi) Abnormal laboratory test such as anemia, leukopenia/leucocytosis, thrombocytosis, etc.

Exclusion criteria were similar for BD I patients having recurrent manic episodes, however it was understood that they had prior history of mood disorders. The sample size included 20 patients in each of the 3 groups comprising of 1st episode mania, recurrent mania and control group. Patients fulfilling eligibility criteria were enrolled by consecutive sampling until the required sample size was achieved.

In the patients Young Mania Rating Scale (YMRS) was employed to measure the severity of manic symptoms. For the measurement of complete blood count blood samples from the participants were collected in the morning hours using full aseptic techniques and sent to the laboratory in vacutainer tubes containing ethylene diamine tetra acetic acid as anticoagulant. The ratio NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count and PLR by dividing the absolute platelet count by the absolute lymphocyte count.

The IBM SPSS version 23.0 was used for the sake of statistical analysis of the data. To find association between categorical variables Chi-square test was used, while for data which was not normally distributed the Kruskal–Wallis test was employed. To determine the relationship of NLR and PLR with the severity of mania Spearman's correlation co-efficient analysis was utilized. For all tests the statistical significance was standardized as $P \leq 0.05$.

Results

Table I associates patients and HC with regards to demographic variables like age, BMI and gender distribution and shows that these are mostly

comparable. It also demonstrates that the severity of mania was generally the same in 1st episode mania and recurrent mania groups as revealed by the mean YMRS scores (Table I).

With respect to blood cell indices, Table II shows that 1st episode mania cases in comparison to control subjects had a significantly higher mean value of neutrophil count and NLR and a lower number of mean lymphocyte count. When the recurrent mania group was compared to HC, it was shown that total neutrophil count and mean value of NLR was statistically significantly higher in the patients with a significantly lower mean lymphocyte count (Table II).

Table II further demonstrates that as compared to recurrent mania, 1st episode mania patients had a significantly higher mean value of neutrophils and NLR, whereas there was no difference in the mean lymphocyte count between the two groups (Table II).

Lastly, it was shown that no significant difference existed among the study groups with respect to mean platelet count and PLR (Table II).

With regards to correlation between YMRS scores and NLR and PLR in 1st episode and recurrent mania groups, the results did not reach statistical significance.

Table I: Study Participants Group-Wise Characteristics

variable	1st episode mania N = 20	Recurrent mania N = 20	Healthy control N = 20
Age (mean±SD)	27.35±6.25	30.29±8.44	28.44±7.23
BMI (mean±SD) Kg/m^2	26.25±1.55	25.99±1.46	25.76±1.39
YMRS (mean±SD)	31.74±6.59	30.77±5.89	-
Male	12 (60%)	14 (70%)	10 (50%)
Female	8 (40%)	6 (30%)	10 50%)

BMI – Body Mass Index; SD – Standard Deviation; YMRS – Young Mania Rating Scale

Table II: Complete Blood Count (Absolute Numbers) And Ratios

Variable	1st episode mania N = 20 (Mean±SD)	Recurrent mania N = 20 (Mean±SD)	Healthy control N = 20 (Mean±SD)	*P*1	*P*2	*P*3
Neutrophils ($10^3/\mu l$)	6.29±1.26	5.11±1.67	3.04±0.59	<0.001	<0.001	<0.001
Lymphocytes ($10^3/\mu l$)	2.05±0.39	2.08±0.46	2.85±0.27	<0.001	<0.001	0.053
Platelets ($10^3/\mu l$)	198.32 ± 97.58	194.65 ± 70.12	203.54 ± 43.83	0.143	0.063	0.071
NLR	3.06±1.14	2.45±0.62	1.06±0.36	<0.001	<0.001	<0.001
PLR	96.58±42.63	93.26±30.89	71.22±18.99	0.127	0.385	0.096

*P*1 – 1st episode mania v/s HC; *P*2 – recurrent mania v/s HC; *P*3 – 1st episode mania v/s recurrent mania

Discussion

In the present study, compared to HC both index episode and recurrent mania groups showed a significantly greater number of neutrophils and NLR and lower lymphocyte counts. These facts link mania with sub-clinical inflammation and are in line with other published studies.[9] Overall, the findings of studies addressing the question of immune-inflammatory markers in bipolar disorder are unclear; nonetheless, mania reportedly has been associated with increased levels of proinflammatory cytokines, acute-phase reactant proteins and complement components.[10]

Innate immune responses are exemplified by neutrophils while lymphocytes mediate adaptive immunity, so that NLR can be an indicator of the balance between these two biological mechanisms. When challenged by injury or infection neutrophils

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serve as the first-line of defense in the body and initiate the protective response by secreting various cytokines, chemokines and other chemical mediators. Since lymphocytes are activated latter in the immune response, they have a regulatory function in directing bodily defenses. In this regard, absolute or relative lymphopenia may point towards increased biological vulnerability associated with poor physiologic functioning. Neutrophil to lymphocyte ratio is an incorporated variable of the two canonical immune pathways and exactly for this reason is more useful than either integer alone. Because of this value NLR may act as a potential biomarker for BD in the manic state.[11] In addition, as compared to single leukocyte parameters NLR is less influenced by such factors as physical exercise, dietary changes, autonomic arousal, etc. and remains useful in the presence of confounding variables.

In addition to NLR, in major psychiatric disorders an association between platelet parameters such as absolute platelet numbers, PLR and mean platelet volume is also documented. Platelets serve as initiators of the protective response as these have a specific function in the activation of neutrophils and macrophages along with the regulation of endothelial permeability. Therefore, PLR can be employed as a biomarker of inflammatory response in mood disorder patients. To extend this argument further, a meta-analysis demonstrated higher value of PLR in BD subjects as compared to controls.[12] Yet, in our study no significant difference in platelet count and PLR was revealed in the investigated groups. This finding is also in line with previous studies investigating the matter.[13]

Our study included drug naïve 1st episode mania subjects, ruling out an effect of psychotropic medications vis-à-vis the inflammatory status of the cases. Interestingly, a significant variance was seen between the patient groups with regards to blood cell indices as neutrophil counts and NLR were significantly higher in index mania versus recurrent mania groups, suggesting less severe inflammatory response in the latter. In this respect, it is worth stating that a recently published study had similar findings.[14] Since the recurrent mania group was on psychotropic medications, it could be surmised that these agents were exerting anti-inflammatory effect which was reflected in blood cell indices. To extend the argument further, animal and human studies are available suggesting an anti-inflammatory effect of various psychotropic medications.[15] Finally, in our study a significant association between NLR and PLR and the severity of mania (increased scores on YMRS) was not established which could be because of the presence of confounding variables like diet, exercise, smoking, etc.[16].

Limitations

i) The study had a cross-sectional design which did not permit for establishing a causative association between higher NLR values and BD.
ii) In conjunction with blood cell indices we did not evaluate other inflammatory indicators, most importantly peripheral pro-inflammatory cytokines.
iii) In the absence of other markers of inflammation it was not practicable to assess the significance of higher NLR values as a standalone marker of a pro-inflammatory state in bipolar disorder.

Conclusion

The present study suggested likely inflammatory mechanisms in the development of mania. Moreover, it showed greater value of inflammatory parameters in cases with index manic episodes as compared to BD subjects suffering from recurrent manic episodes. Since 1st episode mania patients were psychotropic drug naïve, our finding suggested that possibly these medications exerted an anti-inflammatory effect in cases with recurrent mania. Finally, it must be noted that NLR was an easily done and low-cost blood test, such that its utility as a biomarker in bipolar disorder called for further investigations.

Recommendations:

i) Future research having greater number of participants and prospective design is much needed to validate NLR and PLR as potential biomarkers of bipolar disorder.
ii) This research should preferably include multiple sites from different international locations.
iii) Blood cell indices should be combined with other biomarkers of inflammation to corroborate the diagnosis of bipolar mania.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Treatment Outcome of Kwashiorkor in Children as Per World Health Organization Guideline at Nutrition Stabilization Center Multan, Pakistan

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ABSTRACT

Objective: To assess the treatment outcomes and associated factors among children with kwashiorkor (Edematous Severe Acute Malnutrition) at Nutrition Rehabilitation Centre the Children Hospital and The Institute of Child Health, Multan.

Study Design: Retrospective Descriptive research.

Place and Duration of Study: This study was planned at the nutritional rehabilitation center of The Children Hospital and The Institute of Child Health, Multan from 01 January 2012 till 30 December 2020.

Materials and Methods: The record register of stabilization center was utilized to gather the required information for the study. Baseline statistics and medical signs and symptoms of kwashiorkor, complications and treatment outcome of children were recorded. Patients of age 1 month to 60 months with kwashiorkor (weight/height less than -3SD with edema) were included who were treated according to WHO guidelines for Severe Acute Malnutrition (SAM).

Results: during the year 2012-2020, a total of 2393 children were admitted with severe acute malnutrition out of which 222 (9.4%) were edematous SAM (Kwashiorkor). 222 kwashiorkor patients 25 (11.2%) were less than 6 months while 197(88.7%) were more than 6 months old. 120 (54%) were males and 102 (46%) were females. Out of total kwashiorkor patients, 40% presented with diarrhea, about 30% had pneumonia, hypoglycemia was recorded in 10% children, Urinary Tract Infection 15% and other diseases like celiac disease nephrotic syndrome and complication included the 5% of total. Almost 90% of patients recovered and got discharged and 8% passed away, only (2%) patients left against medical advice (LAMA).

Conclusions: Kwashiorkor is the second most prevalent form of severe acute malnutrition in south Punjab and usually difficult to diagnose due to masking effects of edema. Kwashiorkor can be successfully managed by using the WHO guidelines for sever acute malnutrition. WHO guidelines also show treated patients discharged mostly with a lower percentage of mortality and comorbidities.

Key Words: *Edema, Kwashiorkor, Protocols, Severe Acute Malnutrition, Treatment Outcome, World Health Organization Guidelines*

Introduction

Malnutrition is a significant universal issue and nearly 20 million children under five years of age ae facing this disastrous problem mainly in third world countries.[1,2] Malnutrition is also a major contributor in about half of pediatric mortalities in under five years of children. Malnutrition in children below 5years suffers the most from severe acute malnutrition as it hinders their growth, physical and mental development and decreases their IQ levels as well.[3,4]

According to National Nutrition Survey 2018, in Pakistan 28.9% of children are underweight, 17.7 % are wasted and while 40% are stunted.[5] Severe acute malnutrition and protein energy malnutrition works havoc on every physiological system of the human body. All the bodily systems start shutting down and slowing leading to reductive adaptation of all body functions.[6,7] In 1999, WHO established protocols for the treatment and handling of under five-year-old pediatric population suffering from SAM. For the meticulous treatment special therapeutic formulas and diets were designed with all the macro and micronutrients in the desired amount to facilitate the rehabilitation of SAM children. WHO protocols

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are roughly classified in a couple of stages, the initial stage of management is known as stabilization phase and the second phase of recovery and weight gain is kwon as the rehabilitation phase.[8,9]

Malnutrition is dominantly classified into marasmus, kwashiorkor, and marasmic kwashiorkor.[10,11] Kwashiorkor (Edematous malnutrition) is a severe form of childhood malnutrition defined by oedema. If advanced, there may be vomiting, diarrhea, anorexia, loss of muscle mass, growth, loose subcutaneous tissues, dermatitis, and increased susceptibility to infections, and edema which can mask the weight loss.[12] Eventually, there is stupor, coma, and death due to Infection, sepsis, electrolyte imbalances, and heart failure.[13,14]

The CH & ICH, Multan is providing health care facilities to the SAM children of South Punjab as well as Baluchistan as burden of SAM is high in these areas due to illiteracy, myths, food insecurity and recent natural disasters. There isn't much data available regarding treatment outcomes of kwashiorkor using WHO guidelines in hospital facilities and in outpatient departments as well. Our study research was carried out to figure out the occurrence, presentation and treatment outcomes of kwashiorkor using WHO guidelines for SAM among the children who were admitted and treated in Nutrition Rehabilitation Center of the CH & ICH, Multan by using WHO feeding protocols.[15,16]

