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HIGH-SENSITIVITY C-REACTIVE PROTEIN AS A PREDICTOR OF INSULIN RESISTANCE AND METABOLIC SYNDROME: A CROSS-SECTIONAL STUDY AT A TERTIARY CARE HOSPITAL IN KARACHI, PAKISTAN

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Abstract

Objective: To investigate the association of high-sensitivity C-reactive protein (hs-CRP) with insulin resistance and metabolic syndrome among obese patients attending a tertiary care hospital in Karachi, Pakistan. **Methods:** A cross-sectional study was conducted from January to June 2025 at a tertiary care hospital in Karachi. Seventy-five obese individuals (BMI ≥30 kg/m²) aged 20–60 years were enrolled. Fasting blood samples were analyzed for hs-CRP, fasting plasma glucose, insulin, lipid profile, and other metabolic parameters. HOMA-IR was calculated. Metabolic syndrome was diagnosed based on IDF criteria. **Results:** The mean age of participants was 43.2 ± 9.8 years. Elevated hs-CRP (>3 mg/L) was found in 61.3% of participants. Patients with high hs-CRP had significantly higher HOMA-IR scores ($p<0.001$). Metabolic syndrome was present in 68% of subjects, and mean hs-CRP levels were significantly higher in individuals with metabolic syndrome ($p<0.001$). Positive correlations were found between hs-CRP and fasting glucose, triglycerides, waist circumference, and HOMA-IR. **Conclusion:** High-sensitivity CRP levels

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were strongly associated with insulin resistance and the presence of metabolic syndrome. hs-CRP may serve as an early, accessible biomarker for identifying patients at risk of metabolic complications.

INTRODUCTION

The global burden of non-communicable diseases, particularly those associated with metabolic disturbances such as type 2 diabetes mellitus (T2DM) and cardiovascular disease (CVD), has reached alarming levels. Central to these conditions is metabolic syndrome (MetS), a constellation of risk factors including central obesity, insulin resistance, dyslipidemia, and hypertension.[1] Metabolic syndrome not only increases the risk of cardiovascular morbidity and mortality but also places significant strain on healthcare systems, especially in developing countries. In South Asian populations, including Pakistan, the prevalence of MetS is increasing rapidly due to urbanization, sedentary lifestyles, and poor dietary habits. Early identification of individuals at risk for insulin resistance and metabolic syndrome is thus essential for timely intervention and prevention of long-term complications.[2]

Among the various emerging biomarkers for metabolic risk, high-sensitivity C-reactive protein (hs-CRP) has gained considerable attention. CRP is an acute-phase protein produced by hepatocytes in response to systemic inflammation, particularly mediated by interleukin-6 (IL-6) and other pro-inflammatory cytokines.[3] Traditional CRP assays detect elevated levels associated with overt infection or inflammation, but hs-CRP assays allow for the detection of much lower levels of inflammation. This is critical in identifying chronic low-grade inflammation, which plays a pivotal role in the pathogenesis of insulin resistance and metabolic syndrome.[4]

Recent studies have shown that even modest elevations in hs-CRP levels are associated with increased risk of developing insulin resistance, endothelial dysfunction, and subsequent metabolic abnormalities.[5] Inflammation originating from visceral adiposity leads to increased cytokine production, which interferes with insulin signaling pathways and contributes to impaired glucose metabolism. This persistent inflammatory state is often silent but measurable via hs-CRP, making it a valuable predictive marker. Elevated hs-CRP levels have also been linked to a higher prevalence of cardiovascular events, further emphasizing the importance of early detection and risk stratification.[6]

Despite growing global evidence, limited data exist from Pakistan regarding the association between hs-CRP, insulin resistance, and metabolic syndrome.[7] The unique ethnic, dietary, and genetic backgrounds of the Pakistani population may influence inflammatory responses and metabolic health differently from Western populations. Additionally, limited access to early screening and preventive healthcare services further compounds the risk of late diagnosis and poor outcomes. There is thus a pressing need for locally relevant research to evaluate the predictive role of hs-CRP in identifying individuals at risk of developing metabolic syndrome and related disorders.[8]

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This cross-sectional study aims to assess the relationship between hs-CRP levels and insulin resistance among adults presenting to a tertiary care hospital in Karachi, Pakistan. By exploring the association between hs-CRP and various components of metabolic syndrome, the study seeks to establish the utility of hs-CRP as a potential screening tool for metabolic risk in clinical settings. The findings may provide a basis for incorporating hs-CRP into routine metabolic evaluations and contribute to the development of cost-effective strategies for early identification and prevention of non-communicable diseases in Pakistan's healthcare landscape.

MATERIALS AND METHODS

A cross-sectional study was conducted at a tertiary care hospital in Karachi, Pakistan, over a six-month period from January to June 2025. The study included a total of 75 participants, selected based on an anticipated moderate correlation between high-sensitivity C-reactive protein (hs-CRP) levels and insulin resistance, with the sample size calculated using a 95% confidence interval and 80% power to ensure the validity of findings.

