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Case Report

Editorial

ARTIFICIAL INTELLIGENCE, ENTHUSIASM AND EQUITY- A NUANCED TAKE ON THE USE OF AI IN THE GLOBAL SOUTH

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Artificial Intelligence and generative AI may as well be the biggest turning point of the century, but this also presents the greatest equity paradox-While institutions in the Global North approach AI with measured caution, the Global South continues to embrace these technologies with great enthusiasm and at an accelerating pace. The disparity shown here is not just a question of fast /slow adoption rates of technology, but it also represents the complex interplay of educational gaps, economic imperatives, colonial legacies and contesting visions of the future of medical education. As medical educators in Pakistan and the wider global south, we need to navigate this paradox optimistically, but at the same time with critical vigilance. Multinational research surveys report that medical students have significantly more positive attitudes regarding AI integration in the Global South, as compared to their counterparts in the Global North.[1,2] A cross-sectional study involving 4596 medical, dental and veterinary students from 192 institutions across 48 countries reported that students from Latin America, Africa and Asia reported stronger beliefs in the transformative potential of AI and were more willing to adopt it than the global north.[3] This is not just limited to perception but also implementation. Another study showed that 92.3% respondents from the global south contexts believed that AI has a role in patient care, compared to 58.5% North American participants.[3] This presents a very striking contrast-while the Global North institutions debate ethical frameworks and regulatory boundaries, Global South medical schools are actively integrating artificial intelligence into clinical training, curricula and health care delivery. This enthusiasm is driven by several factors, the first being in that in the resource constraints presented in Global South healthcare systems, there are some urgent needs that AI promises to effectively address, such as diagnostic support in settings with physician shortages, educational tools and generative AI uses that can supplement limited faculty resources and facilitate as a fast fix for time constrained faculty.[4] Second, the concept of "leapfrogging" whereby one skips over some technological stages to go directly to the next one significantly impacts the discussions in those areas where the traditional infrastructure had been poorly developed throughout history.[5] Third, the digitally native populations in the Global South embrace technological solutions with very less scepticism than their Global North counterparts.[6] The Global North's measured approach stems from different priorities and historical experiences. The United Kingdom's AI Safety Summit, The European Union's AI Act and the United States' Executive Order on AI Safety all reflect concerns about misuse, privacy violations, algorithmic bias, and loss of human agency.[7,8] These regulatory frameworks have been generated from contexts where the overreach of technology has already led to backlash by the public- form controversies in facial recognition to issues with discriminatory algorithmic decision making in social services and even criminal justice. The World Health Organization also urges caution in AI, particularly generative AI use in healthcare, stressing upon issues like misinformation, premature deployment of technology that has

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not undergone sufficient validation, risk of bias etc. [9] The Global North's hesitancy symbolizes its role as the main inventor and seller of AI technologies; these countries are accountable for technologies that might bring about negative consequences if used all over the world. Moreover, strong data protection measures such as the General Data Protection Regulation (GDPR) set up legal structures that unavoidably delay the use of AI but at the same time are expected to safeguard people's rights.[10] Global south's rapid AI adoption can be explained if we see the historical patterns of knowledge dependency and technology extraction that characterized colonial medicine. It bears significant similarities to the current AI revolution.[11,12] There is a concept of 'data colonialism' which discusses how human life in the GS region is increasingly appropriated for data extraction only to be used within asymmetrical systems under control of Global North corporations.[13,14] Research on AI in healthcare reveals that out of 109 significant machine learning models, 101 were developed in the United States, Western Europe, or China, with only two originating from Global South countries.[16] The problem with this situation is that GS institutions are all consuming technology that has been designed elsewhere, embedding foreign epistemologies into their medical education systems while ultimately the data generated is contributing to enrichment of external corporations. The Global North technology giants still have a major share of the game when it comes to AI infrastructure software, hardware, and cloud storage—with almost total control.[14] In the GS, when medical schools choose to implement AI-based educational resources, they may become reliant on the continuous payment of international proprietary algorithms, and cloud services, which in turn, raises the issues of data rights, long-term costs, and the question of who really controls the technology. This dependency is very much akin to the colonial times in which the colonies were only allowed to supply raw materials, while all the manufacturing, knowledge generation, and control of the processes remained in the colonial centers. Apart from the extraction of resources, the use of AI in medical education in the Global South might result in ethical issues—specifically, the gradual destruction and taking away of local knowledge systems, clinical reasoning and understanding of health and illness practices which are specific to the culture. [15,16] The AI medical decision support systems that are trained solely on the medical literature and patient groups of the Global North are the ones that foster certain diagnostic frameworks, treatment algorithms, and evidence hierarchies while at the same time pushing to the side local clinical wisdom, traditional healing knowledge, and context-specific disease presentations. A study examining development of chatbots with AI for health information, found that those systems that lacked a local stakeholder involvement usually failed to account for community-based health beliefs, cultural idioms if distress, linguistics nuances and community-based health beliefs that majorly shape how patients actually describe and understand illnesses.[17] However, it would still be a very simplistic approach if the whole thing about AI adoption is viewed only from the perspective of colonial exploitation. The Global South's acceptance of AI is not only a sign of their cooperation, inventiveness, and the rightful hunt for answers to urgent health problems but also a symbol of their struggle. AI, when carefully brought into the picture, especially in the context of teaching and healthcare, really has the potential of being one of the major solutions to the problem of inequality in those areas. Many researches from low- and middle-income countries have shown how incredibly useful AI applications are in diagnostic support, telemedicine and decision making. Even having made improvements in treatment outcomes and reduced diagnostic errors in settings lacking specialised expertise.[18,19] These tools work to augment the clinical force where there is a shortage of health care workers. An important point is that the Global South cannot be labelled just as the helpless receiver of AI technologies, rather it is in the process of becoming a stronger source of innovation. For instance, the creation of an Amharic-speaking AI chatbot in Ethiopia is based on participation from various end-users, local patients and health workers, and a 95.7% accuracy rate is an indication of such an

approach in the development of AI that is culturally sensitive and linguistically appropriate.[18,20] This way of looking at the situation gives a positive twist to what has been considered as a negative scenario of the technology-dependent place: communities as co-creators, together with AI systems that enclose local wisdom instead of obliterating it. Pakistan's own technology industry that keeps growing with the help of the National Centre for Artificial Intelligence and other initiatives indicates the potential of the country to come up with solutions that meet its healthcare needs and educational contexts. South-South collaboration—sharing AI tools, training data, and expertise among Global South countries—paves the way to technological sovereignty that is not subject to the dependence on Global North companies nor to the exploitation that is characteristic of the extractive models.[21] Specifically for medical educators, AI powered assessment offers objective, standardized evaluation in settings where due to a smaller number of faculty comprehensive clinical skills assessment is a challenge.[22] The question now arises that given this landscape in the global south that is fraught by complexities, how do medical educators of this region approach AI integration? Outright rejection or overzealous embracing are both counterproductive. Instead, we propose here principles for equity based and careful AI adoption: several principles for thoughtful, equity-oriented AI adoption: Before adoption of any AI tool for medical education, a rigorous overview of the training data is needed to ensure it reflects our context.[23] Local capacity building and ownership should be preferred over passive usage of precooked softwares. Advocacy should be done for policies that encourage health data to be monitored by robust governance frameworks and under national leadership. A deep engagement of all stakeholders- community, health care professionals, students and patients is needed to understand whether the AI model is applicable contextually. Participatory design approaches that involve communities as co-creators rather than subjects yield more effective, equitable technologies.[24,25] The intention to use AI in medical education is an augmentation to support medical teaching. However, areas that need human mentorship should be shielded such as bedside teaching, reflective discussions and patient storytelling.[26] This is a call for action to global south regions. We must think reflectively in terms of equity and ensure that AI usage does not make disparities larger instead of shrinking them. If more students are from less affording backgrounds. Minority communities or remote areas, ensure that they have equitable opportunities to use the AI tools as their peers, otherwise do not push for adoption. The issue at hand is not whether to choose AI usage or not but how to incorporate it in our setups while not overlooking our contextual limits. A critical optimism that it will be beneficial for the global south with South-South collaboration and solid representation only. From us, this asks for intellectual honesty bearing in mind social disparities and inequalities, colonial heritages and the degree to which technology can act as an enabler or an inhibitor of progress.

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Original Article

SELF REPORTED FACTORS AFFECTING CHOICE OF PRESCRIPTION OF DRUGS AMONG DENTAL SURGEONS IN PUNJAB PAKISTAN

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Abstract:

Background: To assess the self-reported factors influencing drug-prescribing practices among dental surgeons in Punjab, Pakistan, and to determine the association of formal or refresher training in drug prescription with prescribing behavior.

Material and Methods: This cross-sectional questionnaire-based study was conducted over 9 months (Feb–Nov 2025) among dentists working in three dental institutes in Punjab, after the approval of the IRB of Azra Naheed Dental College, on 300 dentists using convenience sampling. A structured self-administered questionnaire assessed demographics, training, supervision, confidence, and other influencing factors on drug prescription. Data was analyzed using SPSS Version 25. Chi-square test was applied with significance set at $p<0.05$.

Results: A total of 300 dental surgeons participated (mean age: 24.56±1.60 years); 71% were females (n=213). Training in drug prescription had been received by 68% (n=204). Need for supervision was reported "sometimes" by 61% (n=183), with a significant association with training (p=0.004). Confidence in self-prescribing was "somewhat" high in 55.7% (n=167), also significantly associated with training ($p<0.001$). Supervisor influence was high (93.3%; n=280), and degree of influence did not differ significantly between trained and untrained respondents (p=0.181). Pharmaceutical company influence was not significant (p=0.924), but prescribing in response to pharmaceutical representatives was significantly associated with training ($p<0.001$). Influence from fellow colleagues was significant (p=0.019). Other factors, including senior colleagues, self-judgment, books, and internet resources, showed no significant differences.

Conclusion: Formal or refresher training in drug prescription significantly improves confidence, reduces reliance on supervision, and promotes more cautious prescribing behavior, particularly in response to pharmaceutical marketing.

Keywords: Drug Prescriptions; Pharmaceutical Preparations; Prescription Drugs; Pakistan; Self Report

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INTRODUCTION

Drug prescribing is a critical component of safe and effective dental practice. Dental surgeons routinely prescribe analgesics, antibiotics, anti-inflammatory agents etc., for the management of pain, infection, and post-operative sequelae.[1] However, global literature reported considerable variation in prescribing patterns between dentists and across settings, with frequent reports of over-prescription, inappropriate drug selection, and deviation from evidence based guidelines.[2] Inappropriate use of antibiotics and analgesics in dentistry can lead to adverse drug reactions, but

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antimicrobial resistance and healthcare costs.[3] Previous studies have reported patterns of drug prescription in dental outpatient departments and teaching hospitals, highlighting issues such as polypharmacy, preference for brand names, and excessive use of antibiotics.[4-6] These patterns are influenced by a complex interplay of individual, institutional, and external factors.[7] At the individual level, knowledge of pharmacology, clinical experience, competence, and personal attitudes towards risk and uncertainty affect decision making among dentists.[8] External influences such as pharmaceutical marketing, promotion of brands, and interactions with sales representatives also play a significant role and have been associated with changes in prescribing behavior in both physicians and dentists.[9] In dentistry, pain and infection control as the most common reasons for prescribing medication. Studies have shown that dentists frequently prescribe analgesics and antibiotics, sometimes in situations where only local treatment is sufficient.[10, 11] Recent reviews indicate that antibiotic prescriptions are often given as a substitute for to delay operative treatment, and that the dentist choices are influenced by habits formed during training, continuing education courses, and patient expectations.[6, 7] The drug prescription decision making process is multifactorial which is evident from literature and shows that clinicians rely on factors including colleagues, senior faculty, clinical guidelines, textbooks, continuing professional development, and internet.[3] For newer dentists, supervisors, peer influence and senior faculty may strongly shape prescribing behavior, either through directives or by informal norms and expectations in the clinic.[3, 12]. Moreover, dentists with lower pharmacological competence may refer to supervisors, specialist colleagues or drug information by pharmaceutical representatives.[13] Despite increasing interest in dental prescription, few studies have examined the factors of dentist choice of drugs using a structured, questionnaire based approach. Previous studies have quantified drugs prescription, rather than why these choices are made. Moreover, surveys suggest that modifiable factors like reliance on non-evidence based information and pharmaceutical promotion exert a greater influence on prescription.[8, 14, 15] This can help in establishing guidelines and regulatory measures that encourage more rational, patient-center and evidence based drug prescription in dentistry. The present study aims to explore the self-reported factors affecting the choice of prescription of drugs among dental surgeons using a structured questionnaire in Punjab, Pakistan.

MATERIAL AND METHODS

This analytical cross-sectional study was conducted among dental surgeons working in three dental institutes in Punjab, Pakistan where dental surgeons are routinely involved in prescribing medications for dental conditions. The study was approved from the Ethical Review Board of Azra Naheed Dental College (ANDC/RAC/2025/48-A). The institutes involved were Azra Naheed Dental College, Lahore Medical and Dental College, and Institute of Dentistry, CMH Lahore Medical College, The study was carried out over a period of 9 months from February 2025 to November 2025. The study population comprised qualified dental surgeons (BDS or equivalent and above) who were currently involved in clinical practice and were authorized to prescribe medications. The inclusion criteria were dentists and house officers with at least 6 months of clinical experience after graduation, currently practicing during the data collection period and were willing to consent to be a part of the study. The exclusion criteria were interns or undergraduate students not independently prescribing drugs, dentists exclusively in administrative or non-clinical roles and non-respondents after two contact attempts by focal persons. The minimum sample size of 216 was calculated for this cross-sectional survey using Cochran's formula for proportions: $n=Z^2 p(1-p)/d^2$, with a 90% confidence level, a margin of error of 5% (d=0.05), and anticipated frequency of 27.5%.[3] To compensate for potential non-response and incomplete questionnaires, the calculated sample size was raised to 300 dentists. The data was collected using convenience sampling technique. Data was collected using a structured, self-administered questionnaire developed after reviewing relevant literature on dental and medical prescribing behavior and adapted from existing surveys where applicable. The questionnaire had three sections, **s**ocio-

demographic, sources of information and supervision-related factors, and other related factors. The formal or refresher training in drug prescription included structured lectures or workshops during clinical years (i.e., final year and house job), focusing on pharmacology, drug prescribing, and safe antibiotic use. The questionnaire was distributed via WhatsApp by contacting a focal person from each institute who circulated the link of the questionnaire in the groups of the dentists with repeated reminders within their institutes. Informed consent was mentioned in the questionnaire. Completed questionnaires were downloaded in excel sheets. Data was imported into IBM SPSS Statistics Version 25 (IBM Corp., Armonk, NY, USA) for analysis. Descriptive statistics were used to summarize socio-demographic characteristics and responses to individual questionnaire items. Chi-square test was applied to compare categorical variables and when expected frequencies were <5, Fisher's exact test was applied. A p-value<0.05 was considered statistically significant.

