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October - December 2024 Volume 06 Issue 04

Editorial

- Tsunami of Metabolic Syndrome (MetS). Rizwan Zafar 127

Original Article

- Development of Nutrient Enriched Flour Blend from Oats, Chia Seeds and Spinach Aqsa Nadeem, Anosh, Anusha Sajjad, Syeda Sani e Zahra, Anoosha Ramzan, Farwa Rani 130

- Comparison of Lipid Profile in Cardiovascular Disease Patients with and without Diabetes Mellitus Shanzay Saeed, Amna Iram, Saba Khalid; Sheikh Danial Hanan, Muhammad Numair Younis, Shamayam Saeed 138

- Classification of Glanzmann's Thrombasthenia Patients on Flow Cytometry Saira Gul, Moizza Sahar, Tooba Fateen, Faheem Shahzad, Ghulam Mustafa, Ismat Ullah 146

- Assessment of Empathy Scores Among Medical Students of a Private Medical College, Lahore, Pakistan Seema Hasnain, Ammad Ali, Ayesha Safdar, 153

- Prevalence and Factors Associated with Stress Management Among Healthcare Professionals in Lahore Nyama Shafique, Rubeena Zakar 162

Case Report

- A Dual Neurological Insult: Ipsilateral Subacute Subdural Hematoma and Ischemic Stroke in an Elderly Patient with Contralateral Weakness Omair Farooq, Fiza Ashfaq, Siddiqua Rehman 170

Instruction to Authors

Letter of Authorship

175

Editorial**Tsunami of Metabolic Syndrome (MetS)**Rizwan Zafar¹doi: <https://doi.org/10.51127/JAMDCV06I04editorial>**How to cite this:**

Zafar R. Tsunami of Metabolic Syndrome (MetS) JAMDC. 2024;6(4): 127-129

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Metabolic syndrome is a cluster of different diseases comprising obesity, dyslipidemia, hypertension and insulin resistance. It is also designated as Reaven syndrome or Syndrome X. Patients fulfilling the criteria of metabolic syndrome are prone to develop type 2 diabetes mellitus, cardiovascular disease, and premature death.¹

Metabolic syndrome is a global epidemic and has emerged as a formidable challenge for clinicians & research workers worldwide. According to International Diabetic Federation (IDF), the prevalence of MetS is 34.6 percent in Eastern Mediterranean region, 33.4 percent in USA, 31.5 percent in European region and 28.1 percent in South East Asia.² Even more alarming fact is that, the prevalence of many risk factors associated with cardiovascular disease & MetS will increase over the next 30 years in America and globally.³

The tsunami of Metabolic syndrome and its components hits Pakistan hard. Pakistan ranks number three in the world in terms of Diabetic population, and number 1 regarding comparative prevalence rate of diabetic patients.⁴ Pakistan stands at number eight among most obese nations in world.⁵ Every third Pakistani after age of 45 years suffers from “The Silent Killer”, hypertension. Overall 34% Pakistanis are hypertensive and prevalence increases with age. Metabolic syndrome is diagnosed if anyone meets any three out of these five

following criteria:

1. Waist circumference more than 102 cm (40 in) in men and more than 88 cm (35 in) in women reflecting abdominal obesity
2. Serum triglycerides more than 150 mg/dL (1.7 mmol/L) or if patient is taking medicines to decrease triglycerides
3. Serum high-density lipoprotein (HDL) cholesterol less than 40 mg/dL (1 mmol/L) in men and <50 mg/dL (1.3 mmol/L) in women or if patient is taking medicines to manage low HDL cholesterol
4. Blood pressure more than 130/85 mmHg or if patient is on antihypertensive drugs
5. Fasting blood glucose is more than 100 mg/dL (5.6 mmol/L) or if patient is on antidiabetic drugs.⁴

Visceral obesity plays a key role in pathogenesis of MetS. It leads to insulin resistance. Various factors involved in pathogenesis include, genetic factors, excessive dietary intake, lack of exercise, IL-1, IL-6, IL-18, Resistin, TNF-alpha, CRP & Adiponectin (an anti-inflammatory cytokine reduced in metabolic syndrome). MetS is associated with multiple other diseases like, (but not limited to) fatty liver, cirrhotic liver, hepatic malignancy, cholangiocarcinoma, Polycystic ovarian syndrome, Chronic kidney disease, sleep disorders, stress & depression, dementia, osteoarthritis, fertility issues, impaired immunity and infections.⁵ What needs to be done to fight against tsunami of metabolic syndrome is to educate public about preventive and life style modifications.

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“Prevention is better than cure”. One of most fundamental strategy of lifestyle modifications is to reduce weight. People need to be informed to keep their weight within normal BMI for Asian population (18.5 to 22.9 kg/m²). Reduction in weight of 3–7% from baseline value has beneficial effects on diabetic and cardiovascular outcomes. After achieving weight reduction, it is even more important to maintain it on long term basis. More than 10% of weight loss on long term basis leads to significant metabolic health benefits. We can expand “Ramadan Fasting” benefits to whole year by observing fasts three times per month for whole year to gain health related as well as religious benefits.⁵

Dietary instructions should emphasize intake of predominantly foods in their natural state and without addition of chemicals or industrial treatment (unprocessed foods). One should avoid sweet, carbonated cola and fizzy drinks because they are source of extra calories and lead to weight gain. Similarly intake of junk food, nehari, (as they contain saturated fats), roghni nan should be restricted in diet. Diet, rich in vegetables, fiber (25 to 30 grams per day), low glycemic index foods, nuts, whole grains, olive oil, low fat dairy products without added sugar, lean fish & chicken are safer options.

Physical activity, for example, 30 minutes of brisk walk is recommended five times per week. It is worth noting that Salah (Namaz) is one of best forms of physical activity and exercise in world. There are movements at joints, gentle contraction and relaxation of muscles and smooth postural changes of body at different angles during Namaz. These simple and harmonious physical activities during namaz are doable by both genders and in all ages. (zurairifm.wordpress.com/2009). The recommendation by American Heart Association of brisk walk of 30 minutes 5

times per week can be easily accomplished by walking to nearby local mosque for prayers 5 times a day.

Other life style modifications include quitting smoking, taking 3/4th of meals in breakfast, lunch and dinner, taking water before meals, taking early dinner, having “uninterrupted” 6 to preferably 8 hours sleep, going to bed early and getting up early in the morning. These life style interventions reduce the health hazards associated with metabolic syndrome and people may be saved not only from the costs of tests and treatment but also from enormous expense of angioplasties, dialysis, and CABG.

We also need to adopt latest digital health approaches like mobile apps, web & AI based data clouds, telehealth services, to prevent cardiometabolic syndrome.⁷

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Original Article

DEVELOPMENT OF NUTRIENT ENRICHED FLOUR BLEND FROM OATS, CHIA SEEDS AND SPINACH

Aqsa Nadeem¹, Anosh², Anusha Sajjad³, Syeda Sani e Zahra⁴, Anoosha Ramzan⁵, Farwa Rani⁶

ABSTRACT:

Background: Diet and nutrition play an important role in general health, highlighting the importance for incorporating nutrient dense foods in diet. Particularly those made from plant-based ingredients; offer a promising approach to improving public health. Oats, chia seeds, and spinach powder are rich in essential nutrients such as fibre, protein, healthy fats, vitamins, and minerals, which can contribute to better overall health.

Materials and Methods: In this interventional study flour blend from oats, chia seeds, and spinach powder was developed along with its nutritional profile and sensory attributes evaluation. Two formulations were prepared utilizing locally sourced ingredients, Group 0 utilized (4:1:1) and experimental Group 1 utilized (5:2:2) of oats, chia seeds and spinach powder respectively. Proximate analysis and Sensory evaluation of both flours in the form of tortilla wraps was conducted and data was analysed in SPSS using independent sample t test at 95% level of confidence.

Results: Group 1 has higher crude protein, crude fiber, fat, ash, contains lower amount of carbohydrates and moisture compared to Group 0 flour. Mineral analysis revealed that Group 1 flour is enriched in iron, potassium, contains moderate amount of magnesium and phosphorus but least amount of calcium whereas statistical analysis shows that there is no significant difference in sensory attributes such as colour, texture, taste, appearance and general acceptability ($p > 0.05$) between both flours. Group 1 flour exhibited enhanced nutritional properties, making it suitable for individuals with specific dietary needs such as high protein or Fiber intake, and lower carbohydrate requirements.

Conclusion: Group 1 has higher crude protein, crude fiber, fat, ash, but contains lower amount of carbohydrates and moisture compared to Group 0.

Key words: Crude protein, Oats, Dietary Fibers

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INTRODUCTION

Diet and nutrition are important for maintaining optimal body function and general health of populations. Total quantity of foods consumed by individuals is referred as diet whereas the process of utilizing food for the growth, metabolism, repair and maintenance of tissue is called nutrition. The association between diet,

nutrition and health is bilateral, nutrient deficiency can affect overall health status and vice versa.¹ According to data by Institute for Health Metrics and Evaluation presented that poor diet contributed to 10.6% of all deaths in 2021.² highlighting the urgent need for incorporating nutrient dense foods in our diet. The quality of the energy we obtain is directly influenced by the nutritional value of our diet, which should ideally include a variety of wholesome and nutrient rich foods. Among the healthy dietary options available, a particularly nutritious choice is a flour that has been enriched through the blending of oats, chia

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seeds, and spinach. This nutrient enriched flour represents a sophisticated approach to health-conscious eating, combining the benefits of three powerful ingredients. By incorporating this blended flour into one's diet, this offers versatile and nutrient-dense ingredient that supports a balanced and healthful lifestyle. Whether used in baking, cooking or as a base for various dishes, this flour not only adds nutritional value but also aligns with contemporary dietary trends that emphasize whole plant-based foods including fresh fruits and vegetables, legumes, seeds, nuts are healthier alternatives to fulfil nutritional demand in comparison to animal-based ingredients such as fatty and processed meats³. Oats have unique proteins called globulins, unlike other cereals that have prolamins. They contain the most fat among cereals being lower in quantity of saturated fats and higher in essential unsaturated fats, which can lessen the risk of heart diseases. Oats are abundant in soluble fiber mainly B glucan which is very favourable for health. B-glucan helps lowering blood cholesterol and glucose absorption, thus favourable for prevention of cardiovascular diseases, dyslipidaemia, hypertension, inflammation, and type 2 diabetes. Moreover, antioxidants are present in abundant quantity in oats.⁴ Oats food with B-glucan have been also affirmed by the European Food and Safety Authority and the US FDA for helping to lower cholesterol and lessen the risk of cardiovascular diseases. Besides B-glucan oats also contain favourable compounds one of these are, avenanthramides (AVAs), is an antioxidant that intercepts impairment to LDL cholesterol. AVA-enriched oats extracts, chiefly when combined with vitamin C, can also lessen LDL oxidation. AVAs have distinct health advantages including reducing inflammation, preventing cell growth and protecting from cancer.⁵ Chia seeds carry many nutrients and used more often because they have many health advantages and are enriched in protein, fiber and omega 3 fatty acids. In contrast to other cereals, chia seeds are enriched with protein and are gluten free, making them applicable for

people with celiac disease. They also carry essential amino acids and provide a substantial quantity of dietary fiber, contributing to daily fiber needs. Chia seeds have variety of health benefits, including supporting heart health, aiding brain development during pregnancy, and helping manage diabetes.⁶ Furthermore, by lowering triglycerides and blood pressure, the addition of omega 3 fatty acids from chia seeds promotes cardiovascular health.⁷

Spinach is a readily available green leafy vegetable being familiar for its enhanced nutritional benefits. It is enriched with many essential vitamins and minerals, including iron, manganese, zinc and magnesium. Spinach contains low quantity of calories, but higher quantity of fat, comes antioxidants and anti-inflammatory properties. Consuming spinach may lessen risk of certain cancers and improve health outcomes, for its extended shelf-life spinach offers dehydrated and processed powder for easier storage and use.⁸ Chia seeds and spinach powder have antioxidant qualities.^{9,10} that can help fight oxidative stress and lower the chance of developing chronic illnesses including cancer and heart disease. Numerous studies focused on individual applications of these ingredients like use of spinach powder in ultra-filtered soft cheese cake,¹¹ gluten free bread with chia seeds,¹² biscuits were prepared using oats,¹³ durum wheat bread was fortified with spinach powder,¹⁴ despite the combined use of these ingredients has not been explored in existing literature.

The objective of this study is to analyze the chemical and sensory properties of a flour developed from oats, chia seeds and spinach. The rationale behind this research is to explore the potential of this flour as a functional food, by analyzing its nutritional composition including fiber, protein, fat, carbs, moisture and minerals, as well as sensory characteristics of taste, texture, appearance, general acceptability and color. The study seeks to contribute valuable insights into the development of plant-

based, health promoting foods. The findings will provide a better understanding on how the combination of these ingredients can improve the nutritional composition and sensory attributes of plant-based food products, contributing to healthier alternatives in food industry.

MATERIALS AND METHODS

Its interventional study design focused on the development of flour blends and comparison of their nutritional composition and sensory performed under ethical approval from the IRB (RE = 087-2023 dated 19/05/2023) of University of Management and Technology. The study duration was of 5 months (13-11-2023 to 30-03-2024), during which the experiment was performed. The eligibility criteria for ingredient selection in study included buying fresh oats, chia seed and spinach from local market of Lahore. Spinach was sun dried for three days to conserve its nutrients and then we grinded oats, chia seeds and dried spinach separately from each other in electrical spice grinder to prepare flour of these ingredients.

A previous study, utilized an oat- chia composite in a proportion of (4:1) as a filler, and were added at concentrations of 3 and 5% in yogurt (200 ml total volume). Thus, instead of yogurt spinach powder was used in (4:1) oats-chia seeds composite making two new samples. Group 0 (4:1:1) of oats, chia seeds, spinach powder which is standardized and referred as control, and Group 1 (5:2:2) referred as experimental group.