Materials and Methods

Retrospective descriptive research was organized at Nutrition Rehabilitation Centre the Children Hospital and The Institute of Child Health, Multan from 1st January 2012 to 30th December 2020. The samples were children suffering from severe acute malnutrition as defined by WHO: “a very low weight for height (below -3 z scores1 of the median WHO growth standards), by visible severe wasting, or by the presence of nutritional oedema.”[3] Permission was taken from the IRB committee of the institute (reference #CHC200120). A questionnaire was designed by the lead investigator to collect the desired information and trained staff nurses of nutrition rehabilitation center collected the data. The required data was collected from record registers and files of nutrition rehabilitation center also known as the stabilization center. Main variables were age, gender, and treatment outcomes. The patients were treated as per protocols defined by the world health organization for SAM. The treatment of SAM patients is divided into two phases the initial phase is known as Management phase and the second phase is knows as Rehabilitation phase predominately characterized by reduction of oedema and weight gain in child with return of appetite. Therapeutic feeds F75 and F100 were given to patients during hospital stay. F-75 is a starter formula fed to children who cannot intake regular food, it contains 75 kcal/100 ml and 0.9g protein/100 ml and F- 100 is the 'catch-up' diet started after the child the child has been stabilized and enters rehabilitation phase. F-100 has 100kcal and 2.9g protein per 100 ml. Upon admission at nutrition rehabilitation center, 2hourly F75 feed was started, 100ml/kg/day.[7,8] The therapeutic feed intake of every patient was recorded on a 24-hour intake chart. F100 was added in transition phase. Throughout the recovery stage, also known as rehabilitation, phase the number of feeds were decreased to only six times/day and the quantity was increased up to 220ml/kg/day. The feeding pattern and amount consumed during each feed was written on the daily feeding chart. All the patients admitted to nutrition rehabilitation center were examined for anthropometry daily including weight, height and MUAC on WHO standardizes anthropometric equipment, and the appetite and general demeanor of patients was also noted. When all the food related complaints were resolved, appetite improved, the intravenous antibiotics were finished, , the child started gaining weight 10gm/kg/day and edema settled and caregiver of child was trained to feed and look after the child at home, to look out for danger signs, the child started smiling, the patients were discharged from the nutrition stabilization center. Treatment outcomes comprises of whether the child reached desirable weight/height (wt/ht) ratio i.e., less than -2SD or resolution of edema, discharged after treatment, discharged on request DOR, expired/death, left against medical advice LAMA. The data was analyzed statistically using SPSS version 20.0, Mean, medians and percentages were calculated accordingly.

Results

Overall, 222 children with kwashiorkor were included in the research (Fig1). Of the 222

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respondents 120 (54%) were males and 102 (46%) were females. 25 (11.2%) were less than 6 months while 197(88.7%) were more than 6 months (Table I). 70% were from rural areas while 90% of the total belonged to poor socio-economic status. Out of total kwashiorkor patient 40% were presented with diarrhea, 30 % children had pneumonia, (table II). Total of 198 (90%) children were discharged from ward after being treated and stabilized and 8% passed away due to complications, rest of 2% Left against medical advice (LAMA) and discharge on request. Only 5 patients developed refeeding syndrome while the majority 75% developed pneumonia, 50% diarrhea as complication.

Table I: Demographic Characteristics (n=222)

	Total	Percentages
Gender		
Male	120	54%
Female	102	45%
Residence:		
Urban	67	30%
Rural	155	70
Age:		
Age under 6 months	25	11%
Age more than 6 months	197	89%

Table II: Clinical Presentation at Time of Admission (n=222)

Illness	Total
Diarrhea	97 (44%)
Pneumonia	69 (31%)
Urinary tract infection	54 (24%)
Hypoglycemia	23 (10%)
Other complications (celiac disease, nephrotic syndrome)	11(5%)

Discussion

Current study assessed the presentation and treatment outcomes of kwashiorkor according to WHO guidelines at nutrition center Multan. In our study among all the children admitted during study period only (9.4%) were edematous SAM (Kwashiorkor) and among the kwashiorkor children majority were boys from rural areas with low socioeconomic level. This signifies the socio-economic indicators affecting the nutrition level of under children. Most of the patients were discharged after getting treated successfully. While a study reported (8.1%) cases of kwashiorkor.[17] Lack of proper knowledge regarding feeding and complimentary diets, and poor socio-economic status were major factors associated with kwashiorkor.

In this study the majority of patients were between 6 to 24 months. Among all , 11.2% were below six months of age while 88.7% were between 6-60 months, 54% were boys and 46% were girls contrasting to study where (64.3%) were females.[18,19] Similar results were shown by a study where majority of patients were between 13 to 60 months.[4] Among the results by different studies conducting in Pakistan on severe acute malnutrition, more boys are documented to be suffering from Severe acute malnutrition as compared to girls.[20,21] Which is contrasting to the social context and gender discrimination and cultural significance given to boys. In common households in Pakistan, boys are given preference over girls regarding everyday care, and well-balanced nutritious meals comprising of proteins and meat. Still more boys are documented with kwashiorkor and SAM than females. It can also be since girl child is not brought the hospitals for treatment, and they expire due to untreated SAM in homes. More in depth data regarding this gender disparity of Kwashiorkor children is required to make apt analysis.

In our study 90% of children were discharged after getting recovery and treated. 8% of patients expired due to complications, however another study showed 60% of children getting discharged and 10 % expiries .[15] The usual duration of admission in our study was 10-12 days with the weight gain of 10mg/kg/day with F-75 formula feed. Same numbers were also noted regarding limited hospital stay and low income by Aliyu et al but contrasting to a study in which avg stay was 24.5 days.[22,23] The need for shorter hospital stays has been reported by numerous studies and thus a new CMAM program was introduced to address this issue.

Sepsis and infections were significant risk issues in our study and comparable findings were noted by Aliyu et al.[24,25] The most common infections included 40% diarrhea/loose motions and 30% children had pneumonia 30%, hypoglycemia was present in 10%, UTI in 15% and other disease like celiac disease nephrotic syndrome and complication included the 5% of total. Major presenting symptoms were grading 3 edema 90.9%, followed by poor appetite

85.5%, fever 69.8%, diarrhea and dermatitis 67.5% each similar results were reported by study.[19] 52.2% developed eye signs with the majority having eye redness, 51.8% had hepatomegaly while 33.7% had hair changes.

The WHO guidelines for treatment for kwashiorkor are beneficial and prove to be effective. However, limited health facilities, less awareness, low socioeconomic status, and short hospital stay are major factors that hinder effective outcomes. Our study has limitations regarding time duration and limited resources. A major study on the national level including all nutritional rehabilitation centers following WHO protocols needs to be conducted to provide more accurate details about the application, implementation, and results of WHO Community management of acute malnutrition program.

Conclusions

Kwashiorkor is the second most prevalent form of severe acute malnutrition in south Punjab and usually difficult to diagnose due to masking effects of edema. Kwashiorkor can be successfully managed by using the WHO guidelines for sever acute malnutrition. WHO guidelines also show treated patients discharged mostly with a lower percentage of mortality and comorbidities.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Comparison of Perinatal Outcomes in Growth Restricted Fetuses with Abnormal and Normal Umbilical Artery Doppler at a Tertiary Care Hospital

Rabia Channa[1], Faisal Nadeem[2], Sabiha Nasir[3], Muneeb Ullah[4]

ABSTRACT

Objectives: To compare perinatal outcomes in growth restricted Fetuses based on normal and abnormal umbilical artery doppler studies.

Study Design: Prospective Cohort Study.

Place and Duration of Study: This Study was conducted in Civil Hospital Karachi. Duration of the study was 6 months, from 24th November 2018 to 25th May 2019.

Materials and Methods: 232 growth restricted Fetuses were divided into two equal groups, 116 with normal umbilical artery doppler studies (Group A) and 116 with abnormal umbilical artery doppler studies (Group B). Inclusion criteria were pregnant patients with age 20-35 years and excluding malformations. Doppler assessment used 3-5 MHz probe (GE PRO-V, USA) for umbilical artery and vein, noting absent/reversed flow. Follow-up included delivery, neonatal assessment, and mortality recording.

Results: The mean age in our study was 28.92 ± 5.71 years, while gestational age was 33.97 ± 2.58 years. The normal umbilical artery doppler group experienced a 14.66% rate of premature deliveries compared to 52.59% in the abnormal group (*p*-value: 0.0001). NICU admissions were reported at 26.72% in the normal umbilical artery doppler group and notably higher at 76.72% in the abnormal group (*p*-value: 0.0001). A striking observation was the threefold increase in perinatal deaths within the abnormal umbilical artery doppler group (18.10%) as opposed to the normal group (7.76%) (*p*-value: 0.024).

Conclusion: Adverse perinatal outcomes were associated with abnormal umbilical artery Doppler in Fetuses with growth restriction. Timely preventive measures should be taken to reduce perinatal morbidity and mortality.

Key Words: *Doppler, Umbilical artery, Growth Restriction, Perinatal, Outcomes.*

Introduction

Fetal growth restriction (FGR) is characterized by weight at birth below 10th percentile for a specific age of gestation. Those infants whose weight falls below 10th centile for gestation age are considered as small for gestational age (SGA).[1] Another criterion for SGA involves fetal measurements of abdominal circumference that fall below an arbitrary percentile, often ranging from 2.5th to 10th percentiles as per charts derived from representative fetal samples.[2] Incorporating abnormal umbilical artery doppler waveforms into the FGR diagnosis is a practice followed by some, extending beyond size criteria alone. The aetiology of FGR is multifaceted.[3] FGR increases the risks of respiratory distress syndrome, necrotizing enterocolitis, intraventricular haemorrhage, clotting disorders, organ failure, premature birth, and perinatal mortality.[4,5] Although maternal circulation abnormalities contribute to FGR's pathophysiology, the feto-placental vasculature's role in normal development is equally significant. Studies underscore that FGR with absent or reversed end-diastolic umbilical artery velocities face poor fetal outcomes in comparison to FGR with preserved end-diastolic velocities.[6] Umbilical artery doppler assessment is recommended for FGR pregnancies with high risks.[7] The use of doppler techniques especially in obstetrics was initially explored by Fitzgerald and Drumm and has remained

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a focal point of research.[8] Doppler velocimetry's potential to assess uterine, placental, and fetal circulations has been widely investigated.[8,9] Doppler assessment helps in FGR cases to examine potential small vessel disease in feto-placental and utero-placental blood circulation. Different criteria for doppler study regarding FGR have been proposed. Among these the systolic/diastolic ratio (S/D) is the crucial measure.[10] S/D ratio of more than 3 after 30 weeks of pregnancy is considered abnormal. Factors such as low fetal weight, reduced volume of amniotic fluid, and mother's hypertension are reliable predictors of FGR.[6,11]

Given the scarcity of data regarding the relationship between perinatal outcomes in FGR and the status of umbilical doppler in our region, this prospective study becomes paramount. It aims to emphasize the clinical relevance of umbilical artery doppler studies in fetal growth restriction management, particularly in guiding decisions about the timing and mode of delivery. This cohort study will furnish essential evidence for timely interventions, ultimately improving perinatal outcomes in pregnancies with FGR.

Materials and Methods

Prospective cohort study was carried out in the Obstetrics and Gynaecology department of Civil Hospital Karachi from 24th November 2018 to 25th May 2019. Ethical approval letter numbered OBG-2016-183-7258 is attached. The sample size determination was guided by considering the proportion of perinatal death in both normal and abnormal umbilical artery doppler groups, statistical power (80%), significance level (5%), and an estimated error of estimation (5%). Consequently, the final sample size was established as 232; 116 participants in each Group A and Group B. Group A had normal umbilical artery doppler studies while Group B had abnormal umbilical artery doppler studies. Nonprobability consecutive sampling technique was used. Inclusion criteria included pregnant women, age between 20 to 35 years, primigravida and multigravida with single fetus between gestational age 28 to 38 weeks and lastly those who were at risk of having FGR. Those who had already been detected with congenital malformations during antenatal check-up were excluded. Patients were enrolled after obtaining informed consent. Ultrasound doppler was carried out by colour pulsed wave doppler electronic probe of machine GE PRO-V (USA). The abnormal flow findings included absent or reversed umbilical artery end diastolic flow in umbilical artery and pulsatile flow in ductus venosus or umbilical venous system. Follow-up extended to delivery, with neonatal assessment encompassing 1-minute Apgar scores and birth weight. Cases of neonatal death, stillbirths, and admissions/shifting to neonatal intensive care unit (NICU) were documented using pre-approved forms. All the data and all the follow up were documented under the supervision of same doctor (researcher). Analysis of data was done using SPSS version 20.0. Quantitative variables such as age, parity, gestational age, and birth weight were presented as means ± standard deviation (SD). Qualitative variables including low birth weight, gestational diabetes mellitus, pre-eclampsia, and outcomes like preterm birth, perinatal death, and NICU admission were expressed as numbers and percentages (%). A Chi-square test was employed to compare outcome variables between the two groups and a p-value of < 0.05 was deemed statistically significant. Relative risk calculations were utilized to identify significant effect modifiers and confounders, such as gestational age, parity, gestational hypertension, diabetes mellitus, pre-eclampsia, and low birth weight, with control achieved through stratification. Subsequently, post-stratification Chi-square tests were applied, and relative risk was computed.

