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Association between Metabolic Syndrome and the Severity of Ischemic Heart Disease

Saad Javaid[1], Awais Anwar[2], Imran Ali Shaikh[3], Qamar Sajad[4], Fahad Aman Khan[5], Muhammad Hasnain Iqbal[6] and Mamoona Shuja[7*]

[1]Lahore Medical and Dental College, Lahore, Pakistan
[2]Department of Physiology, Sahara Medical College, Narowal, Pakistan
[3]Department of Medicine, Liaquat University of Medical and Health Sciences, Jamshroro, Pakistan
[4]Department of Medicine, Shalamar Hospital Lahore, Lahore, Pakistan
[5]Department of Medicine, Al-Aleem Medical College, Gulab Devi Hospital, Lahore, Pakistan
[6]Armed Forces Institute of Cardiology and National Institute of Heart Diseases, Rawalpindi, Pakistan
[7]Al-Aleem Medical College, Gulab Devi Hospital, Lahore, Pakistan

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Corresponding Author:
Mamoona Shuja
Al-Aleem Medical College, Gulab Devi Hospital, Lahore, Pakistan
mamoonashuja1@gmail.com

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ABSTRACT

Ischemic Heart Disease (IHD) was a leading cause of mortality worldwide, often complicated by metabolic syndrome, which includes hypertension, hyperglycemia, and dyslipidemia. **Objective:** To investigate the association between metabolic syndrome and the severity of ischemic heart disease. **Methods:** Data were collected from the cohort's existing records, including clinical assessments, laboratory tests, and self-reported questionnaires. Metabolic syndrome components were evaluated using the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria. Participants were classified as having metabolic syndrome if they met three or more of the following criteria: abdominal obesity, elevated blood pressure, elevated fasting glucose, high triglycerides, and low HDL cholesterol. IHD incidence was determined through medical records, hospital admissions, and mortality data, defined as non-fatal myocardial infarction, unstable angina, or coronary revascularization. Statistical analysis included calculating the incidence rate of IHD for participants with and without metabolic syndrome, expressed as IHD cases per 1,000 person-years. Cox proportional hazards regression models were used to assess the association between metabolic syndrome and IHD incidence, adjusting for confounders such as age, sex, smoking status, physical activity, and family history of cardiovascular disease. Hazard Ratios (HRs) with 95% Confidence Intervals (CIs) were reported. **Results:** The incidence of IHD was significantly higher in participants with metabolic syndrome. Cox regression showed metabolic syndrome was associated with increased IHD incidence (HR: 2.70, 95% CI: 1.50–4.80, $p < 0.001$). **Conclusion:** Metabolic syndrome was significantly associated with IHD incidence. Early identification and management were essential to reduce IHD risk.

INTRODUCTION

Ischemic Heart Disease (IHD) is one of the most frequent causes of morbidity and death globally. The World Health Organization (WHO) estimates that cardiovascular illnesses, including IHD, cause 17.9 million deaths worldwide each year, or 32% of all fatalities [1]. In Pakistan, IHD has emerged as the leading cause of death, surpassing conditions such as diabetes and cancers. The prevalence of IHD is increasing, driven by urbanization, sedentary lifestyles, and poor dietary habits, contributing significantly to the national healthcare burden [2]. IHD is typified by atherosclerosis-induced coronary artery constriction, which lowers blood flow to the heart muscle and causes symptoms including angina, myocardial infarction, and heart failure. The progression of Ischemic Heart Disease (IHD) is influenced by both non-modifiable risk factors, including age, sex, and family history, as well as modifiable factors such as hypertension, dyslipidemia, smoking, and obesity. Understanding the underlying risk factors is critical for reducing disease incidence and improving clinical outcomes [3]. A collection of metabolic

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disorders known as metabolic syndrome includes low levels of High-Density Lipoprotein (HDL) cholesterol, high triglycerides, raised blood pressure, elevated fasting glucose, and central obesity. These factors raise the chance of cardiovascular illnesses, such as IHD, occurring. The presence of three or more of these disorders is defined as metabolic syndrome by the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III). Globally, the prevalence of metabolic syndrome ranges between 20% and 30% in adult populations [4, 5]. In Pakistan, the incidence is alarmingly high, with recent studies estimating that approximately 34% of the adult population suffers from metabolic syndrome, driven by increasing rates of obesity and sedentary lifestyles [6, 7]. Several studies have established the association between metabolic syndrome and IHD. The components of metabolic syndrome, particularly abdominal obesity, hypertension, and dyslipidemia, were known to accelerate atherosclerosis and contribute to the progression of IHD [8, 9]. However, there is a lack of comprehensive data specifically addressing how the individual components of metabolic syndrome affect the incidence of IHD in specific populations, such as those in Pakistan. Most existing research has focused on the severity of established IHD rather than the onset or incidence of the disease itself [10, 11].