Standardized measurement of 1 teaspoon equivalent to 5 grams was used for calculating amount of each ingredient in both flours. For Group 0 (4:1:1), formulation consisted of 20 g of oat flour, 5g chia flour and 5 g spinach powder and for Group 1 formulation consisted of 25g of oat flour, 10g chia flour and 10 g spinach powder. Additionally, scaling factor was used to calculate the proportion of 100g for

both flours. For Group 0, the flour consisted of 66g of oat flour, 17 g of chia flour and spinach powder. Similarly, for Group 1, the flour comprised 56g of oat flour, 22 g of chia flour and 22 g of spinach powder.¹⁵

Scaling factor= (Desired weight)/ (Total weight of ingredient)

The study was conducted at University of Management and Technology with standardized methods. The variables in the study included proximate composition which as determined in laboratory using (hot air oven for moisture, Kjeldahl for crude protein, fiber analyser for crude fiber, muffle furnace for ash, Soxhlet system for fat) and mineral analysis (atomic absorption spectrophotometer for iron, calcium, flame photometry for potassium and magnesium and spectrophotometer for phosphorus) as well as sensory attributes for appearance, color, texture, taste and general acceptability of both flours was determined using a questionnaire. For investigating the organoleptic properties, tortilla wraps were prepared from both flour samples. Sensory evaluation panel from the Department of Nutrition and Dietetics of the University of Management and Technology evaluated the wraps using standard questionnaire. The questionnaire was based on a 9-point hedonic scale with scores ranging from 1 to 9, designating 1 (least undesirable), 2 (dislike very much), 3 (dislike moderately), 4 (dislike slightly), 5 (neither like nor dislike), 6 (like slightly), 7 (like moderately), 8 (like very much), 9 (most desirable). Panellist evaluated both the samples based on these scores for sensory attributes of color, texture, taste, appearance and general acceptability of both samples. The sensory evaluation data for each was analysed in SPSS version 26 using independent sample t test to compare the sensory attributes of both samples at 95% level of confidence. Potential biases were limited by conducting blinded sensory assessment and assuring standardized preparation and serving of the samples.

RESULTS

Group 1 flour has increased amount of dry matter 92.17%, crude protein 13.20%, crude fiber 11.85%, fat 8.0%, ash 6.63% but lower amount of moisture 7.83%, carbs 60.32% and energy 365 Kcal compared to Group 0 dry matter 63.63%, Crude protein 12.10%, Crude fiber 4.62%, ash 2.30%, fat 4.25%, moisture 36.37%, Carbs 76.73% and energy 393 Kcal. (Table-1).

Table 1: Proximate Analysis of Both Flours

Type of test in percentages %	Group 0 (4:1:1)	Group 1 (5:2:2)
Dry matter	63.63	92.17
Moisture	36.37	7.83
Crude Protein	12.10	13.20
Crude fiber	4.62	11.85
Fat	4.25	8.0
Ash	2.30	6.63
Carbs	76.73	60.32
Energy (Kcal/100g)	393	365

Group 1 (5:2:2) flour has increased K (112.0 mg/L), Fe (95.0 mg/L), moderate amount of P (25.6 mg/L), Mg (15.0 mg/L), and least amount of Ca (6.79 mg/L). (Table-2).

Table 2: Mineral Analysis of Group 1 Flour

Test	Fe (mg/L)	Mg (mg/L)	Ca (mg/L)	P (mg/L)	K (mg/L)
	95.0	15.0	6.79	25.6	112.0

Independent sample t test group statistics shows that the mean and standard deviation for

Proximate analysis of both flours shows that appearance of flour for Group 0 is 6.87 ± 1.302 & for Group 1 is 7.40 ± 1.121 , color of product for Group 0 is 6.93 ± 1.163 & for Group 1 is 7.00 ± 1.254 , texture of product for Group 0 is 6.80 ± 1.373 & for Group 1 is 7.47 ± 0.990 , taste of product for Group 0 is 7.67 ± 0.976 & for Group 1 is 7.73 ± 1.223 , general acceptability of product for Group 0 is 7.80 ± 1.014 and for Group 1 is 8.00 ± 0.845 . Since all the features have ($p > 0.05$), it means that there is no significant difference between color, appearance, taste, texture and acceptability of both flours. (Table-3).

Table 3: Comparison of Sensory Attributes

Sensory Attributes	Group 0 (4:1:1)	Group 1 (5:2:2)	P value
Appearance	6.87 ± 1.302	7.40 ± 1.121	0.239
Colour	6.93 ± 1.163	7.00 ± 1.254	0.881
Texture	6.80 ± 1.373	7.47 ± 0.990	0.138
Taste	7.67 ± 0.976	7.73 ± 1.223	0.870
General acceptability	7.80 ± 1.014	8.00 ± 0.845	0.562

DISCUSSION

The results of the current study presented notable variations in both the nutritional and sensory analysis of flour blends, Group 0 (4:1:1) and Group 1 (5:2:2)

A key finding from the sensory evaluation of tortilla wraps made from both flour mixtures was the impact of spinach powder on the color of product. Inclusion of spinach powder in both Group 0 and Group 1 flour produced green color, where Group 1 presented a darker green color than Group 0 which aligns with the findings of the study that prepared dried noodles using different proportions of spinach powder demonstrated that increasing the

amount of spinach powder in dough results in a darker green color.¹⁶ Furthermore, the ingredient ratio in both flours noticeably affected water holding and retention capacity of the doughs. Group 0 dough with lower chia seeds content, exhibited better water retention and absorption capacity, resulting in dough that was easy to knead, shape and roll out and doesn't become excessively sticky. In comparison, the Group 1 dough with higher chia seeds content contributed to improved water retention but became more vulnerable to sticking, needing more efforts and adjustments during the kneading process to reach the intended consistency. The findings align with the study that prepared chicken meat sausages using different proportion of chia seeds presented that increasing chia seeds content resulted in increased water holding capacity of chicken meat sausages.¹⁷

Proximate analysis manifests that Group 1 flour has increased amount of crude protein, fiber, fat, ash, but lower amount of moisture and carbohydrates compared to Group 0 flour. Increased protein content in Group 1 flour may increase its demand among individuals seeking to improve their protein intake for exercising regularly,¹⁸ whereas the increased fiber content can contribute to improved bowel movements and digestion whereas higher amount of chia seeds contributed to lower moisture content of Group 1 flour,¹⁹ the lower carbohydrate content of Group 1 flour is suitable for individuals with diabetes,²⁰ as it provides a source of complex carbohydrates and higher fat content of Group 1 which contains polyunsaturated and monounsaturated fatty acids is valuable for patient with heart disease as it help lowers cholesterol and is associated with reduced risk of developing type 2 diabetes mellitus and CVD.²¹ Furthermore, it is also beneficial for patients with iron deficiency and elevated blood pressure as it is enriched in iron and potassium. Statistical analysis shows that both flours are equally acceptable based on sensory attributes of color, general acceptability, texture, taste and appearance. The current study strives to prepare a flour blend from plant-based

local ingredients oats, chia seeds and spinach powder for promoting the health of community. Chia seeds are known for higher amounts of protein and fiber²² and contains abundant quantity of fatty acids, vitamins, minerals and dietary fiber²³ contributing valuable addition to any food. Spinach carries lower amount of carbohydrate,²⁴ but abundant quantity of many minerals comprising calcium, potassium, zinc, iron, sodium.²⁵ Oats contain abundant quantity of fiber, iron and zinc.²⁶

While many studies have looked at the nutritional benefits of oats, chia seeds and spinach powder individually while modifying traditional foods, but the outcomes of this study highlight the importance of combining all three ingredients to create a nutrient enriched flour. For instance, one study found that fortifying traditional wheat flour biscuits with oats flour enhanced protein, fat, fiber and mineral content of the biscuits.²⁷ Whereas, spinach powder was utilized in preparing cookies compared to wheat flour cookies enhances its nutritional profile.²⁸ Similarly, chia seeds were used with corn flour for enhancing nutritional profile of gluten free products for celiac patients. and incorporation of chia seeds resulted an increase in fat, fiber and mineral content compared to corn flour gluten free product without chia seeds.²⁹

The limitation of the study is that all ingredients were purchased from local markets of Lahore. The nutritional content and quality of ingredients from different regions or seasons could affect the consistency of the results. While the sensory evaluation was conducted blind, probable biases could have been introduced due to panellists preferences, familiarity with ingredients used and subjective nature of sensory assessments whereas the evaluation was performed by 15 trained panellist which could not be a representative of broader population.

CONCLUSION

The study highlights that the flour created from the incorporation of oats, chia seeds and spinach powder can improve nutritional value

while retaining favourable sensory attributes. The findings manifest that Group 1 flour offers more protein, fiber, fat and mineral content in contrast to Group 0 flour making it highly beneficial for individuals who wants to improve dietary status. The combination of these three ingredients not only amplify nutritional profile but also promote nutritional benefits for individuals with diabetes, cardiovascular diseases, bowel problems and nutrient deficiencies. Furthermore, the outcomes manifest that these ingredients can be advantageously combined for promoting the health of community through locally available plant-based ingredients to develop healthier food alternatives.

CONFLICT OF INTEREST

None

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None

AUTHOR'S CONTRIBUTIONS

AN: Manuscript writing

A: Interpretation of data

AS: Study design

SSZ: Data collection

AR: Data analysing

FR: Study concept

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Original Article

COMPARISON OF LIPID PROFILE IN CARDIOVASCULAR DISEASE PATIENTS WITH AND WITHOUT DIABETES MELLITUSShanzay Saeed¹, Amna Iram², Saba Khalid³, Sheikh Danial Hanan⁴, Muhammad Numair Younis⁵, Shamayam Saeed⁶**ABSTRACT**

Background: Dyslipidaemia accounts as a major contributing factor to the severity of most prevalent non-communicable diseases such as cardiovascular diseases and diabetes mellitus. Lipid profile test is being widely used for the diagnosis of abnormal lipid levels acting as a primary diagnostic parameter. The objectives of the current study were to compare lipid profile parameters in patients of cardiovascular diseases with and without diabetes mellitus and to determine the relationship of age and gender with abnormal lipid profile parameters.

Material and Methods: A case-control study was conducted at Fatima Memorial Hospital (FMH) Lahore over a period of three months. Total of 94 subjects fulfilling the inclusion criteria were included. Total sample size was further divided into two groups of 47 individuals in each. Group A included cases (cardiovascular disease patients with diabetes mellitus) and Group B included controls (cardiovascular disease patients without diabetes mellitus). Lipid profile parameters (HDL, LDL, TAG, CHOL, VLDL and CHOL/HDL Ratio) of all individuals were determined and compared.

Results: Group A had 23(46.9%) males and 24(53.3%) females whereas, Group B had 26(53.1%) males and 21(46.7%) females. The mean age of Group A and Group B subjects was 64.87 ± 10.1 , 61.1 ± 11.5 respectively. Group A had higher abnormal levels of lipid profile parameters as compared to Group B (P values < 0.05). Gender had no association with lipid profile parameters (P values > 0.05). Age had a positive significant correlation with abnormal lipid profile parameters. Group A had higher risk of developing abnormal lipid profile parameters as compared to Group B (RR >1).

Conclusion: This study concluded that elderly male and female having cardiovascular disease with diabetes mellitus presented with significantly higher abnormal lipid levels.

Keywords: Cardiovascular Diseases, Diabetes Mellitus, Dyslipidemia, Lipid Profile.

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INTRODUCTION

Cardiovascular diseases (CVDs) and Diabetes

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mellitus (DM) are among the most prevalent non-communicable diseases throughout the world and is prevailing in Pakistan as well.¹ CVDs include a wide range of diseases including not only heart blood vessels disease termed as coronary artery disease i.e., myocardial infarction but also cerebrovascular disease i.e., stroke, peripheral artery disease (PAD) i.e., limb diseases, and aortic atherosclerosis i.e., aneurysm.² DM a metabolic disorder, is being characterized by imbalanced blood glucose levels. Type-2 DM is the predominant type of diabetes characterized by body's resistance to naturally produced insulin.³ CVDs are being

considered the biggest killer disease causing approx. 1 in 3 deaths in the world. As per the British Heart Foundation report 2024, 523 million people are currently living with CVDs globally.⁴ Global burden of disease 2019, reports that the incidence of CVD was found to be 918.18/100,000 in Pakistan.⁵ Diabetes on the other hand has a rising prevalence in the world. As per the International diabetes federation (IDF) report 2021, 537 million people are living with DM and the prevalence of diabetes in Pakistan is 26.7%^{6,7}. Pakistan ranks as the fifth most populous country globally thus, facing with a dual challenge of non-communicable diseases such as cardiovascular diseases and diabetes mellitus.^{1,5} As per the estimate done in 2021, Type-2 DM specifically is diagnosed in 33 million living in Pakistan.⁸

A number of factors have been associated with such diseases which contribute to their severity such as obesity, tobacco use, high blood pressure, hyperglycemia, dyslipidemia, high-calorie diet, saturated fats, liquor consumption, and lack of exercise.⁹ Risk for developing CVD and DM increases as the person ages. As per the AHA and IDF reports, the approximate age for developing CVDs and Type-2 DM is above 45years.^{10,11} Due to the rise in unhealthy living and industrialization the younger population is at stake for developing such lethal diseases. Therefore, there is a need of proper evaluation and treatment of subjects who are at the risk.

Dyslipidemia a generalized term for abnormal or dysregulated lipid levels. Decreased high density lipoprotein (HDL) level and raised low density lipoprotein (LDL), very low-density lipoprotein (VLDL), triglycerides (TG), cholesterol (CHOL) levels and cholesterol/high density lipoprotein (CHOL/HDL) ratio are categorized as dyslipidemia.