RESULTS

A total of 300 dental surgeons participated in the study. The mean age of respondents was 24.56±1.60 years. The demographical data and prior experience of refresher training course on drug prescription is exhibited in Table 1.

Table 1. Demographic characteristics of participants (N = 300)

Variables	Frequency (n)	Percentage (%)
Gender		
Male	87	29.0
Female	213	71.0
Departments		
Prosthodontics	24	8.0
Surgery	60	20.0
Operative Dentistry	61	20.3
Diagnostics	61	20.3
Periodontology	57	19.0
Pedodontics	14	4.7
Orthodontics	23	7.7
Refresher course/training of drug prescription in clinics		
Yes	204	68.0
No	96	32.0

A majority of dental surgeons sometimes needed supervision when prescribing drugs (61%; n=183). There was a significant difference between those who were taught or had refresher course in drug prescription during clinics regarding need for supervision (p=0.004) More than half of participants reported feeling somewhat confident (55.7%; n=167) prescribing a drug independently. Moreover, there was a significant difference between those who were taught or had refresher course in drug prescription during clinics regarding confidence after self-prescribing (p<0.001).

Table 2. Comparison of prescription-related behaviors between dentists who received formal / refresher training in drug prescription and those without such training

Category	n (%)	Received training n (%)	Not Received training n (%)	χ^2	p-Value
Need for supervision					
Always	63 (21)	28 (9.3)	35 (11.7)	19.31	0.004
Sometimes	183 (61)	63 (21)	120 (40)		
Rarely	52 (17.3)	5 (1.6)	47 (15.7)		
Never	2 (0.7)	0 (0)	2 (0.7)		
Confidence in self-prescribing					
To a great extent	82 (27.3)	8 (2.7)	74 (24.6)	45.49	<0.001
Somewhat	167 (55.7)	65 (21.7)	102 (34)		
Very little	47 (15.7)	19 (6.3)	28 (9.4)		
Not at all	4 (1.3)	4 (1.3)	0 (0)		

Analysis of influence-related factors revealed several important patterns regarding the prescribing behavior of dental surgeons in relation to whether they had received formal training or refresher teaching in drug prescription. Overall, supervisory influence remained high across both groups, although the association between receiving training and

simply feeling influenced by a supervisor was not statistically significant (p=0.074). Moreover, when the *degree* of influence was evaluated, no significant association was observed (p=0.103), indicating that those without refresher training were more likely to report stronger supervisor influence (senior faculty or clinical supervisors) compared to those who had received training (Table 3). Influence from pharmaceutical companies did not differ significantly between trained and untrained respondents (p=0.924), and the degree of such influence was similarly nonsignificant (p=0.406). Despite this, prescribing behavior in response to pharmaceutical marketing showed a strong and significant association with training status (p<0.001). Respondents without training were more likely to "always" or "sometimes" prescribe drugs promoted by pharmaceutical representatives, whereas those who had received training demonstrated more cautious prescribing patterns (Table 3). Additionally, reliance on fellow colleagues as a major factor influencing drug choice showed a significant association with training (p=0.019), suggesting that dentists lacking refresher training in drug prescription tended to depend more on peer opinions. Factors such as senior colleagues, self-judgment, pharmaceutical companies, supervisors, and internet resources did not show statistically significant differences between trained and untrained groups. Books as a major influencing factor approached significance (p=0.052), indicating that trained respondents were somewhat more likely to consult textbooks. Overall, the results indicate that formal or refresher training in drug prescription enhances independent decision-making, reduces reliance on non-evidence-based sources, and is associated with more cautious prescribing behavior in response to pharmaceutical promotion (Table 3).

Table 3: Influencing factors and their comparison between those who received refresher training and those who did not

Category	n (%)	Received training *(Yes)*	No training *(No)*	χ^2	P-Value
Supervisor					
Yes	280 (93.3)	194 (64.7)	86 (28.6)	3.19	0.074
No	20 (6.7)	10 (3.3)	10 (3.3)		
Degree of influence by supervisor					
High/ Moderate Influence	261 (87.0)	181 (60.3)	80 (26.7)	1.96	0.181
Low/No influence	39 (13.0)	23 (7.7)	16 (5.3)		
harmaceutical companies					
Yes	98 (32.7)	67 (22.3)	31 (10.3)	0.009	0.924
No	202 (67.3)	137 (45.7)	65 (21.6)		
Degree of influence by pharmaceutical companies					
Influenced	93 (31.0)	58 (19.3)	35 (11.7)	1.67	0.202
Low/No influence	207 (69.0)	146 (48.7)	61 (20.3)		
Pharma representative					
Frequently influenced	191 (63.7)	146 (48.7)	45 (15.0)	**17.20**	**<0.001**
Rarely/ Never influenced	109 (36.3)	58 (19.3)	51 (17.0)		
Fellow colleagues					
Yes	109 (36.3)	65 (21.7)	44 (14.7)	**5.51**	**0.019**
No	191 (63.7)	139 (46.3)	52 (17.3)		
Senior colleagues					
Yes	207 (69.0)	135 (45.0)	72 (24.0)	2.38	0.123
No	93 (31.0)	69 (23.0)	24 (8.0)		
Self-judgment					
Yes	178 (59.3)	118 (39.3)	60 (20.0)	0.587	0.444
No	122 (40.7)	86 (28.7)	36 (12.0)		
Clinical Supervisor					
Yes	215 (71.7)	147 (49.0)	68 (22.7)	0.048	0.826
No	85 (28.3)	57 (19.0)	28 (9.3)		
Internet					
Yes	113 (37.7)	82 (27.3)	31 (10.3)	1.74	0.187
No	187 (62.3)	122 (40.7)	65 (21.7)		
Books					
Yes	88 (29.3)	67 (22.3)	21 (7.0)	3.79	0.052
No	212 (70.7)	137 (45.7)	75 (25.0)		

DISCUSSION

In the present study, 68% dentists reported that they had received a refresher training or refresher course in drug prescription before or

during clinics, while 32% did not, which suggests that most fresh dentists are engaged in some level of prescription training activity. Recent studies suggest that targeted training in drug prescription has reportedly improve prescribing ability and confidence of dentists.[2, 11, 13] A previous study found that targeted education and a prescribing tool among Australian dentists achieved a significant reduction in unneeded antibiotic prescriptions (44.6%) and overall antibiotic use (40.5%).[11] It has been reported that a single training session can have significant improvement.[16] In the current study, one third dentists without refresher course or training before entering clinics indicate a need for repeated training sessions, workshops etc., before prescribing in clinics. The current study reported that 61% of respondents "sometimes" needed supervision when prescribing drugs, with 21% "always" needing supervision with a significant difference between those who had training and those who did not. The dentists with training required less supervision, which aligns with the findings reporting that training improves self-efficacy and need for supervision.[3, 11, 13] A qualitative study on antimicrobial prescription in dental settings identified "beliefs about capabilities" and "access to resources" as key factors on prescribing behavior.[17] The findings of the current study shows that formal training enhances dental knowledge and confidence to prescribe independently. In the current study, more than half of participants (55.7%) felt "somewhat confident" prescribing a medicine independently with a significant difference between trained vs untrained dentists, which was in agreement with the previous literature indicating that targeted education improves competency of prescription writing.[3, 11, 16] A systematic review reported that knowledge gaps correlate with less evidence-based prescribing.[18] The formal or refresher training before entering clinics significantly improves prescribing confidence among dentists, which in turn can promote more autonomous, efficient and focused drug prescription. The study reported that 93.3% participants felt influenced by supervisors, but there was no significant between training status. However, untrained dentists were more likely to be influenced when it comes to the extent of influence. Previous studies on dental and medical prescribing report that peer norms, hierarchical influence, and organizational expectations affect decision-making.[19] Therefore, supervisory influence a persuasive factor, but receiving formal training can reduce the extent of that influence.[3, 20] This study showed no significant difference between trained and untrained dentists in terms of being influenced except when it comes to pharma representatives and fellow colleagues with untrained respondents more likely to prescribe such promoted drugs. These findings were consistent with the previous literature reporting that pharmaceutical representatives are positively associated with increased prescription of the products of that company deviating from evidence based choices.[21, 22] Moreover, in this study, the fellow colleagues were a major influencing factor in drug prescription and it was significantly reported in untrained dentists. Other factor like senior colleagues, self-judgment, supervisors, and internet resources did not show significant differences. Consulting books showed significance difference with trained dentists more likely to consult textbooks. These findings were in agreement with the previous literature showing textbook learning as influencing factors, however, very limited data is available regarding peer influence in drug prescription.[23, 24] The significant differences between dentists who had refresher courses or training in prescription and those who did not, suggest that standardized education in drug prescription should be integrated into undergraduate dental curricula during clinic al years and reinforced through continuous professional development at level of house job and final year where they actually and initially have to write prescriptions. Moreover, mentorship and clinical leadership need to shift toward promoting critical thinking and independent decision making rather than directive behavior.

CONCLUSION

Dental surgeons who received refresher training/courses on drug prescription were significantly less dependent on supervision during clinics, exhibited higher confidence in independently prescribing medications, and showed lower pharmaceutical promotional influence. These findings highlight the value of refresher trainings and workshops, continuing professional development and institutional support especially in clinical years (final year

and house job) in strengthening rational prescribing in dental clinics.

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CONFLICT OF INTEREST

None

AUTHOR'S CONTRIBUTION

HH: Conception and design
SF: Analysis and interpretation of the data
AS: Critical revision of the article for important intellectual content
MH: Collection and assembly of data, Data analysis,
SUK: Critical revision of the manuscript
SH: Data curation

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Original Article

EVALUATION OF SAFETY PROFILE OF *ALPINIA OFFICINARUM* AND *HYMENOCRATER SESSILIFOLIUS* BY ACUTE TOXICITY STUDY IN ALBINO RATS

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Abstract:

Background: *Hymenocrater sessilifolius* and *Alpinia officinarum* extracts have known for their folkloric uses but no potential toxicity has been described yet. This project was aimed to find the safe dose range and biological response of both extracts in rats by analyzing hematological parameters, liver and renal function tests and histopathological study.

Material and Methods: *Hymenocrater sessilifolius* and *Alpinia officinarum* extracts were administered to albino rats orally. The sighting study was carried out with following doses of plant extract 5, 50, 300 and 2000 (mg/kg) of body weight. Furthermore, the highest dose, 2000 mg/kg body weight was selected for the main test of the acute oral toxicity experiment. Three groups (control group and two plants treated group) each having 5 rats were studied. After administration of (2000 mg/kg) to the rats, general behavior, untoward action, and death rates were checked 2 weeks. Blood was collected for hematological, liver and renal function tests and histological necroscopy after sacrificing the plants treated and the control group of rats. Data was statistically analyzed by Graph Pad Prism using one-way ANOVA, and for comparison Bonferroni was employed.

Results: Results showed no significant alterations in hematological, liver and renal function tests when compared against the control group. The vital organs did not reveal any gross and histological necroscopy.

Conclusions: *Hymenocrater sessilifolius* extract and *Alpinia officinarum* extract did not show any toxicological effects. However, sub-acute and chronic toxicity studies will provide the complete profiles of their safety.

Keywords: Acute toxicity, Albino Rats, *Hymenocrater sessilifolius* extract, *Alpinia officinarum*

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INTRODUCTION

One of the components of complementary and alternative medicines is herbal medicine and it is gaining privilege across the globe. It is generally considered that treatment with plants is natural and safe. Nevertheless, when natural remedies are not taken in correct manner, not only failure of treatment is experienced but hazardous results are also observed.[1] However, , in many areas around the world herbal plants are considered non-toxic and relatively safe. People using natural remedies from these areas have common belief that herbal treatment has less adverse effects actions as compared to synthetic medicines. However, the common belief that herbal treatment is free from all side effects is not completely true.[2] In fact, the administration of these enriched medicinal plants for prolonged periods will be a big problem for patients. Thus, this study is of utmost importance to assure the safety profile

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of valuable medicinal plants that are used traditionally. The family Lamiaceae; genus Hymenocrater; consists of almost 21 species. The only specie present in Pakistan is *Hymenocrater sessilifolius* (HS). *H. sessilifolius* mainly grows in Quetta. Herbs of genus Hymenocrater are taken as sedative, anti-inflammatory, antiallergy,[3] against bacterial infection[4] and fungal infection and as antioxidant agents.[4,5] However, HS (voucher no. GC.Herb.Bot.3691) is taken by residents for the treatment of cardiovascular disorder, gastrointestinal disorder, respiratory issues and urinary tract related problems. The major active chemical constituents of HS are aromatic oil and flavonoids.[6,7] HS is an ethno-medicinal herb that Iranians have used in the past to improve cardiac efficiency.[8] *Alpinia officinarum* (AO) grows in China and it is a pungent plant while its rhizome has an aromatic constituents whereas in Europe, its rhizomes have been added in foods as condiments for over thousands of years.[9] In traditional Chinese and Ayurvedic medicines, it has also been used for medicinal purpose for better functioning of stomach, pain relief and as an antiemetic.[10] This herb majorly exerts its effect on alimentary canal and its accessory organs such as stomach and spleen. Furthermore, it is also used for the treatment of gastric pain, cold, for revitalizing the blood circulation system and for decreasing swelling.[11] Although pharmacological effects of HS extract and AO extracts are beneficial and have been used by local people for prolonged period but a comprehensive scientific information on their toxicity potential is not available yet. Therefore, the objective of the acute toxicity study involved the safety evaluation of plant extracts, determination of their dose and finding particular untoward actions of these plant extracts in albino rats.