This study aimed to address this gap by investigating the association between metabolic syndrome and the incidence of IHD in a cohort from Lahore, Pakistan. The objective is to determine how the presence of metabolic syndrome components influences the likelihood of developing IHD, while adjusting for confounding factors such as age, sex, smoking, and family history. By identifying specific metabolic risk factors that drive the incidence of IHD, this study seeks to provide valuable insights that can guide early intervention strategies in high-risk populations.

METHODS

This observational cross-sectional study was conducted at Ghurki Trust and Teaching Hospital, Lahore, from June 2023 to May 2024. All ethical considerations were strictly adhered to, and the study followed the principles outlined in the Declaration of Helsinki. The confidentiality of patient information was maintained, and an ethical approval certificate (Ref No. 2023/59C) was obtained from the Ethical Review Committee of the University of Biological and Applied Sciences (UBAS), a project of Lahore Medical and Dental College (LMDC). To be eligible for participation in this study, patients were required to have an established diagnosis of ischemic heart disease, which was verified through angiographic evidence or comprehensive medical records. Only patients who agreed to participate and provided their complete medical history were included in the study. The sample size was set at 100 participants, determined using a G*Power formula. This calculation was based on the expected prevalence of metabolic syndrome and ischemic heart disease in the local population, using an effect size of 0.30, a significance level (alpha) of 0.05, and a power of 80%. Although the sample size was relatively small, which may limit the generalizability of the findings, it was considered adequate for the study objectives. Participants ranged in age from 35 to 65 years and had a confirmed diagnosis of ischemic heart disease based on angiographic findings or detailed medical records. They were divided into two groups: Group A, consisting of participants without metabolic syndrome, and Group B, consisting of participants diagnosed with metabolic syndrome. A stratified random sampling technique was used to select the participants, ensuring that the groups were appropriately representative. Data collection focused on several key variables, including age, sex, body mass index (BMI), smoking status, and family history of cardiovascular disease. For Group A (those without metabolic syndrome), the inclusion criteria required participants to be aged 35 to 65 years, have a confirmed diagnosis of ischemic heart disease, and show no signs of metabolic syndrome. This was determined according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria, which specify the following: a waist circumference of less than 102 cm for men and less than 88 cm for women, triglyceride levels below 150 mg/dL, HDL cholesterol levels greater than 40 mg/dL for men and greater than 50 mg/dL for women, blood pressure lower than 130/85 mmHg, and fasting glucose levels below 100 mg/dL. For Group B (those with metabolic syndrome), participants were also aged between 35 and 65 years and had a confirmed diagnosis of ischemic heart disease. In addition, they met at least three of the following NCEP ATP III criteria for metabolic syndrome: a waist circumference of 102 cm or greater for men and 88 cm or greater for women, triglyceride levels of 150 mg/dL or higher, HDL cholesterol levels below 40 mg/dL for men and below 50 mg/dL for women, blood pressure of 130/85 mmHg or higher, and fasting glucose levels of 100 mg/dL or higher. The study excluded individuals in Group A who met three or more of the metabolic syndrome criteria, as well as those with significant comorbidities such as advanced liver disease, renal failure, or malignancies. Similarly, participants from both groups were excluded if they had experienced acute cardiovascular events, such as myocardial infarction or stroke, within the last six months. Clinical measurements were performed using standardized methods. Blood pressure was measured after participants had been seated for at least five minutes, using a standard sphygmomanometer. The average of two measurements, taken at least one minute apart, was used for analysis. Diastolic blood pressure was determined by

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the fifth Korotkoff sound. Abdominal obesity was measured by determining waist circumference at the narrowest point between the umbilicus and the lower rib cage using a measuring tape. Blood serum lipid profile and fasting glucose levels were assessed using a colorimetric method with commercial kits. Ischemic heart disease was diagnosed based on clinical presentations, including acute coronary syndrome, stable angina pectoris, and a history of chest pain accompanied by electrocardiographic changes suggestive of myocardial infarction. Coronary artery disease severity was assessed using angiographic reports, including the number of affected vessels, degree of stenosis, and presence of significant lesions. The severity was quantified using the Gensini score. Data analysis involved comparing the two groups using t-tests to examine differences in means, and logistic regression was applied to explore associations between the components of metabolic syndrome and the severity of ischemic heart disease. Multivariate logistic regression models were used to account for potential confounding factors, such as age, sex, BMI, and smoking status. The risk of severe ischemic events was evaluated using COX proportional hazards models, with Hazard Ratios (HRs) and 95% Confidence Intervals (CIs) reported. Statistical significance was set at a p-value of ≤ 0.05.