Dyslipidemia, particularly secondary dyslipidemia is strongly associated with the comorbidities such as CVDs and DM. Dyslipidemia is a hallmark for the development of atherosclerotic plaque in vessels which causes the vessels narrowing and hinders the blood flow and ultimately leads to CVDs. Type-2 DM

characterized by insulin resistance and insufficient insulin production causes increased free fatty acid in blood impairing use of lipoprotein which deposits in vessels and forms atheroma and ultimately leads to CVDs.¹² Consequently, DM has been recognized as a significant determinant for CVDs.¹³

Lipid profile a medical laboratory blood test determines different levels of lipid in blood. It analyses high density lipoprotein known as good cholesterol, low density lipoprotein and very low-density lipoprotein known as bad cholesterol, TG, CHOL and CHOL/HDL ratio. HDL, LDL, VLDL, CHOL levels and CHOL/HDL ratio are the hallmark for atherosclerotic changes in vessels leading to coronary artery disease. TGs levels act as an indicator for metabolic disease such as DB. Raised levels of LDL, VLDL, TGs, CHOL, CHOL/HDL ratio and low level of HDL are an indicator of dyslipidemia in CVDs and DM patients. Thus, lipid panel test is a strong diagnostic test for patients presenting with symptoms of cardiovascular diseases and diabetes mellitus.¹⁴

The objectives of the current study were to compare lipid profile parameters in patients of cardiovascular diseases with and without diabetes mellitus and to determine the relationship of age and gender with abnormal lipid profile parameters. The widespread occurrence of CVDs and DM provoked a thought for the determination of lipid profile role in assessing the severity and risk of these conditions in affected patients. Therefore, the findings of this study will assist clinicians in the effective management and timely treatment of patients who are at the risk of developing dyslipidemia. Additionally, this study will raise awareness among individuals about the severe risks associated with elevated lipid levels and the importance of maintaining a healthy lifestyle to mitigate these hazards.

MATERIAL AND METHODS

A case-control study constituting of 94 subjects was conducted at Indoor and Outdoor departments of Fatima Memorial Hospital (FMH) Lahore from May 2024 to July 2024. 94 subjects

were divided into two groups of 47 individuals in each. Group A subjects consisted of CVDs and DM (cases). Group B subjects consisted of CVDs without DM (controls). Non-randomized purposive sampling technique was used to collect the sample fulfilling the criteria. This study included subjects of both genders, aged 40 to 80 years, with cardiovascular diseases, including both diabetic and non-diabetic individuals. This study excluded subjects with renal failure, cardiac arrest, or stroke.

Data collection was initiated after taking approval from Institutional review Board (IRB) of FMH with a Reference No.FMH-04/03/2024-IRB-1364. Informed consents duly signed by patients, were obtained before blood sampling.

Demographic factors and disease history of patients were recorded using a proforma. After 9-12hr of fasting, venous blood samples were taken in the morning and analyzed for lipid profile parameters (HDL, LDL, VLDL, Triglyceride, CHOL, and CHOL/HDL Ratio). HDL level < 40mg/dL in males and < 50mg/dL in females was taken as abnormal or raised. LDL level > 100mg/dL, VLDL > 50mg/dL, TG level > 150 mg/dL, CHOL level >200 mg/dL, and CHOL/HDL Ratio > 5 were taken as abnormal or raised. Lipid profile parameters (HDL, LDL, VLDL, Triglyceride, CHOL, and CHOL/HDL Ratio) of all individuals were determined by automated ROCHE Cobas Analyzer using enzymatic method (spectrophotometry technique).^{15,16}

All the data collected was entered into SPSS version 26 and subjected to statistical analysis. The continuous variables were expressed as mean \pm SD and categorical data as frequency and percentage. The mean of lipid profile variables HDL, LDL, VLDL, TG, CHOL and CHOL/HDL ratio were compared using independent t-test among two groups. Pearson correlation and chi-square test was used to determine the relationship of age and gender with lipid profile variables.

Relative Risk (RR) was used to find the risk. p value < 0.05 was deemed to be statistically significant.

RESULTS

The present study included 94 subjects, with 47 participants in each of the two groups, Group A and Group B. Group A had 23(46.9%) males and 24(53.3%) females whereas, Group B had 26(53.1%) males and 21(46.7%) females. The mean age of Group A and B subjects was 64.87 ± 10.1 and 61.1 ± 11.5 respectively.

Mean \pm SD for each of the lipid profile parameters in both Group A and Group B were calculated separately. The p values were found to be significant (p < 0.05) (Table. 1).

Table 1: Comparison of lipid profile parameters among group A and group B

LIPID PROFILE	Group A (CVD & DIABETICS)	Group B (CVD & NON-DIABETICS)	p Value
HDL	39.87 \pm 11.14	46.38 \pm 13.96	0.014
Male Female	36.78 \pm 9.54 42.83 \pm 11.93	43.19 \pm 15.24 50.33 \pm 11.32	
LDL	127.68 \pm 30.62	111.04 \pm 39.90	0.026
Male Female	123.83 \pm 32.52 131.38 \pm 28.8	114.73 \pm 42.08 106.38 \pm 37.52	
VLDL	71.96 \pm 28.33	58.68 \pm 27.70	0.024
Male Female	68.87 \pm 28.05 74.92 \pm 28.89	59.65 \pm 26.60 57.48 \pm 29.63	
TG	234.40 \pm 111.94	188.77 \pm 81.66	0.029
Male Female	224.48 \pm 118.02 243.92 \pm 113.61	193.04 \pm 82.51 183.48 \pm 82.32	
CHOL	255.60 \pm 71.05	224.45 \pm 59.91	0.024
Male Female	243.17 \pm 67.97 267.50 \pm 73.31	227.54 \pm 45.36 220.62 \pm 75.22	
CHOL/HDL Ratio	7.17 \pm 3.28	5.72 \pm 3.28	0.036
Male Female	7.31 \pm 3.52 7.03 \pm 3.10	6.39 \pm 3.63 4.89 \pm 2.64	

CVD; cardiovascular diseases, HDL; high density lipoprotein, LDL; low density lipoprotein, VLDL; Very low-density lipoprotein, TG; triglyceride, CHOL; cholesterol, CHOL/HDL Ratio: cholesterol/high density lipoprotein ratio.

Table 2: Abnormal distribution of Lipid Profile parameters in Group A and B according to Gender

LIPID PROFILE PARAMETERS	Group A (CVD & DIABETICS)		Group B (CVD & NON - DIABETICS)	
	Male (N=23)	Female (N=24)	Male (N=26)	Female (N=21)
HDL	14 (45.2%)	17 (54.8%)	11 (57.9%)	8 (42.1%)
LDL	17 (44.7%)	21 (55.3%)	16 (57.1%)	12 (42.9%)
VLDL	19 (47.5%)	21 (52.5%)	17 (54.8%)	14 (45.2%)
TG	18 (46.2%)	21 (53.8%)	17 (56.7%)	13 (43.3%)
CHOL	20 (48.8%)	21 (51.2%)	19 (57.6%)	14 (42.4%)
CHOL/HDL Ratio	17 (45.9%)	20 (54.1%)	13 (65.0%)	7 (35.0%)

Gender had no association with abnormal lipid profile parameters HDL ($p=0.66$), LDL ($p=0.52$), VLDL ($p=0.62$), TG ($p=0.65$), CHOL ($p=0.83$), CHOL/HDL ($p=0.90$). Lipid profile parameters such as LDL, VLDL, TG, CHOL, CHOL/HDL have a direct relationship with the degree of abnormality except HDL which has an inverse relationship the abnormality. Age had a positive significant correlation with all lipid profile parameters HDL ($p=0.004$), LDL, VLDL, TG, CHOL, CHOL/HDL ($p=0.000$) The Pearson

correlation value of -2.94 doesn't represents negative correlation of HDL with age as it's already been described above that HDL has an inverse relationship with abnormality. Thus, -2.94 represents a positive correlation with age like all other factors (Table. 3).

Table 3: Correlation between age with lipid profile parameters.

Lipid Profile Parameters	Pearson Correlation value	p- value
HDL	-2.94	0.004
LDL	0.471	0.000
VLDL	0.468	0.000
TG	0.352	0.000
CHOL	0.582	0.000
CHOL/HDL Ratio	0.374	0.000

Group A subjects had high risk of developing abnormal lipid levels ($RR>1$) (Table. 4).

Table 4: Risk estimation of Group A having abnormal lipid profile values.

LIPID PROFILE PARAMETERS	GROUP A (CVD & DIABETICS)
HDL	1.63
LDL	1.35
VLDL	1.29
TG	1.30
CHOL	1.24
CHOL/HDL Ratio	1.85

DISCUSSION

Dyslipidemia is a key contributor to the severity of many common non-communicable diseases, including cardiovascular diseases and diabetes mellitus leading to high morbidity and mortality. Dyslipidemia is a broad term for abnormal or deranged lipid levels in the blood. It constitutes of low HDL, high LDL, VLDL, TG, CHOL and CHOL/HDL ratio defined as mixed dyslipidemia.

Elevated lipids in the blood deposits in the vessels increasing the intima media thickness, forming atherosclerotic plaques leading to narrowing and blockage of blood vessels compromising the blood flow through the body and progressing to CVDs. DM on the other hand is caused by a combination of insulin resistance, where the cells of the body do not effectively utilize insulin due to various underlying factors and inadequate insulin production by the pancreas which results from the gradual loss of pancreatic islet function or cell count. This change in lipid levels is associated to a higher risk of both macrovascular (peripheral vascular disease, cerebrovascular disease, ischemic heart disease) and microvascular (retinopathy, nephropathy, neuropathy) complications in individuals with diabetes.¹⁷

DM is a major contributing factor for the development of CVDs however, as per the recent study CVDs can also contribute to the development of DM specifically in patients with abnormal lipid levels such as mixed dyslipidemia¹⁸. Thus, deranged lipid levels are deemed as risk factors for such lethal diseases.

Lipid profile assessment is the base line diagnostic tool for determining the risk and severity of CVDs and DM as it provides the key information about the levels of different types of fats in the blood. An accurate and timely evaluation of dysregulated lipid levels is essential for delivering optimal patient care.

In current study, patients with CVDs and DM were compared to those with cardiovascular diseases but without diabetes mellitus. To the best of our knowledge this is an only study which included a broad range of cardiovascular diseases while, previous researches focused only on specific heart conditions without encompassing cardiovascular diseases as a whole. This highlighted the need for research that encompasses all types of CVDs to more effectively compare lipid profiles between diabetic and non-diabetic patients with CVDs.

This study included 94 subjects aged between 40-80 years. Total subjects were divided into two groups of 47 in each having nearly equal ratio of male to female. Group A had CVD & DM and Group B had CVD-Non-DM subjects.

In this study HDL in Group A and B was 39.87 ± 11.14 and 46.38 ± 13.96 . LDL in Group A and B was 127.68 ± 30.62 and 111.04 ± 39.90 . TG in Group A and B was 234.40 ± 111.94 and 188.77 ± 81.66 . CHOL in Group A B was 255.60 ± 71.05 and 224.45 ± 59.91 .

HDL was found abnormal in 31 (62.0%), 19 (38.0%) subjects of Group A and B. LDL was found abnormal in 38(57.6%), 28(42.4%) subjects of Group A and B. TG was found abnormal in 39(56.5%), 30(43.5%) subjects of Group A and B. CHOL was found abnormal in 41(55.4%), 14(42.4%) subjects of Group A and B.

A study was conducted to compare lipid profile in ischemic heart disease patients with and without diabetes found that HDL in diabetics and non-diabetics with IHD was 43.17 ± 14.042 mg/dL and 45.98 ± 16.142 mg/dL. LDL in diabetics and non-diabetics was 103.31 ± 37.397 mg/dL, 85.84 ± 28.344 mg/dL. TG in diabetics and non-diabetics with IHD was 159.14 ± 56.139 mg/dL, 124.43 ± 50.341 mg/dL. CHOL in diabetics and non-diabetics with IHD was 175.86 ± 41.410 mg/dL, 156.64 ± 25.756 mg/dL. The results were comparable to our study (P value < 0.05). Abnormal lipid profile parameters HDL, LDL, triglyceride and cholesterol was found in

61(46.92%) 46 (35.38%) 68 (52.30%) and 50 (38.46%) individuals respectively.¹⁹

Al Shaer et al compared lipid profile in type-2 diabetes mellitus subjects with and without CADs. HDL in Non-CAD and CAD group was 1.98 ± 0.07 , 1.82 ± 0.09 . (p value > 0.05). LDL in Non-CAD and CAD group was 126.82 ± 12.91 , 156.17 ± 17.9 . TG in Non-CAD and CAD group was 5.21 ± 1.8 , 12.46 ± 2.1 . (p value < 0.05). The findings were concerned to our study with (P value < 0.05), however, HDL of this showed insignificant difference among two groups.²⁰

In another study lipid parameters in diabetic and non-diabetic atherosclerotic patients were compared. Diabetic atherosclerotic individuals had low level of HDL in comparison to non-diabetic atherosclerotic and normal control individuals. Diabetic atherosclerotic individuals had high level of LDL, VLDL, TG, CHOL and CHOL/HDL in comparison to non-diabetic atherosclerotic and normal control individuals.²¹ These results were comparable to current study.

Few previously published studies have been conducted on comparison of lipid profile between diabetic and non-diabetic subjects. They reported dyslipidemia in diabetics as compared to non-diabetics. This finding is in the support of pathophysiological mechanism of diabetics having abnormal lipid levels.^{22,23}

In this research a positive significant correlation of age with all lipid profile parameters was found. This finding was consistent with other studies^{19,21}. Gender found no significant association with either of the abnormal lipid levels. This was found contrary to other article findings as they showed female and male association with abnormal lipid levels.^{19,20,21} Our finding suggests that both male and female are equally affected by these highly morbid and mortal diseases.