MATERIAL AND METHODS

Extract was prepared from aerial parts of *Hymenocrater sessilifolius* Benth (HS) (Sursandh) (20kg) which was purchased from Plant market in Quetta, Balochistan and a voucher of the specimen (GC.Herb.Bot.3691) was deposited. The whole plant of HS was shade dried and grounded into powder form and soaked in methanol: water (70:30) for 3 days. The mixture was filtered by means of a muslin cloth and afterwards with the help of Whatman filterpaper (qualitative grade 1). This procedure was performed two more times; then the filtrate was gathered and subjected to rotary evaporator (at 35 to 40ºC under reduced pressure of –760 mmHg), that gave a viscous brown colored material, called as crude extract of HS and its yield was 14.8%. The solubilization of HS crude extract was poor in water so it was suspended in carboxymethylcellulose sodium (CMC-Na) (1%).[12]*Alpinia officinarum* (AO) extract was purchased from Salus Company (China). AO with batch number 180720 was catered with small portion of extract along with analytical report to Pharmacy Department of Government College University, Faisalabad (GCUF), Pakistan. The experimental procedures involving animals were approved by the Institutional Review Board (IRB 761) and performed in compliance with relevant ethical and institutional guidelines. This 14 days pre-clinal study that was performed in GCUF by housing rats at temperature-controlled environment (23±2 ºC) and exposed to 12/12 hours of light/ dark cycle each 24-hour period. The rats were fed with standard laboratory rat food pellets and water ad libitum. Animals selected for study were 10-week-old and weight ranging from 130g to 170g. Being most sensitive gender, the female albino rats were selected to check the response of treatment.[13,14] Rats having any sign and symptoms of disease, pregnancy, lactating rats, animal with prior exposure to any drug or plant extract within last 30 days were excluded from the study. Rats were deprived of food 3 hour prior to dosing but water was allowed. After the completion of fasting period, rats were weighed and plants' extracts were given orally as single dose of 5, 50, 300 and 2000 (mg/kg) as preliminary test when it was observed that all rats survived then main experiment was conducted with dose of 2000mg/kg. Control group, HS (2000mg/kg) treated group and AO

(2000mg/kg) treated group were consisting of 5 rats per group. The volume for the extract administered was 1ml/kg body weight (BW) of the rats. The randomized study was chosen to avoid biasness of healthier and heavier rats or on the basis of ages of rats. During the first 24 h, after the administration of dose, all rats were observed individually at intervals of 30 min, for first 4 hours the rats were attended with particular care, and after then observed them daily, for a total of 14 days while symptoms of sickness, health or behavioral alterations were done twice a day. According to Organization for Economic Co-operation and Development (OECD) guidelines for Testing of Chemicals number 420 (OECD, 2001), acute oral toxicity study was performed which is an *in vivo* toxicity evaluation in rats. Following monitoring must be done in response to treatment, including deaths, moribund, sickness, alteration in skin, fur, eyes, mucus membranes, behavioral manner and tremors. Weekly observed the weight of each rat and the difference of the BW at the start of study and on 14th day of study was recorded. The quantity of food (200g) and water 200ml in the bottle that was sufficient for a week, was kept in the food tray and quantity of food and water remained were calculated at the end of the week to get the quantity of consumed food and water. At the end of study (14th day of experiment), under the effect of chloroform anesthesia, blood was collected via cardiac puncture before the autopsy. The blood was collected in vacutainer tube without EDTA for serum collection to perform the evaluation of hematological, liver function test (LFT) and renal function test (RFT). The hematological parameters that were measured included erythrocyte, leukocyte, platelets, hemoglobin, hematocrit (HCT), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), lymphocyte %, and mean cell volume (MCV). For LFTs, the parameters were alkaline phosphatase (ALP), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) while the RFT was based on the following parameters, urea and uric acid. Gross autopsy study was performed to see any modification in organ such as aorta, heart, liver, stomach and kidney. For histopathological evaluation, slices of each organ (aorta, heart and kidney) were fixed in buffered solution of formalin (10%) for 24 hours. The organs of rat were exposed to different concentrations of alcohol including absolute alcohol then the tissue was embedded in molten paraffin wax that became semi-solid block of paraffin wax on cooling. This block of paraffin having embedded tissue was mounted on rotary microtome to have section cutting of 4 µm thickness. The section cuttings obtained were shifted carefully to water bath and place in oven at 58 ° for overnight. The slides were then stained by using histological stains (hematoxylin & eosin). Xylene was added to avoid presence of bubbles and thereafter covered with cover slips. The prepared slides were placed in light microscope to observe any anomaly or structural variation in the tissue.

GraphPad Prism7.0 software was employed for calculation and statistics. All values were presented as mean± standard error of the mean (SEM). The values were statistically analyzed with the help of one- way analysis of variance (ANOVA) followed by Bonferroni test. Values with $p< 0.05$ were considered statistically significant. The ethical approval of this study was taken from GC University Faisalabad under IRB number 761 dated 09-09-2020.

RESULTS

The visual observation did not show any signs of toxic response in preliminary study performed with the following doses 5, 50, 300 and 2000 mg/kg BW of rats, for both plants HS and AO extracts. As all the rats survived so the main test was carried out with the dose of 2000 mg/kg BW. The acute toxicity study neither showed any death of treated groups of rats nor toxic responses were found throughout the duration of test (14 days). The BW of the plant extracts-treated and untreated rats (Table 1). It was observed that there was gradual rise in BW in all three groups. HS extract treated and AO extract treated groups revealed that the

variation in BW and food and water consumption were not statistically significant when compared against rats of the control group. The utilization of food and consumption of water of the HS extract treated and AO extract treated groups were also not changed significantly in comparison to the rats of control group (Table 1).

Table 1: Body weight (g), utilization of food (g) and usage of water (ml) of control and treated groups of rats given HS extract and AO extract

Groups	Body weight (g)		Utilization of food (g)		Usage of water (ml)	
	Day7	Day 14	Day 7	Day 14	Day 7	Day 14
Control	145.0 ±9.97	156.8 ±11.12	91.2 ±9.18	94.0 ±6.32	246.8 ±7.08	251.4 ±5.22
HS 2000mg/kg	137.6 ±7.27	151.6 ±6.58	90.0 ±6.28	98.0 ±6.12	238.8 ±7.22	244.4 ±8.20
AO 2000mg/kg	158.2 ±14.3	169.6 ±16.45	87.2 ±7.43	92.8 ±6.53	231.0 ±14.74	239.2 ±7.66

Results of n=5 are shown as mean ± standard deviation

Results related to hematology, LFT and RFT are revealed in Table 2. Hematological parameters revealed a non-significant rise in leukocytes, erythrocytes, hemoglobin, HCT and platelets of HS extract and AO extract treated groups as compared to control group of rats. Similarly, insignificant decrease in MCV, MCH and MCHC of HS extract and AO extract when compared to control group and it was found that they were within normal range (control limits). The clinical values of ALP, AST, ALT, urea and uric acid of the HS extract and AO extract treated groups were not remarkably varied when compared against the control (Table 2). All observed parameters were normal at 2000mg/kg of rat. This revealed the both extracts, HS plant and AO plant, did not cause toxicity. Thus, the median lethal dose (LD_{50}) of both extracts exceeds 2000 mg/kg body weight. Therefore, the administration of a single dose of HS extract or AO extract had no adverse effects. Substances having LD50 > 2,000mg are considered as relatively safe according to Globally Harmonised Classification System (GHS). Hence, HS extract or AO extract can be classified as Category 5 according to GHS

Table 2: Hematological values of control and treated rats with HS extract and AO extract

Parameters of hematology	Control	HS extract (2000mg/kg)	AO extract (2000mg/kg)
Leukocyte	4.04±1.25	4.14±1.04	4.44±1.04
Hemoglobin	13.58±0.51	14.22±0.68	14.60±0.57
Erythrocyte	6.58±0.69	7.50±0.43	7.97±0.44
Hematocrit	35.72±3.17	39.66±4.35	43.78±4.14
MCV	65.47±4.44	62.29±2.49	57.02±2.26
MCH	26.22±0.97	25.44±1.27	22.57±2.72
MCHC	37.74±1.96	34.36±1.03	33.29±2.61
Platelets	1133.56 ±247.80	1162.46 ±261.98	1179.27 ±271.48
Values of liver profile and renal profile of control and rats treated with HS extract and AO extract			
Serum analysis	**Control**	**HS extract (2000mg/kg)**	**AO extract (2000mg/kg)**
Liver profile			
ALP (U/L)	281.70 ±32.60	297.85 ±41.88	304.00 ±20.78
AST (U/L)	163.27± 28.47	168.23 ±23.98	174.87 ±9.62
ALT (U/L)	52.64 ±5.98	59.18 ±4.60	65.18 ±7.13
Renal profile			
Urea (mmol/L)	5.23 ±1.18	6.38 ±0.90	7.16 ±1.16
Uric acid (umol/L)	144.35 ±25.32	152.23 ±28.96	166.30 ±19.33

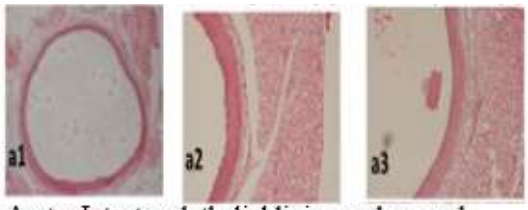
Results are showed as mean ± standard deviation (n = 5)

MCV – Mean corpuscular volume
MCH – Mean corpuscular hemoglobin
MCHC – Mean corpuscular hemoglobin concentration

No physical signs of toxicity have been observed during the study period in rats of HS treated group and AO treated group.

Gross study of various organs inside the body showed normal texture and no apparent sign of abnormality. The aorta sections from rats treated with HS extract and AO extract showed normal histological architecture, with intact endothelial lining and no signs of inflammation, necrosis, or vascular damage (Figure 1). The tunica intima, media, and adventitia layers were well-preserved, indicating no adverse effects of the extract on aortic tissue. The cardiomyocytes appeared healthy, with no signs of degeneration or vacuolization, indicating that HS extract and AO extract did not induce cardiac toxicity in treated rats (Figure 1). Renal histopathology showed preserved glomerular and tubular structure, with no signs of tubular necrosis,

inflammation, or glomerular damage (Figure 1). The renal corpuscles and tubules appeared normal, indicating that HS extract and AO extract did not cause nephrotoxicity in treated rats. Thus, no significant treatment related histopathological abnormality was noted in internal organs such as aorta, heart and kidney.



Aorta: Intact endothelial lining and normal wall architecture.

Heart: Normal cardiac muscle fibers with no signs of necrosis or inflammation.

Kidney: Preserved renal structure with intact glomeruli and tubules, indicating normal histology.

Figure 1. Representative photomicrographs of hematoxylin and eosin-stained rat organ sections. (1) Aorta: Intact endothelial lining and normal wall architecture. (2) Heart: Normal cardiac muscle fibers with no signs of necrosis or inflammation. (3) Kidney: Preserved renal structure with intact glomeruli and tubules, indicating normal histology.

DISCUSSION

As mentioned before, HS extract or AO extract have traditional uses so are used by locals as decoction or spices as well. Although many studies have been carried out on AO extract and very few studies have been performed on HS extract, there is a huge study gap for their toxicity safety profile. This study showed that all groups of animals remained alive in acute toxicity study performed with dose of 2000mg/kg on HS extract or AO extract. According to GHS classification of toxic substances, HS extract or AO extract with oral LD_{50} ranging between 2000–5000 (mg/kg BW) have relatively low toxicity.[15] Both extracts have no effect on body weight and utilization of food and water of extracts treated groups when compared to control group. The rise in BW of all three groups is nominal and normal supported by Halim *et al*.[16] Normally, on exposure of toxic material there is reduction in the body weight which is a sensitive index of toxicity. Variations in BW is indicator of adverse action of medicine or chemical substance. This indicator becomes significant when the reduction of body weight is 10% from initial value.[17] This rise in BW is directly proportional to increase in consumption of food and water. Blood parameters gives the idea about the response of human body to trauma, wounds, inflammation and starvation. In this study, the doses of both extracts did not affect differentiation of leukocytes so non-significant variation of number of leukocytes was found when control group was compared against HS-extract and AO-extract. The mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, hemoglobin, hematocrit and erythrocytes are observed as they are important parameters to evaluate anemia[18,19] and in this study, data indicate that HS- or AO- extract do not cause anemia. Though the blood parameters were high in HS- or AO- extract treated groups but it was insignificant variation as compared to control group of rats. This rise may be due to the synthesis of growth factors.[20] Changes in serological and biochemical parameters are important to estimate effect of toxic substance.[21] Toxic effects of xenobiotics on liver and kidney are assessed by liver function test and renal function test as both organs are responsible for the metabolism and excretion of

xenobiotics.[22] The most frequently studied liver enzymes AST, ALT and ALP showed insignificant variation when HS extract- or AO extract – treated groups were compared to control and showed no significant variations between treated and control groups supported by study of Balaji and Ganesan.[23] The urinary system is sensitive to xenobiotics like medicines or active constituents of ethnomedicinal plants which may result in kidney failure.[24] Insignificant variation in the amount of urea and uric acid suggested no kidney injury occurred in HS extract- or AO extract – treated groups. No gross lesions were found in the aorta, heart and kidney after the extract was given for 14 days supported by study of Akintimehin *et al*.[25]

CONCLUSION

Hymenocrater sessilifolius extract and *Alpinia officinarum* extract did not show any toxicological effects. However, sub-acute and chronic toxicity studies will provide the complete profiles of their safety.