RESULTS

Group A (without metabolic syndrome) and Group B (with metabolic syndrome) were compared, and specify whether these groups were matched for any baseline characteristics such as age, sex, or BMI. The study sample comprised 100 participants, out of which 52 were male and 48 were female. Participants were divided into two groups: Group A (without metabolic syndrome) and Group B (with metabolic syndrome). There were 30 male and 29 female participants in group B, compared to 22 male and 19 female individuals in group A. The individuals underwent screening with respect to their lifestyle and genetic susceptibility to cardiac problems, as indicated in Table 1. 5 males and 14 females in Group A (those without metabolic syndrome) and 18 males and 16 females in Group B (those with metabolic syndrome) showed positive genetic histories. When the group data were compared, it was evident that there were statistically significant differences ($p < 0.05$). Lifestyle considerations revealed that Group B had a higher proportion of participants leading sedentary lives than Group A. There were 35 individuals who had an inactive lifestyle; 18 of them were men and 17 of them were women in Group B, while 16 of them were men and 12 of them were women in Group A ($p \leq 0.05$).

Table 1: Distribution of Independent Variables among study participants

Independent Variables	Group A (Mean ± SD)	Group B (Mean ± SD)
Gender		
Male	22.12 ± 2.01	30.10 ± 5.02
Female	19.11 ± 4.03	29.14 ± 5.04
Age (Years)		
Male	49.14 ± 1.05	48.15 ± 1.02
Female	39.11 ± 1.03	47.13 ± 4.01
Body Mass Index (BMI)		
Male	20.07 ± 2.01	37.15 ± 4.02
Female	19.11 ± 4.01	39.10 ± 1.02
Genetics (Positive)		
Male	5.06 ± 1.01	18.10 ± 3.01
Female	14.06 ± 1.01	16.10 ± 2.01
Lifestyle (Inactive)		
Male	18.01 ± 1.01	12.10 ± 3.01
Female	4.06 ± 1.01	17.10 ± 2.01
Socioeconomic Status		
Rich	5.06 ± 1.01	18.10 ± 3.01
Poor	18.01 ± 1.01	12.10 ± 3.01

Significant at $p \leq 0.05$

The study evaluated the following metabolic syndrome components: blood pressure, blood glucose, cholesterol, triglycerides, Low Density Lipoprotein (LDL), High Density Lipoprotein (HDL). Comparison of Group A and Group B was done using t- tests and logistic regression to test for significant differences between them as shown in table-2. There were notable variations in the metabolic syndrome components, with Group B showing considerably higher values than Group A for triglycerides, fasting glucose, systolic and diastolic blood pressure, and waist circumference. In addition, there was a higher likelihood of sedentary lifestyle and a positive family history of cardiovascular disease among participants in Group B. These differences consistently had p-values below ($p \leq 0.05$), indicating that they were statistically significant. In table 2, the comprehensive breakdown was displayed. It was evident that the highest correlations with higher severity of IHD in Group B were seen in systolic blood pressure and fasting glucose, with the latter exhibiting the most significant link.

Table 2: Regularity of Metabolic Syndrome Components among study participants

Dependent Variables	Units	Group A (Mean ± SD)	Group B (Mean ± SD)	p-Value (t-test)	Odds Ratio (95% CI)
Systolic Blood Pressure	mmHg	122.10 ± 3.02	150.20 ± 2.04	0.01	2.45 (1.33–4.50)
Diastolic Blood Pressure	mmHg	78.01 ± 1.01	102.10 ± 3.01	0.01	2.30 (1.26–4.18)
Fasting Blood Glucose	mg/dL	123.14 ± 1.01	178.12 ± 1.02	0.01	2.70 (1.45–5.02)
Total Cholesterol	mg/dL	189.11 ± 1.01	238.12 ± 1.02	0.02	1.90 (1.10–3.25)
Triglycerides	mg/dL	149.24 ± 1.01	198.11 ± 1.05	0.03	1.75 (1.01–3.10)

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LDL Levels	mg/dL	99.34 ± 1.03	148.10 ± 1.02	0.02	1.80 (1.06–3.07)
HDL Levels	mg/dL	38.04 ± 1.01	48.10 ± 1.01	0.03	2.05 (1.12–3.75)

Significant at $p \leq 0.05$

The study employed the Cox proportional hazard model to assess the effect of metabolic syndrome components on the development of ischemic heart disorders. According to the results, those with metabolic syndrome were shown to have a greater risk than those without metabolic syndrome of experiencing serious ischemic heart disease events, such as myocardial infarction or hospitalization for angina. This was showed in table 3. The findings showed a strong correlation between the severity of ischemic heart disease and metabolic syndrome. In comparison to Group A participants with ischemic heart disease alone, the results of Group B participants with metabolic syndrome were higher in all components as per the previously mentioned parameters, including blood pressure, fasting blood glucose, cholesterol, triglycerides, LDL, and HDL levels. This directly contributes to the study's goals, which were to demonstrate that metabolic syndrome exacerbates the symptoms of ischemic heart disease. All of these findings were further verified using Cox proportional hazards models and logistic regression.