Overall, the findings of this study provide an insight to the alarming lipid levels in cardiovascular diseases patients with diabetes mellitus. A significant but not highly significant difference in lipid levels has been observed in

present study among both groups particularly CHOL/HDL ratio which has been reported a better parameter to for the identification of dyslipidemia is less significant among both groups with p-value 0.03.^{9,18,21} These results suspect the development of diabetes in near future in control group and increases chances of more adverse form of cardiovascular diseases. Moreover, both elderly male and female have been found to be equally affected by such lethal diseases. Therefore, this suggests a need of appropriate lipid management in both genders particularly of aged individuals.

CONCLUSION

The current study concludes that CVD patients with DM presented with mixed dyslipidaemia having significantly higher levels of LDL, VLDL, CHOL, CHOL/HDL ratio and low level of HDL as compared to CVD patients without DM. These findings highlight the need for proactive management in such cases.

CONFLICT OF INTEREST

None

SOURCE OF FUNDING

None

AUTHOR'S CONTRIBUTIONS

SS: Conception and drafting of the work

AI: Proof reading

SK: Data interpretation

SDH: Revision of work

MNY: Revising of work critically for important intellectual content

SS: Data collection

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Original Article

Classification of Glanzmann's Thrombasthenia patients on flow cytometry

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Abstract:

Background: Glanzmann's Thrombasthenia (GT) is an autosomal recessive platelet disorder caused by mutations in the ITGA2B and ITGB3 genes, leading to partial or complete deficiency of the GPIIb/IIIa (CD41/CD61) complex on platelets, causing quantitative or qualitative defects of platelet fibrinogen receptors α IIb β 3 glycoprotein complex. This results in abnormal platelet aggregation, diminished clot retraction and mild to severe bleeding episodes. Affected individuals suffer from lifelong moderate to severe bleeding, mostly mucocutaneous in nature. The present study was designed to characterize GT subtypes through quantitative flow cytometry

Material and Methods: A descriptive study was conducted on 46 GT patients attending Allama Iqbal medical college / Jinnah Hospital. After obtaining written informed consent, blood samples were taken, severity of bleeding was assessed by Glanzmann's Thrombasthenia Italian Team protocol (GLATIT) and expression of platelet integrin was determined by quantitative flow cytometry.

Results: On flow cytometry 20 patients were categorized as type I (43.5%), 07(15.2%) as type II and 19(41.3%) as type III according to the level of receptor deficiency.

Conclusion: Type I is the most common followed by type III then type II. Most cases were severe bleeders followed by mild then moderate bleeders. Initial yet important account of clinical and phenotypic characterization of GT in local patients, which may spark further studies to help molecular diagnosis, optimal disease management and genetic counselling-based prevention efforts.

Keywords: Glanzmann's Thrombasthenias; Inherited Platelet Disorder Platelet, Glycoprotein GPIIb-IIIa Complex;

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INTRODUCTION

Glanzmann Thrombasthenia (GT; MIM # 273800), first identified by Edward Glanzmann in 1918 as "hereditary hemorrhagic thrombasthenia"¹, is a rare autosomal recessive bleeding disorder with an estimated incidence of 1 in 1 million population.¹ It results in life-long,

moderate to severe mucocutaneous bleeding.

Key features include prolonged bleeding time, abnormal clot retraction, normal platelet count, and abnormal responses to ADP, epinephrine, and collagen, though aggregation with Risto cetin remains normal.² Clinical manifestations include epistaxis, gum bleeding, petechiae, purpura, easy bruising, prolonged bleeding from injuries, bleeding post-circumcision in males, and menorrhagia in females. The bleeding severity varies from minimal bruising to severe, potentially fatal hemorrhages, with over two-thirds of patients needing blood or platelet transfusions, underscoring the disorder's severity.¹ Bleeding severity was categorized into

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mild (trauma-related), moderate (spontaneous but non-life-threatening), or severe (recurrent and

life-threatening, requiring transfusion) as defined by the GLATIT protocol.

Glanzmann Thrombasthenia (GT) is a rare bleeding disorder with a prevalence of about one in a million, more common in populations with high consanguinity, such as in the Middle East, Europe, and Pakistan, where it is the most prevalent platelet functional disorder.³ This study aims to classify GT patients in Pakistan using flow cytometry, providing insights into diagnostic and treatment variations in this underrepresented population. Flow cytometry is used to assess platelet integrin $\alpha\text{IIb}\beta\text{3}$ (CD41/CD61) expression, crucial for platelet aggregation. It identifies severe $\alpha\text{IIb}\beta\text{3}$ deficiencies in types I and II and rare variant forms like type III, making it the gold standard for GT diagnosis.^{2,4} Seven novel variants have been identified, highlighting the importance of flow cytometry in carrier detection, prenatal diagnosis, and reducing the GT burden.⁵

This study aims to classify Glanzmann's Thrombasthenia (GT) in 46 Pakistani patients using flow cytometry to identify diagnostic and treatment variations. By focusing on an underrepresented population, the research seeks to improve global understanding of GT and develop tailored diagnostic and therapeutic strategies. It examines the link between bleeding severity and surface receptor expression in these patients

MATERIALS AND METHODS

This cross-sectional descriptive study was conducted at the Hematology Department of Allama Iqbal Medical College/Jinnah Hospital Lahore, spanning from December 2022 to December 2023, with ethical approval granted (ERB144/11/09-06-2023/S1). A total of 46 unrelated patients diagnosed with Glanzmann's Thrombasthenia (GT) were enrolled based on clinical and laboratory confirmation. The sample size was determined using the World Health Organization's (WHO) formula for health studies version 2.0.21.13

$$n = \frac{Z^2_{1-\alpha/2} P(1-P)}{d^2} \text{ with a 95\% confidence level}$$

($Z = 1.96$), an anticipated proportion of 3%, (prevalence of disease) and a margin of error of 5%.⁽³⁾ Convenient sampling was used to select patients, with inclusion criteria based on a history of mucocutaneous bleeding, prolonged bleeding time with normal platelet count and coagulation profile, and platelet aggregation failure when tested with ADP, epinephrine, and collagen, while showing a normal response to Risto cetin. Patients with acquired bleeding disorders, those on anticoagulant or antiplatelet therapy were excluded. Data on demographic details, bleeding history, transfusion requirements, and bleeding severity, were collected. Bleeding severity was categorized into mild (trauma-related), moderate (spontaneous but non-life-threatening), or severe (recurrent and life-threatening, requiring transfusion) as defined by the GLATIT protocol.

Flow cytometry was performed in the department of Immunology University of Health Sciences Lahore on BD FACS Caliber flow cytometer. Peripheral blood samples were collected from patients and controls after informed consent. Five milliliters of blood was drawn into EDTA vials for flow cytometric analysis. Expression of $\alpha\text{IIb}\beta\text{3}$ integrin (CD41/CD61) was assessed using monoclonal antibodies against CD41 (GPIIb) and CD61 (GPIIIa). A forward vs. side scatter (FSC/SSC) dot plot was used to identify the platelet population (R1 region), followed by analysis of CD41 and CD61 markers. Patients were categorized into GT type I, II, or III based on the percentage of $\alpha\text{IIb}\beta\text{3}$ expression:

- Type I: <5% $\alpha\text{IIb}\beta\text{3}$ expression
- Type II: 5-20% expression
- Type III: >20% expression

Isotype controls were used to correct for non-specific binding.

Key outcome variables included GT subtype (flow cytometry), bleeding severity (GLATIT protocol), and hematological parameters (Hb, MCV, MCH, MCHC, platelet count). Descriptive statistics summarized continuous variables (mean \pm SD) and categorical variables (frequencies/percentages). One-way ANOVA test analyzed differences between GT subtypes and

clinical manifestations. Pearson or Spearman correlation assessed the association between α IIb β 3 expression and bleeding severity. Statistical significance was set at $p < 0.05$ and analyses were conducted using SPSS software version. 20.

RESULTS

GT patients were enrolled based on following hematological data: the mean hemoglobin (Hb) level 9.8 ± 2.5 g/dL, with RBCs indices indicating chronic bleeding and iron deficiency anemia (MCV 69.6 ± 15.5 fl, MCH 21.9 ± 6.9 pg and MCHC 31.6 ± 2.2 g/dL). Bleeding time of 11 minutes was recorded in all patients, normal platelet count (median $314 \times 10^9/L$), and normal PT, and APTT values were in concordance with GT diagnosis. The demographic data according to the clinical assessment and history are provided in the table below:

Table.1: The Demographic Data of GT patients (n=46)

Clinical Detail of GT Patients	No. of Patients (n=46)	Percentages (%)	
Gender			
Male	27	58.7%	
Female	19	41.3%	
Cousin Marriage	44	95.70%	
Purpura	46	100%	
Bruises	46	100%	
Nose Bleed	43	93.50%	
Gum Bleed	35	76.10%	
Gastrointestinal Bleed	7	15.20%	
Hematuria	8	17.40%	
Menorrhagia	5	26.30%	
Family History of GT	26	56.50%	
Transfusion History	38	82.60%	
Severity of Bleeding	Mild	6	13.00%
	Moderate	2	4.30%
	Severe	38	82.60%

Samples were analyzed using FACSCalibar (BD Biosciences) Cell Quest pro software, where 10,000 events were sampled from each reaction. Quantitative flow cytometric analysis of platelet integrin GPIIb/IIIa (α IIb β 3) was performed on 46 GT patients, revealing all the three types of GT. The level of glycoprotein receptor were $< 5\%$ of normal for type I, 5-20 % of normal for type II and $> 20\%$ of normal for type III. The α IIb β 3 (GPIIb/IIIa or CD41/CD61) levels on the platelet surfaces were quantified, identifying 20 (43.5%) type 1 GT cases with a mean α IIb β 3 level of 1.78 ± 2.2 % of normal. Seven (15.2%) patients were diagnosed with type II GT with a mean α IIb β 3 levels of 12.39 ± 3.92 % and CD 41 $<$ CD 61. Nineteen (41.3%) patients were diagnosed with type III GT having a mean value α IIb β 3 $50 \pm 2\%$ of normal platelets with level of CD 41 $<$ CD 61 in all the patients with type 3 GT (represented in Figures 1, 2, 3 & 4).

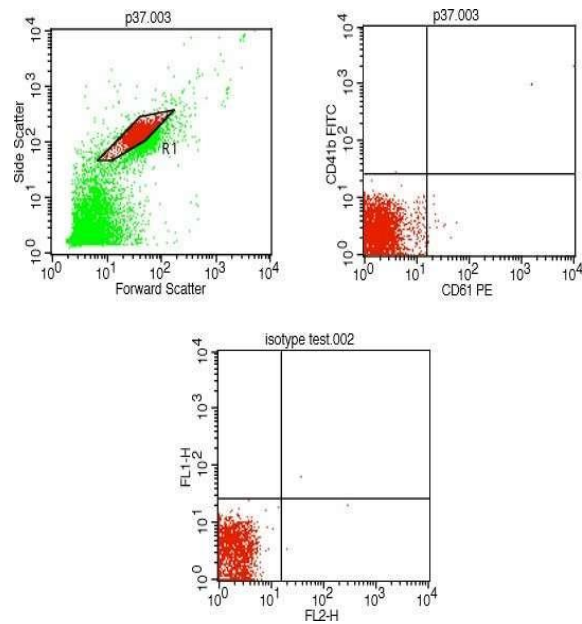


Figure 1:

Representative flow cytometric dot plots of Glanzmann's Thrombasthenia (GT) patient and control: (a) R1 shows platelet gating based on physical properties in forward vs side scatter dot plot (b) normal CD41 and CD61 marker activity in a healthy control (indicating normal activity of GPIIb/IIIa on platelets (c) Isotype control (d) reduced CD41 and CD61 activity in a GT patient, indicating diminished GPIIb/IIIa activity on platelets.

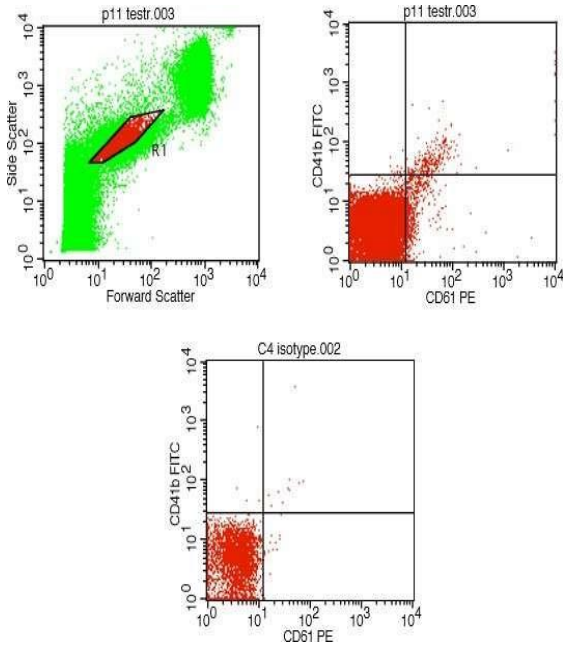


Figure 2:

The dot blot from a GT patient, platelets showed no activity of CD41 or CD61, indicating the absence of GPIIb- IIIa complex, which is consistent with type I GT

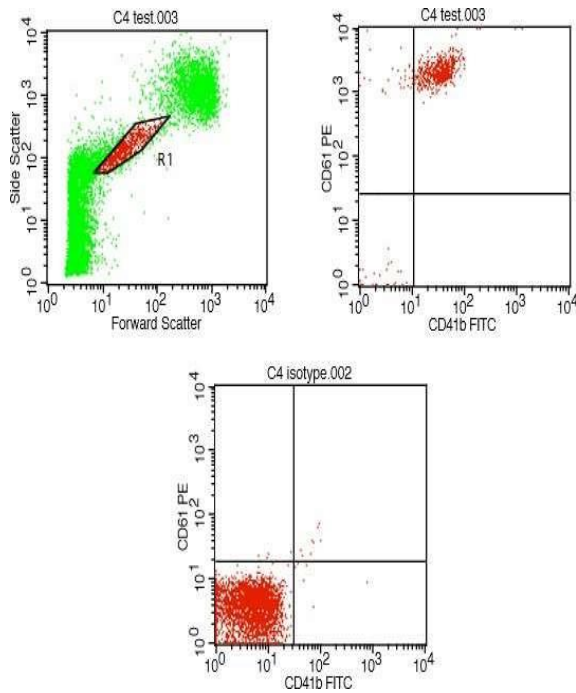


Figure 3:

The dot plot from a type II GT patient shows activity of CD 41 (0.35%) and CD 61 (13.65%). The patients had a family history of GT and consanguinity, but no history transfusions.