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CONFLICT OF INTEREST

None

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None

AUTHOR'S CONTRIBUTION

FJ: Performed experiment, writing the manuscript, statistical analysis,
SFF: Experimental planning and statistical evaluation, critical evaluation of manuscript,
KS: Statistical evaluation, layout of manuscript,
AS: Data evaluation, editorial assessment of Manuscript

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Original Article

EMOTIONAL INTELLIGENCE AS A PREDICTOR OF ACADEMIC STRESS AND BURNOUT AMONG MEDICAL STUDENTS

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Abstract

Background: Burnout among medical students is an alarming issue worldwide. It can be manifested as depersonalization, cynicism and reduced personal and professional efficacy. It contributes in deterioration of quality of life, mood disorders, reduced professionalism, poorer academic performance and lower empathy and the chances of burnout. The objective of this study was to examine the roles of emotional intelligence and academic stress in influencing and developing burnout in undergraduate medical students.

Materials and Methods: This study has a cross-sectional research design. Convenience sampling was used to recruit 270 medical students from a private medical college. Brief Emotional Intelligence Scale (BEIS-10), Academic Stress Scale & Burnout Assessment Tool for Students (BAT-S) were used for data collection. Person correlation analysis, regression analysis were carried out using SPSS version 25.

Results: Burnout had a significant positive correlation with academic stress ($r=0.52$, $p<.001$) and significantly negatively correlated with emotional intelligence ($r=-0.41$, $p<.001$). Academic stress was negatively correlated to emotional intelligence ($r=-0.28$, $p<.001$). Increased academic stress predicted higher burnout ($\beta = 0.47$, $p < .001$), while increased emotional intelligence predicted lower burnout ($\beta = –0.33$, $p < 0.001$).

Conclusion: Greater academic stress increases the susceptibility of burnout, but higher emotional intelligence (EI) decreases its likelihood among medical students. These results highlight critical need of emotional intelligence training, stress management training and curricula redesign to promote academic growth and overall well-being of medical students.

Keywords: Burnout, Stress, Academics, Intelligence, Medical students

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INTRODUCTION

Burnout among medical students is an alarming issue worldwide. Recent evidence shows that 37.2% of medical students experience burnout during medical school. It manifests as depersonalization, cynicism and reduced personal and professional efficacy.[1] This prevalence has even approached to 50% especially in those students who are under some sort of perceived stress.[2] Burnout is not just feeling tired, it contributes in deterioration of quality of life, mood disorders, reduced professionalism, poor academic performance and lower empathy.[3] Given its consequences, it is necessary to find out factors contributing towards its development. One of the strongest contributors in development of burnout in medical students is academic stress. Recent studies have shown a positive relationship between academic stress and burnout in students. In a recent Malaysian study, it was found out that academic stress, when combined with psychological distress has direct relationship with the development of burnout in

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students.[4] Academic stress in medical students contributes to burnout by increasing fatigue, stress, inefficiency and sleep problems. It is often linked to high workload and emotional demands of the curriculum.[5] A recent Pakistani study found that private medical college students reported more academic stress and burnout than public medical college students.[6] Emotional intelligence (EI) is the ability to perceive, understand, manage and use emotions effectively. It is extensively studied as a positive and protective individual personality trait.[4] EI helps students manage their emotions to deal with environmental challenges and the high emotional demands of medical curriculum, thereby reducing the chances of burnout. It was found that increase in one unit of EI led to decrease in 12 units of burnout.[7] It can be said that higher EI can contribute to better coping against external stressors.[8] Studies show that improving EI may prevent burnout in students.[9] However, despite all these studies there is still a gap as EI and academic stress have been either separately linked to burnout or they have been studied as mediator or moderators. Secondly the cultural, curricular and institutional support context matters. They may interfere in how these associations play out. Given the high prevalence of burnout and its severe negative effects, it is critical to find out what increases burnout (academic stress) and what protects medical students against it (emotional intelligence). Therefore, this study aimed to examine the roles of emotional intelligence and academic stress in influencing and developing burnout in undergraduate medical students. It could help inform curricular redesign, regular EI- trainings and stress management trainings for students in medical schools.

MATERIALS AND METHODS

This was a cross-sectional correlational study conducted to examine the role of academic stress and emotional intelligence in the development of burnout in medical students. IRB No. IRB2024/165, dated 02 September 2024. Convenience sampling was used and 270 students that were currently enrolled in a private medical college undergraduate program were recruited in this study. Brief Emotional Intelligence Scale (BEIS-10), Academic Stress Scale & Burnout Assessment Tool for Students (BAT-S) were used for data collection. Socio-demographic information like age. Gender, year of study was also recorded. Incomplete or partially filled questionnaires were discarded. Analysis was run on a total of 250 participants. Person correlation analysis, regression analysis was carried out using SPSS version 25.

RESULTS

Data from 250 students from medical students across all 5 years was analyzed. Mean age in years was 21.3 ± 1.7 years.

Table 1. Demographic Characteristics of Participants (N=250)

Variables	Frequency (n)	Percentage (%)
Gender		
Male	105	42
Female	145	58
Year of Study		
1st Year	50	20
2nd Year	45	18
3rd Year	55	22
4th Year	50	20
5th Year	50	20

145 were female 58%, and 105 were male 42%. Descriptive statistics showed moderate burnout, moderate to high academic stress and moderate emotional intelligence.

Table 2. Pearson Correlation between study variables (N=250)

Variables	1	2	M	SD
Burnout (BAT-S)	-	-	2.87	0.64
Academic Stress Scale (ASS)	.52***	-	3.24	0.59
Emotional Intelligence (BEIS-10)	-.41***	-.28***	3.61	0.54

Analysis revealed that burnout had a significant positive correlation with academic stress (r=0.52, p<.001) and was significantly negatively correlated with emotional intelligence (r=-0.41, p<.001). Academic stress was negatively correlated to emotional intelligence (r=-.028, p<.001).

Table 3. Multiple Regression Analysis Predicting Burnout

Predictor	B	SE B	β	t	p
Constant	1.02	.28		3.64	
Academic Stress	.49	.07	.47	7.02	0.52
Emotional Intelligence	-0.38	.08	-0.33	-4.75	0.41
Gender	.09	.10	.05	.90	0.37
Year of Study	-.04	.03	-.07	-1.25	0.21

R^2= .36, F (4, 245), p <.001

Multiple regression analysis revealed that both emotional intelligence and academic stress were significant predictors of burnout, with academic stress being a better predictor. The overall model was significant ($F(3, 246) = 45.27$, $p < .001$, $R^2 = 0.36$), explaining 36% of the variance in burnout scores. Increased academic stress predicted higher burnout ($\beta = .47$, $p < .001$), while increased emotional intelligence predicted lower burnout ($\beta = –0.33$, $p < .001$) when the effects of gender and year of study were controlled for.

DISCUSSION

The results indicate that while both emotional intelligence and academic stress had a significant impact on burnout in medical students, academic stress was the stronger predictor. Higher emotional intelligence was reported in students with lower burnout, showing it to have a potential protective function. Neither gender nor year of study significantly affected burnout in this sample. In line with previous research, results showed that academic stress was positively correlated with burnout, and negative with emotional intelligence. These variables, collectively, explained about 36% of the burnout score variance, indicating their strong contribution to defining the psychological health of medical students. The high positive correlation between academic stress and burnout agrees with previous research that has shown that the rigors of medical training lead to emotional exhaustion and decreased academic effectiveness.[10,11] Academic stress has been identified as the most stable predictor of burnout among Asian medical students. The current findings thus affirm the imperative for stress management strategies and curriculum reform to foster a more healthful academic climate.[4, 16] In contrast, emotional intelligence (EI) showed a buffer effect against burnout. Those with higher EI scores reported lower levels of burnout, implying that emotional self-awareness, empathy, and good emotional regulation could protect against the effects of academic difficulties. This finding replicates earlier findings that EI increases resilience and coping capacity for health professional students.[12, 13] Emotional intelligence allows students to interpret academic failure positively and handle interpersonal stressors during training. These findings reinforce the argument that EI is not an individual trait but a learnable ability that can lower the risk of burnout when incorporated into curricula in medicine.[14, 15, 17] Together, these results highlight the need to address risk (academic stress) and protective (emotional intelligence) factors alike during medical education. Emotional intelligence training, peer support groups, and counseling services should be considered by institutions for integration into education in order to enable students to develop effective coping strategies. Faculty mentorship and pacing of curriculum may also mitigate undue academic pressure.

CONCLUSION

It can be concluded that greater academic stress increases the susceptibility of burnout, but higher emotional intelligence (EI) decreases its

likelihood among medical students. These results highlight critical need of emotional intelligence training, stress management training and curricula redesign to promote academic growth and over all well-being of medical students.

LIMITATIONS

The study's cross-sectional research design limits causal association. Moreover, all measures were self-reported and there could be a chance of potential biasness.

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None

CONFLICT OF INTEREST

Authors reported no conflict of interest.

AUTHORS' CONTRIBUTION

MT: conceived the study idea, designed the research framework, and prepared the initial draft of the manuscript.

KJ: supervised the study, provided critical revisions, and approved the final version.

JT: contributed to data collection and statistical analysis.

HS: assisted in literature review and interpretation of results.

ASB: helped in data entry, formatting, and reference management. All authors read and approved the final manuscript.

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Original Article

GLYCEMIC INDEX AND POSTPRANDIAL GLUCOSE RESPONSE OF WHOLE WHEAT MUFFINS PREPARED WITH DIFFERENT SWEETENERS IN YOUNG ADULTS

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Abstract

Background: As global diabetes cases are on rise, interest in low-glycemic food sources is growing. Despite existing knowledge on coconut palm sugar's general glycemic advantages, its metabolic impact and consumer acceptance in widely consumed baked products like muffins remain understudied. Objective of this study was to examine the glycemic effect of coconut palm sugar (CPS) versus refined white sugar in whole wheat muffins by providing in-vivo data of both sugars, a critical step towards developing healthier bakery options.

Materials and Methods: Twenty healthy volunteers from different BMI groups received both coconut palm sugar and refined sugar muffins in randomized crossover manner. Fasting and 45, 90, and 120 minutes post-prandial blood glucose was measured.

Results: Coconut palm sugar muffins had a lower overall glycemic index (GI = 49.61) compared to refined sugar muffins (glycemic index = 70.37), especially in participants with normal BMI ($p < 0.05$). While inconsistent responses were observed in the underweight group, overall coconut palm sugar muffins produced lower peak glucose and recovery to baseline values.

Conclusion: The results confirm coconut palm sugar as a potential natural sweetener for diabetic bakery products. Future research should explore long-term glycemic effects of coconut palm sugar in larger, more diverse populations and optimize its use across a broader range of bakery products to further establish its suitability as a healthier sweetener alternative.

Keywords: Glycemic Response, Coconut Palm Sugar, Whole Wheat Muffins, Table Sugar, Young Adults, Sugar Alternatives, Diabetes Mellitus.

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INTRODUCTION

The role of diet in the prevention and management of chronic diseases, as diabetes mellitus and obesity, is very crucial. According to the International Diabetes Federation (IDF) Diabetes Atlas, about 11.1% of the adult population (20-79 years) has diabetes, with over 4 in 10 unaware that they have it.[1] IDF estimates that one in eight adults or 853 million people would have diabetes by 2050, a 46% rise. As per the World Health Organization (WHO), physical inactivity and unhealthy eating habits are among the most important risk factors for these conditions which can be modified. The glycemic index (GI) has emerged as a valued tool for assessing how rapidly the carbohydrate-containing foods show effect on postprandial blood glucose levels in comparison to a reference food (commonly glucose or white bread) in the same

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individual. Low-GI foods encourage more gradual rises and better glycemic management thus using coconut palm sugar instead of refined sugar in muffins can result in a lower-glycemic index, healthier version of a popular snack,[2] whereas high-GI foods i.e. GI > or = 70 cause fast spikes in blood glucose and increases risk of diabetic complications.[2,3] Thus, glycemic index can help diabetic patients improve their health outcomes by making better food choices.

Muffins are popular bakery item consumed globally, traditionally made with refined white sugar, which has a high GI and is inappropriate for individuals requiring strict glucose control. To address this, multiple researchers have explored natural sweeteners with low GI. Honey and molasses have medium glycemic index while coconut palm sugar, sorbitol and mannitol have low glycemic index.

Coconut palm sugar, a natural sweetener is often promoted as having a lower glycemic index (35–54) relative to cane sugar (commonly 60–70). Coconut palm sugar is created by evaporating coconut sap so variations occur in heating duration, additives (like lime to prevent fermentation), and degree of crystallization, all of which alter sugar composition and impact glycemic index. This lower glycemic index of coconut palm sugar is partly due to its inulin content (approx. 4.7 g/100 g), a soluble fiber known to delay glucose absorption. Its fiber content varies depending on the source of sap (e.g., hygienic vs. fermented neera), which influences glycemic index.[4] Moreover, coconut palm sugar preserves trace minerals (potassium, magnesium, iron, zinc) and antioxidants like polyphenols due to minimal processing. However, compositionally, coconut palm sugar is similar to refined sugar as the former consists of approximately 89% sucrose and 3% of reducing sugars (glucose and fructose) each, whereas the latter is nearly 94% sucrose.[5] Therefore, any potential glycemic index advantage must be interpreted cautiously, as there is only a minor difference, when incorporated into complex food matrices like muffins. According to certain reviews and in vitro research, coconut palm sugar lowers the estimated GI and starch digestibility of wheat based meals, suggesting its use as a functional sweetener in baked products.[6]

Despite promising claims, the effects of coconut palm sugar on glycemic response in muffins remains unclear. Most of researches have been done in vitro, which do not accurately mimic the dynamics of human digestion, including hormonal reactions and metabolic variations, therefore do not predict real blood glucose impact accurately.[7] Limited human trials reveal inconsistent results; for instance, some studies found that utilizing coconut palm sugar decreased GI values, while other studies found no apparent change when coconut jaggery is compared to cane sugar (GI: 65.19 vs. 60.76), classifying both as moderate GI sweeteners.[8] Furthermore, baking may alter chemical composition and affect the glycemic response of the final product that is why it is unclear whether coconut palm sugar sustains its low-GI qualities in baked products or not.