Results

Study participants had a mean age of 28.92 ± 5.71 years while gestational age was 33.97 ± 2.58. Mean of parity was 2.80 ± 1.01. Gestational hypertension was seen in 25% (n=58) patients, pre-eclampsia was seen in 8.19% (n=19) patients while gestational diabetes was seen in 31.03% (n=72) patients. The detail distribution of age, gestational age, parity, gestational hypertension, pre-eclampsia, gestational diabetes, low birth weight, between Group A and Group B is in Table I.

The average weight of babies born to Group A and Group B was 3.26 ± 1.03 kg and 3.01 ± 0.79 kg respectively. Significant distinctions in perinatal outcomes emerged between the normal and abnormal umbilical artery doppler groups.

Table I: Distribution of Variables between Group A and Group B

Group	Mean Age	Gestational Age	Parity	Gestational Hypertension	Pre-eclampsia	Gestational Diabetes	Low Birth weight
	Mean ± SD	Mean ± SD	Mean ± SD	N (%)	N (%)	N (%)	N (%)
Group A (n=116)	28.90 ± 5.71	34.08 ± 2.60	2.82 ± 1.07	30 (25.86%)	10 (8.62%)	37 (31.9%)	46 (39.66%)
Group B (n=116)	28.95 ± 5.71	33.85 ± 2.57	2.79 ± 1.03	28 (24.14%)	9 (7.76%)	35 (30.17%)	45 (38.79%)
Total	28.92 ± 5.71	33.97 ± 2.58	2.80 ± 1.04	58 (25%)	19 (8.19%)	72 (31.03%)	91 (39.22%)

Particularly, the normal umbilical artery doppler group A experienced a 14.66% (n=17) rate of premature deliveries compared to 52.59% (n=61) in the abnormal umbilical artery doppler group B. NICU admissions were reported at 26.72% (n=31) in the normal umbilical artery doppler group and notably higher at 76.72% (n=89) in the abnormal group. A striking observation was the threefold increase in perinatal deaths within the abnormal umbilical artery doppler group (18.10%) as opposed to the normal group (7.76%). Their *p*-values and details are shown in Table II.

Table II: Perinatal Outcomes between the Group A and Group B

Outcome Variable		Group A	Group B	*p*-value	RR
Preterm Delivery	Yes	17 (14.66%)	61 (52.59%)	0.0001	3.59
	No	99 (85.34%)	55 (47.41%)		
NICU Admission	Yes	31 (26.72%)	89 (76.72%)	0.0001	2.87
	No	85 (73.28%)	27 (23.28%)		
Perinatal Mortality	Yes	9 (7.76%)	21 (18.10%)	0.024	2.33
	No	107 (92.24%)	95 (81.90%)		

Discussion

Utero-placental blood flow alterations, observed in conditions like hypertension and FGR, have prompted doppler ultrasonography for early analysis and surveillance of fetal growth, in addition to being non-invasive, economical, and simple method.[12] In this context, we carried out a study to determine the relationship between perinatal outcomes in FGR with normal and abnormal umbilical artery doppler study. Our findings revealed significant differences in perinatal outcomes between the normal and abnormal umbilical artery doppler groups (*p*-value 0.0001). Some authors advocated use of umbilical artery doppler screening in second and third trimesters for risk assessment of premature delivery while some recommend its use in all three trimesters.[13,14,15] Meanwhile our study was based on third trimester screening and notably, the abnormal group showed a markedly higher proportion of premature deliveries compared to the normal group. Admission to NICU was significantly elevated in abnormal umbilical artery doppler group compared to the normal group. This was also noted in an International Research.[16] Importantly, perinatal mortality was higher in abnormal umbilical artery doppler group than in the normal group consistent with international data.[17] This aligns with similar comparative studies that underscored the adverse impact of abnormal umbilical artery doppler on perinatal outcomes.[18] Previous research by Rochelson, Berkowitz, Alfirevic, and others emphasized the link between abnormal umbilical artery doppler and increased perinatal morbidity and mortality.[4,19] The role of doppler in estimating poor outcomes and the potential benefits of its integration into high-risk pregnancy surveillance protocols have also been established.[11,12,20] However, Doppler's use in low-risk populations has shown no advantage over standard fetal surveillance.[10,21] Abnormal venous Doppler waveforms and umbilical artery reversed flow have been associated with increased neonatal deaths, perinatal morbidity, and adverse fetal outcomes.[22,23] Abnormal Doppler findings, like those in the umbilical artery, can independently predict NICU admissions beyond low-birth-weight considerations.

Limitations of our study included being a single tertiary care study. Doppler analysis was performed during the third trimester of pregnancy. The expertise of doctor performing doppler study was

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variable and depended upon available doctor at the time of study. Long-term outcomes such is completion of milestones, neurological and physiological development were not followed in current study.

This study however forms the basis for future research regionally that will ultimately lead to local recommendations of screening doppler velocimetry studies in fetal growth restriction cases as a diagnostic tool along-with serial fundal height estimation and fetal biometry. Doppler studies may also be used as a diagnostic tool in addition to screening for prediction of pre-eclpamsia in high-risk cases.

Conclusion

This study confirmed the adverse perinatal outcomes associated with abnormal umbilical artery doppler in FGR. This calls for timely preventive measures and mitigate perinatal mortality and morbidity for both mothers and fetuses.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Single Stage Laparoscopic Orchiopexy for Impalpable Low Abdominal Undescended Testis in Children- Analysis of Outcome

Mumtaz H Khan[1], Amna H Khan[2] Naila Yaqub[3]

ABSTRACT

Objective: To evaluate clinical efficacy of single stage laparoscopic orchiopexy by modified Prentiss procedure for the treatment of impalpable undescended testis within 2.5 cm from deep ring in children.

Study Design: This was a retrospective case series study design.

Place and Duration of Study: Department of surgery, section of pediatric surgery. Northern Area Armed Forces Hospital Hafer Al Batin, Saudi Arabia, from June 15, 2011, to Sep 15, 2021.

Materials and Methods: All the children admitted with diagnosis of impalpable undescended testis were treated by single stage laparoscopic orchiopexy by modified Prentiss technique during the study period from June 15, 2011, till Sep 15, 2021. The total number of patients was 22. The age of the patients ranged from 1 year to 7 years. Seventeen (77.26 %) children had unilateral (10 with left sided and 7 with right sided) impalpable undescended testis. Five (22.72%) children had bilateral impalpable undescended testis. All the patients were evaluated by ultrasound and MRI abdomen to confirm the abdominal location. The patients were operated by single stage laparoscopic orchiopexy using modified Prentiss technique by single senior pediatric surgeon after confirming the location of testis within 2.5 cm from deep inguinal ring. All the patients were followed up in out-patient clinic after 1 week, after 6 months and after 1 year.

The operative time, degree of post- operative pain, per operative and post- operative complications and follow up results were analyzed to evaluate the clinical outcome in terms of testicular location in the scrotum and size.

Results: A total of 22 children were treated successfully by single stage laparoscopic orchiopexy by modified Prentiss technique. The age ranged from one year to 7 years at the time of surgery. Ten (45.45%) patients had left sided non-palpable testis, 7 (31.81%) had right sided and 5 (22.72%) children were having bilateral non palpable testis. There was no per-operative complication. One patient (4.54%) had scrotal hematoma which resolved spontaneously. All the children had successful outcome in terms of testicular size and location within scrotum after surgery on follow up of more than one year. There was no case (0%) of testicular atrophy in this series. Thirteen (59%) patients had testis in lowest position of scrotum, eight (36.36%) patients had testis in the middle scrotum and one (4.54%) patient had testis in the neck of the scrotum.

Conclusion: Single stage Laparoscopic orchiopexy by modified Prentiss procedure is feasible, safe and effective technique to treat children with impalpable low abdominal undescended testis in children.

Key Words: *Abdominal Testis, Complications, Impalpable Undescended Testis, Laparoscopic Orchiopexy, Single Stage, Testicular Atrophy*.

Introduction

Undescended testis (UT) is an important condition that needs surgical treatment in children. The incidence of UT is about 1-4.6% in full term neonates and it is 20-30 % in premature neonates weighing less than 2.5 kilogram. [1]The problems with UT are reduction of potential of fertility, testicular malignancy and torsion in addition to psychological effects.[2] To avoid these complications, orchiopexy is recommended to treat UT not later than one year of age.[3]

Impalpable undescended testis (IUT) is classified as vanished testis, intra-canalicular testis or intraabdominal testis.[4] After exclusion of vanished testis various strategies are used to manage IUT.[5]

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Traditional inguinal exploration for IUT is limited and usually unsatisfactory.

Intra-abdominal high UT may be treated by single or two stage Fowler Stephen laparoscopic orchiopexy (LO) using Shehata technique.[6] Staged laparoscopic traction orchiopexy is another option to treat high intraabdominal testis.[7] Low intra-abdominal and intra-canalicular testis are treated by single stage LO either by laparoscopic trans-inguinal orchiopexy (LTIO) or by laparoscopic orchiopexy by modified Prentiss maneuver (LOMP).[8]

Prentiss et al in 1955 described the technique of retro-peritoneal dissection to mobilize testicular vessels and by dividing inferior epigastric vessels, fascia transversalis and lateral spermatic ligament to gain extra length to bring the testis within scrotum without any tension on testicular vessels.[9]

Later, Ayub et al described small incision in fascia transversalis above pubic tubercle avoiding division of inferior epigastric vessels.[10] Recently, laparoscopy and LO using LOMP procedure has become gold standard treatment of IUT.[11] Laparoscopy has made mobilization of testicular vessels and vas deference in abdominal cavity possible under direct vision.[12] Laparoscopy makes precise path of descent possible for testis medial to inferior epigastric vessels. Single stage LOMP is effective and safe method of treatment of abdominal testis within 2.5 cm of distance from deep ring. Retraction of testis or testicular atrophy are complications found on follow up of LOMP.

Our study was a retrospective analysis of 22 children with impalpable low abdominal undescended testis treated by single stage LOMP during the period from June 15, 2011, till Sept 15, 2021, to evaluate the clinical outcome in terms of testicular size and location within the scrotum.

Materials and Methods

This was a retrospective study of 22 children diagnosed as impalpable testis located in abdomen within 2.5 cm from deep ring and treated successfully by single stage LOMP at Northern area Armed Forces Hospital, Saudi Arabia, during the period from June 15, 2011, till Sep 15, 2021. The electronic data was collected by the operating pediatric surgeon after getting permission from the hospital ethical committee.

All the patients were referred from primary health care center to pediatric surgery out- patient clinic with diagnosis of UT. The age ranged from 1 year to 7 years. Clinical examination was done to confirm the diagnosis of IUT and to exclude any associated congenital anomaly. Seventeen (77.27%) children (10 on left side and 7 on right side) had unilateral IUT and five (22.72%) children had bilateral IUT.

All the patients were evaluated by ultrasound abdomen and MRI abdomen to confirm the presence and abdominal location of testis. All the children were admitted one day prior to surgery through out-patient clinic for elective surgery. The surgery was performed under general anesthesia by single senior pediatric surgeon at Northern Area Armed Forces Hospital Hafer Al Batin, Saudi Arabia.

Laparoscopic evaluation was done to confirm the location of testis or exit of testicular vessels and vas through deep ring. Blind ending vas and vessels were found in cases of vanished testis within abdomen or on groin exploration.

