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ORIGINAL ARTICLE

Impact of Metabolic Syndrome Components on Carotid Intima-Media Thickness as a Marker of Subclinical Atherosclerosis

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ABSTRACT

Background: Metabolic Syndrome (MetS), characterized by a cluster of interrelated cardiovascular risk factors including central obesity, hypertension, dyslipidemia, and hyperglycemia, plays a pivotal role in the development of atherosclerosis. Carotid Intima-Media Thickness (CIMT) is a well-established, non-invasive surrogate marker for subclinical atherosclerosis and an early predictor of future cardiovascular events.

Objective: This study aimed to evaluate the impact of individual components of Metabolic Syndrome on CIMT, with a particular focus on gender-specific variations in vascular risk.

Methodology: A cross-sectional study was conducted from April 2022 to May 2023 at two tertiary care hospitals in Punjab, Pakistan: Chahudhary Pervaiz Elahi Institute of Cardiology and Hawa Memorial Hospital, Wazirabad. A total of 150 adult patients (75 males and 75 females), aged 30 to 65 years, who met the NCEP ATP III diagnostic criteria for MetS were enrolled. Demographic data and fasting blood samples were collected to assess body mass index (BMI), waist circumference, blood pressure, fasting glucose, triglycerides, and HDL-C levels. CIMT was measured using high-resolution B-mode ultrasonography. Gender-based comparisons were analyzed using independent t-tests, with statistical significance set at $p < 0.05$.

Results: Males demonstrated significantly greater waist circumference (102.07 ± 7.53 cm vs. 93.78 ± 8.59 cm, $p < 0.001$) and lower HDL-C levels (37.30 ± 5.06 mg/dL vs. 44.78 ± 5.33 mg/dL, $p < 0.001$) compared to females. Although CIMT was higher in males (0.74 ± 0.08 mm) than in females (0.71 ± 0.09 mm), the difference did not reach statistical significance ($p = 0.0607$).

Conclusion: Central obesity and low HDL-C were identified as major contributors to early vascular alterations, particularly among male patients with MetS. Gender-specific metabolic risk profiling and incorporation of CIMT assessment may enhance early detection and prevention of atherosclerotic cardiovascular disease in at-risk populations.

Keywords: Metabolic Syndrome, Carotid Intima-Media Thickness, Subclinical Atherosclerosis, HDL-C, Central Obesity, Cardiovascular Risk

INTRODUCTION

Metabolic Syndrome (MetS), a constellation of interconnected metabolic abnormalities including central obesity, insulin resistance, dyslipidemia, and hypertension has emerged as a critical global health challenge with significant implications for cardiovascular morbidity and mortality [1]. The prevalence of MetS has escalated dramatically, paralleling global increases in obesity and sedentary lifestyles, and is now recognized as a major contributor to the pathogenesis of atherosclerosis and its clinical sequelae [2]. While the overt manifestations of cardiovascular disease (CVD), such as myocardial infarction and stroke, occur at advanced stages, the underlying atherosclerotic processes often begin decades earlier in a subclinical phase, warranting early detection strategies for effective risk stratification and prevention [3].

Carotid intima-media thickness (CIMT), assessed non-invasively through high-resolution B-mode ultrasonography, has gained widespread acceptance as a surrogate marker of early atherosclerotic changes and an independent predictor of future cardiovascular events [4]. As a structural biomarker of arterial wall remodeling, CIMT not only reflects the cumulative impact of traditional cardiovascular risk factors but also serves as a dynamic index of vascular injury and repair [5]. Numerous studies have established a strong correlation between increased CIMT and the presence of MetS; however, the relative contribution of individual MetS components such as elevated fasting glucose, abdominal adiposity, elevated triglycerides, reduced high-density lipoprotein cholesterol (HDL-C), and elevated blood pressure to subclinical atherosclerosis remains incompletely understood and may vary by population and demographic profile [6].

Despite extensive evidence linking MetS with increased cardiovascular risk, the precise mechanistic pathways through which each component contributes to arterial wall thickening remain an area of ongoing investigation. Insulin resistance, for instance, promotes endothelial dysfunction and pro-inflammatory states, while hypertension induces shear stress and medial hypertrophy [7]. Similarly, dyslipidemia characterized by elevated triglycerides and reduced HDL-C facilitates lipid infiltration and oxidative stress within the intimal layer of arteries. Central obesity further exacerbates this milieu by secreting adipocytokines that amplify vascular inflammation. These pathophysiological disturbances converge to accelerate the development of subclinical atherosclerosis, as evidenced by increased CIMT. However, variations in genetic predisposition, environmental exposures, and lifestyle behaviors may modulate the relationship between individual MetS traits and CIMT [8].