There seem to be several gaps in the literature regarding coconut palm sugar as a substitute for refined sugar in bakery products. First, controlled human studies evaluating the postprandial glycemic response and glycemic index of coconut palm sugar-based muffins are missing, leaving uncertainty about their actual metabolic impact. Second, influence of BMI categories (underweight, normal, overweight/obese) on glycemic response of CPS-containing baked goods has not been explored. Lastly, despite the fact that CPS is frequently promoted as a healthy sweetener, there is not enough empirical data to support these claims when used in frequently consumed baked goods. Current evidence suggests that coconut palm sugar in muffins may slightly reduce glycemic impact in vitro. However, the actual effect in vivo remains inconclusive. In future, researches should directly measure the glycemic index of coconut palm sugar -based muffins in controlled human studies with appropriate sample size. The objectives of this study were to develop whole-wheat muffins

using coconut palm sugar and compare their postprandial glycemic response and glycemic index with refined sugar muffins across different BMI categories (underweight, normal, overweight/obese) as well as overall. Furthermore, the study aims to estimate whether coconut palm sugar shows its low glycemic index properties when added to muffins and assess its prospective as a healthier alternative for diabetics and health-conscious individuals. The hypothesis is that whole-wheat muffins prepared with coconut palm sugar show a lower glycemic index as well as lower and steadier mean postprandial glycemic response (0–120 min) compared to the muffins sweetened with refined white sugar.

MATERIALS AND METHODS

It was a randomized, experimental in vivo study conducted at the University of Management and Technology, Lahore Pakistan, in June, 2025. RCT registration number RE-069-2024, dated 12-06-2024. The duration of the study was 3 weeks. According to the ISO-26642 and glycemic index studies that have been conducted, sample size must have at least 10 or more subjects, either only males, females or both. A sample size of 20 participants was selected using convenience sampling as per previous studies.[9,10,11] Participants were informed about study protocols; written consent was obtained. Participants were acknowledged for their voluntary participation and time as per research ethics. Participants aged 18-25 years, fasting blood glucose of 80-110 mg/dL, no past medical history, non-smokers, with no dietary restrictions, and those not involved in any kind of sports or athletes were included.

The exclusion criteria was individuals having diabetes or other medical conditions, smokers, fasting blood sugar > 110 mg/dL, history of medications, food allergies or intolerances, and those who had undergone any surgery in the recent past. The muffins were prepared following the technique described with alterations under standardized laboratory conditions to ensure homogeneity. All the ingredients were purchased from local supermarket in Lahore. The mixture contained whole wheat flour (128 g), salt (2 g) milk (100 ml), baking powder (5 g), white sugar (50 g), olive oil (30 ml), and egg (1). The mixture was beaten at low speed for 80 seconds. Another mixture with the same quantities was prepared with coconut palm sugar (50 g) instead of white sugar. The mixtures were then weighed in cups and baked in the preheated oven for 15-20 minutes at 180ºC. The recipe was repeated in order to get the desired yield of muffins. Each serving of muffin contained 25 g of available carbohydrates which resulted in 63 g and 64 g batter of white sugar muffin and coconut palm sugar muffin respectively. The muffins were made on the prior day in the evening and stored at room temperature after cooling. For reference food, glucose solution (27.7 g of glaxose-D in 250 ml water) was used which provided 25 g of available carbohydrates.

The experiment was completed in three sessions. The participants were blinded to the type of test meal. They were given glucose solution and two test meals on separate days. According to the glycemic index methodology and evidenced by multiple researches, 50 or 25g of available carbohydrates can be served in each portion.[14,15] There was a washout period of 2-3 days between sessions. The trial started in the morning at 8:30 AM after 8-12 hours fast overnight. The fasting blood glucose of participants was checked. After that, they consumed the test meal within 10-15 minutes along with 250 ml distilled water. Participants consumed glucose solution, table sugar muffin, and coconut palm sugar muffins in random order. Blood samples of participants were collected at fasting then 45, 90, and 120 minutes postprandial. The physical activity of the participants was kept to minimum and was asked to be seated for most of the time during test period. Blood glucose monitoring was performed with the help of validated Accu-Chek ®Performa glucometer following a standardized finger-prick methodology. Participants warmed their hands to enhance peripheral blood flow before testing. Capillary

blood samples were obtained using sterile lancet puncture, with gentle hand massage. To ensure reliable measurements, the first two blood drops were wiped away to prevent potential contamination, the third drop was analyzed by the glucometer. After recording the blood glucose levels from 0-120 minutes, a curve was constructed for each individual for test samples and reference food.

The incremental area under the curve (IAUC) was geometrically calculated using the trapezoid rule, ignoring the area under the baseline (fasting level of the individual). Glycemic index of the food i.e. the mean glycemic index

for entire sample size, was calculated using the formula:

$$\frac{IAUC\ for\ the\ test\ food}{IAUC\ for\ the\ reference\ food} \times 100$$

A statistical analysis was conducted using SPSS v25. Data and figures were processed in Microsoft Word. IAUC and GI values were calculated using trapezoid method. Data was interpreted as mean ± standard deviation. Pair wise comparisons were done by applying paired t-test. The criteria for significance was a two-tailed $p < 0.05$.

RESULTS

A sample comprising 20 participants was selected, of which 12 were females and 8 were males. The mean age of participants was 21.40 ± 1.64 years. The mean height was 164.30 ± 7.88 cm, while mean weight was 57.40 ± 13.52 kg. The sample consisted of individuals from different BMI categories, of which 2 were underweight, 14 were normal, 4 were overweight/obese, in Table 1. As shown in Table 2, the glycemic index (GI) values of table sugar muffins and coconut palm sugar (CPS) muffins were calculated and compared across BMI groups. In participants with normal BMI (n = 14), the GI of coconut palm sugar muffins (41.0 ± 24.1) was significantly lower than that Among overweight/obese participants (n = 4), no significant difference was found between of table sugar muffins (67.51 ±43.95; $p < 0.05$). coconut palm sugar muffins (5.75 ± 6.18) and table sugar muffins (78.28 ± 85.07; $p > 0.05$). Similarly, in underweight participants (n = 2), no significant difference was observed between coconut palm sugar muffins (197.55 ± 215.60) and table sugar muffins (74.55 ± 55.79; $p > 0.05$). Standard deviations were large in some groups, particularly underweight and overweight/obese indicating high inter-individual variability in glycemic responses.

Table: 1 Demographic of Participants

Gender	Frequency (n)	Percentage (%)
Male	8	40
Female	12	60
Underweight (>18.5)	2	10
Normal (18.5- 24.9)	14	70
Overweight (25-29.9)	3	15
Obese (<30)	1	1

Table: 2 Glycemic index (GI) values and its classification among different BMI categories

Participants	n	Table Sugar Muffin	Coconut Palm Sugar Muffin
Overall response	20	70.37 ± 51.47	49.61 ± 74.91
Normal BMI	14	67.51 ± 43.95	41.0 ± 24.1
Overweight / Obese	4	78.28 ± 85.07	5.75 ± 6.18
Underweight	2	74.55 ± 55.79	197.55 ± 215.60

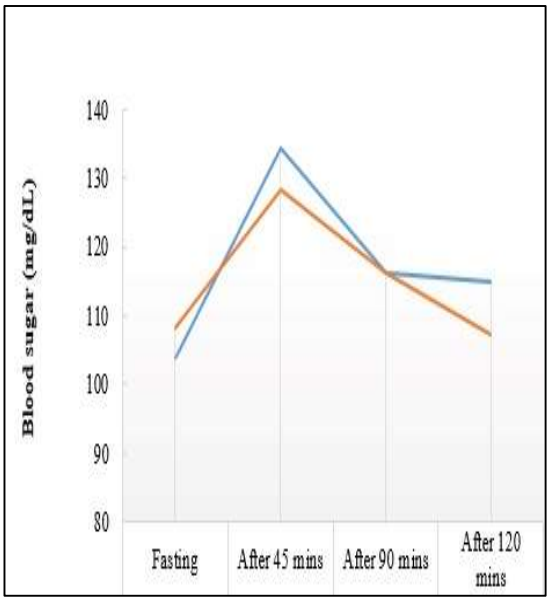

Figure: 1

Figure 1. Illustrates mean postprandial blood glucose (mg/dL) of the entire sample after consuming table sugar vs. coconut palm sugar muffins 0-120 minutes

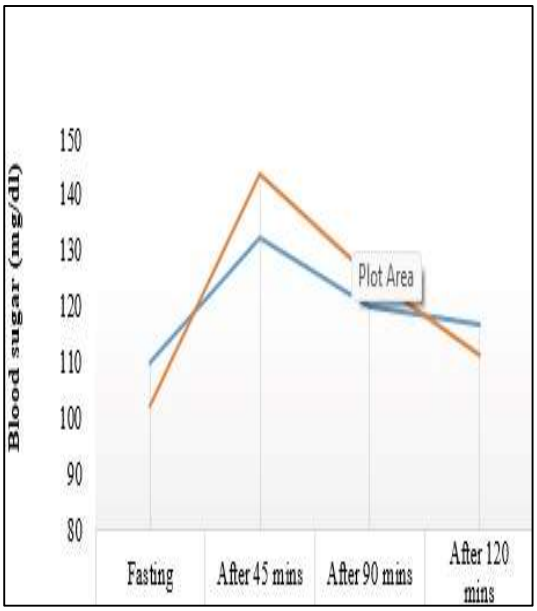

Figure 2

Figure 2. Illustrates mean postprandial blood glucose (mg/dL) of the underweight BMI after consuming table sugar vs. coconut palm sugar muffins from 0-120 minutes. Figure

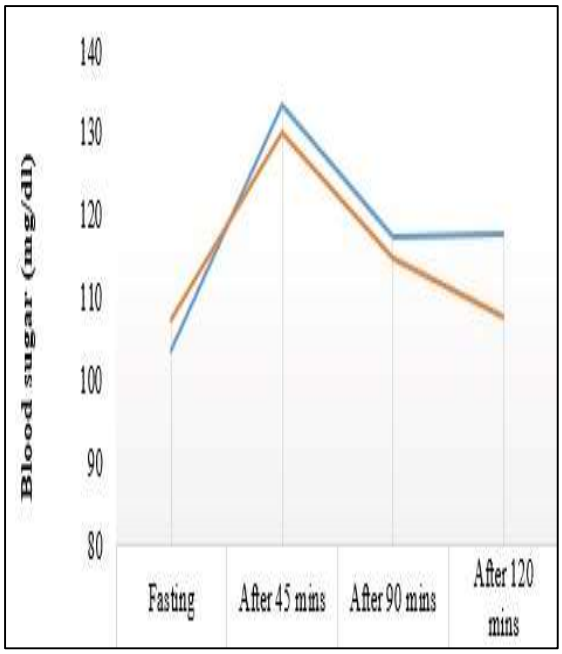

Figure: 3

Figure 3. Illustrates mean postprandial blood glucose (mg/dL) of the normal BMI after consuming table sugar vs. coconut palm sugar muffins 0-120 minutes

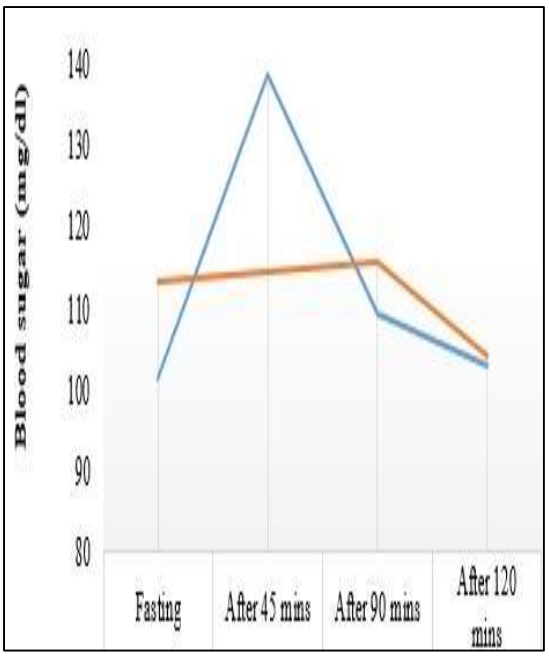

Figure: 4

Figure 4. Illustrates mean postprandial blood glucose (mg/dL) of overweight/obese BMI after consuming table sugar vs. coconut palm sugar muffins 0-120 minutes.