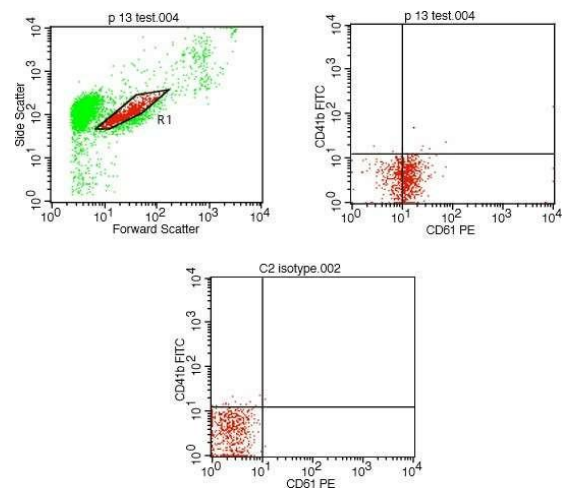


Figure 4:

In the type III GT patients, platelets showing activity of CD 41 (0.12%) and CD 61 (77397 %). The patients had a family history of GT, consanguinity, and history of transfusions.

Table-2: Association of Age and Laboratory Parameters with the types of GT

Lab Parameters	GT Type 1 (n = 20) Mean ± SD Median (IQR)	GT Type 2 (n = 07) Mean ± SD Median (IQR)	GT Type 3 (n = 19) Mean ± SD Median (IQR)	P-value
Age (years)	8.05 ± 6.5	17.0 ± 13.4	10.37 ± 4.3	0.024
Hb (g/dL)	10.2 ± 2.6	10.3 ± 2.2	9.3 ± 2.5	0.464
Platelets (x10 ³ /μL)	316.4 ± 110.8	288.5 ± 81.8	340 ± 122.3	0.55
Bleeding Time (Minutes)	11.60 ± 2	11.8 ± 1.1	11.3 ± 1.2	0.636
CD 41 Expression (%)	0.62 ± 0.97	0.67 ± 0.42	0.46 ± 0.6	0.751
CD 61 Expression (%)	1.16 ± 1.5	11.72 ± 3.5	49.62 ± 19.4	0.00
CD 41/61 Combine Expression (%)	1.95 ± 1.3	13.25 ± 4.24	50.74 ± 19.1	0.00

Association of age and laboratory parameters with the types of GT (Table 2) showed that only the age of the patients, expression of CD61 and combined CD41/ CD61 levels were found to be statistically significant. *P*-value <0.05.

Table: 3 Association of Glanzmann's Thrombasthenia (GT) type on Flow cytometry with Severity of Bleeding as per GLATIT score

GT Type	Severity of Bleeding			P-Value
	Mild	Moderate	Severe	
GT Type I (n= 20)	03	0	17	0.549
GT Type II (n = 07)	01	0	06	
GT Type III (n = 19)	02	02	15	

The association of clinical presentation, as per the GLATIT bleeding score, with the type of GT on flow cytometry is given in Table 3. It reveals that the majority of the patients were classified as severe bleeders among all the three types of GT, with no statistically significant correlation found between the type of GT and the severity of bleeding

DISCUSSION

Glanzmann's thrombasthenia (GT; MIM# 273800) is a rare autosomal recessive platelet disorder, with an incidence of approximately 1 in 1 million, but higher in regions like Pakistan where consanguinity is common. This study involved 46 GT patients (27 males, 58.7%, and 19 females, 41.3%), reflecting a male predominance similar to Iranian reports.⁶ The median age of patients was 9 years, consistent with studies from Turkey.⁴ USA⁷ and Iraq,⁸ and 65% were under 10 years old, aligning with Indian data.⁹ High consanguinity (95.7%) was noted, mirroring Iranian studies.^{4,10} Family history of bleeding was present in 56.5% of cases, slightly higher

than previous Pakistani studies,¹¹ with 43.5% lacking a family history, suggesting possible new mutations.¹² Common symptoms included epistaxis (93.5%), gum bleeding (76%), hematuria (17.4%), gastrointestinal bleeding (15.2%), and menorrhagia (26.5%), consistent with findings from the USA and China.^{13,14} Severity was classified as 13% mild, 4.3% moderate, and 82.6% severe.^{5,15} with most severe cases occurring in those under 10 years old. Over 84% required transfusions,^{6,16} highlighting the disorder's severity.

Hematological parameters showed a mean Hb of 9.8 ± 2.5 g/dL, with RBC indices indicating chronic bleeding and iron deficiency anemia, consistent with studies in Pakistan and India.^{1,17} All patients had prolonged bleeding time (11 minutes), a sign of poor platelet aggregation, though bleeding time is less specific than PFA-100.¹⁸ Platelet count, PT, and APTT were normal, which is characteristic of GT.¹⁹

Flow cytometry classified 20 patients (43.5%) as type I GT with a mean α IIb β 3 level of $1.78 \pm 2.2\%$ of normal, 7 patients (15.2%) as type II with a mean α IIb β 3 level of $12.39 \pm 3.92\%$, and 19 patients (41.3%) as type III with a mean α IIb β 3 level of $50 \pm 2\%$ of normal. CD41 was lower than CD61 in all type III cases, consistent with previous studies.²⁰ Type I GT was most common, followed by type III, as noted in India and Iraq.⁸ The study found no significant correlation between GT type and bleeding severity, aligning with previous research.^{7,21} Flow cytometry of GPIIb/IIIa in relatives may aid in detecting carrier status.²²

The study highlights the need for a thorough assessment of disease-causing mutations in GT patients from highly consanguineous Pakistani populations. This approach could provide new insights into α IIb β 3 integrin biology and enhance therapeutic options, including gene therapy, through the identification and characterization of novel mutations.

CONCLUSION

The novelty of this study lies in its focus on the Pakistani population, where consanguinity increases the prevalence of autosomal recessive disorders like Glanzmann Thrombasthenia (GT). As the first local study to use flow cytometry for GT classification, it provides essential baseline data for genetic counseling, explores GT subtype-bleeding severity correlations, and suggests improved management strategies.

CONFLICT OF INTEREST

None

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None

AUTHOR'S CONTRIBUTIONS:

SG: Manuscript Writing

MS: Date Collection

TF: Supervision

FS: Manuscript Editing

GM: Thesis Working

IU: Manuscript Writing

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Original Article

ASSESSMENT OF EMPATHY SCORES AMONG MEDICAL STUDENTS OF A PRIVATE MEDICAL COLLEGE, LAHORE, PAKISTAN

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ABSTRACT:

Background: The most vital component of healthy physician-patient relationships is empathy, which is strongly linked to better patient outcomes. The objective of this study was to determine the empathy score among medical students across the academic years and to find out the association of empathy scores with gender, year of study and specialty chosen by the students.

Materials and Methods: A cross-sectional study was conducted among the medical students after having approval from institutional review board on a validated self-reported Jefferson scale of empathy –student version (JSE-S) from August 23 to January 24. Data was collected from the students who were present on the day of data collection by convenience sampling technique. Data was analyzed by SPSS 25 version.

Results: Out of 619 students 594 filled the questionnaire. The mean empathy score was 88.1±10.31. There was no statistically significant relationship of gender with mean score of empathy p Value (0.08) but there was statistical difference of the empathy score with academic years(p=0.002). There is statistically significant association of gender with perspective (p=0.00) and compassion (p=0.024) subscales of JSE-S version. However, there is significant statistical difference of perspective, compassion and walking in patient shoes subscales in relation to academic years (p-value=0.001, 0.001 and 0.026 respectively).

Conclusion: The empathy score was low in this study. The empathy score was high in first year and fourth year. No relationship was demonstrated depending on the career preference. Year of medical training and preclinical/ clinical categories has strong and significant relationship with empathy levels.

KEYWORDS: Empathy, Medical students, Assessment, Jefferson scale of empathy

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INTRODUCTION

The ability to feel other people's emotions, see things from their point of view, and put yourself in their position is known as empathy. In essence, it involves taking on people's perspective and experience their feelings.¹ Health care professionals

universally recognize the necessity of empathy as a vital skill for cultivating interpersonal interactions between patients and doctors. Furthermore, empirical evidence demonstrates that empathy increases both patient and physician satisfaction, enhances patient compliance, improves diagnostic accuracy, and positively influences therapeutic outcomes.² Therefore, for medical students to thrive as doctors, it is imperative that they nurture and uphold their clinical empathy competence

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throughout their training. They can develop the skill of empathy via education.³ Physicians' empathic attitude raise diagnostic accuracy and clinical competence, minimize emotional distress, improve quality of life and increase therapeutic outcome in patients.⁴ Medical students must study about empathy because it is a crucial aspect of their profession.⁵ Empathy is divided into two categories: affective (emotional) empathy and cognitive empathy. The capacity to comprehend another person's circumstances without making them one's own is cognitive empathy.⁶ Development of empathy is a slow and gradual process. The initial steps are active listening, thinking and comprehending followed by communicating the awareness empathically, and ultimately comes the sense that your counterpart has understood you.⁷ Medical institutions and professional organizations promote a balance between clinical detachment and over involvement, characterizing empathy as accurately recognizing another person's emotional state without going through that state themselves.⁸ Nurturing empathy in medical practice, as the art of history taking and physical examination are necessary for patient's satisfaction and better therapeutic outcome.⁹ Many studies have supported empathy-enhancing interventions for undergraduate medical students. These interventions range from experiential learning exercises with simulated patients, focus on communication skills, reflective writing exercises, and role-playing.¹⁰ According to a longitudinal study carried out in Pakistan, targeted empathy-enhancing activities included patient-centered modules in 3rd year and stress management workshops for final year students. This study assessed the evolution of empathy consecutively from 2015 to 2019 by use of Jefferson Scale of Empathy. The improvement in empathy scores in the third year students and in internship may have influenced by the patient-centered module, which concentrates on exercises that promote empathy. It might be possible to help medical students to develop empathy by scheduling repeated formal events throughout all of their clinical years.¹¹ The

medical school system in Pakistan place little emphasis on developing humanistic qualities and primarily concentrate on imparting the knowledge needed practice medicine.¹² The absence of empathy development in Pakistan's medical curriculum, as highlighted by the study conducted in Lahore, raises concerns about the holistic approach to medical education.^{13,14} As empathy plays a very important role in health care, the current study evaluated the level of empathy among undergraduate students from first to final year and also determined the relationship of empathy scores with gender, year of study and priority of specialty among them.

MATERIALS AND METHODS

A cross-sectional study was conducted in a private medical college among the medical students from August 2023 to January 2024. Out of 619 participants across the five years, 594 were included who were present on the day of data collection through convenience sampling. Research was conducted after approval from IRB Fatima Memorial Hospital College of Medicine and Dentistry letter # FMH-25/08/2023-IRB-1295. The exclusion criteria included those students who were absent on the day of data collection. The dependent variable was empathy and independent variables were age, gender, year of study and specialty. The JSE-S version was used to assess the empathy score which is a self-reported standardized validated questionnaire. Written permission was obtained from Jefferson Thomas University before employing this tool for data collection. This questionnaire includes 20 Likert-type items with a seven-point scale ranging from "strongly disagree" to "strongly agree". Items 2, 4, 5,9,10,13,15,16,17 and 20 were positively scored on Likert scale (i.e. Strongly disagree =1.... Strongly agree=7 whereas items 1,3,6, 7, 8, 11,12,14, 18 and19 were reverse scored (i.e. ,Strongly agree=1....Strongly disagree=7) . The score ranged from 20-140. Higher score indicate more empathy among the students. Specialties were divided into three categories:

technology-oriented, people-oriented, and other specialties. Regarding the likelihood of pursuing each expertise, students indicated their career specialty intentions. After getting permission from the heads of departments 2-3 students of 4th MBBS of Batch A went to the lecture halls from 1st to final year and briefed the students about the questionnaire. Then the questionnaire was distributed among the students after taking verbal informed consent from them. Data was entered, cleaned, and analyzed using SPSS 25.0. The negatively worded items were recorded to re-score them in the positive direction. Categorical variables were described using proportions and percentages, whereas continuous variables such as age and scores of Jefferson scale of empathy were described using mean and standard deviation. The ANOVA test was applied to compare the mean empathy score of students for five years, career aspirations and two age groups for statistical significance. To determine the statistical significance of empathy score with gender, an independent sample t-test was applied. For this investigation, a p-value of ≤ 0.05 was deemed significant.