The cases of the peeping testis, cryptorchidism associated with syndromes, patients with history of hormonal therapy and vanished testis were excluded from the study. All the patients were treated by single stage LOMP technique by descending the adequately mobilized testis through a path medial to inferior epigastric vessels to reach within scrotum. We have used a 2-point fixation with tunica albuginea of testis. We didn't close the deep ring in our patients.

All the patients were given prophylactic intravenous cefuroxime and were discharged home after 72 hours of surgery in good health. All children were followed up in out- patient clinic after 1 week, after 6 months and after 1 year. We used color Doppler evaluation on follow up after 6 months and after 1 year in all our patients to evaluate the blood flow and volume of the testis and found good blood flow and increase in volume of testis.

The hospital electronic data including operative time, per-operative and post- operative complications, post- operative pain and outcome of surgery with evaluation of scrotal location, testicular blood flow and volume of testis on follow up was analyzed by the operating pediatric surgeon to evaluate the efficacy and safety of LO.

The statistical analysis was done via SPSS version 21. Chi square test was applied to categorical variable

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(testis location in lowest art of scrotum vs testis location in middle/ neck of scrotum} with p-value 0.083.

Based upon our experience with limited number of patients, it is found that single stage LOMP has a better position of testis within scrotum. However more studies with a bigger number of patients are needed to analyze the clinical outcome.

Results

A total of 22 children with IUT in abdomen within 2.5 cm from deep ring were treated successfully by single stage LOMP procedure. The age of the patients ranged from one year to 7 years at the time of surgery.

Ten (45.45%) patients had left sided IUT, 7 (31.81%) had right sided IUT and 5 (22.72%) children were having bilateral IUT. The abdominal presence and location of testis was confirmed at diagnostic laparoscopy. All the patients with vanished testis were excluded from the study. All the patients had abdominal testis within 2.5 cm from the deep ring and were treated by single stage LOMP by descending the adequately mobilized testis medial to inferior epigastric vessels (Figure 1, 2, 3 and 4).

The operation time was (Min) = 41.32+- 5. There was no per-operative complication. One patient (4.54%) had post-operative scrotal hematoma which resolved spontaneously. All children were followed up in out- patient clinic after 1 week, after 6 months and after 1 year. We used color Doppler evaluation on follow up after 6 months and after 1 year in all our patients to evaluate the blood flow and volume of the testis and found good blood flow and increase in volume of testis.

Based upon our experience, it is suggested that single stage LOMP has a better position of testis within scrotum. After 6 months and one year of follow up, we found that the testis was in lower scrotum in 13 (59%) patients, in the mid scrotum in 8 (36.36%) patients and at the scrotal neck in one (4.54%) patient.

No patient (0%) had testicular atrophy. No retraction (0%) of testis was seen on follow up. We found single stage LOMP as safe and effective method of treatment for IUT within 2.5 cm from deep inguinal ring (Table 1 and 2)

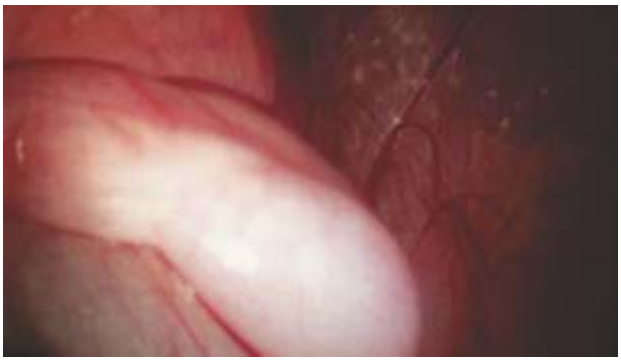

Figure 1 : Intraabdominal Location of Testis within 2.5 cm from Deep Ring

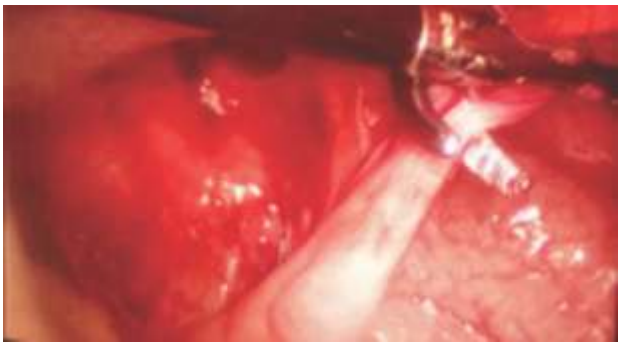

Figure 2: Establishment of Channel for Descent of Testis Medial to Inferior Epigastric Vessels

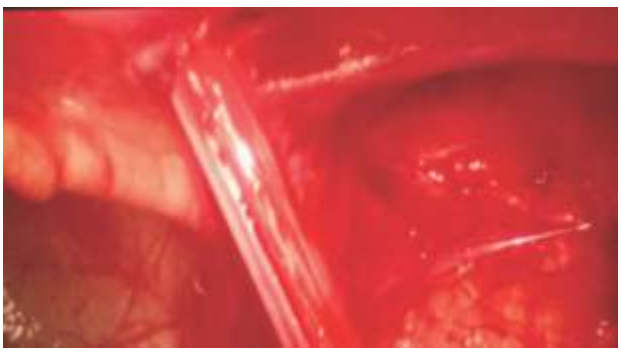

Figure 3: Testis being Brought Down into the Scrotum Through the Channel Medial to Inferior Epigastric Vessels

Figure 4: The Testis Brought Down within the Scrotum

Table I:Pre-Operative and Intraoperative Data

No of patients	22
Age (months)=	12+_ 84
Laterality of IUT	Left sided IUT=10 (45.45%) Right sided IUT=7 (31.81%) Bilateral IUT=5 (22.72%)
Location of IUT in the abdomen	In the abdomen Within 2.5 cm from deep ring

*IUT: Impalpable Undescended testis

Table II: Per-Operative and Postoperative Complications

Complications	Number of patients (%)
Per-operative complications	0 (0%)
Post-operative complications	Scrotal hematoma=1 (4.54%) Hernia or hydrocele =0 (0%) Testicular retraction= 0 (0%) Testicular atrophy= 0 (0%)
Testicular position in the scrotum	Low scrotum=13 (59 %) Mid scrotum= 8 (36.36 %) Scrotal neck=1 (4.54 %)

Discussion

Twenty to 35 % of children with UT present with IUT.[13] To avoid future complications, orchiopexy is recommended to treat UT not later than one year of age. [14] Traditional inguinal exploration for IUT is limited and unsatisfactory. LO is performed to treat IUT located inside the abdomen.

Yang et al, Elderwy et al and Prentiss et al have reported that LOMP shortens the distance of descent of testis. [15] Agrwal et al believed that primary LO is feasible when the distance from deep ring is less than 2.5 cm .[16] Begga et al suggested that single stage LO is considered when the distance from deep ring is less than 1 cm.[17] We found that singe stage LO is feasible if the distance from deep ring is less than 2.5 cm.

Many authors have noted that when testis can reach the contralateral deep ring after mobilization, it makes single stage LO feasible.[18] This is one of the modes of evaluation but if the testis is more than 3 cm away from the deep inguinal ring, staged orchiopexy should be considered.[19]

In our series, we used LOMP technique to treat all our patients with impalpable abdominal testis located within 2.5 cm from the deep ring.

Closure of peritoneum at deep ring is described in some series.[20] We did not close the peritoneum at the deep ring in any of our patients and found no complication of inguinal hernia or hydrocele on follow up.

There was no per-operative complication in our series. Poor wound healing and scrotal hematoma is reported in literature after LO.[21] There was no complication of poor wound healing in our patients. In this series, 4.54% of patients developed scrotal hematoma which was resolved spontaneously.

Color Doppler ultrasonography is used to evaluate testicular blood flow and volume in follow up evaluation status of testis.[22]

We used Color Doppler evaluation on follow up after 6 months and after one year in all our patients to evaluate the blood flow and volume of the testis and found good blood flow and increase in volume of testis. Testicular atrophy is defined as loss of more than 50% of post-operative testicular volume.[23] In our series none (0%) of the patients developed testicular atrophy.

Testicular retraction is described as a complication of single stage LO.[24] In our series adequate testicular mobilization and a proper dartos pouch was found critical for testicular fixation within scrotum. We have used a 2-point fixation with tunica albuginea of testis. There is no case (0%) of testicular retraction in our series. We found that the testis was in lower scrotum in 59% patients, in the mid scrotum in 36.36% patients and at the scrotal neck in 4.54 % patients.

Older patients tend to face difficulty in obtaining satisfactory testicular position as the distance from testis to scrotum increases with age.[25] The morphology of the spermatic cord may be tense and small in some patients and tortuous and thick in others.[25] All the factors including age, distance from the deep ring and laxity of spermatic cord should be considered for single stage LO.

Our study has limitations of small number of patients. More studies are needed in future to evaluate the clinical outcome of single stage LOMP. Based upon our experience, it is suggested that single stage LOMP has a better position of testis within scrotum.

Conclusion

Single stage LOMP procedure is feasible, safe, and effective technique to treat children with impalpable low abdominal undescended testis within 2.5 cm from deep inguinal ring.

Conflict of interest

The authors declare that there are no conflicts of interest with respect to the authorship and publication of this article.

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CONFLICT OF INTEREST

Authors declared no conflicts of Interest.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Self-Medication of Antibiotics Among Medical Students: A Cross Sectional Study

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ABSTRACT

Objective: To determine the frequency and perception regarding self-medication of antibiotics among medical students of Al-Nafees medical college, Isra university.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: It was conducted in Al-Nafees Medical College from 1st April- 30th June 2019.

Materials and Methods: This study was conducted among medical students of Al-Nafees Medical College. A total of 220 students were included in the study, via convenient sampling technique, 44 students from each year, with male to female ratio of 1:1. A structured questionnaire comprising of 12 multiple choice questions along with a demographic details section was used to collect the data. The data was entered and analyzed using Statistical Package for Social Sciences (SPSS) version 22.0.

Results: Out of 220 students (mean age 21 +/-4 years), 74% of students were self-medicating. 26.8% said prior experience of use was the reason for self-medication while 2.7% wanted to maintain privacy. About 39.50% of students used antibiotics to treat fever, whereas 5.90% for genitourinary infections. About 38.2% reported that the major source of information was acquired from other students, while 7.7% from friends or internet. Type of antibiotic was put under consideration by 40.5% of the students while self-medicating, 38.6% consulted doctor for selecting dosage. Dosage was changed during course of treatment by 16.8% , major reason (28.6%) behind it was improvement in health condition. Twenty-two percent stopped taking antibiotics before course completion on disappearance of symptoms while 29.5% labelled it as an unacceptable practice.

Conclusion: The trend of antibiotics' self-medication is quite high among medical students which may result in an increase in antibiotic resistance.