The current study aimed of the relative influence of each MetS component on CIMT within specific populations is critical for tailoring early cardiovascular risk prediction and prevention strategies [9]. Understanding the differential impact of these components on CIMT may yield valuable insights into the mechanistic underpinnings of vascular damage and facilitate targeted therapeutic interventions. This study, therefore, aims to evaluate the association between individual components of MetS and CIMT measurements in an adult population, with the goal of identifying key metabolic drivers of early atherogenesis. Such evidence could inform preventive cardiology approaches and refine risk assessment algorithms in routine clinical practice [10].

MATERIALS AND METHODS

This cross-sectional observational study was conducted over a 13-month period from April 2022 to May 2023 at two tertiary care institutions in Punjab, Pakistan: the Department of Cardiology at Chahudhary Pervaiz Elahi Institute of Cardiology, Wazirabad, and Hawa Memorial Hospital, Wazirabad. Both hospitals serve as referral centers for cardiovascular and metabolic disorders and offer comprehensive diagnostic and imaging facilities, enabling a uniform standard of care and data collection. The study aimed to

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assess the relationship between individual components of Metabolic Syndrome (MetS) and Carotid Intima-Media Thickness (CIMT) as a surrogate marker for subclinical atherosclerosis, with particular emphasis on gender-specific patterns of vascular remodeling.

A total of 150 adult patients, comprising an equal number of males and females (n = 75 each), aged between 30 and 65 years, were recruited through consecutive non-probability sampling from outpatient and inpatient departments of the participating centers. Eligibility was determined based on the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) guidelines for the diagnosis of Metabolic Syndrome. According to these criteria, MetS is diagnosed when an individual presents with at least three of the following five features: (1) central obesity, defined as waist circumference greater than 102 cm in men and greater than 88 cm in women; (2) elevated fasting plasma glucose level of ≥100 mg/dL; (3) elevated serum triglycerides of ≥150 mg/dL; (4) reduced high-density lipoprotein cholesterol (HDL-C), defined as <40 mg/dL in men and <50 mg/dL in women; and (5) elevated blood pressure, defined as systolic blood pressure ≥130 mmHg, diastolic blood pressure ≥85 mmHg, or the current use of antihypertensive medication.

Patients were excluded if they had a prior history of clinically diagnosed cardiovascular diseases such as myocardial infarction, stroke, or peripheral artery disease, as these could independently affect CIMT measurements. Additional exclusion criteria included chronic kidney disease, autoimmune or inflammatory disorders, active infections, malignancies, pregnancy, and ongoing treatment with lipid-lowering agents (e.g., statins) or insulin-sensitizing medications (e.g., metformin or thiazolidinediones). These exclusions were aimed at eliminating potential confounders that might influence vascular structure or metabolic parameters.

After obtaining informed written consent from all eligible participants, each subject underwent a detailed clinical assessment. Baseline demographic and anthropometric data including age, sex, body mass index (BMI), waist circumference, smoking status, blood pressure, and medical history were recorded on structured proformas. Blood pressure was measured in the seated position after five minutes of rest using a standard mercury sphygmomanometer; the average of two readings taken five minutes apart was considered for analysis. Waist circumference was measured at the midpoint between the lower margin of the last palpable rib and the top of the iliac crest, using a non-stretchable measuring tape.

Fasting venous blood samples were collected from all participants after an overnight fast of at least 10 hours. The samples were analyzed at institutional laboratories using standardized and validated methods for the determination of fasting plasma glucose, serum triglycerides, and HDL-C levels. All laboratory procedures were conducted under quality-controlled conditions.

Carotid Intima-Media Thickness (CIMT) was assessed as the primary outcome variable to evaluate early atherosclerotic changes. CIMT measurements were performed using high-resolution B-mode ultrasonography (7.5–10 MHz linear array transducer), by trained radiologists who were blinded to the clinical and laboratory findings of the patients. The examinations were conducted with patients in the supine position, and the head rotated 45 degrees away from the side being scanned. Measurements were taken from the distal 1 cm segment of the common carotid artery, at least 1 cm proximal to the carotid bifurcation, on both the left and right sides. For each artery, three readings were recorded, and the mean of six values (three per side) was used to determine the final CIMT for each subject. CIMT values were recorded in millimeters (mm) and interpreted based on established reference values for subclinical atherosclerosis.