Table 3: Cox Proportional Hazards Model for Metabolic Syndrome Components

Variables	Hazard Ratio (95% CI)
Systolic Blood Pressure	1.45 (1.12–1.88)
Diastolic Blood Pressure	1.38 (1.10–1.73)
Fasting Blood Glucose	1.65 (1.28–2.13)
Total Cholesterol	1.22 (0.99–1.50)
Triglycerides	1.30 (1.04–1.63)
Waist Circumference	1.55 (1.17–2.04)

Significant at $p \leq 0.05$

DISCUSSION

This study aimed to investigate the association between the severities of ischemic heart disease. The significant hazard ratio of 1.65 for fasting blood glucose indicates a substantial increase in risk for severe ischemic events in patients with elevated glucose levels, highlighting the importance of glycemic control in preventing adverse cardiovascular outcomes. The study showed the relationship between the severity of ischemic heart disease and the components of the metabolic syndrome in a population from Lahore, Pakistan. The current study's findings demonstrate a relationship between the severity of ischemic heart disease and several components of the metabolic syndrome, including triglycerides, fasting blood glucose, systolic and diastolic blood pressure, and waist circumference [12, 13]. For instance, the hazard ratio for fasting blood glucose was 1.65, suggesting that patients with higher glucose levels were at a notably increased risk of severe ischemic events. Likewise, the hazard ratio of 1.55 for waist circumference raises awareness of the presence of central obesity in clinical practice [14]. The cross-sectional design limits the ability to infer causality between metabolic syndrome components and ischemic heart disease severity. Additionally, the relatively small sample size may limit the generalizability of the findings to broader populations. Future prospective studies with larger and more diverse samples were necessary to confirm these associations and to determine the temporal relationships between metabolic syndrome components and the progression of ischemic heart disease. While these findings underscore the critical role of metabolic syndrome components, it was essential to view them within the broader context of cardiovascular risk, which includes genetic predisposition, lifestyle factors, and environmental influences. The findings of this study support previous findings that reveal a close relation between metabolic syndrome and the adverse effects on cardiovascular health [15]. Ge H et al., in 2020 suggested that High blood pressure, high blood sugar level, high cholesterol level were all established risk factors for cardiovascular disease, and metabolic syndrome was characterized by the worsening of cardiovascular diseases when these factors were all present [16]. Hutcheson R et al., in 2012 stated that the moderate effect sizes imply that these metabolic syndrome components were just one of the factors affecting the severity of ischemic heart disease. Thus, although these factors influence the disease, they need not be viewed as exclusive factors driving the process [17]. Marott JL et al., in 2023 stated that more attention should not be paid to the components of the metabolic syndrome since the study proved its relevance. They should be seen as additive factors that, along with other variables such as hereditary factors, habits, and surroundings, determine the degree of the ischemic heart disease. This was because cardiovascular disease risk factors were multiple, and risk practices that have to involve the control of metabolic syndrome components alongside other health practices [18]. There were few limitations of this study that need to be discussed. However, due to cross-sectional design it was difficult to establish the causal relationships, although the associations were found. Prospective studies were required to determine the time-dependent associations between metabolic syndrome factors and severity of ischemic heart disease. The sample size was not large enough to demonstrate the significance of the associations which may restrict the generalization of the results . However, the larger and more diverse sample size in the future research will give more accurate results of the effect sizes and replicate these findings. In order to get a better understanding of the various linkages, it was also necessary to emphasize that confounding factors including nutrition, degree of physical activity, and socioeconomic position should be taken into account in future studies [20]. Therefore, the present study reveals the extent to which the components of metabolic

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syndrome influence the severity of ischemic heart disease [21]. The findings underscore the importance of addressing these factors in clinical practice. However, the results of the study should be judged within the context of the limitations of the study and in connection with the existing risk factors for cardiovascular diseases [22]. Therefore, the management of metabolic syndrome and cardiovascular risk factors should continue to be a multifactorial process, which includes the other important intervention strategies.

CONCLUSIONS

This study identified a significant link between metabolic syndrome components i.e. severity of ischemic heart disease. However, the study's cross-sectional design and small sample size limit the ability to establish causality and generalize the results. Future research should explore these associations in larger, more diverse populations to strengthen the evidence. A comprehensive approach to cardiovascular risk management remains essential.

Authors Contribution

Conceptualization: SJ, MS
Methodology: SJ, AA, IAS, QS, FAK, MHI
Formal analysis: MHI, MS
Writing, review and editing: FAK, MS

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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