Key Words: *Antibiotics, Cross sectional study, Frequency, Medical students, Prescription.*

Introduction

Antibiotics are medications prepared to treat or prevent bacterial infections, dispensed to patients depending on the prescription of a certified health care provider. Antibiotics are essential therapeutic agents, particularly in the developing world where infectious diseases are highly prevalent and still a leading cause of mortality.[1]

However, the indiscriminate use of antibiotics can lead to most health problems. A major global health public problem is the increasing use of non-prescribed antibiotics, in other words known as self-medication.[2] Self-medication is defined as the use of drugs to treat self-diagnosed disorders or symptoms without a prescription or guidance from a physician.[3,4]

Multiple factors contribute to the use of antibiotics including influence of family and friends, unchecked sales, time and financial constraints, customer attitudes and expectations and impact of media. Moreover, a few reasons for self-medication with antibiotics in low-income countries include over-the-counter sale, high cost of medical consultation, low satisfaction with doctors, and misunderstandings about the effectiveness.[5,6]

The inappropriate consumption of antibiotics may lead to adverse outcomes, which include antibiotic resistance, treatment failure, and drug toxicity. Widespread irrational use of antimicrobials with no background of medical consultation can ultimately result in an increased likelihood of inappropriate, incorrect, or delay in therapy along with missed diagnosis, and increased morbidity. Ultimately this may lead to chronic illnesses, frequent health care consultations, prolonged hospital stays, the

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necessity for costly medications, and even mortality.[7] The ascent in antimicrobial resistance, due to incomplete course of treatment is harmful to individuals as well as societies.[8]

Antibiotic resistance is documented as the world's most predominant public health issue. The emergence of multidrug-resistant bacterial strains has raised an alarming concern about antibiotic resistance globally.[9,10] In Pakistan, antibiotics, along with other medicines, are readily available to the population without requiring a prescription; a similar situation is encountered in many poor countries. Throughout the years, complications of self-prescription particularly with antibiotics have achieved increasing recognition worldwide as well as in Pakistan. In Pakistan, few research have been conducted on self-medication. Surveys related to self-prescription of antibiotics in Pakistan reported prevalence of 32.5%.[11]

A study done in Nigeria reveals prevalence of self-medication among medical students to be high. Reasons being having satisfactory pharmaceutical information, and almost half of them purchased these medicines from the community pharmacy. Most of them used patient information leaflet for dosage and duration of medication.[12]

Research conducted in Nepal amongst students of nursing department in November 2016 showed that more than half of them acknowledged engaging in self-medication of antibiotics over the past one year. Fever was the most frequently treated symptom using antibiotics. The practice amongst nursing students was common due to their confidence in their medical knowledge, followed by the thinking that doctor's advice is not required for common illnesses, and to save time and money.[13]

Research in Saudi Arabia focused on antibiotics usage in the Middle East, addressing symptoms like cough, sore throat, and urinary tract infections. Self-medication was prevalent due to poorly implemented policies on antibiotic availability, socio-economic factors, the belief in the efficacy of antibiotics for quicker recovery, and the practice of storing antibiotics at home for self-administration or sharing among family and friends.[14]

The research in Mekelle, Ethiopia, focused on self-medication among Health Sciences students, revealing a 50% prevalence of the practice. Common ailments prompting self-medication included headaches, cough/common cold, dysmenorrhea, and dyspepsia. Students cited personal experience and perceived mildness of conditions as key motivations. Accessibility of drugs in informal settings, such as open markets and kiosks, played a significant role in the widespread adoption of self-medication among the student population.[15]

Keeping in view the situation regarding self-medication of antibiotics among medical students, limited studies have been done in the local context. Therefore, this study was performed with the objective of assessing the magnitude of this problem.

Materials and Methods

This descriptive cross-sectional study was performed on MBBS students of Al-Nafees Medical College for duration of 2 months from 1st April- 30th June 2019. A total of two hundred and twenty students were selected using Raosoft sample size calculator at 95% confidence interval and 5% margin of error. Among them 110 were males and 110 were females. Students who gave consent were included in the study. Data was collected simultaneously from students in five academic years, encompassing first year to final year. The sample included a total of 44 students, with an equal distribution of 22 males and 22 female. Convenient non-probability sampling technique was used. Verbal informed consent was taken, after approval by the Institutional Review Committee.

A self-administered, pre-tested self-constructed questionnaire was used as a tool to conduct this study with closed ended questions. Pre-testing was done by conducting a pilot study on 10 participants whose data was not used in the results. The questionnaire gathered demographic data such as name, age, gender, and education level of participants. It also contained 12 multiple choice questions. Participants were asked whether they have ever treated themselves with antibiotics or not. Participants who confirmed self-medication were asked the reason, purpose, source of information, frequency, usage and name of antibiotics.

SPSS version 22 was used for data entry and analysis. Descriptive statistical analysis was carried out to document frequencies and percentages of study variables.

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Results

Table I: Demographic Profile

Demographic Profile	Number	Percentage (%)
Class		
1st year	44	20
2nd year	44	20
3rd year	44	20
4th year	44	20
5th year	44	20
Gender		
Male	110	50
Female	110	50
Age Groups		
17-19	38	17.2
20-22	125	56.8
23-25	57	25.9

The major use of antibiotics was due to prior experience of use that is 26.8% while 2.7% wanted to maintain the privacy as shown in figure 1.

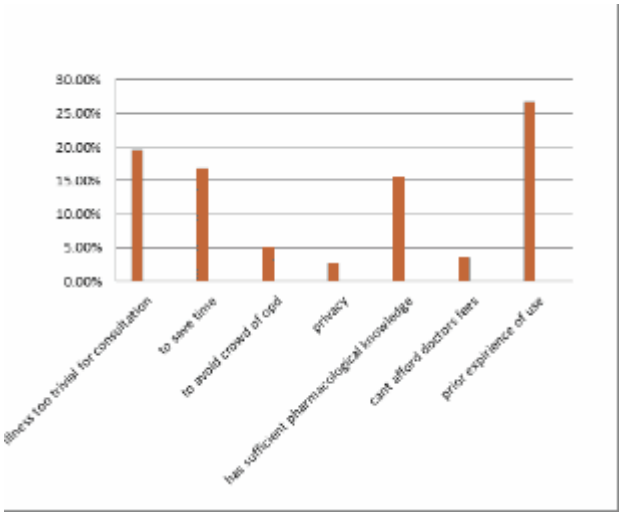

Figure 1: Reasons for Self-Prescription of Antibiotics Complaints for which Antibiotics was Self Prescribed

The most common complaints students reported for self-treating with antibiotics were fever followed by respiratory tract infection, GIT infections, skin infection and genitourinary infections.

Source of Information

The major source of information to take antibiotic for self-prescription was from old prescription whose frequency was 38.2 % among the students, followed by use of antibiotic by some other family member that is 29.1 % common. Some community pharmacists also recommended common antibiotics (16.4%). Other sources of antibiotics included drug advertisement sources (7.7%) and friends or internet (3.6%).

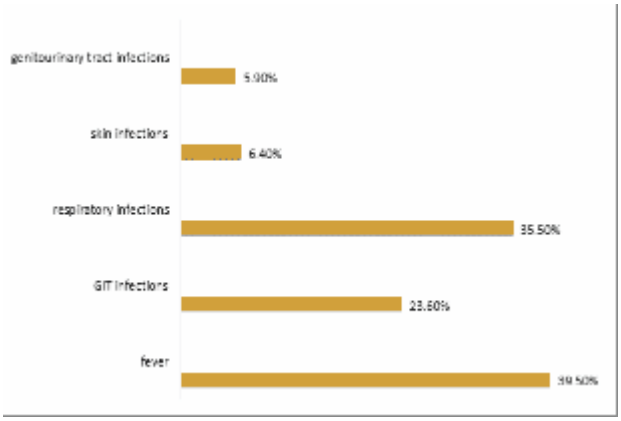

Figure 2: Common Complaints for Using Antibiotics.

Antibiotic Selection

While selecting an antibiotic people considered multiple factors. In our survey 40.5% of students considered the type (group) of antibiotics, 15.9% chose antibiotic with minimal side effects, 13.2% chose according to brand name, 4.1% consider the prices of antibiotic.

Frequency and Usage

According to the survey 38.6% took according to consultation of a doctor, 19.5% of participants checked the package insert in the medicine for getting knowledge regarding dose for self-prescribed antibiotic, 3.6% by consulting a pharmacist. 1.4% used antibiotics by consulting a senior at university, 4.1% by the help of lecture notes and 6.4% consulted internet for correct antibiotic dosage.

Change of Dosage

The frequency of students who changed the dosage of antibiotic during the course was 16.8% while 28.2 % people never changed the antibiotic or its dose during the course. On the other hand, 28.6% changed the antibiotics sometimes as shown in figure III.

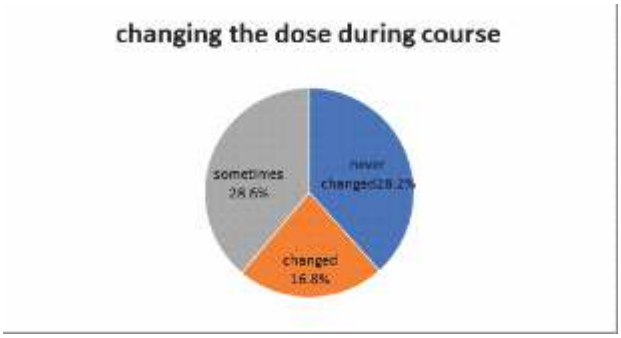

Figure 3: Frequency of Students Who Changed the Dosage of Antibiotic During the Course.

Reason Behind Change of Dosage

In our study, one of the major reason behind the change of dosage was due to improvement in students' health (28.6%) while 9.5% changed it due to worsening conditions. There is a small percentage of 11.4% students who changed the dose to reduce the side effects of antibiotics.

Cessation of Antibiotic Intake

When we explored the reasons behind cessation of antibiotic intake, we saw that 21.8% stopped taking antibiotics after their symptoms disappeared while 14.5% stopped taking antibiotics after few days of recovery. Some of them stopped taking antibiotics after few days regardless of their outcome their frequency was 4.5%, 2.7% stopped taking after antibiotics ran out, 29.5 stopped taking after completion of the course, and 1.8 stopped taking antibiotics after consulting a doctor.

Experiencing Adverse Reaction

Some people experienced an adverse reaction, and their frequency was 18.2%, while 55.5% did not experience any adverse reaction. The people who had experienced an adverse reaction 25% of them stopped taking antibiotics, 7.3% switched to other antibiotics, 30.5% consulted a doctor, some of them consulted a pharmacist their frequency was 0.5%, 0.9% consulted their family or friends while 9.5% did not consult anyone.

Opinions About Self Prescription

Twenty percent of the subjects thought that self-medication was a good practice, 24.5% considered it as an acceptable practice, and 29.5% labelled it as an unacceptable practice.

Among people who self-medicate with antibiotics, 33.6% of them speculated that they could successfully treat infectious disease all by themselves, 30.5% among were not sure, while 10% of them thought they couldn't treat it.

Discussion

Self-medication is the selection and use of medicines by individuals to treat self-recognized illnesses or symptoms. [16] Historically people have shown vigilance regarding their health for which they have practiced self-medication. Self-medication has its pros and cons but that varies with who uses it and how it is used.[17] This study was conducted to assess the frequency of self-medication among the medical students of Al-Nafees medical college which was found to be 74%, that is closely similar to 74.4% found in the study conducted among the medical students of south-east of Iran.[18] In another research a higher rate of 88% was recorded by Bangladeshi Undergraduate Pharmacy Students .[19] Kumari R did similar observation among the medical students of Jammu, with the percentage of 79%.[20] While a lower frequency was found in the study among medical college students in West Bengal.[21]

In our study two most frequently reported reasons for self-medication were previous experience (26.8%) and illness too trivial to be consulted (19.5%). Similar findings were reported in studies conducted in Iran[22] and Karachi.[23] Different surveys also stated that low severity of illness being one of the major reasons for self-prescription.[24] However, another study stated that the commonest reason for students to practice self-medication was saving time.[25] In another research done by Gupta V among the students in Malwa Punjab the most widely reported reason for self-medication was for quick relief.[26]

In present study 15.5% students responded themselves as having sufficient pharmacological knowledge this resulted in our prevalence rate being lower as compared to rate of 45% in a study stated by medical students of coastal south india.[25]

In the present study the majority (38.2%) of the students gained knowledge about self-medication from the formerly prescribed medicines by physicians. Our data coincided with the research work conducted in the past.[19] Similar results could be seen in research work conducted by Pereira C.M from two Brazilian universities.[27] Fever 35.50% and respiratory infection 39.50% were the most common complaints reported by students followed by GIT infections, skin infection and genitourinary infections. Conversely, the most predominant symptoms stated in the prior study in Asmara, Eritrea were wound infection and sore throat.[28] Similar to some previously published articles, headache, common cold, fever, pain, and vomiting were the most common symptoms for self-administration of medications mentioned by the participants.[29]

Multiple studies have identified a higher rate of self-medication with antibiotics in Asia, ranging from 4% to 7.5%. This prevalence surpasses that observed in Northern Europe, where the self-medication rate

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with antibiotics is reported to be 3%.[30] Our study considered only antibiotics self-medication. On the contrary, according to the study conducted by medical students of Karachi[23] analgesics were commonly used followed by antipyretics and antibiotics; the study conducted by Abrar Hussain Azad also reported analgesics to be the most widely used drug group (51%) followed by antibiotics contributing 44.3% of the total share.[31]

Self-medication has become prevalent throughout the world. Although, when practiced with caution in a community with good literacy rate and with limited classes of drug, is time saving and cost effective for the patients where professional care is comparatively expensive and not available promptly but at the other hand, misuse of these drugs can lead to numerous health hazardous.