DISCUSSION

The present findings are interpreted within the context of the composite food matrix in which the sweetener was incorporated. Unlike isolated sugar testing, the muffins contained whole wheat flour, fat, and protein, all of which are known to influence gastric emptying and carbohydrate digestion rates. The interaction between sweetener type and the structural properties of a baked product may therefore play a critical role in determining postprandial glycemic behavior. This highlights an important practical consideration: evaluating sweeteners within realistic food systems provides more meaningful dietary insight than testing sugars in isolation, as glycemic response is strongly influenced by mixed food composition, formulation, and processing conditions.[11,12,13] From a translational perspective, the study reflects real-world consumption patterns, as individuals typically consume sugars as part of mixed meals rather than in pure form. Thus, the glycemic behavior observed in this study contributes applicable evidence regarding how sweetener substitution performs under practical dietary conditions Another important aspect of this study is the focus on healthy young adults, a population often overlooked in glycemic research that predominantly targets individuals with diabetes. Early dietary modifications during young adulthood may contribute to long-term metabolic risk reduction, particularly in regions where refined carbohydrate intake is high. By using a randomized crossover design and standardized available carbohydrate portions (25 g), the study minimized inter-individual variability and allowed each participant to serve as their own control, thereby strengthening internal validity. Although the sample size was modest, this controlled experimental framework enhances confidence that observed differences were attributable to sweetener substitution rather than external dietary factors. These findings support the concept that incremental formulation changes in commonly consumed bakery products may serve as feasible preventive strategies within broader nutritional interventions.[12] The overall findings that coconut palm sugar may serve as a lower-glycemic index alternative in baked products align with previous glycemic index and palm sugar comparison studies.[9,10] Coconut palm sugar showed lower glycemic index and moderate post-prandial glucose levels, specifically in normal BMI range individuals, which is consistent with previous in vitro and human studies,[6] which suggest that minimally processed sugars like coconut palm sugar can reduce glycemic response when compared to refined sugars. This characteristic is often attributed to its natural polyphenols and inulin content, which may slow down glucose absorption and contribute to better glycemic control.[4] According to the research by Rayappa,[6] a reduction in in vitro digestibility of starch and estimated glycemic index occurs when substituting cane sugar with coconut palm sugar. Whereas a study by Pathirana et al[8] observed no significant difference in glycemic index between coconut jaggery and cane sugar in human trials, and classified both as moderate glycemic index sweeteners, similar to findings reported in palm sugar glycemic response studies.[10] In our study, there is statistically significant difference in glycemic index seen in the normal BMI group, and exceptionally high glycemic index observed in the underweight group for coconut palm sugar muffins. This coincides with previous research showing variability in glycemic response depending on nutritional formulations, metabolic status, and supplement composition.[13,14,15] This variability highlights the importance of the complex interaction within a food matrix and individual physiological responses. The high standard deviation across all participants also highlights this inconsistency, reinforcing the point that in vitro estimates do not always accurately predict real blood glucose response.[7] The drawback faced while performing the study was that blood glucose response might be affected by individual differences in insulin sensitivity, metabolism, and lifestyle which might alter results.

CONCLUSION

Replacement of refined sugar with coconut palm sugar in whole wheat muffins lowered the glycemic response especially in the individuals with normal BMI indicating an improved postprandial glucose control.

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AUTHORS CONTRIBUTION

AN: Study Concept
SND: Data Analysis
EZ: Interpretation of Data
KA: Manuscript Writing
MF: Review of literature

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CONFLICT OF INTEREST

None

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Original Article

EFFICACY OF NALBUPHINE IN ATTENUATION OF HEMODYNAMIC RESPONSE TO LARYNGOSCOPY AND OROTRACHEAL INTUBATION

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ABSTRACT

Background: Laryngoscopy and orotracheal intubation produce significant hemodynamic responses including hypertension and tachycardia, which may be detrimental in high-risk patients. Nalbuphine, a synthetic opioid with both agonist and antagonist properties, may attenuate these cardiovascular responses. This study aimed to compare the efficacy of nalbuphine versus placebo in controlling mean arterial blood pressure (MAP) changes during laryngoscopy and intubation.

Materials and Methods: This randomized controlled trial was conducted at the Operation Theatres of Hayatabad Medical Complex, Peshawar, from March 2024 to December 2024. A total of 122 American Society of Anaesthesiologists (ASA) grade I patients aged 18-60 years undergoing elective surgery were randomly allocated into two groups. Group A (n=61) received intravenous (IV) saline, while Group B (n=61) received nalbuphine 0.2 mg/kg IV, five minutes before induction with propofol and atracurium. MAP was recorded at baseline, three minutes after drug administration, immediately after intubation, and at one-minute intervals for five minutes post-intubation.

Results: The mean age was 44±12.77 years in Group A and 46±13.12 years in Group B. Group B demonstrated significantly lower MAP (95.17±4.09 mmHg) compared to Group A (98.33±4.18 mmHg) following intubation (p=0.0001). This significant reduction was consistent across all age groups, both genders, weight categories, and ASA classification (p=0.0001 for all stratifications).

Conclusion: Nalbuphine represents a safe and effective option for maintaining hemodynamic stability during airway manipulation.

Keywords: Anaesthesia, Hemodynamic; Intubation: Laryngoscopy; Arterial Pressure; Nalbuphine; Analgesics, Opioid; Premedication.

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INTRODUCTION

Laryngoscopy and intubation are very important steps in general anaesthesia but rank among the most excitatory experiences for the anaesthetic patient.[1] The mechanoreceptor activation of the laryngopharyngeal region leads to a sympathoadrenal response with the subsequent release of catecholamines, causing profound cardio-vasoactive responses that mainly manifest as an increase in blood pressure, heart rate, and cardiac oxygen demand, with potential dangers for a patient with vulnerable cardiac, cerebral, or ocular systems.[2] The severity of the hemodynamic reaction induced by laryngoscopy and intubation differs among individuals, but the reaction reaches its peak in the first 30 to 45 seconds following the procedure and recovers after five to ten minutes.[3,4] However, even such transient periods of instability could induce myocardial ischemia, arrhythmias, cerebrovascular bleeding, and intracranial hypertension in susceptible individuals.[5] In

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view of these considerations, numerous pharmacologic methods have been explored to reduce such stress responses, such as the use of opioids, beta-blockers, alpha-2 agonists, calcium channel blockers, and local anaesthetics.[6] Opioids are extensively investigated for their use in general anaesthesia because of their capacity to abolish the hemodynamic reflex response associated with laryngoscopy and intubation by reducing the outflow of the sympathetic nerves as well as circulating levels of catecholamines.[7] Nalbuphine is a synthetic opioid analgesic compound with Kappa opioid receptor agonist as well as Mu receptor antagonist properties.[8] This combination of pharmacological properties confers several benefits: they produce reliable analgesia with a ceiling effect in respect to pulmonary depression; they have less abuse liability and they produce less CV depression at therapeutic doses.[9] Although fentanyl and other classical mu-opioid agonists have long been used for this, nalbuphine is a promising alternative with fewer side effects.[10] While the effectiveness of nalbuphine has been proven in pre-existing papers for different applications in the field of surgery, its role in blunting intubation-induced changes in the hemodynamic of the patient is still to be explored.[11] Several controversies exist as to the optimal dose and agent of choice to be used among the opioids that provide hemodynamic stability. Although some authors prefer the higher doses or even combinations of the opioids, others stress the need to avoid the side effects of the opioids such as respiratory distress and nausea.[12] Furthermore, the relative effectiveness of other opioids such as nalbuphine compared to the existing methods used in contemporary aesthetic practice is not well understood.[13] Despite the theoretical advantages, the role of nalbuphine in blunting the effects of intubation response has yet to be comprehensively assessed, particularly in Pakistani populations, where ethnic differences in drug pharmacokinetics and conventional baseline values of the subjects' cardiovascular systems might play a vital part in the efficacy of the pharmacologic agent used. In the setting of the Hayatabad Medical Complex and most Pakistani medical institutions, premedication with opioids for healthy ASA I subjects is not a common and systematic approach; hence, the transient response of the cardiovascular system remains self-limiting and well-tolerated. Saline solution as the control agent reflects the true modern ease of practice in the hospital setting. This study aims to be the first systematic appraisal of the efficacy of intravenous nalbuphine, with a total dosing of 0.2 mg/kg for the purpose of stabilizing the cardiovascular system with the onset of intubation procedures among Pakistani subjects.

MATERIALS AND METHODS

The trial was conducted at the Operation Theatre of Hayatabad Medical Complex, Peshawar, Pakistan. The trial had a prospective, randomized controlled design. It was approved by the Institutional Review/ Ethics Committee (Approval No: 2231) on 5th January 2024, and all patients gave their prior written consent before participating in the trial. The trial was carried out for a period of ten months, commencing on the 1st of March 2024, and ending on the 15th of December 2024. This study was also registered at ClinicalTrials.gov (NCT07348159) prior to the finalization of data analysis. The sample size was calculated using the online sample size calculator for the comparison of two independent means, using a 95% confidence interval, and 80% power. Taking hypothetical values for the MAP values at five minutes post-intubation, 96.76 mmHg and 94.82 mmHg, respectively, for the control and intervention groups, with a standard deviation of 3.95 mmHg and 3.66 mmHg, respectively, a total of 122 patients, 61 in each group, were regarded sufficient to demonstrate a statistically significant difference. A consecutive sampling method was used, where all eligible patients were enrolled irrespective of the time of reporting to the operation theatre. Patients comprised males and females 18-60 years of age, graded ASA physical status class I, and were scheduled for elective surgeries requiring tracheal intubation under general anaesthesia. Patients were if the following conditions existed: suspected or known difficult airway anatomy; history of hypertension or administration of antihypertensive medications;

known allergy or hypersensitivity to opioids, including nalbuphine; existing cardiovascular disease, including coronary disease, congestive heart failure, and significant valvular disease; hepatic disease or chronic liver dysfunction; existing renal disease, including chronic kidney disease; pregnancy and breastfeeding; administration of monoamine oxidase inhibitors or other medications having potential interactions; and unwillingness to give full consent. The patients were randomly assigned to one of the two groups through the lottery method. In Group A, the patients acted as the controls and were given 0.9% normal saline (quantity equivalent to that of the test drug), whereas the patients in Group B received nalbuphine 0.2 mg/kg IV. The random allocation was carried out by an independent research assistant who did not involve himself with the patient care or data collection. The drugs for the trial were prepared by the anaesthesia nurse who was not participating in the trial. The hemodynamic variables were collected by the independent observer who was blind to the allocation group. On entering the operation theatre, the hemodynamic variables were recorded as baseline (T0), that is, heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), MAP, and peripheral oxygen saturation (SpO2). Standard ASA monitoring was used for all participants, which included continuous electrocardiography (ECG), non-invasive blood pressure, pulse oximetry, and capnography. Five minutes prior to induction of anaesthesia, IV normal saline as placebo was administered to patients in Group A, and IV nalbuphine 0.2 mg/kg was administered to those in Group B. Preoxygenation was done with 100% oxygen for three minutes. MAP was then recorded three minutes after administration of the study drug (T1). Anaesthesia induction was standardized with propofol 2 mg/kg IV and atracurium 0.5 mg/kg IV for facilitating neuromuscular blockade. During the 90-second period after atracurium injection, patients were manually ventilated with 33% oxygen and 66% nitrous oxide to maintain normocapnia with end-tidal CO_2 of 35 to 40 mmHg. Macintosh laryngoscopy and blind orotracheal intubation were achieved by experienced anaesthetists in 15 seconds. Endotracheal tubes of appropriate sizes were chosen based on patient profile (7.0 to 7.5 mm inner diameter for females and 8.0 to 8.5 mm inner diameter for males). Blood pressure measurements were taken immediately after endotracheal intubation (at T2) and at one-minute intervals for five minutes thereafter as T3, T4, T5, T6, and T7, respectively. All measurements were recorded on a standardized data collection proforma sheet. Anaesthesia management thereafter was achieved with isoflurane and the oxygen-nitrous oxide mixture with further injection of atracurium as required. Any untoward events such as bradycardia with HR< 50 per minute, hypotension with MAP< 60 mmHg, oxygen desaturation with SpO_2< 90% and prolonged periods of apnea were noted and further managed as per protocol and Hospital Standard Procedures respectively. All data were entered and analysed using SPSS version 26.0. Mean and standard deviation were used in representing the quantitative variables age, weight, and MAP. On the other hand, frequency and percent were employed to represent the categorical variables gender and ASA Physical Status. Comparison among the two groups was undertaken using the independent samples t-test while the Chi-square test was employed in the categorical variables. Stratification was employed using the variables age (18-30 years, 31-40 years, 41-50 years, 51-60 years), gender (male, female), weight classes (≤75 kg, >75 kg), and ASA Physical Status. Both the independent samples t-test was employed in comparing the MAP among the two groups. P-value ≤0.05 was considered significant.

RESULTS

The study started with the enrolment of 122 ASA grade I patients. However, the study lost a total of 15 patients (12.3%) because of reasons such as violation of the study protocol

(6 patients), conversion to emergency surgeries (4 patients), problematic intubation procedures (3 patients), and patients revoking the consent for the study (2 patients). Therefore, a total of 107 patients completed the study and were selected for the final analysis: 53 patients belonging to group A (Saline/control group), and the remaining 54 patients belonging to group B (nalbuphine). The flow of participants through the study phases is summarized in Figure 1. The demographic and baseline parameters of the patients were similar and not significantly different between the groups, as depicted in Table 1.

Table 1: Baseline demographic and clinical characteristics

CATEGORY	GROUP A (SALINE) n=53	GROUP B (NALBUPHINE 0.2 MG/KG) n=54	P-VALUE
AGE DISTRIBUTION			
18-30 years	9 (17%)	8 (15%)	0.4127
31-40 years	13 (24%)	14 (26%)	
41-50 years	15 (28%)	15 (28%)	
51-60 years	16 (31%)	17 (31%)	
MEAN±SD	44±12.77 years	46±13.12 years	0.4289
GENDER DISTRIBUTION			
Male	36 (68%)	35 (65%)	0.8541
Female	17 (32%)	19 (35%)	
WEIGHT DISTRIBUTION			
≤75 KG	33 (62%)	32 (59%)	0.8873
>75 KG	20 (38%)	22 (41%)	
MEAN±SD	**75±10.83 KG**	**75±8.37 KG**	**0.9621**

From the primary outcome analysis, there was a statistically significant difference in the results of Mean Arterial Pressure (MAP) between the groups post-laryngoscopy and intubation (see Table 2).