RESULTS

Out of 619 respondents of all medical years, 594 (95.9%) filled the questionnaire. Out of 152 students of second year 150 (98.6%) responded to the questionnaire followed by first year in which out of 149 students 145(97.3%) responded. About 352 (59.3%) students were less than twenty years with mean age of 21.56 ± 1.99 years and 400 (67.3%) were females. The Jefferson score ranges from 86-90 among 149 (25.1%) students followed by 81-85 among 114 (19.2%) medical students whereas mean score was 88.1 ± 10.31 (Table-1). The mean score of JSE-S was almost similar among undergraduates less than 22 years (88.24 ± 10.04) and more than 22 years (88.00 ± 10.72) with no statistical difference ($p=0.78$). The mean score of empathy among the males and females is 87.10 ± 11.37 and 88.65 ± 9.7 respectively

reporting no statistically significant association in relation to gender ($p=0.08$). Statistically significant association of JSE-S mean score in relation to academic years ($p=0.002$) was reported. (Table-2). Whereas the mean score of females in perspective taking, compassionate care and standing in the patient's shoes is greater as compared to males. There is statistically significant association of gender with perspective ($p=0.00$) and compassionate ($p=0.024$) subscales of JES-S version. However, there is significant statistical difference of perspective, compassionate and walking in patient shoes subscales in relation to academic years (p -value= 0.001 , 0.001 and 0.026 respectively) (Table -3).

Table 1: Frequency distribution of empathy scores among the medical students

Score intervals	Frequency	Percent
≤ 75	53	8.9%
76-80	59	9.9%
81-85	114	19.2%
86-90	149	25.1%
91-95	99	16.7%
96-100	55	9.3%
101-105	36	6.1%
106-110	17	2.9%
111-115	7	1.2%
116-120	4	0.7%
126-130	1	0.2%
Total	594	100.0%

Table 2: Mean Empathy score distribution according to socio-demographic characteristics of the students.

Variables	N (Percentage)	Mean \pm SD	t-test & P-value
Age			
Less than 22years	352 (59.2%)	88.24 \pm 10.04	t-test 0.279 P - 0.781
More than 22years	242 (40.7)	88.00 \pm 10.72	
Gender			
Male	194 (32.6%)	87.11 \pm 11.38	t-test 1.711 P - 0.088
Female	400 (67.3%)	88.65 \pm 9.73	
Academic year			
1st year	145 (97.3%)	57.599 \pm 7.21	ANOVA30.43 P-0.002
2 nd year	150 (98.6%)	54.647 \pm 8.00	
3 rd year	91 (94.7%)	51.80 \pm 9.76	
4 th year	109 (96.4%)	58.64 \pm 7.06	
Final year	99 (90.8%)	50.74 \pm 10.95	
Pre-clinical/Clinical			
Preclinical	295 (49.6%)	88.26 \pm 9.40	t-test 0.268 P-0.788
Clinical	299 (50.3%)	88.03 \pm 11.16	
Career preference			
Patient oriented	299 (50.3%)	88.07 \pm 10.65	F=0.050 P-0.951
Technology oriented	239 (40.2%)	88.30 \pm 9.88	
Undecided	56(9.42%)	87.91 \pm 10.50	

Table -3: Frequency of mean score JSE-S in relation to its three subscales

Subscales of JSE	Perspective	Compassionate	Walking in patient shoes
Age of students	Mean \pm SD	Mean \pm SD	Mean \pm SD
<22 years N=	55.63 \pm 8.23	24.71 \pm 8	7.9 \pm 2.53
>22years	54.46 \pm 9.8	54.46 \pm 7.48	25.7 \pm 7.48
T-test –P-value	1.53, p=0.13	-1.46, p=0.14	-1.9, p=0.06
Gender			
Male (194)	52.98 \pm 10.38	26.13 \pm 7.25	7.99 \pm 2.50
Female (400)	55.99 \pm 8.06	24.60 \pm 7.98	8.07 \pm 2.46
t-test &p-value	-3.85&p=0.00	2.26 &p=0.024	-0.348&p=0.72
Year of medical training			
Ist year	57.56 \pm 7.22	22.59 \pm 6.99	7.79 \pm 2.48
2nd year	54.65 \pm 8.01	26.23 \pm 8.58	7.7 \pm 2.54
3 rd year	51.8 \pm 9.77	27.98 \pm 7.81	8.67 \pm 2.23
4 th year	58.64 \pm 7.07	23.22 \pm 7.01	8.22 \pm 2.53
5 th year	50.75 \pm 10.95	26.51 \pm 6.86	8.14 \pm 2.41
F-ratio &P=value	17.67, p=0.001	10.76&p=0.001	2.77&p-valu=0.026
Preclinical/Clinical			
Preclinical N=	56.08 \pm 7.75	24.44 \pm 8.03	7.75 \pm 2.5
Clinical N=	53.95 \pm 9.96	25.76 \pm 7.47	8.33 \pm 2.4
t-test &p-value	2.91 &p=0.004	-2.07&P=0.039	-2.91 &p=0.004
Choice of specialty			
Patient oriented N=	55.42 \pm 8.83	24.55 \pm 7.99	8.1 \pm 2.44
Technology oriented	54.58 \pm 9.02	25.77 \pm 7.47	7.95 \pm 2.5
Undecided N=	54.59 \pm 9.73	25.21 \pm 7.76	8.11 \pm 2.49
Age of students			
F-ratio &p-value	0.655& p=0.520	1.658&p=0.191	0.245&p=0.783
Less than 22 years N=	55.63 \pm 8.23	24.71 \pm 8	7.9 \pm 2.53
More than 22years	54.46 \pm 9.8	54.46 \pm 7.48	25.7 \pm 7.48
T-test –P-value	1.53, p=0.13	-1.46, p=0.14	-1.9, p=0.06
Gender			
Male (194)	52.98 \pm 10.38	26.13 \pm 7.25	7.99 \pm 2.50
Female (400)	55.99 \pm 8.06	24.60 \pm 7.98	8.07 \pm 2.46
t-test &p-value	-3.85&p=0.00	2.26 &p=0.024	-0.348&p=0.72
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Patient oriented N=	55.42 \pm 8.83	24.55 \pm 7.99	8.1 \pm 2.44
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Undecided N=	54.59 \pm 9.73	25.21 \pm 7.76	8.11 \pm 2.49
F-ratio &p-value	0.655& p=0.520	1.658&p=0.191	0.245&p=0.783

DISCUSSION

This study was conducted among the medical students across the academic years to find out the empathy score as it is a very important skill for cultivating interpersonal interactions between patients and doctors. The current study revealed that mean empathy score among medical students was 88.18 ± 10.31 . However, there is marked variation in empathy scores globally as reported in various studies: India.¹⁵(105.77 ± 18.5), Bangladesh.¹⁶ (110.41), Malaysia.¹⁷(106.2 ± 13.5), Iran¹⁸ (106.42 ± 14.8), and Spain¹⁹ (120 ± 11.92). On the contrary in, a study of Lahore.²⁰ the mean over all empathy level was 90.63 ± 11.5 which is comparable to our result. Whereas a study of Sukker. stated the mean empathy score of 98.11 ± 12.31 .²¹ The marked variation in empathy score in various countries may be due to differences in cultural factors, customs, ethnicity, spiritual belief, educational system, due to variations on empathy training, varying nature of interactions and work load in different health care systems. The mean empathy level among females was slightly higher (88.65 ± 9.73) as compared to males (87.11 ± 11.38) but there is no statistically significant association of empathy level ($p=0.088$) with gender. An Islamabad study results corroborate with our study reporting no significant statistical association ($p=0.302$). Contrary to this a study of Iran ($p=0.001$), India. ($p<0.001$) and Malaysia ($p=0.004$) depicted significant statistical association between mean empathy score and gender.^{15,17,18,22} Non-significant association between empathy scores and gender can be attributed to several factors for example these medical students undergo similar training and socialization process regardless of gender which can lead to similar levels of empathy among male and female students. Also cultural and societal changes due to which younger generations may experience less rigid gender socialization, leading to more similar empathy levels. Individual differences like personality, experiences and education may overshadow gender differences. Understanding

these factors can provide insight into why studies might not find significant differences in empathy in relation to gender. Nevertheless, significant association between empathy and gender can be described as females are often socialized to be more emotionally attuned, enhancing empathy, while males may emphasize independence. Use of expressive communication and brain differences related to emotional processing may contribute to higher empathy in females.

A significant statistical relationship between empathy score and year of academic session was reported in this study($p=0.002$). Same results were reported by a study conducted in Islamabad ($p=0.003$). The highest empathy score was reported by the 4th year medical students followed by first year. The lowest score was reported by the final year students in the current study. Whereas a Kerala study revealed that students of first year had higher empathy score as compared to fourth year with p -value <0.001 .¹⁵ Studies have identified various factors for this consistent finding. As students progress through their training, the cumulative stress can diminish their ability to empathize with patients. Increased work load and responsibilities limit time for empathetic patient interactions. Desensitization can also occur due to repeated exposure to patient suffering. Another reason can be due to lack of focus on empathy in assessments and feedback reduces its development. A Malaysian study depicted no difference between academic years and empathy score ($p=0.15$).¹⁷ There is no statistical difference between career preference and empathy score as seen in this study ($p=0.951$). The results of Kerala. (0.9), Chatterjee study (0.054) and Turkey (0.5) are congruent with this study.^{15,23,24} Contrary to this, Mirani SH et al, reported significant differences in empathy score between those who chose people oriented specialty as their future preference when compared to those who chose technology oriented or remained undecided.²⁵ There is significant difference of gender with

perspective ($p=0.00$) and compassionate (0.024) subscale but no association with walk in shoes subscale (0.72) in the recent study. An Iranian study reported statistical relationship between three subscales of JSE-S with the gender.¹⁸ Whereas a study conducted in private medical college of Lahore, the mean values of perspective taking, compassionate care and standing in patients shoes was almost similar among males and females and thus showing no statistical significance in JSE subscale.²⁶

These results suggest that gender differences exist in specific aspects of empathy with females scoring higher in perspective taking and males scoring higher in compassionate care, while both genders show similar scores in the ability to metaphorically walk in a patient's shoes. The higher compassionate care score for males may be due to variations in how empathy is self-assessed across genders or the fact that compassionate expressions are sometimes viewed differently by male students.

The ANOVA test reveals significant differences in empathy scores across different years of medical school for all three categories which are perspective ($p<0.001$), compassionate ($p=0.001$, and patient shoes ($p=0.02$) respectively. This suggests that empathy levels, as measured by these scores, fluctuate throughout medical education, with the most significant variations observed in the perspective and compassionate categories in the present study. On the other hand, Mirani et al. study revealed a downward trend in three subscales in five years of medical school.²¹ Long work hours, sleep deprivation, and added obligations that accompany the later years of medical school were blamed for this.

As the number of medical school years increased, so did the compassionate domain of empathy ratings ($F=8.32$, $p=0.004$).¹⁹ A study of Oman has depicted not much difference between the year of medical training and the three subscales of JSE-S.²⁷ Whereas in another study, perspective taking was higher in third year students, compassionate care scores were

higher among first year students while mean score of walking in patient shoes was higher in final year students. There is significant difference of higher empathy scores among clinical students as in compassionate care ($p=0.039$). The Malaysian study results corroborates to our study in relation to compassionate care but the cognitive empathy scores remain unchanged. According to one theory, affective empathy, which is more of an autonomic and basic process than cognitive empathy, may have developed as a result of the student's clinical encounter with the patients.

CONCLUSION

Medical students showed a low mean empathy score of 88.65 ± 9.7 . Empathy scores varied significantly across academic years, but not by gender. However, gender and academic years influenced specific subscales of empathy, such as perspective and compassionate care.

RECOMMENDATIONS

1. Empathy training should be incorporated in curriculum of the students which should include empathy courses, role playing and narrative medicine to help students connect with patients' experiences
2. Communication skills should be taught to the students e.g.; active listening, validating emotions and showing understanding can greatly improve empathy
3. Interdisciplinary training with nursing, social work, and other healthcare fields allows students to learn empathy by appreciating diverse roles and perspectives within patient care.
4. Address burnout through mental health support, work-life balance and self-care to sustain empathy throughout training.
5. Patient feedback after interactions can offer valuable insight into the student's ability to

communicate and express empathy.

CONFLICT OF INTEREST

None

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AUTHOR'S CONTRIBUTION

SH: Conceptualization

AA: Manuscript writing and Data Analysis

AS: Data Collection & Review

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Original Article

PREVALENCE AND FACTORS ASSOCIATED WITH STRESS MANAGEMENT AMONG HEALTHCARE PROFESSIONALS IN LAHORE

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Abstract

Background: Elevated stress levels can significantly impact both the mental and physical well-being of healthcare professionals. This chronic stress can lead to burnout, anxiety, and various health issues, which in turn can compromise the quality of care they provide. Consequently, effective stress management techniques become essential tools for their well-being and for enhancing their overall performance. The objective of the study was to investigate the prevalence and risk factors of stress management among Health Care Professionals (HCPs) in Lahore.

Materials and Methods; In this study, data was collected from 277 HCPs from public and private tertiary care hospitals in Lahore, through a self-reporting questionnaire. This is a cross-sectional study. The questionnaire consisted of 43 items, identifying many risk factors of stress. The Perceived Stress Scale (PSS), developed by Cohen et al. in 1981, was utilized to evaluate the stress levels of participants. The relationship between stress and associated risk factors was analyzed. Additionally, the coping strategies employed by participants were documented. The data has been analyzed using SPSS version 21.0.

Results: The prevalence of stress among HCPs in Lahore in this study was 49.2%. Various environmental factors caused stress in 88.4% of HCPs. Social stress was experienced by 63.2% of HCPs in their lives while 56 % faced organizational stress. A significant association was observed between PSS scores and environmental factors like traffic, pollution, finances, biological factors, social factors, and organizational factors like overwork and work politics. Certain coping strategies like thinking positively and controlling emotional responses were used by HCPs to decrease their stress levels.

Conclusion: HCPs in Lahore are experiencing a high level of stress in their work place as well as personal lives.