Strengths and limitations

The strength of this study is that this kind of study has never been done on medical students in Pakistan where its frequency seems to be high, and antibiotics are available over the counter without any prescription. Limitation is the non-probability sampling technique and single centered study.

Conclusion

The trend of antibiotics' self-medication is quite high among medical students which may result in an increase in antibiotic resistance. This needs to be evaluated further. Awareness programs about hazards of self-medication can be run in the community. The reasons for self-medication should be addressed appropriately. Legislations for over-the-counter antibiotic sale should be made and enforced in our country. Pharmacists should be counseled for not dispensing drugs without prescription.

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Correlation of Academic Performance with Student Attendance in Pre-Clinical and Clinical Years of Undergraduate Medical Education

Amjad Ali Khan[1], Usman Mahboob[2]

ABSTRACT

Objective: To investigate the correlation between student attendance and academic performance in undergraduate medical education, with a focus on exploring potential similarities or differences in correlation patterns between pre-clinical and clinical years.

Study Design: Retrospective cross-sectional, correlational study.

Place and Duration of Study: Saidu Medical College Swat Pakistan from 1st March 2018 to 26th November 2020.

Materials and Methods: A total of 450 students from preclinical and clinical years were studied. Student attendance and marks obtained during their annual exams were converted to percentage values. To measure the strength of correlation, the Pearson Correlation coefficient was calculated using SPSS version 25.

Initially, the correlation coefficient of Pre-clinical and Clinical students was calculated independently, the results were then compared against each other to understand the difference between the two cohorts. Scatter plots and regression analysis were calculated to depict the relation between variables. A p-value < 0.05 was deemed statistically significant.

Result: A statistically significant positive correlation between class attendance and academic performance of pre-clinical students was found ($r = 0.227$, $p < 0.001$). The mean attendance of Pre-Clinical Students was (86.4) with a standard deviation of SD ± 5.638. Analysis of clinical students revealed a very weak negative but statistically insignificant correlation, ($r = -0.037$, $p < 0.73$). Mean attendance was measured to be (83.1) with a standard deviation of SD ± 5.83.

Conclusion: This study points to a previously unexplored dissimilarity in the correlation between lecture attendance and academic performance among clinical year as compared with pre-clinical year students, underscoring the dynamic nature of the relationship between attendance and academic performance throughout different phases of medical education. Further research exploring the factors influencing academic performance in clinical years is required to understand the complex interplay between attendance and academic performance.

Key Words: *Academic Performance, Attendance, Clinical, Correlation, Pre-Clinical, Undergraduate Medical Students.*

Introduction

Medical education is an ever-changing and highly challenging field. The extensive curriculum and the addition of newer information as a result of continuous advancement in technology and a better understanding of disease conditions through research have rendered the medical profession, one of the most challenging professions.[1]

The gradual decline in student attendance at medical schools[2] prompted researchers to identify factors that hamper the academic performance of medical students in class and their professional performance. Studies were carried out trying to find a link between attendance and the resulting academic performance.[3] Moreover, researchers also strived to identify the causes of poor attendance in classes and the perspectives of faculty and students regarding the importance of attendance.[4,5]

A vast literature in this regard pointed towards a positive correlation between attendance and academic performance in undergraduate medical students.[6] Student attendance is so much emphasized in Pakistan that major universities in

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Pakistan are barring students with lower attendance from appearing in exams.[7]

Research, however, also suggests that the failure to attend classes may not be attributed merely to the lack of interest in classes. Mandal identified a lack of motivation leading to decreased concentration and diminished interest as one of the factors affecting student academic performance during undergraduate medical studies however their findings also suggested that there was no significant link between academic performance and attendance.[8]

A few decades back, attending lectures was the primary source of learning. The only learning material a student could take back with him were the notes he took or the concepts he understood and memorized. The advent of modern technology, social media, and access to online learning resources, also raise the possibility that students who are failing to attend classes may be opting for better learning avenues.[9] Alternative reasons for student absenteeism may also exist where either a student does not perceive any value in attending classes or may have found a better alternative to attending class. Questions are now being raised on mandatory attendance.[10]

This necessitates the reassessment of the correlation of lecture attendance with academic performance in undergraduate medical education. Furthermore, the different requirements of participation and interaction during pre-clinical and clinical years in undergraduate medical education also warranted research to understand the correlation in this perspective.

The correlation in terms of pre-clinical and clinical years was also unexplored and required further research.[3] The main objectives of this study were to investigate the correlation between students' class attendance and academic performance in undergraduate medical education, with a focus on exploring potential similarities or differences in correlation patterns between pre-clinical and clinical years.

Materials and Methods

We used an explanatory correlational design for our study. Two cohorts of students at Saidu Medical College were studied. One from pre-clinical students (n=359) between 1st March 2018 to 26th November 2020 and the second cohort (n=91) from clinical years between 1st March 2018 to 25th December 2019.

The convenience sampling technique was adopted. The sample size for this study was determined for a desired confidence level (α) of 0.05 and, power (1 - β) of 0.80, aligning with conventional standards. A smaller effect size (r = 0.1) was chosen to reflect the nuanced and potentially subtle correlation anticipated between the attendance of pre-clinical and clinical years. A sample size of n=50 was considered sufficient to demonstrate the presence of a relationship.[11]

IRC Approval, (Ref # Riphah/IRC/22/2018), was obtained from the Institutional Review Committee to pursue the research and analyze and use the data for research purposes. Institutional permission was sought to have access to the overall class attendance (not including practical and bedside teaching) and annual professional exam result data along with student identification data. (Ref # 100/SMC/PF). The attendance data obtained was anonymized. Once an anonymous number was assigned to each student the original student record was returned to the student affairs section. There was no direct interaction of the authors with students at any stage of the study.

Student attendance data and student's annual academic scores, converted to percent attendance and percent marks, were selected as independent and dependent variables. Students who were due to appear in supplementary exams were excluded from the study as studies have listed upcoming exams as a cause of low attendance [12]. Students with below 75% attendance were also excluded from the study as the University has a minimum 75% attendance criteria for eligibility to appear in the annual professional examination [7].

To measure the strength of correlation, the Pearson Correlation coefficient was calculated using SPSS version 25. Bivariate data analysis was also carried out. Descriptive statistics, Scatter plots, and regression analysis were calculated. A p-value < 0.05 was statistically significant.

Results

Attendance and academic performance data of the two cohorts, (n=359) preclinical students and (n=91) clinical students were analyzed.

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Pre-Clinical Students Data Analysis

Among the 359 Preclinical Students, 275 (76.6%) were male, and 84 (23.4%) students were female. The mean attendance of Pre-Clinical Students was (86.4) with a standard deviation of SD ± 5.638. A two-tailed, Pearson correlation coefficient for attendance and academic performance for pre-clinical students was calculated to be (r = 0.227, $p < 0.001$) as shown in (table. II). This shows the likelihood of a significant positive correlation between the two variables.

A scatter plot as shown in (Fig. 1) indicated a linear positive relationship between the attendance and the academic performance of pre-clinical students.

In preclinical years, the mean attendance and performance of male students was 85.19 and 72.38 respectively, in contrast, female students in the clinical years showed a higher mean attendance of 90.37, accompanied by a mean performance of 74.43. An independent sample t-test revealed a statistically significant difference between class attendance of both genders in Preclinical students. (t = -7.998 p=0.001). (Table. I)

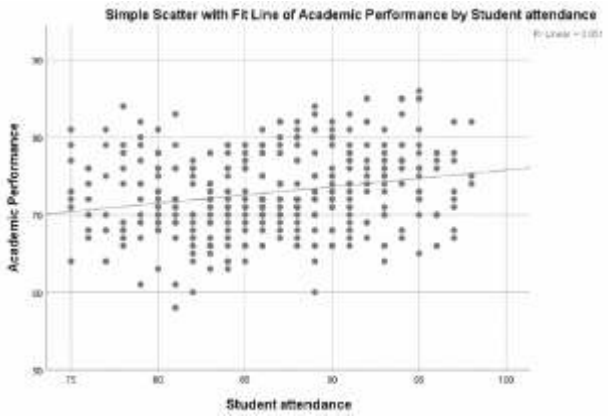

Figure 1: Simple Scatter Plot with Fit Line of Academic Performance by Pre-Clinical Students' Attendance

Table I : Gender-Based Independent Sample T-Test, Pre-Clinical and Clinical Students

Student Attendance		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig.	Mean Diff	Std. Error Diff	95% (C.I.) of the Difference	
									Lower	Upper
Pre-Clinical	Equal variances assumed	0.842	0.360	-7.998	357	0.000	-5.184	0.648	-6.458	-3.909
Clinical		0.032	0.858	-1.767	89	0.081	-2.140	1.211	-4.546	0.267

Clinical Students Data Analysis

A total of 91 Clinical students' data were analyzed, 48 (52%) of the students were male and 43 (47%) were female. Mean attendance was measured to be (83.1) with a standard deviation of SD ± 5.83. The Two-tailed, Pearson correlation coefficient for attendance and academic performance for Clinical students was calculated to be (r = -0.037, $p < 0.73$) as shown in (table. II). This showed that there is a very weak negative association between the two variables and a P value greater than 0.05 showed that the correlation was insignificant in the case of Clinical students.

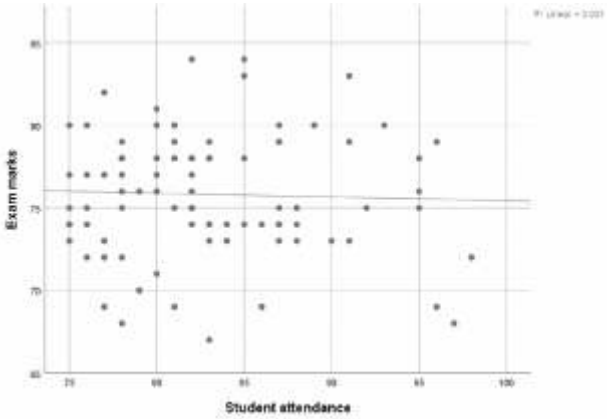

Figure 2 : Simple Scatter Plot with Fit Line of Academic Performance by Clinical Student's Attendance

In the case of Clinical students, the scatter plot (Fig. 2) indicated a linear weak negative relationship between attendance and the academic performance of pre-clinical students. The mean attendance and performance of male students was 82.00 and 75.44 respectively, while female students in the clinical years showed a slightly higher mean attendance of 84.14, accompanied by a mean performance of 76.26. An independent sample t-test showed a statistically insignificant difference between class attendance of both genders (t = -1.767 p = 0.081). (Table. I)

Table II : Comparative Statistics, Attendance, and Academic Performance

Preclinical & Clinical			Student Attendance	Exam marks
Pre-clinical N=359	Student Attendance	Pearson Correlation	1	.227**
		Sig. (2 - tailed) *p*=		.001
	Exam marks	Pearson Correlation	.227**	1
		Sig. (2 - tailed)	.001	
Clinical N=91	Student Attendance	Pearson Correlation	1	-.037
		Sig. (2-tailed) *p*=		.726
	Exam marks	Pearson Correlation	-.037	1
		Sig. (2 - tailed)	.726	
*** Correlation is significant at the 0.01 level (2-tailed).*				

From our analyses of the datasets of the two cohorts it is quite clear that in clinical years, student attendance does not affect their academic performance the same way as observed during pre-clinical years.