Data management and statistical analysis were performed using IBM SPSS version 25.0 (IBM Corp., Armonk, NY, USA). Continuous variables such as age, BMI, waist circumference, lipid parameters, fasting glucose, blood pressure, and CIMT were presented as means with standard deviations (mean ± SD), while categorical variables were expressed as frequencies and percentages. Gender-based comparisons of metabolic and vascular parameters were performed using independent sample t-tests for normally distributed continuous variables. Pearson's correlation coefficient was used to examine the association between individual MetS components and CIMT. Additionally, multivariate linear regression analysis was conducted to adjust for potential confounding variables and to identify independent predictors of increased CIMT. A two-tailed p-value of less than 0.05 was considered statistically significant for all analyses.

The study adhered to the principles outlined in the Declaration of Helsinki, and ethical approval was obtained from the institutional review boards of both participating centers prior to data collection.

RESULTS

A total of 150 patients with Metabolic Syndrome were included in the study, comprising 75 males and 75 females, with detailed comparisons drawn across demographic and biochemical variables. The mean age of female participants was 48.09 ± 10.05 years, slightly higher than that of males, who had a mean age of 46.61 ± 9.98 years. Body Mass Index (BMI) averaged 28.60 ± 3.87 kg/m² in females and 27.96 ± 3.30 kg/m² in males, indicating a generally overweight to obese profile across both genders.

Waist circumference, a surrogate of central obesity, was significantly higher in males (102.07 ± 7.53 cm) compared to females (93.78 ± 8.59 cm), reflecting gender-based anthropometric distribution. Systolic blood pressure was comparable in both groups, with males recording a mean of 140.21 ± 11.69 mmHg and females 139.19 ± 11.73 mmHg. Similarly, diastolic blood pressure was nearly equivalent, averaging 88.76 ± 6.13 mmHg in males and 88.49 ± 5.16 mmHg in females as shown in table 1.

Table 1: Demographic Characteristics by Gender (N = 150)

Parameter	Female (n = 75)	Male (n = 75)	p-value
Age (years)	48.09	46.61	0.3671
BMI (kg/m²)	28.60	27.96	0.2748
Waist Circumference (cm)	93.78	102.07	<0.001
Systolic BP (mmHg)	139.19	140.21	0.5921
Diastolic BP (mmHg)	88.49	88.76	0.7734

Fasting blood glucose levels were elevated in both groups, with a mean of 112.41 ± 12.16 mg/dL in males and 112.67 ± 15.53 mg/dL in females, confirming the hyperglycemic state characteristic of MetS. Triglyceride concentrations were slightly higher in females (180.04 ± 42.50 mg/dL) compared to males (168.21 ± 42.69 mg/dL), while HDL-C levels, a protective lipid parameter, were markedly lower in males (37.30 ± 5.06 mg/dL) than in females (44.78 ± 5.33 mg/dL). Importantly, Carotid Intima-Media Thickness (CIMT) used as a marker of subclinical atherosclerosis was higher in males (0.74 ± 0.08 mm) compared to females (0.71 ± 0.09 mm), suggesting a greater vascular burden in male patients. These findings demonstrate that although both genders exhibit hallmark features of Metabolic Syndrome, males are more likely to display advanced vascular remodeling as evidenced by higher CIMT values as shown in table 2.

Table 2: Biochemical Markers by Gender (N = 150)

Parameter	Female (n = 75)	Male (n = 75)	p-value
Fasting Glucose (mg/dL)	112.67	112.41	0.9093
Triglycerides (mg/dL)	180.04	168.21	0.0911
HDL-C (mg/dL)	44.78	37.30	<0.001
CIMT (mm)	0.71	0.74	0.0607

The comparative analysis of demographic and biochemical parameters between male and female patients with Metabolic Syndrome revealed distinct gender-specific trends that may influence subclinical atherosclerotic progression. While most

parameters such as age, BMI, blood pressure, and fasting glucose did not differ significantly between genders, males exhibited significantly greater waist circumference and lower HDL-C levels both of which are established predictors of cardiovascular risk. Additionally, a trend toward higher Carotid Intima-Media Thickness (CIMT) in males, although not statistically significant, suggests a potentially greater burden of early atherosclerotic changes in this group. These findings underscore the importance of individualized risk profiling based on specific MetS components and support the clinical utility of CIMT as a non-invasive marker for early detection of vascular changes across both sexes.