Table 2: Primary outcome - mean arterial pressure after laryngoscopy and intubation overall map (mmHg)

GROUP A (SALINE) N=53	GROUP B (NALBUPHINE 0.2 MG/KG) N=54	MEAN DIFFERENCE	P-VALUE
98.33±4.18	95.17±4.09	3.16	0.0001

In group A (saline/control), the mean value of MAP recorded was 98.33 ± 4.18 mmHg, while in group B (nalbuphine), the significantly lower mean value of 95.17 ± 4.09 mmHg was recorded (p = 0.0001). This makes the difference of 3.16 mmHg in the attenuation of the hemodynamic response achieved with nalbuphine; although this is small and needs careful consideration. The results of subgroup analysis, being stratified for the underlying demographic variable, were consistent across all categories (Table 3).

Table:3 Subgroup analysis of mean arterial pressure by demographic starta

CATEGORY	GROUP A (SALINE) MAP (mmHg)	GROUP B (NALBUPHINE) MAP (mmHg)	P-VALUE
AGE GROUP			
18-30 years (n=17)	98.45±7.59	94.27±3.22	0.0001
31-40 years (n=27)	97.87±4.56	94.53±6.35	0.0011
41-50 years (n=30)	98.33±4.18	95.17±4.09	0.0001
51-60 years (n=33)	99.77±3.22	93.52±2.53	0.0001
GENDER			
Male (n=71)	98.73±3.38	93.51±2.63	0.0001
Female (n=36)	99.75±4.56	94.55±2.48	0.0001
BODY WEIGHT			
≤75 KG (N=65)	98.21±3.51	95.34±4.12	0.0001
>75 KG (N=42)	98.30±4.22	94.31±3.17	0.0001
ASA GRADE			
Grade I (N=107)	98.33±4.18	95.17±4.09	0.0001

For the different age groups, the effect of nalbuphine showed variability. For the 18-30 years age group, the MAP value for Group A was 98.45 ± 7.59 mmHg, while that of Group B was 94.27 ± 3.22 mmHg (p=0.0001). However, the value for Group A had a large standard deviation, making the result unreliable. For the

31-40 years age group, the value was 97.87 ± 4.56 mmHg for Group A, while for Group B, the value was 94.53 ± 6.35 mmHg (p=0.0011). For the 41-50 years age group, the value for Group A was 98.33 ± 4.18 mmHg, while that for Group B was 95.17 ± 4.09 mmHg (p=0.0001). For the 51-60 years age group, the value was 99.77 ± 3.22 mmHg for Group A, while that for Group B was 93.52 ± 2.53 mmHg (p=0.0001). The result of gender analysis revealed that in both male and female subjects, the MAP was reduced by nalbuphine. In the case of the male subjects, the MAP was recorded to be 98.73 ± 3.38 mmHg in Group A and 93.51 ± 2.63 mmHg in Group B (p=0.0001), showing a reduction of 5.22 mmHg. In the case of female subjects, the MAP was recorded to be 99.75 ± 4.56 mmHg in Group A, whereas in Group B it was 94.55 ± 2.48 mmHg (p=0.0001), showing a reduction of 5.20 mmHg. However, it was observed that the reduction was similar between genders. Weight stratification showed variable responses. In patients weighing ≤75 kg, the value of MAP was 98.21±3.51 mmHg in Group A and 95.34±4.12 mmHg in Group B (p=0.0001) for a variation of 2.87 mmHg. In ≥75 kg patients, the value of MAP was 98.30±4.22 mmHg in Group A and 94.31±3.17 mmHg in Group B (p=0.0001) with a variation of 3.99 mmHg. This indicates a greater variation in heavier patients potentially benefiting from nalbuphine dosing according to total body weight. Adverse events were also closely watched throughout the duration of this study (Table. 4).

Table 4: Adverse events during study period

GROUP A (SALINE) n=53	GROUP B (NALBUPHINE) n=54	P-VALUE
MILD BRADYCARDIA (HR 50-55 BPM)		
0 (0%)	3 (5.6%)	0.0862
MILD NAUSEA		
0 (0%)	2 (3.7%)	0.1573
TRANSIENT HYPERTENSION (MAP >110 MMHG)		
1 (1.9%)	0 (0%)	0.3125
TOTAL ADVERSE EVENTS		
1 (1.9%)	5 (9.3%)	0.0951

During intraoperative events, three patients in Group B had transient bradycardia with heart rate of 50-55 bpm, which resolved spontaneously without intervention. Two patients in Group B had mild nausea in the immediate postoperative setting. One patient in Group A had transient hypertension with mean arterial pressure >110mmHg for about 3 minutes following intubation. No severe adverse events in hypotension, respiratory depression that required intervention, or in allergic reactions occurred in both groups. The incidence of adverse events was considerably higher in Group B with 9.3% in comparison with Group A with 1.9% though not significantly different (p=0.0951).

DISCUSSION

This RCT carried out at the Hayatabad Medical Complex, Peshawar, proves that premedication with intravenous nalbuphine 0.2 mg/kg administered five minutes prior to anesthetic induction resulted in a significantly higher reduction in MAP post-laryngoscopy and intubation compared to the saline extension of the envelope alone – the placebo group. The significance of these observations needs to be examined in the context of the Pakistani healthcare system. A difference of 3.16 mmHg in MAP is statistically significant but reflects only a small hemodynamic response. Avenues of great importance are raised regarding the implications of clinical and statistical significance of such a small response, especially regarding patients with ASA grade I classification and adequate CVS reserve to withstand short periods of hypertension without risk of untoward effects.[14,15] Although the sympathoadrenergic response of laryngoscopy and intubation because of the mechanical stimulation of the pharyngal and laryngeal receptors tends to become spontaneous with 5-10 minutes in healthy patients, the implications of a 3 mmHg decrease in MAP and its significances of such a response have become equivocal and even less important in

comparison to the transient nature of the response of intubation.[16] Our results show partial confirmation with other studies regarding opioid premedication during intubation, although there are relevant discrepancies. For instance, a local Pakistani study by Ahsan-ul-Haq and Kazmi similarly demonstrated that nalbuphine 0.2 mg/kg IV effectively prevented marked rises in both heart rate and mean arterial pressure during laryngoscopy and orotracheal intubation in a comparable setting.[17] This supports the efficacy observed in our trial, where nalbuphine achieved a statistically significant (though modestly smaller) MAP reduction of 3.16 mmHg post-intubation. In one study, similar efficacy was shown for nalbuphine and fentanyl, with MAP decreases around 8-10 mmHg—one order of magnitude larger than the 3.16 mmHg shown in our results.[18] Perhaps differences in the type of patients studied, baseline hemodynamic condition, methods of anaesthesia, or the effect of the attrition rate in our results could explain the evident discrepancy. In fact, similar differences in hemodynamic changes after nalbuphine premedication compared to our findings were noted by other authors.[19] On the other hand, few studies have demonstrated the lack of clinical differences from placebo among healthy individuals after premedication with opioids, casting doubt on the justification required by the side effects.[20] However, it is a matter of careful interpretation to determine the reasons behind the variation in the effect of nalbuphine in various age groups. The maximum decrease in MAP in the age group between 51-60 years (6.25 mmHg) might vary due to various physiological changes due to aging, pharmacokinetic changes, or may be due to the variability in sampling in smaller subgroups due to study attrition.[21] The large standard deviation in young patients indicates a large variation in the result, a phenomenon also evident in the literature concerning anesthesiology.[22] Some people have also suggested in their studies that due to a large variation between individuals, one cannot give general advice about hemodynamic variation, but one needs to personalize premedication according to patient risk factors.[23] As far as body weight is concerned, the fact that the greater decrease in MAP was seen in patients weighing >75 kg (3.99 vs. 2.87 mmHg in those weighing ≤75 kg) may imply a dose-response relation. As nalbuphine was dosed according to body weight (0.2 mg/kg), there was a greater absolute dose in heavier patients, which may suggest that there is a dose threshold below which the sympathoadrenal response cannot be adequately blunted. As far as gender is concerned, there were similar effects; however, the larger absolute level of MAP and the variability in the control females (n=36) could either represent gender differences in stress response or merely a smaller number in this category. In a pragmatic context, as it applies to Pakistani medical practice, a number of issues arise. The 12.3% attrition rate that occurred in our study, though not unexpected in clinical research, is a function of unanticipated difficulties in airway management, deviations, and patient issues. Although the study was initially powered for 122 patients, only 107 completed the trial. Despite this reduction, the difference in MAP between groups remained statistically significant, suggesting that the observed effect of nalbuphine is robust; however, the smaller sample may reduce the precision of the effect estimate. The attrition rate is, as expected, commensurate with other research studies on anesthesia administration in Pakistan, yet underscores a significant discrepancy between clinical research conditions and real-world outcomes.[24] The availability and cost-effectiveness of Nalbuphine relative to another commonly used drug, such as fentanyl, administration training to effectively use it, and availability regarding facilities for managing postoperative complications contribute significantly to our ability to translate our findings into clinical practice recommendations. In a clinical setup where substantial patient volume is a challenge,

as is common in most Pakistanis hospitals, employing another form of premedication as a regular option may pose risks that far surpass our modest findings regarding MAP reduction. The mild adverse events noted in our study (bradycardia three patients, nausea two patients) were to be expected given the pharmacologic profile nalbuphine and did not require intervention. Nonetheless, our monitoring primarily focused on intraoperative hemodynamic changes, and we may potentially underestimate incidence of postoperative complications. Certain trials reported a higher incidence of complications such as nausea, dizziness, and somnolence among patients treated with nalbuphine compared to our data.[25] However, although overall incidence of complications for Group B (9.3%) was not significant (p=0.0951), it should not be overlooked that a notable trend existed towards postoperative complications. The close proximity to statistical significance implies that, among a larger population, these complications could potentially become a significant demerit. The lack of any serious adverse reactions is comforting but should be interpreted with caution, considering our small study population and the exclusion of high-risk patients who are potential candidates for adverse reactions to opioids, given that our study population consisted of healthy ASA I patients. Several researches have questioned the practice of opioid administration for hemodynamic control in low-risk patients. The transient nature of intubation response and the strong buffering capacity in healthy patients indicate that aggressive pharmacological management could be both ineffective and harmful, contributing to new complications (respiratory depression, prolonged recovery, increased health expenses) to overcome a transient physiological phenomenon.[26] This outlook assumes particular significance in our study population of ASA I patients, in whom the inherent risk of complications from transient hypertension remains low. Patients with known hypertension, coronary artery disease, cerebrovascular disease, and increased intracranial pressure—the very patients requiring hemodynamic control—are systematically excluded in our study, thereby preventing us from giving our recommendation to these high-risk groups in which the modest advantage offered by nalbuphine could assume significance. There are a number of significant limitations in this study, which may influence the interpretation of results and their generalizability. The study did not account for the timing of surgery, which may have introduced unmeasured time-related variability in hemodynamic responses. The ASA grade I population makes it difficult to generalize to a population with a high risk of complications who would benefit predominantly by means of hemodynamic management. The 12.3% rate of attrition may have led to less precise estimates and may have also introduced a risk of a self-selected group of patients, which may have systematically differed from the ones who were retained for analysis. The results are based solely on the measurement of mean arterial pressure, and a complete evaluation of cardiovascular parameters such as HR, RPP, and CO may have led to a different assessment of a significant effect. The results are also not contrasted with active comparison arms such as fentanyl, remifentanil, and dexmedetomidine, and hence it is also difficult to compare the relative benefits of nalbuphine. The survey of adverse effects was restricted to the intraoperative period only and may, therefore, have underestimated its risks. The results of this survey may also not be generalizable to Pakistani healthcare settings, which may also include resource-limited and different populations of this country. Multiple comparison correction was also not performed for subgroup analysis, and there is a significant probability that some of the significant results may also have occurred by chance. The results of this survey may also have limited utility in suggesting a clinical significance because it is restricted to a short period of anaesthesia, and there is no information about patient-centred

outcomes such as complications, in-hospital stay, patient satisfaction, and cost. The results of this survey may also have a significant limitation that it may also have failed to optimize a strategy for a Pakistani population because different doses were also not considered for a comparison.

CONCLUSION:

Nalbuphine was found to have a significant effect in reducing the blood pressure change associated with the intubation process among healthy patients.

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AUTHOR'S CONTRIBUTION

AHA: Conceived the study, data collection, drafting of the manuscript
MO: Study design, data interpretation, and final approval.
SM: Supervision, critical intellectual input, and manuscript review.
JM: Data collection, case documentation, and literature review.
MSK: Data analysis, manuscript editing, and reference management
MZW: Data acquisition and critical review of the manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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Case Report

ANTI TUBERCULOSIS THERAPY INDUCED DRESS SYNDROME

Omair Farooq[1], Haseeb Jan Gurmani[2], Ibtahaj Mohsin Iqbal,[3] Umer Saleem[3], Muhammad Rauf Mustafa[5], Muhammad Omar Rashid[6]

ABSTRACT:

Background: Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) represents a rare yet potentially fatal hypersensitivity reaction. Although various medications have been associated with this condition, rifampicin is an infrequent culprit.

Case Presentation: A 72-year-old male with hypertension and a history of spinal surgeries presented with fever, widespread pruritic rash, and edema following three weeks of empirical treatment with Rifampicin. Assessment using RegiSCAR criteria resulted in a score of 6, confirming a definitive diagnosis of DRESS syndrome. Laboratory tests indicated eosinophilia (30%), elevated liver enzymes, and increased serum IgE levels (409 IU/ml). The patient was treated with intravenous corticosteroids, followed by a tapering oral regimen, which resulted in significant clinical and biochemical improvement.

Conclusion: Timely identification and immediate cessation of adverse effect of drug are crucial for achieving favorable outcomes in DRESS syndrome. This case underscores the importance of clinical awareness, even with frequently prescribed medications such as Rifampicin.