It is important to understand that our study of correlation provides a likely association between the two variables in both cohorts but does not imply causation.[13]

Discussion

Our study explored the relationship between students' lecture attendance and academic performance in pre-clinical as well as clinical years of undergraduate medical education. Notably, a significant positive correlation was observed in pre-clinical years, indicating that higher class attendance was associated with improved academic performance during annual exams. Other studies, exploring the correlation between attendance and academic performance during pre-clinical years reached the same conclusion. A correlational study conducted at Rawalpindi Medical University involving (n=317) students of first and second year MBBS, found a positive correlation between attendance and academic performance. Similarly, a positive correlation was observed between the two variables for individual subjects.[14] Another study conducted at Rehman Medical College involving (n=99) students explored the correlation between attendance and academic performance in third-year MBBS students and found a strong positive correlation. This study, however, was limited to the subject of pharmacology, considering the overall attendance including lectures and Practicals while students' academic performance was derived from internal exam results. Another study conducted at Eastern Medical College, Kabila, Bangladesh on (n=314) students of third and fourth-year MBBS also found a similar positive correlation between the two variables.[15]

Although in the case of pre-clinical years, our findings are consistent with the majority of the studies one study spanning over six weeks, conducted at the University of Central Florida, College of Medicine found no correlation between attendance and academic performance however, there was one significant difference in the attendance policy, where academic sessions were divided into 12 mandatory TBLs, CBL session and 29 lectures where attendance was voluntary, and all course material was made available online. [16]

However, in clinical years, our study found a weak and statistically insignificant correlation, suggesting a differing pattern in the relationship between lecture attendance and academic performance during different phases of medical education. This finding contrasts with other studies conducted limited to clinical subjects. A study conducted at a teaching Hospital in Dublin, Ireland where attendance of (n=147) students (tutorials and clinical teachings combined, in Obstetrics and Gynecology clinical rotations) were correlated with students' annual examination scores in the subject found a significant positive correlation. [17] Another study took a slightly different path by correlating absenteeism and academic performance in medicine and

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pediatrics, involving (n=310) students, found a negative correlation suggesting that poor attendance led to lower performance, This study also correlated the overall attendance i.e. the combination of both tutorials and clinical teaching. [18]
More recently a study conducted at the Arabian Gulf University, Bahrain also concluded a significantly positive correlation between student attendance during their surgical clerkship and corresponding academic scores. in this case, the attendance was not limited to lecture attendance but the combination of hospital-based activities, simulation sessions, and problem-based activities. [3]
Research exploring correlations during clinical years was scarce and primarily limited to individual disciplines. All three instances involving research in clinical disciplines discussed above employed combined attendance of lectures/tutorials and hospital-based sessions for their studies. Our study was limited to correlating lecture attendance only, with academic performance considering that research points towards diminishing attendance during lectures. [19]
The gender-based analysis of pre-clinical students' data revealed notable disparities in attendance rates between male and female students, with female students exhibiting higher attendance and achieving corresponding higher academic scores than their male counterparts. A similar trend was observed among clinical students, although the gender gap was significantly narrower in this cohort. This finding is in line with other studies comparing attendance and academic performance of male and female students.[3,20]
Didactic lectures are predominantly used as the primary teaching method in Pakistan during pre-clinical years, while more interactive, hospital-based bedside teaching, is employed during clinical years [21]. This difference in the mode of information transfer during clinical years appears to positively influence learning thereby enabling students to perform better and also explain the minimal effect of skipping didactic lectures on overall performance.
Additionally, Transition from adolescence to adulthood occurs between the ages of 18 years to 24 years [22]. So, one could argue that the students during their preclinical years are largely influenced by their experience as pedagogical learners, and this gradually changes when the student reaches the clinical years, hence their predilection of self-directed learning and independent decision making about the choice of study pattern. Apart from that, a major portion of our population as of 2022 had little to no access to the internet and digital resources [23]. This leaves only a small number of students with resources and access to online learning. These factors could explain the significant effect of attendance on academic performance.
Considering self-determination theory, during the pre-clinical phase, autonomy is linked to expressing opinions and collaborating with peers, emphasizing in-class learning for academic success.[24] However, during clinical years, a shift in autonomy toward self-directed study, time management, and class selection is observed. Competence achievement becomes tied to personalized study strategies, allowing clinical students to balance online resources and self-study, minimizing the impact of reduced classroom attendance on academic performance.
A few limitations were observed during this study. Since the attendance was manually registered by the students via an attendance sheet circulated in class during lectures, the possibility of proxies could not be ruled out. Secondly, only a quantitative approach was used. Conducting a parallel analysis of attendance during bedside teaching sessions in clinical rotations could have provided a more comprehensive understanding of the correlation dynamics. The limited scope of this study, conducted within a single institution, also constrains its generalizability to broader contexts.
These findings underscore the importance of considering the dynamic nature of the attendance-academic performance relationship across distinct educational phases. Tailored interventions may be warranted to address the varying impact of attendance on academic success in pre-clinical and clinical years. Importantly, our study cautions against inferring causation from correlation, emphasizing the need for further research to explore the multifaceted factors influencing academic performance in clinical settings.

Conclusion

This study points to a previously unexplored dissimilarity in the correlation between lecture

attendance and academic performance among clinical year as compared to pre-clinical year students, underscoring the dynamic nature of the relationship between attendance and academic performance throughout different phases of medical education. It also emphasizes the need for further research exploring the factors influencing academic performance in clinical years to enhance our understanding of the correlation between attendance and academic performance.

Recommendations

Future research should consider a mixed-methods approach to delve deeper into the reasons behind student absenteeism, providing a better understanding of factors influencing attendance and academic performance. Comparative studies across diverse institutions, longitudinal analyses tracking changes over the entire medical education journey, and a qualitative exploration of the clinical years are recommended.

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CONFLICT OF INTEREST

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DATA SHARING STATMENT

The data that support the findings of this study are available from the corresponding author upon request.

ORIGINAL ARTICLE

Motivation and Attitude of BDS Students and House Officers in Their Postgraduate Career Selection

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ABSTRACT

Objective: The objective of this research was to explore the motivational factors among BDS students and house officers for post graduate career selection.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: The research was conducted from 3rd October to 19th December 2022 at Lahore Medical and Dental College.

Materials and Methods: A total of 226 participants (77 from third year BDS, 84 from 4th year BDS and 65 House Officers) were asked to fill a questionnaire in which the first part consisted of biodata and the second part was based on questions related to motivation of students for post-graduation and their preferred field of choice either clinical sciences or basic sciences. Descriptive statistical analysis was done and significance testing between the variables was done using chi-square test. Significance level was set at 0.05.

Results: Results of the study showed a significant difference (p=0.018) between the groups in reasons for choosing dentistry as a profession where majority 51.3% were internally motivated. It was found that 61% students were motivated for post-graduation and majority (68.5%) wanted to choose clinical subjects as compared to 13.2% for basic sciences. There was significant difference between the groups (p=0.00) as a clear majority (71.6%) believed that there were not enough options for post-graduation in Pakistan and 85.3% wanted the institute to conduct seminars for career counselling (p=0.048).

Conclusion: The dental students were motivated to do post-graduation out of which a clear majority opted to pursue clinical studies. The students wanted the institute to conduct career counselling sessions to help them plan their career choices.

Key Words: *Basic Sciences, Career Choices, Career Counselling, Dental Students, Motivation.*

Introduction

Specialization and post graduate studies in dentistry have gained a lot of importance over the years. The competition created for a limited number of seats has led to saturation of all the key training posts therefore making the right career choice is one of the most important decisions in a dental student's life.[1] The motivation for pursuing post-graduation has been widely researched including the factors contributing to the demographics of speciality choices.[2] There are many factors that have been identified as playing a key role in career selection by students including their academic performance, expected income from the speciality, social status, duty timings, personal preferences, awareness and helping the community.[3] According to the three dimensional framework theory of career selection, an individual may be intrinsically motivated due to personal choices or extrinsically motivated due to his environment or interpersonal dimension based on the social interactions with friends, family and peers.[2]

While career choices in dentistry have been widely researched, there are few studies that have researched the factors affecting the choice of specialization between basic sciences and clinical subjects. After graduating, students have two choices of a career path either in clinical subjects or basics sciences.[4] There is a clear majority of students who opt for clinical subjects rather than

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specialization in basic sciences.[4] In a study conducted in Nepal, it was found that students only considered specialization in basic sciences when they had failed their luck trying in clinical fields and it was necessary to highlight the role of good mentoring as the most ascertainable factor in career choice of young graduates.[5,6]

Shortage of teaching faculty in basic sciences has also been identified as one of the factors responsible for this trend as reported in a study in Japan, where there was a 24.5% rate of interest in basic sciences.[7] A study conducted in a private medical college in Karachi revealed that 91.1% students wanted to pursue post graduate studies of which Oral and Maxillofacial surgery was the most popular choice followed by Orthodontics and Restorative dentistry.[8] In another multi survey study conducted across different government and private dental institutes in Karachi, it was found that 51.5% students wanted to pursue post graduate studies out of which 75.3% opted for clinical subjects and only 14.4% for basic sciences.[9]

In Pakistan, Fellowship of College of Physicians and Surgeons (FCPS) has proved to be the most popular post graduate degree pursued by graduates even though there is a shortage of training posts in dental institutes.[10,11,9] Studies have shown that knowledge of basic sciences is a pre requisite to handle clinical scenarios and students should be motivated and guided to pursue research careers.[6] Therefore the reasons for this lack of inclination towards basic sciences must be explored in order to inspire students to make informed choices.

The aim of our study was to find the factors that lead graduates of Lahore Medical and Dental College in making career choices. The objectives of the study were to find the reasons for an inclination towards clinical training and what is the role of the institute in motivating their students to make these choices. The reasons for choosing dentistry and awareness of options for post-graduation were determined to understand the inclination of students towards clinical degrees.

Materials and Methods

A cross sectional comparative study was conducted at Lahore Medical and Dental College (LMDC), Lahore, Pakistan, between October and December 2022. Permission was obtained from the Ethical Review Board of LMDC to conduct the study, FD/1930/22, 24-5-2022. Non-probability convenience sampling was done and a total of 226 students were included in the study out of which 77 were from third year BDS, 84 were from 4th year BDS and 65 House Officers. First year and 2nd Year BDS students were excluded from the study based on their limited exposure to clinical work.

A questionnaire was prepared consisting of 13 multiple choices, close ended questions. The purpose of the study was stated, and confidentiality of the data was ensured. The first part of the questionnaire consisted of biodata and the second part was based on questions related to motivation of students for post-graduation and their preferred field of choice either clinical sciences or basic sciences. Each question had three options and two questions had five options stating the benefits of field of choice. The survey form was pretested and pre validated in a pilot study first. Participation was voluntary and out of 234 questionnaires distributed, 226 were filled and their responses were recorded.

Data was collected and analysed using Statistical Package for Social Sciences (SPSS) version 26.0. The data was subjected to descriptive statistical analysis and qualitative variables were described as percentages and frequencies. Pearson's Chi square test was used to compare the differences between the groups. The *p*-value < 0.05 was taken as significant.

Results

A total of 226 participants were included in the study out of which 153 (67%) were females and 73 (32%) were males. The mean age of the participants was 20±2 years. Out of 226, there were 77 (34.1%) students from 3rd year BDS, 84 (37.2%) students from 4th year BDS and 65 house officers (28.8%). Table Ⅰ shows the frequency of responses given to the questions asked about motivation for post-graduation and their associated p values. Table Ⅱ shows frequency of responses to questions asked about preference for clinical or basic science subjects. There was a significant difference (p=0.018) between the groups in reasons for choosing dentistry as a profession where majority 51.3% were internally motivated. There was also a significant difference between the groups (p=0.012) for motivation for post-graduation after BDS. Third year

and 4th year students were more motivated, 68.8% and 64.2% respectively as compared to house officers (47.6%). There was a highly significant difference between the groups (*p*=0.00) as a clear majority (71.6%) believed that there were not enough options for post-graduation in Pakistan and 85.3% wanted the institute to conduct seminars for career counselling (p=0.048).

Results showed that the biggest hurdle faced by students in pursuing post-graduate studies was lack of career counselling (30.9%) and shortage of seats for training (37.6%). A clear majority (68.5%) were more inclined towards choosing clinical sciences as compared to only 13.2% for basic sciences. There were however 18.1% who wanted to keep both options open. The benefits of clinical fields given by students as most appealing were better job prospects (25.6%) and better financial stability (29.2%). The benefits of basic sciences by majority of students were better job prospects (26.1%) and less training time (22.1%).