Key Words: Stress management, prevalence, risk factors of stress, Health Care Professionals

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INTRODUCTION

Stress is the body's natural response to situations that require us to take action. It can serve as a motivating force, helping us navigate challenge and stay focused in demanding

circumstances. Whereas a certain amount of stress is important to accomplish certain tasks, too much stress is the precursor to many health problems.¹ Be it mental, biological, or social, many health issues arise due to continuous, high levels of stress. Many diseases like diabetes, Hypertension, and stomach ulcers are linked to high stress levels in individuals.²

The World Health Organization has identified stress as a global epidemic of the 21st century. Due to digitalization, overpopulation, and inflation, everyone is experiencing increased

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stress levels in their everyday lives, all over the world. Although people living under the poverty line are affected more, it seems that the professionals are experiencing their fair share of stress. The prevalence of stress among HCPs was found to be 59% in India.³ Medical professionals suffer from higher levels of stress than other professionals.⁴ This study aims to highlight the major everyday hassles causing stress to health professionals in the cosmopolitan city of Lahore. The perceived stress scale designed by Cohen et al. is used to measure the levels of stress.⁵ The participants analyzed their own stress and reported on the questionnaire. The participants helped in identifying the various kinds of stressors they experience. The participants also stated whether they performed certain activities to alleviate their daily stress and whether that helped them.

A mentally and physically healthy individual can contribute more to society than an overstressed, exhausted person especially can, especially in the field of healthcare. Better mental health in HCPs diffuses at large to better mental health of our whole society. It is stated that daily hassles including stress on a small and regular basis causes more cumulative stress than a big stressful incident.⁶ Therefore, it is important to find the prevalence of stress in Lahore among the HCPs and to identify the risk factors affecting them daily. Stress has become a global epidemic.⁷ Among Australian nurses' the prevalence of stress was found to be 41.2%.⁸ The prevalence of stress among HCPs was found to be 44.86% in Bangladesh.⁹ The prevalence of stress in Pakistan among HCPs was around 35% in Karachi.⁴ The gravity of the situation needs to be examined and necessary action needs to be taken to alleviate stress.

There are many global issues like air pollution, water pollution, and lack of resources, that cause stress in a community but it appears that these issues are more profound and severe in Pakistan. The result is that everyone appears stressed. Stress is not only an issue of developing countries like Pakistan but many developed countries are suffering from it as well.¹⁰ Both the social and physical environments play a critical

role in shaping physical and mental health, exerting their effects through the neuroendocrine and immune systems.¹¹ This study plans to explore the risk factors contributing to stress among HCPs and their coping strategies in Lahore

MATERIAL AND METHODS

The cross-sectional study was conducted in Lahore (from February 2023 to July 2023), after approval from Departmental Doctoral Program Committee (DDPC) Institute of Social and Cultural Studies, Letter no: D/119/ISCS University of Punjab Lahore. The research instrument employed was a questionnaire encompassing four distinct sections. Convenience sampling technique was used. Questionnaires were distributed in four different hospitals; two of the hospitals were public and two were private Hospitals. The sample included 277 participants, ensuring a 95% confidence interval and a margin of error of 5%. The study respondents are the Health Care Professionals working in these hospitals. The HCPs who were working full-time were included in this study. HCPs include doctors, nurses, lab technicians, nutritionists, and physiotherapists. Anyone who did not consent and was not a direct employee of the hospital were excluded from the study. Convenience sampling was used for questionnaire distribution in the hospitals.

The questionnaire consisted of 4 sections. The first section presented the demographic details, which were age, gender, residence, education, designation, marital status, and family income. This section comprises a total of 13 items. The second part included the Perceived Stress Scale (PSS).⁵ It contains 10 questions with Likert-type scale. The third part helped identify the various factors affecting the stress of individuals. Environmental, social, Biological, and Organizational stressors. Some other risk factors of stress are also mentioned here. There are 13 items in this part of the questionnaire. The fourth part consists of the coping strategies used in stressful situations. They were developed by

Lazaurus and Folkman.¹² The data was analyzed using SPSS (version 21.0). Frequencies and percentages were tabulated. Chi-square was applied to all the parameters and associations were noted by determining the P-value. Taking the cutoff point of the PSS score to be 50%. Low-level stress and High-level stress were categorized and the chi-square test was applied.

RESULTS

A total of 277 Health Care Professionals have participated in the study. The socio-demographic characteristics of participants are presented in Table 1.

Table no 1: Descriptive Statistics of Sociodemographic Characteristics (N=277)

Variables		Frequency (n)	Percentages (%)
Age	20-25 years	99	35.7
	26-30 years	6	34.7
	31-35 years	37	13.4
	36-40 years	16	5.8
	More than 41 years	24	8.7
Gender	Male	84	30.3
	Female	193	69.7
Types of Facilities	Public	181	65.3
	Private	96	34.7
Marital Status	Married	165	59.6
	Single	110	39.7
	Divorced	2	0.7
Designation	Doctors	208	75.1
	Nurses	51	18.4
	Others	18	6.5
Working hours per week	>40 hours	113	40.8
	40 to 60 Hours	103	37.2
	<60 Hours	60	21.7

The demographic data showed that almost 70 percent of the participants were between the ages of 21 years to 30 years. Two-thirds of the participants were females. One-third were males. 60 % of participants were married. Two-thirds of them were doctors. One-third included nurses, physiotherapists, nutritionists. Two-thirds of the participants worked more than 40 hours per week.

Table no 2: Risk Factors associated with Stress levels of HCPs (N=277)

Variables	Low Stress Number (n) Percentages (%)	High Stress Number (n) Percentages (%)	P value
Designation			
Doctors	118 42.6	90 32.5	0.5
Nursing Staff	36 13	22 7.9	
Others	9 3.2	2 0.7	
Working Hours			
40 hours	73 26.4	40 14.4	0.18
40-60 Hours	56 20.2	47 17	
>60 Hours	30 10.8	30 10.8	
Environmental			
None	20 7.2	12 4.3	0.001
Pollution	20 7.2	10 3.6	
Traffic	32 11.6	9 3.2	
Political Situation	25 9	9 3.2	
Finances	22 7.9	30 10.8	
All	41 14.8	47 17	
Social			
None	81 29.2	21 7.6	0.000
Relationship Issues	31 11.1	50 18.1	
Peer pressure	32 11.6	26 9.4	
Daycare issues	14 5.1	13 4.7	
All	2 0.7	7 2.5	

Biological			
None	127 45.8	72 26	0.003
Diabetes	11 4	5 1.8	
Hypertension	4 1.4	9 3.2	
Angina	3 1.0	2 0.7	
Depression	15 3.4	27 9.7	
Other	0 0	2 0.7	
Organizational			
None	79 28.5	43 15.5	0.009
Overworked	52 18.8	38 13.7	
Boss	2 0.7	12 4.3	
Office Politics	26 9.4	23 8.3	
All	1 0.36	1 0.36	
Frequency of Exercise			
Never	116 41.8	95 34.3	0.03
Daily	26 9.4	7 2.5	
>2 times a week	18 6.5	15 5.4	
Frequency of Walk			
Never	71 25.6	72 26	0.01
Daily	45 16.3	29 10.5	
>2 times a week	44 15.5	16 5.8	

Regarding the risk factors, interesting findings were that 40% of the participants spend more than two hours on social media per day. Fifty-one percent of the participants reported that they do not engage in relaxing walks. Furthermore, 76.2% indicated that they do not exercise on a regular basis. The primary sources of stress identified by the participants included financial concerns, the political situation within the country, traffic conditions, and pollution, listed in that order of significance. This research indicates that nearly 30% of healthcare professionals (HCPs) encounter relationship

challenges, while 21% report experiencing various forms of peer pressure. Notably, depression emerges as the predominant biological stressor among individuals in the 21-30 age demographic. Additionally, the leading organizational stressors identified are excessive workloads and office politics.

In this study the prevalence of stress among HCPs was found to be 49.2%. Score of less than 20 was labelled low stress and higher than 20 was labelled high stress using PSS scale values. Chi Square was applied to determine the relationship between various factors and Perceived levels of stress according to PSS scale. No relationship was found between various demographic factors and stress levels. Participant’s age, gender, marital status and number of kids had no significant effect on their stress levels.

The positive findings were: that social stressors like relationship issues and peer pressure caused high perceived stress levels, with a p-value of 0.000. Participants with depression and hypertension scored high on PSS, showing a p-value of 0.003. Office politics, boss issues, and overwork caused high-stress levels, with a p-value of 0.009. The environmental factors which include Pollution, traffic, political situation, and finances also were risk factors for high stress showing a p-value of 0.001.

Among other risk factors participants who never went for a walk had high-stress levels with a P-value of 0.01, similarly participants who never exercised had high-stress levels with a p-value of 0.03.

The chi square analysis showed that among the coping strategies thinking positive, p value 0.02 accepting a new challenge (p value 0.01) and seeking escape from your problems, p value 0.03, were found to be significantly associated with stress.

Table 3: Association of coping strategies with stress levels

		Low Stress	High Stress	P value
		Frequency (n) Percentages %	Frequency (n) Percentages %	
1.	Think positive and learn a lesson			
	Yes	145 52.3	95 34.3	0.02
	No	15 5.4	22 7.9	
2.	Accept a new challenge			
	Yes	143 51.6	92 33.2	0.01
	No	17 6.1	25 9	
3.	Accept that you might be part of a problem			
	Yes	121 43.7	96 34.7	0.18
	No	39 14.0	21 7.6	
4.	You might be perceiving a situation wrong.			
	Yes	126 45.5	95 34.3	0.36
	No	34 12.3	22 7.9	
5.	Seek support from family and friends.			
	Yes	120 43.3	83 30	0.27
	No	40 14.4	34 12.3	
6.	Seek escape from your problems.			
	Yes	50 18	54 19.5	0.03
	No	109 39.3	63 22.7	
7.	Control your own emotional response in stress.			
	Yes	141 50.9	99 35.7	0.3
	No	20 7.2	17 6.1	

DISCUSSION

In the present times of digitalization and social media, life is very much fast-paced. Health Care Professionals are trying to accomplish many tasks, performing many jobs, and managing a to-do list that never ends. Additionally, the emotionally and physically demanding nature of

their work, exposure to patient suffering, and the added burden of decision-making further compound their stress levels.⁶ Travelling distances to work have increased due to the ever-expanding large cities. The traffic situation is quite frustrating due to extreme rush and unlawful traffic situation.

As PSS is not a diagnostic tool, there are no cut-off values for moderate or severe stress. The higher the score on Perceived Stress Scale, the more stressed the person is.¹³ However, in their study Silvia et al took the cut off value of 39% PSS score to be acceptable upper limit of stress.¹⁰ In this study 50% cut off value is taken. The prevalence of stress in HCPs of Lahore, according to this study was found to be 49.2% based on PSS scores. The stress levels in this study were more than those reported by Nochiawong which was 36.5%.¹⁵ In a similar study 74.7% nurses reported stress in a tertiary Hospital in Karachi.⁴ This number is higher than what was reported in this study.

The second objective was identifying the risk factors associated with stress among healthcare professionals. Ninety percent of healthcare professionals encounter various forms of environmental stress. Finances, Political situation and traffic are the main causes of stress, among HCPs in Lahore. In a similar study done in Karachi among nurses 36.5% reported moderate stress while 61.5% reported severe stress.¹⁶ The demands placed on individuals have significantly increased, creating a landscape where higher expectations are the norm. Compounded by the prevalence of chaotic traffic, this environment adds further stress to individuals who may already be feeling exhausted. Additionally, the role of news media and social platforms often exacerbates these pressures, rather than alleviating them. Rather when there is political instability, stressful news shown repeatedly further aggravates stress. Finances are another stressful story that almost all Health Care professionals suffer from. Air pollution and improper waste disposal are significant contributors to an increase in health issues and heightened stress levels.¹⁷ Furthermore, while social media has become an

essential component of modern communication, it often consumes valuable time that could otherwise be spent on relaxation and family interactions. Organizational stress is also an added factor to this. In this study, 62% of HCPs experienced some form of social stress. Most common form of social stress were relationship issues and peer pressure issues. Seventy-one (71%) percent of participants did not report any biological issues. This outcome can largely be attributed to the fact that approximately two-thirds of the participants belonged to the age group of 21 to 35 years. Job dissatisfaction was related to stress (p value: 0.009).¹⁸ Most common biological stressor was depression, The prevalence of depression in this study was thirty percent (30%) - which is alarming in younger HCPs. 54.9% of HCPs experienced some form of organizational stressors. most common were overwork 32.5%, no good chemistry with boss, and office politics 17.3%. According to a similar study in Nigeria 35% HCPs experienced overwork, 29.8% experienced office politics. which is higher than this study.¹⁹

Third objective of this study was to assess the association between stress and various risk factors. To achieve this aim, Chi-square test was employed. No association was found between any demographic factors and stress. This shows that males and females were equally stressed. All age participants are stressed. According to this study participant's marital status and number of kids had no significant effect on their stress levels. Erdogan had similar findings in their study in Turkey¹⁴

In this study no association was found between Perceived Stress and working hours. In a similar study it was found that a greater level of Perceived Stress was caused by overwork.²⁰ A significant association was seen in this study between stress levels and environmental factors (p-value 0.001), social factors (p-value 0.000), biological factors (p-value 0.003), and organizational factors (p-value 0.009). In Nigeria a similar study prevalence of stress due to increased workload and office politics was found to be 15.4%; 9.9% respectively.²¹

According to this study, participants who did not take a walk regularly had high-stress levels with a p-value 0.001. participants who never exercised also had high-stress levels. A p-value 0.002 shows a positive correlation between these factors and stress levels.

The chi-square analysis showed that among the coping strategies (p value: 0.01), accepting new challenges, finding an escape from problems (P value: 0.03), and thinking positively and learning a lesson from their own experience (p Value: 0.02) had significant associations with stress levels. In a similar study 63% nurses found escape in overeating due to high stress levels.²²

Limitation of this study is that the most readily available, and willing participants were the house officers and medical officers. Therefore, the data is short on specialists and nursing staff. Further studies need to be carried out where there is equal participation of all age groups and all designations of HCPs. Additional tools, other than PSS, need to be employed to measure the stress and depression levels to further analyze the mental health of HCPs.