Keywords: DRESS syndrome, Rifampicin, anti-tuberculosis therapy, hypersensitivity reaction, eosinophilia, RegiSCAR, systemic drug reaction, steroid therapy, dermatologic emergency, adverse drug reaction

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INTRODUCTION

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) syndrome is a potentially life-threatening, delayed, type 4 hypersensitivity reaction to drugs. It manifests with multisystem involvement, as well as cutaneous and hematological symptoms, appearing 2-8 weeks after the initiation of the implicated medications, with a mortality rate of 8-10 percent.[1] Although literature on this condition is limited and inadequate in the Pakistani context, the hematological symptoms typically include leukocytosis and significant eosinophilia, along with the presence of atypical lymphocytes. The liver is the most commonly affected organ, involved in 60-80 percent of cases.[2,3] Cutaneous symptoms may begin with prodromal signs such as itching, which can progress to a morbilliform or maculopapular rash, along with other skin manifestations that may persist long after drug exposure. The International Registry of Severe Cutaneous Adverse Reactions (RegiSCAR) criteria are utilized worldwide for clinical diagnosis, relying on clinical signs and symptoms in conjunction with laboratory findings, including eosinophilia, elevated leukocyte counts, and abnormal liver enzymes.[2]

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A total of 44 drugs have been identified in the literature as potential triggers, including antipsychotics, antiepileptics, beta-lactam antibiotics, and antituberculosis medications, with Carbamazepine being the most frequently implicated.[4] Rifampicin is infrequently reported as a causative agent of DRESS Syndrome. We encountered a case of DRESS Syndrome where Rifampicin was determined to be the causative drug, as evidenced by the timing of symptom onset following the initiation of the medication.

CASE PRESENTATION

A 72-year-old male presented to the Emergency Department of Farooq Hospital (Westwood Branch, Lahore) with complaints of fever, generalized rash, generalized edema, and severe itching. He had a history of undergoing spinal fixation twice in the past due to spinal stenosis (Fig.1), which raised concerns for suspected osteomyelitis/infection. Consequently, he had spinal implant removal performed one week prior. The patient had also taken Rifampicin empirically for three weeks. On the third postoperative day, he returned to the hospital with the aforementioned complaints. Prior to this, during his admission for spinal implant removal, he exhibited a mild rash across his body (suspected Interstitial Nephritis secondary to Rifampicin), which nearly resolved by the time of discharge. However, the rash re-emerged with a severe flare-up affecting his entire body, including his face, accompanied by generalized and facial edema. Upon examination, the rash was morbilliform (Fig.3), covering approximately 70-80% of his body, with significant redness and edema. Given the patient's previous history of three weeks of Anti-Tuberculosis Therapy (Rifampicin) and the negative results for the following tests (Antinuclear Antibody, Extractable Nuclear Antigen, Complement component 3, Complement component 4, Mycoplasma Serology, Epstein-Barr Virus Serology, Human Herpes Virus-6 Serology, Varicella Zoster Virus Serology, Herpes Simplex Virus Serology, Hepatitis B and Hepatitis C Serology), a provisional diagnosis of DRESS SYNDROME was established. To confirm the diagnosis, the RegiSCAR scoring system was utilized, which categorizes cases as “negative case,” “probable case,” or “definitive case” of DRESS Syndrome.[2] In this instance, the score was determined to be “6,” thus classifying it as a “definitive case of DRESS Syndrome.” The causative drug was promptly discontinued, and the patient was admitted to the hospital. As fever was also one of the presenting complaints, blood cultures and sensitivity tests were conducted, along with all other baseline assessments, including Serum Immunoglobulin E levels. The patient's Eosinophil count was significantly elevated at 30%, and Serum Immunoglobulin E levels were also increased at 409 IU/ml. In contrast, his Procalcitonin level was recorded at 0.20. He commenced treatment with IV Dexamethasone at a dosage of 4mg every 8 hours for the first two days, after which the dosage was adjusted to 4mg every 12 hours until the fifth day post-admission. The patient was discharged on the fifth day post-admission, transitioning from IV Dexamethasone to oral Prednisolone (Tab Deltacortil) at a daily dosage of 45mg, administered as three tablets orally three times a day (5mg per tablet). Additionally, topical steroids were applied, including a mild topical steroid for facial application. It is noteworthy that this patient had a medical history of hypertension and allergic rhinitis. The DRESS SYNDROME experienced by the patient resulted in an exacerbation of acute asthma, accompanied by abnormalities in the liver profile, likely due to inflammatory changes in the bile ducts and lungs (refer to Fig.2), secondary to the DRESS SYNDROME. Following the prescribed treatment, the rash began to diminish, and the itching reduced significantly, with the rash decreasing by nearly 90% by the seventh day (see Fig.4). There was a marked improvement in his laboratory results, as detailed below:

Furthermore, his blood culture sensitivity indicated no bacterial growth. It is additionally intended to gradually reduce the dosage of Prednisolone on a weekly basis, aiming to reach the minimum dose by the eighth week, thereby discontinuing the steroids entirely. Furthermore, a sequential follow-up of Immunoglobulin E levels, C-Reactive Protein, Liver Function Tests, and Renal Function Tests will be conducted accordingly. Two days post-discharge, the patient showed significant improvement with a 90% recovery in the rash (Fig.4), along with all pertinent systematic profiles.

Table 1: Laboratory Investigations (day wise)

Parameter	Day 1	Day 2	Day 3	Day 4
Eosinophils (%)	30	4	6	9
Total Leukocyte Count (×10⁹/L)	15.0	11.8	10.4	7.6
C-Reactive Protein (mg/L)	178.0	97.2	40.9	36.4
Alkaline Phosphatase (U/L)	1092	1009	1174	987
Gamma Glutamyl Transferase (U/L)	986	1013	1246	1116
Serum Albumin (g/dL)	2.9	3.0	3.1	—
Serum Urea (mg/dL)	44	36	25	35
Serum Creatinine (mg/dL)	1.3	1.1	1.0	—

Table 2: Diagnosis of Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS Syndrome) using Regi SCAR Scoring System

Criteria	Result in our case	Score
Fever (≥ 38.5 oC)	Yes	0
Enlarged lymph nodes	No/Unknown	0
Atypical Lymphocytes	Yes	+1
Eosinophilia	≥ 1500 cells or ≥ 20%	+2
Skin Rash Extent >50%	Yes	+1
At least two of: edema, infiltration, purpura, scaling	Yes	+1
Biopsy suggesting DRESS	No	-1
Internal Organ Involved	≥ 2	+2
Resolution in >15 days	No/Unknown	-1
Alternative diagnosis excluded (by ≥ 3 biological investigations) Yes +1		
Total Score=6 (Definitive Case)		

Table 3: Changings in Investigations (at the time of admission versus at the time of discharge)

Parameter	Normal Value Range	Value at the time of Admission	Value at the time of Discharge
Eosinophils	1-4 %	30%	2%
Total Leukocyte Count	4-11 x 109/L	15.0x109 /l	7.6x109 /l
C-Reactive Protein	Less than 0.700	178.0	36.4
Alkaline Phosphatase U/L	44-147	1092	987
Gamma Glutamyl Transferase U/L	10-40	986	1116
Serum Albumin g/dL	3.5-5.2	2.9	3.1
Serum Urea mg/dL	10-50	44	35
Serum Creatinine mg/dL	0.6-1.1	1.3	1.0

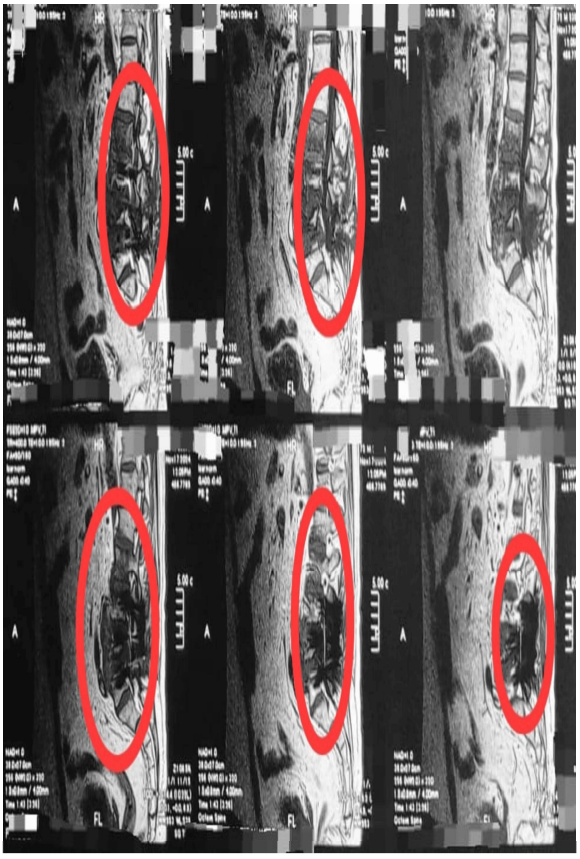

FIGURE 1: MRI Lumbosacral Spine: Stenosis

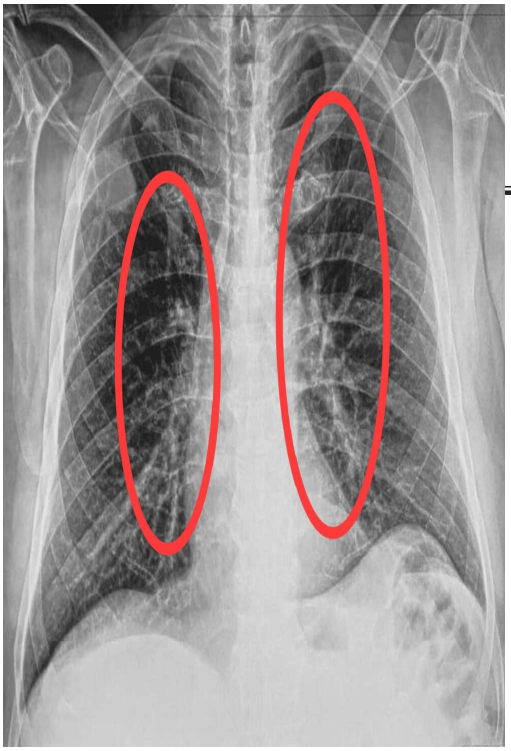

Figure 2: X-Ray Chest: Prominent Hilar Markings

Figure 3: Morbilliform Rash on the day of Presentation (Day 1)

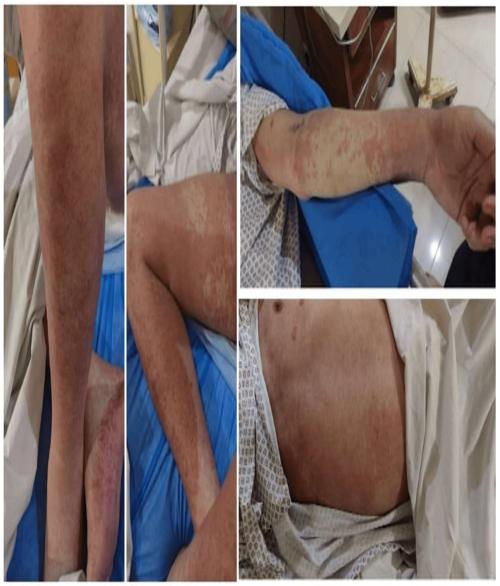

Figure 4: Rash on Day 7 (2 days after discharge); 90% recovery

DISCUSSION

DRESS Syndrome is classified as a Type IV B hypersensitivity reaction, which is marked by symptoms such as fever, an erythematous morbilliform skin rash, facial swelling, and eosinophilia, alongside the involvement of various internal organs, primarily the liver, lungs, and kidneys. Hematological findings typically include leukocytosis and eosinophilia.[3] The diagnosis is challenging due to the varying latency periods associated with different drugs and combinations, as well as the diverse presentation of symptoms. The diagnosis of DRESS Syndrome is established based on the widely accepted RegiSCAR Criteria.[3] The precise pathogenesis of DRESS Syndrome remains unclear; however, three key components involved in its pathogenesis include genetic predisposition linked to specific Human Leukocyte Antigens, the metabolic pathways of drugs, and the reactivation of latent viruses.[4,5] In the case presented, a 54-year-old male had a history of using an Anti Tuberculosis Therapy drug for over three weeks prior to his hospital admission for osteomyelitis, which resulted in DRESS Syndrome characterized by a rash covering more than half of his body, eosinophilia, and other systemic manifestations. This was diagnosed as a definitive case of DRESS Syndrome, with a score of 6 according to the RegiSCAR criteria. The common drug categories implicated in DRESS Syndrome include aromatic anticonvulsants, antimicrobials, antituberculosis agents, anti-inflammatory medications, antivirals, and herbal remedies.[6] Anti Tuberculosis Therapy is a fixed drug combination primarily utilized for tuberculosis; however, in this instance, the patient was using it as an empirical treatment for his spinal osteomyelitis. DRESS Syndrome resulting from first-line Anti Tuberculosis Therapy is exceedingly rare, and identifying the culprit drug is complicated due to the combination of therapies. All Anti Tuberculosis Therapy medications have the potential to induce DRESS Syndrome, but Rifampicin is the most frequently associated drug among first-line Anti Tuberculosis agents. Consequently, it is crucial to recognize the early signs and symptoms of DRESS Syndrome in patients undergoing Anti Tuberculosis Therapy who may be at risk of developing this syndrome.[6,7]

CONCLUSION

Timely identification and immediate cessation of adverse effect of drug are crucial for achieving favorable outcomes in DRESS syndrome. This case underscores the importance of clinical awareness, even with frequently prescribed medications such as Rifampicin.

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AUTHOR'S CONTRIBUTIONS

OF: Concept, Article writing

HJG: Abstract, Introduction

IMI: Case Description

US: Critical Approval

MRM: Data Analysis

MOR: Data Collection

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