Table I: The Results of the Responses to Questions Asked about Motivation for Post-Graduation and their Associated *P*-Value

S.No	Questions asked in the survey	Responses	3rd Year	4th Year	House officers	*p*-value
1	**Choice of Choosing Dentistry**	Influenced by parents	16	13	25	0.018
		Internally motivated	41	50	25	
		Chose as a second option	20	21	15	
2	**Choice of Continuing Dentistry**	Yes	63	77	52	0.279
		No	8	3	7	
		Not Sure	6	4	6	
3	**Motivation for post-graduation**	Yes	53	54	31	0.012
		No	12	11	22	
		Not Sure	12	19	12	
4	**Knowledge of post-graduation**	Yes	20	18	18	0.820
		No	36	42	33	
		Not Sure	21	24	14	
5	**Options of Post-graduation in Pakistan**	Yes	18	2	6	0.00
		No	46	64	52	
		Not Sure	13	18	7	
6	**Role of Institute in motivation**	Yes	27	24	26	0.179
		No	37	44	55	
		Not Sure	13	16	4	
7	**Role of Institute in choosing field**	Yes	32	28	27	0.202
		No	33	50	30	
		Not Sure	12	6	8	
8	**Need for Career Counselling**	Yes	62	76	55	0.048
		No	7	6	9	
		Not Sure	8	2	1	
9	**Hurdles of post-graduation**	Lack of Motivation	10	9	9	0.143
		Financial Barrier	13	4	8	
		Lack of Career Counselling	18	34	18	
		Shortage of Seats	32	28	25	
		Difficult to Pass Exam	4	9	5	
10	**Job Preference**	Academic	11	10	11	0.597
		Private Practice	32	35	32	
		Both	34	39	32	

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Table II: Comparison of Reasons and Frequency of Responses for Preference of Clinical and Basic Sciences

Questions asked in the survey		Level of education			
		3rd Year	4th Year	House officers	*p*-value
Inclination	Clinical	55	60	40	0.682
	Basic	9	11	10	
	Both	13	13	15	
Benefits of Clinical Sciences	Better job prospects	18	23	17	0.738
	Better financial stability	24	25	17	
	Satisfaction of helping people	17	17	10	
	Work is not boring	16	13	17	
	Others	2	6	4	
Benefits of Basic sciences	Better prospects in academia	18	21	20	0.013
	Less training time	20	19	11	
	No Clinical Burden	20	17	9	
	Research work is more interesting	11	21	8	
	Others	8	6	17	

Discussion

This study is done to document the motivation levels of dental students and house officers in LMDC and their choice of field after graduation. There is a significantly higher number of female participants in the current study reflecting the higher ratio of females choosing dentistry as a profession.[12,13,14] However the responses recorded did not show a significant difference in career choices and reasons for choosing any specific field are same for both genders. Both genders reported that the biggest hurdles faced in post-graduation are lack of career counselling and shortage of seats as even though they are motivated but still struggled due to these issues. This trend is in line with similar studies conducted in this region[9] and also with a study conducted in Denmark.[18] In another study conducted in Nepal, the students were very motivated to do post-graduation but were discouraged by the high expenses of specialization.[19]

In our study the majority of students 51.3% are internally motivated for choosing dentistry as a profession out of which 85% want to continue dentistry after BDS and 61% are motivated for post-graduate studies.[25] This is in contrast to a study done in India where 74.4% students chose dentistry

because they failed to get admission in a medical college.[15] In our study there is a significant difference in the groups as undergraduate students of 3rd year and 4th year BDS are more motivated as compared to house officers. The reasons could be that as students the motivation levels are high but after graduation, the reality of post-graduate options available may be different. This contrasts with another study conducted in Karachi, where majority of students were pursuing dentistry to fulfil their parents desire.[9] In another study in India, the reasons cited most for choosing dentistry were good income and a respectable social standing. This study also showed an inclination towards clinical fields as compared to research and basic sciences.[14]

A clear majority (71.6%) of students believed that there are not enough options available for post-graduation in Pakistan and 85.3% want their educational institute to conduct career counselling seminars as only 24.7% had prior knowledge of post-graduate options. The importance of career counselling was highlighted in a study done in Army Medical College, Rawalpindi, in which questionnaires were given before and after the career counselling sessions. The participants were able to select their choice of speciality more effectively after the counselling session.[20] However these sessions must be an ongoing activity as a single session alone does not make a significant difference.[11]

A striking feature of our study is that most students 68.5% want to choose clinical subjects as compared to only 13.2% for basic sciences. This trend has been documented in numerous other studies as well.[9,11,21,22,23] Clinical subjects are preferred by the students because of better financial stability and job prospects. Likewise, better prospects in academia and less training time are the reasons given by students for choosing basic sciences. In a study conducted in 80 medical schools in Japan found that females were more inclined towards career development in basic sciences as the rationale for choosing this was an interest in research whereas in our study only 17.6% were interested in research work highlighting the role of making research more attractive for students.[7] In a study conducted in different dental colleges of Karachi, it was found that 84% students wanted to do post-graduation with 48.3% wanting to get an FCPS degree based on personal interest.[10] In separate studies done in United Kingdom, it was found that the majority (71%) students wanted to pursue dentistry with the most popular fields of choice for specialization were Restorative dentistry and Orthodontics.[24] A study done in Harvard School of Dental Medicine also showed Orthodontics to be the most popular choice[5] and Prosthodontics[12] in a Chinese Medical University reflecting the popularity of clinical sciences.

The importance of basic sciences cannot be ignored as basic science knowledge is critical to clinical decision making and students must be encouraged and inspired to purse a research career and not just join as a second option.[6] The prospects of good earning and financial stability in the future are some of the factors that students look for when choosing a career field.[4] Our study showed that financial stability was the most popular choice for choosing clinical subjects as highlighted in another study in Karachi where financial reward and role models were considered the influencing factors for choosing any speciality.[21]

The authors propose that in order to encourage students to opt for basic sciences, career counselling at an institutional level must be done while at the same time highlighting the positive aspects of a career as an academician and the benefits of research work can all inspire students to pursue basic sciences. This will also reduce the burden of shortage of seats that many students face when applying for clinical training programs. The limitation of our study was that the results were collected from one institute only and they may be compared with other medical colleges of Lahore where career counselling sessions are being given.

Conclusion

A majority of students were motivated to do post-graduation out of which a clear majority opted to pursue clinical studies instead of basic sciences. The students believed that the institute should provide career counselling sessions to help them make informed decisions when choosing a career path.

The Department of Medical Education can play its part in strengthening basic science subjects and ensuring that students choose these specialities so that there is a balance in distribution of specialists.

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CASE REPORT

A Geriatric Case of Acute Motor and Sensory Axonal Neuropathy (AMSAN) following Viral Encephalitis

Ahmad Asim, Abid Saeed Khan, Maham Qudoos Nizami

ABSTRACT

Acute Motor and Sensory Axonal Neuropathy is a rare form of Guillain-Barré syndrome (GBS). The incidence after viral encephalitis is rare in contrast to other variants of GBS. We reported a very rare case of Acute Motor and Sensory Axonal Neuropathy in a 70-year-old man after viral encephalitis, diagnosed by clinical evaluation, Electromyography (EMG) and Nerve Conduction Studies (NCS).

Key Words: *Acute Motor and Sensory Axonal Neuropathy, AMSAN, Guillain-Barré syndrome, Viral Encephalitis, EMG/NCS.*

Case

A 70 years old man presented in the Emergency Room of Capital Hospital, Islamabad with a complaint of high-grade fever for 4 days, sudden onset weakness in left upper limb and altered level of consciousness for 1 day. The level of consciousness according to Glasgow Coma Scale (GCS) of the patient was $E_2M_2V_2$=6/15. The temperature was 102°F. Rest of the physical examination was normal. CRP of the patient was raised to 69 mg/dl while Blood C/S and Urine C/S were negative. CT Scan showed senile cerebral atrophy. The patient was admitted as a case of viral encephalitis and treatment was started. The level of consciousness improved gradually with GCS 15/15 on the 6th day of admission, but the patient had developed quadriparesis with areflexia and loss of vibration and proprioception in lower limbs.

Electromyography (EMG) and Nerve Conduction Studies (NCS) were done that showed the following findings.

- Low compound muscle action potentials amplitude & conduction velocity in (bilateral) Median Nerve, Ulnar Nerve, Tibial Nerve & (Right) Common Peroneal Nerve.
- Unevokable motor response in (Left) Common Peroneal Nerve.
- Unevokable F-wave response in sampled nerves.
- Low sensory nerve action potentials amplitude & conduction velocity in (bilateral) Median Nerve & Ulnar Nerve.
- Unevokable sensory response in (bilateral) Sural Nerve.
- The electrophysiological study, suggestive of AMSAN.

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Introduction

Guillain-Barré syndrome (GBS) is an acute, severe autoimmune polyradiculoneuropathy.[1] Infections with Campylobacter jejuni, CMV, EBV, Mycoplasma pneumoniae, Hemophilus influenzae, HSV and VZV are some of the known antecedent infections in GBS patients.[2] Axonal variants of GBS are AMAN, AMSAN and pharyngeal-cervical-brachial weakness.[3] Acute Motor Sensory Axonal Neuropathy (AMSAN) is a rare and severe variant of GBS having a prolonged recovery course.[4]

We reported a rare case of post encephalitis AMSAN in a 70 years old man.

Discussion

GBS is a form of polyradiculoneuropathy that is immune mediated and can occur after various viral or bacterial infections.[5]

In this article we provide a detailed report of a geriatric case of GBS AMSAN-type after viral encephalitis. According to the Brighton diagnostic protocol, following clinical, neurophysiological and laboratory criteria, the patient fulfilled the Level-2 criteria for GBS diagnosis.[6]

A case of Guillain–Barré syndrome (GBS) caused by Japanese encephalitis virus was reported in China in 2022 but that didn't have sensory nerve involvement.[7] A similar case was also reported in China back in 2014.[8] A number of case reports

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related to AMSAN and COVID 19 are published.[9] But both sensory and motor variant GBS (AMSAN) after viral encephalitis is rare in literature.

Conclusion

There should be more research towards this aspect of viral encephalitis. It should be diagnosed and treated earlier with keeping in mind, one of its complication, AMSAN, a rare form of GBS that usually has a serious clinical course and slower recovery than the common demyelinating form of GBS. So, suspicion of the clinician is important as early diagnosis and intervention with immunotherapy can improve the outcome.[10]

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- Objective
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- Place & Duration of Study
- Materials & Methods
- Results
- Conclusion

Four elements should be addressed: "why did you start?", "what did you do?", "what did you find?" and "what does it mean? “.” Why did you start?" is addressed in the objective. "What did you do?" constitutes the methodology and could include design, setting, patients or other participants, interventions, and outcome measures. "What did you find?" is the 'results', and "what does it mean?" would constitute the conclusions. Please label each section clearly with the appropriate sub-headings. Structured abstract for an original article, should not be more than 250 words. At least 3 key words should be written at the end of the abstract. Review articles, case reports and others require a short, unstructured abstract. Commentaries do not require an abstract.

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- Sampling technique
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- There is clear evidence that the findings are unreliable, either as a result of major error (e.g., miscalculation or experimental error), or as a result of fabrication (e.g., of data) or falsification (e.g., image manipulation)
- It constitutes plagiarism.
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- It contains material or data without authorization to use.
- Copyright has been infringed or there is some other serious legal issue.
- It reports unethical research
- It has been published solely on the basis of a compromised or manipulated peer review process.
- The author(s) failed to disclose a major competing interest that, in the view of the editor, would have unduly affected interpretations of the work or recommendations by editors and peer reviewers.

At times the article may occasionally be retracted for correction of errors in submission or publication and will be replaced with the corrected one.

Retraction Process

JIIMC adopts the following retraction process to ensure best practice of retraction:

1. An article requiring potential retraction will be brought to the attention of JIIMC editor.
2. Managing Editor will follow the step-by-step guidelines according to the COPE flowcharts and will seek the response from the author of the

article as well.

3. JIIMC Publication & Research Integrity Committee will evaluate the evidence of misconduct and response of the authors. Based on the findings, the committee will recommend a final decision whether to retract the publication or otherwise.
4. The final decision is then communicated to the author and, if necessary, any other relevant bodies(PMC, HEC), or the author's institution as deemed appropriate.
5. The retraction-note titled "**Retraction: [article title]"** will be published in the paginated part of a subsequent issue of the journal and listed in the contents list.
6. The text of the retraction should explain why the article is being retracted.
7. The statement of retraction and the original article must be clearly linked in the electronic database so that the retraction will always be apparent to anyone who comes across the original article.
8. The relevant changes in the online version will be reflected through **Crossmark** icon.