CONCLUSION

The findings of this study indicate that the prevalence of stress among healthcare professionals is significantly elevated. Approximately 50% of healthcare practitioners in Lahore experience high levels of stress.

CONFLICT OF INTEREST

None

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None

AUTHOR'S CONTRIBUTION

NS: Data Collection and Analysis

RZ: Manuscript Writing

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Case Report

A DUAL NEUROLOGICAL INSULT: IPSILATERAL SUBACUTE SUBDURAL HEMATOMA AND ISCHEMIC STROKE IN AN ELDERLY PATIENT WITH CONTRALATERAL WEAKNESS.

Omaid Farooq¹, Fiza Ashfaq², Siddiqua Rehman³

Abstract:

This case report discusses a rare occurrence of simultaneous subacute subdural hematoma (SDH) and ischemic stroke in a 95-year-old male patient with a history of chronic obstructive pulmonary disease (COPD) and chronic kidney disease (CKD). The patient presented with contralateral weakness and a series of diagnostic challenges. This report underscores the complexities in the diagnosis and management of these concurrent neurological insults. A detailed analysis of the clinical findings, treatment strategies, and prognostic considerations is provided, with reference to existing literature on similar cases.

Keywords: Subdural hematoma, ischemic stroke, elderly, concomitant pathology, stroke management, anticoagulation, multidisciplinary approach, neuroimaging

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INTRODUCTION

Ischemic stroke and subdural hematomas (SDHs) are common yet distinct neurological conditions, frequently observed in the elderly. SDHs often result from traumatic brain injury (TBI), such as falls, leading to blood accumulation between the dura and arachnoid mater.¹ Presentations can range from acute SDHs, which require immediate neurosurgical intervention,² to subacute or chronic SDHs, which may manifest over weeks to months, particularly in individuals over 65 years of age.^{3,4} Conversely, ischemic strokes typically arise

from thromboembolic events, often associated with atherosclerosis or cardiac emboli.⁵ Symptomatology in ischemic strokes varies based on the affected vascular territory and extent of ischemia.⁶ The concurrent occurrence of SDH and ischemic stroke is rare but poses significant diagnostic and therapeutic challenges, especially in anticoagulated patients, necessitating tailored management strategies for dual pathologies.⁷

65 years of age present with gradual symptoms over weeks to months.

Ischemic strokes most commonly occur due to thromboembolic events caused by atherosclerotic plaques in the carotid or vertebral arteries, or cardiac thrombi. Clinical presentation and symptom progression depend on the location, extent of ischemia, and the affected vascular territory.

CASE PRESENTATION:

A 95-year-old male with a medical history of

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Chronic Obstructive Pulmonary Disease (COPD) and Chronic Kidney Disease (CKD) stage 3 presented to the Emergency Department at Farooq Hospital, Westwood. He complained of shortness of breath, confusion, left-sided body weakness, and slurred speech. The symptoms had progressively worsened over the past 7 days.

Patient presented with the history of fall. However, no symptoms were noted immediately following the incident. Seven days post-injury, the patient developed fluctuating left-sided weakness and disorientation. The weakness was intermittent in the upper and lower limbs which was progressively worsening. Over time, the patient became unable to bear weight or stand independently.

A neurological examination conducted on Day 1, the patient exhibited left-sided weakness, with muscle power rated at 1/5 in both the left upper and lower limbs. A positive Babinski's sign was noted on the left side. The Glasgow Coma Scale (GCS) score was 8/15, with an eye response of E2, a verbal response of V2, and a motor response of M4.

The patient presented with fever and coarse crepitations throughout the chest. Supplemental oxygen was required, administered at 2–3 liters via nasal cannula. The pulse was irregular, and an electrocardiogram (ECG) revealed new-onset atrial fibrillation.

A CT brain scan revealed isodense concavity on the right side, which is indicative of a subacute subdural hematoma (Figure 1). Additionally, an evolving infarct was noted in the right middle cerebral artery (MCA) territory (Figure 2) (Figure 4). Importantly, no mass effect or herniation was observed.

The CT carotid angiography confirmed the presence of an atherosclerotic plaque in the right internal carotid artery, causing 50% stenosis. This was identified as the cause of the ischemic stroke. The echocardiogram revealed severe pulmonary hypertension (PASP 60 mmHg) and moderate tricuspid regurgitation. The likely etiology of these findings was the patient's underlying COPD. The patient's blood work showed an elevated white cell count, indicating an acute infective exacerbation of COPD.

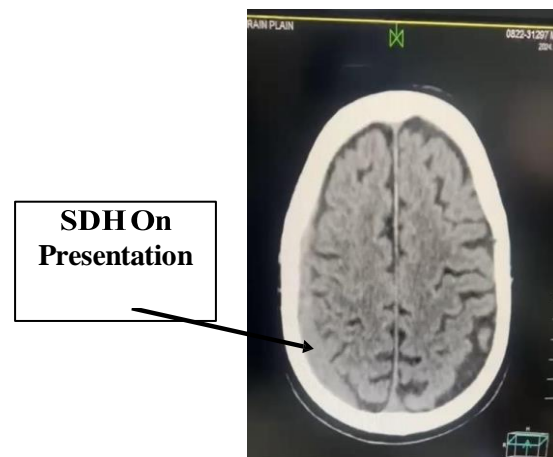


Figure 1: An isodense concavity (subacute subdural hematoma) on the right side.

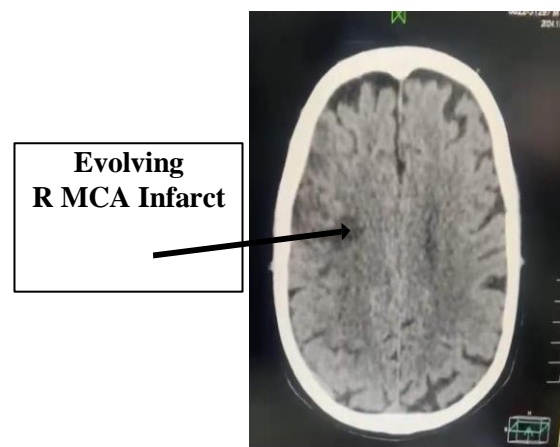


Figure 2: Evolving infarct in Right Middle Cerebral Artery (MCA)

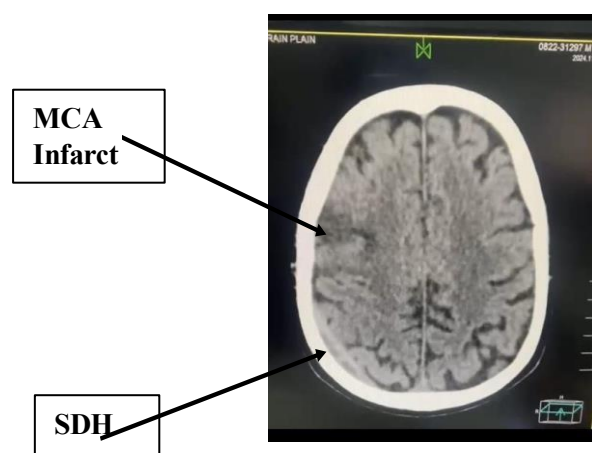


Figure 3: Right MCA Infarct along with SDH

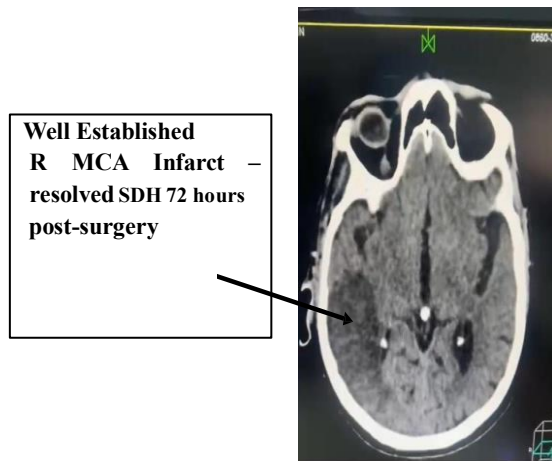


Figure 4: MCA infarct post-surgery

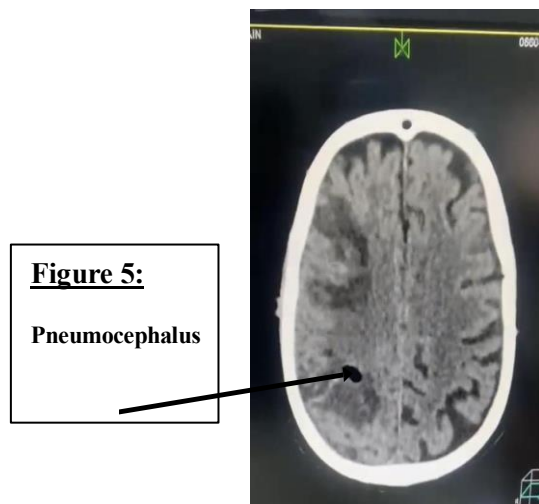


Figure 5: Resolved SDH with Pneumocephalus post -Surgery

The coagulation profile was normal. The patient was admitted to the ICU for close monitoring. Atrial fibrillation was treated with a 300 mg STAT dose of amiodarone, which successfully reverted the rhythm to normal sinus rhythm. A 72-hour Holter monitor showed no significant findings.

CT findings suggested that the stroke had occurred 24–48 hours prior, with symptoms persisting for more than 72 hours. This placed the patient outside the

window for thrombolysis (tPA). Thrombolytics were not used due to the patient's advanced age (95 years) and the concurrent presence of a right-sided subdural hematoma, which increased the risk of bleeding.

A burr hole craniotomy was performed to evacuate the subdural hematoma. The procedure resulted in the complete resolution of the subdural hematoma.

To manage the acute infective exacerbation of COPD, the patient was administered IV antibiotics (Imipenem, Moxifloxacin) and IV steroids for inflammation control. Additionally, nebulization with ipratropium and beclomethasone was provided.

The patient was started on a calcium channel blocker, Diltiazem, to manage the pulmonary hypertension.

A coordinated care approach involving neurosurgery, neurology, pulmonology, and cardiology was implemented to provide comprehensive management for the patient.

DISCUSSION

The concurrent occurrence of ipsilateral subacute subdural hematoma (SDH) and ischemic stroke in elderly patients, presenting with contralateral weakness, is a rare and complex clinical scenario. Such cases pose significant diagnostic and therapeutic challenges, particularly in individuals on anticoagulation therapy.

The current case presented unique challenges in managing an elderly patient with concurrent right-sided subdural hematoma and ipsilateral ischemic stroke, complicated further by comorbidities such as atrial fibrillation, COPD, and severe pulmonary hypertension. The simultaneous presence of SDH and ischemic stroke highlighted the complexities in diagnosis and treatment, particularly in elderly patients with multiple coexisting conditions.

The decision to withhold thrombolytics in the present case, given the patient's advanced age,

the risk of hemorrhagic complications from SDH, and the fact that the patient was outside the thrombolysis window, demonstrates the need for individualized, risk-averse management strategies. The successful burr hole craniotomy for SDH evacuation resulted in the resolution of neurological deficits.

Postoperatively, the patient required ventilatory support due to a severe COPD exacerbation. Antibiotics and steroids helped manage his respiratory infection and inflammation, while calcium channel blockers addressed his pulmonary hypertension.

OUTCOME AND FOLLOW-UP

The patient remained hospitalized for 10 days. His GCS improved from 8/15 on presentation to 15/15 postoperatively. Despite some persistent weakness in his cough and gag reflex, his overall neurological function improved significantly. A nasogastric tube (NGT) was used for feeding during the initial 7 days post-surgery, which was removed upon discharge following improvement in his cough and gag reflex.

The patient was discharged with a follow-up visit in the outpatient clinic, where he demonstrated continued improvement.

One such case was presented by Strahnen et al.⁸ who reported an 83-year-old male on apixaban therapy who developed a right parietal SDH and subsequent ipsilateral ischemic stroke, highlighting the intricacies of managing dual pathologies in anticoagulated patients.

The management included reversing apixaban with specific agents to prevent hematoma expansion, close neurological monitoring, and surgical evacuation of the subacute subdural hematoma to relieve intracranial pressure. Thrombolysis was contraindicated for the ischemic stroke, with supportive care provided instead. Post-stabilization, the patient underwent rehabilitation, and a careful risk-benefit assessment was conducted for resuming anticoagulation therapy to prevent further thromboembolic events.

These cases underscore the importance of

comprehensive neurological assessment and advanced imaging techniques in elderly patients presenting with atypical neurological deficits. A multidisciplinary approach is essential to navigate the challenges of anticoagulation management and to optimize patient outcomes in such complex clinical scenarios.

Gonzalez et al.⁹ emphasized that elderly patients with ischemic stroke and multiple underlying conditions benefit from coordinated care involving specialists from various fields, including neurology, pulmonology, cardiology, and surgery. This approach improves the overall management and outcome by addressing the complex interactions between different medical conditions.

In this case, the collaborative efforts of neurosurgery, neurology, pulmonology, and cardiology teams ensured comprehensive care and targeted interventions, helping to stabilize the patient and address each of the complicating factors.

CONCLUSION

This case highlights the importance of a multidisciplinary approach when managing complex, intersecting pathologies in elderly patients. The successful management of dual neurological insults—subdural hematoma and ischemic stroke—was made possible through tailored treatment strategies that involved neurosurgery, neurology, pulmonary medicine, and cardiology. Future research should focus on refining management strategies for patients with multiple comorbidities and simultaneous neurological insults.

CONFLICT OF INTEREST

None

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None

AUTHOR CONTRIBUTION

OF: Concept, critical review, proof reading

SR: Drafting of literature review

FA: Compilation of data and discussion

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