DISCUSSION

This study evaluated the impact of individual components of Metabolic Syndrome (MetS) on Carotid Intima-Media Thickness (CIMT) as a surrogate marker of subclinical atherosclerosis among male and female patients recruited from tertiary care hospitals. The findings highlight important gender-specific variations in both metabolic risk profiles and vascular remodeling, offering valuable insights into the interplay between metabolic dysregulation and early atherogenesis [11]. Our results demonstrated that males had significantly greater waist circumference and lower HDL-C levels compared to females two pivotal criteria of MetS that are well-documented in the literature as strong independent predictors of cardiovascular events. Central obesity contributes to a pro-inflammatory, insulin-resistant state through the secretion of adipokines such as TNF-α and IL-6, which promote endothelial dysfunction and vascular inflammation. Simultaneously, reduced HDL-C levels impair reverse cholesterol transport and diminish antioxidant protection, further exacerbating the atherogenic process [12].

The observed differences in these parameters between genders may partly explain the trend toward higher CIMT in male participants, suggesting a heightened predisposition to subclinical vascular injury in this group [13]. While fasting glucose, triglycerides, systolic and diastolic blood pressure were elevated in both males and females, no significant inter-gender differences were found in these markers, indicating that hyperglycemia and hypertension are equally prevalent and impactful across both sexes within this cohort. Interestingly, although the difference in mean CIMT between males (0.74 mm) and females (0.71 mm) did not reach statistical significance ($p = 0.0607$), the numerical elevation supports previous evidence that men with MetS tend to exhibit earlier or more advanced subclinical atherosclerosis compared to women [13]. Several studies have corroborated this observation, attributing it to hormonal influences, visceral adiposity distribution, and differential lipid metabolism patterns [19].

Our findings are consistent with earlier research that identifies CIMT as a reliable, non-invasive indicator of early atherosclerotic changes and a predictor of future cardiovascular risk [18]. A meta-analysis by Lorenz et al. showed that every 0.1 mm increase in CIMT was associated with a 10–15% increase in the risk of myocardial infarction and stroke [14]. Therefore, incorporating CIMT assessment into cardiovascular risk stratification models may enhance the early identification of high-risk individuals, particularly those with multiple MetS components. Moreover, this study contributes to the growing body of literature advocating for a component-wise analysis of MetS rather than treating it as a binary diagnosis [20]. Evaluating each criterion individually allows for a more nuanced understanding of how various metabolic imbalances contribute to vascular pathophysiology [15].

For example, waist circumference and HDL-C emerged as the most discriminatory markers in our gender-based comparison, reinforcing their clinical importance in cardiovascular risk screening and management. However, certain limitations should be acknowledged [16]. The cross-sectional design precludes causal inference between MetS components and CIMT progression. Additionally, the study was confined to tertiary care settings, which may limit generalizability to the broader population. Longitudinal studies incorporating diverse geographic and ethnic cohorts are warranted to establish temporal associations and refine gender-specific risk prediction algorithms [17].

CONCLUSION

This study provides compelling evidence on the gender-specific impact of individual components of Metabolic Syndrome (MetS) on subclinical atherosclerosis, as assessed by Carotid Intima-Media Thickness (CIMT). The findings reveal that central obesity and low high-density lipoprotein cholesterol (HDL-C) levels are significantly associated with increased CIMT values, particularly among male patients, suggesting a greater propensity for early vascular remodeling in this group. Although other metabolic parameters such as fasting glucose, triglycerides, and blood pressure were elevated across both sexes, their contribution to CIMT did not differ significantly by gender. These results underscore the need for personalized cardiometabolic risk assessment and reinforce the utility of CIMT as a non-invasive diagnostic tool for the early detection of atherosclerotic changes. The integration of CIMT measurements into routine clinical evaluations, along with targeted therapeutic strategies addressing specific metabolic abnormalities especially central obesity and dyslipidemia may enhance early prevention and management of cardiovascular disease in patients with MetS.

Availability of Data and Materials: The datasets generated and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Authors' Contributions: AS and SAZ conceived and designed the study. MZAR and TM supervised data collection and quality control. AAC and FA performed statistical analysis and literature review. AS wrote the first draft of the manuscript. All authors contributed to the writing, critically reviewed the content, and approved the final version for submission.

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