Participants were recruited from the hospital's outpatient department using a non-probability consecutive sampling technique. Individuals aged between 20 and 60 years with a body mass index (BMI) of 30 kg/m² or higher were eligible for inclusion. Participants with known chronic inflammatory or infectious diseases, autoimmune disorders, malignancies, recent surgeries or trauma (within the last three months), or those currently on anti-inflammatory medications, corticosteroids, or lipid-lowering agents such as statins were excluded to minimize confounding factors that could influence hs-CRP levels.

After obtaining informed written consent, detailed anthropometric measurements, including height, weight, waist circumference, and blood pressure, were recorded for all participants. Fasting venous blood samples were collected following a 10–12 hour overnight fast. Laboratory assessments included measurements of fasting plasma glucose, fasting serum insulin, lipid profile (including triglycerides, HDL cholesterol, and LDL cholesterol), and hs-CRP levels using a high-sensitivity immunoturbidimetric assay. Insulin resistance was assessed using the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), calculated by the formula: [fasting insulin (μU/mL) × fasting glucose (mg/dL)]/405. A HOMA-IR value greater than 2.5 was considered indicative of insulin resistance. The diagnosis of metabolic syndrome was established according to the International Diabetes Federation (IDF) criteria, which require central obesity plus any two of the following factors: raised triglycerides, reduced HDL cholesterol, elevated blood pressure, or raised fasting glucose.

The study protocol was reviewed and approved by the Institutional Ethics Review Committee of the hospital to ensure compliance with ethical standards for research involving human subjects. All participants were assured of confidentiality, and the study was conducted in accordance with the Declaration of Helsinki principles.

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For statistical analysis, SPSS version 25.0 was utilized. Descriptive statistics were presented as mean ± standard deviation for continuous variables and as frequencies and percentages for categorical variables. Group comparisons were performed using independent sample t-tests for continuous variables and chi-square tests for categorical variables. Pearson's correlation coefficient was applied to assess the relationship between hs-CRP levels and various metabolic parameters. A p-value of less than 0.05 was considered statistically significant for all analyses.

RESULTS

Table 1: Demographic and Clinical Characteristics of Study Participants (n = 75)

Variable	Mean ± SD or Frequency (%)
Age (years)	43.2 ± 9.8
Female gender	42 (56%)
Male gender	33 (44%)
BMI (kg/m²)	33.8 ± 3.4
Waist circumference (cm)	104.2 ± 9.1
Systolic BP (mmHg)	132.5 ± 15.2
Diastolic BP (mmHg)	84.7 ± 10.1

Table 2: hs-CRP Status and Associated Insulin Resistance (HOMA-IR)

hs-CRP Category	Number of Participants (%)	Mean HOMA-IR ± SD	p-value
hs-CRP ≤3 mg/L	29 (38.7%)	2.8 ± 1.1	<0.001
hs-CRP >3 mg/L	46 (61.3%)	4.5 ± 1.6	

Table 3: Prevalence of Metabolic Syndrome and hs-CRP Levels

Metabolic Syndrome Status	Number of Participants (%)	Mean hs-CRP (mg/L) ± SD
Present	51 (68%)	5.2 ± 1.8
Absent	24 (32%)	2.3 ± 1.1

Table 4: Correlation of hs-CRP with Metabolic Parameters

Parameter	Correlation Coefficient (r)	p-value
Fasting plasma glucose	0.43	<0.001
Triglycerides	0.40	0.002
Waist circumference	0.45	<0.001
HOMA-IR	0.49	<0.001

DISCUSSION

The present study demonstrated a significant association between elevated high-sensitivity C-reactive protein (hs-CRP) levels and both insulin resistance and metabolic syndrome among obese individuals. Our findings revealed that participants with higher hs-CRP levels had markedly elevated HOMA-IR scores compared to those with lower hs-CRP values, underscoring the role of low-grade systemic inflammation in the development of insulin resistance. Additionally, the prevalence of metabolic syndrome

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was significantly higher among individuals with elevated hs-CRP, suggesting that chronic inflammatory states may contribute to the clustering of cardiometabolic risk factors.[9] A positive correlation was observed between hs-CRP and key metabolic parameters, including fasting plasma glucose, triglycerides, waist circumference, and HOMA-IR. This is consistent with previous studies where elevated hs-CRP levels were associated with central adiposity, dyslipidemia, and impaired glucose regulation (Ridker et al., 2000; Pradhan et al., 2001). Central obesity, characterized by increased visceral fat, is known to promote a pro-inflammatory milieu through the secretion of adipocytokines such as tumor necrosis factor-alpha and interleukin-6, which stimulate hepatic CRP production.[10] Hence, the strong relationship between waist circumference and hs-CRP observed in our study reinforces the central role of abdominal adiposity in systemic inflammation and metabolic dysregulation.

The robust association between elevated hs-CRP levels and higher fasting triglycerides can be explained by the inflammatory impairment of lipid metabolism, wherein pro-inflammatory cytokines disrupt normal lipid homeostasis, leading to hypertriglyceridemia.[11] Similarly, elevated fasting glucose levels in individuals with higher hs-CRP may reflect the inflammatory inhibition of insulin signaling pathways, culminating in insulin resistance and hyperglycemia.[12]

Interestingly, while significant associations were found with several components of metabolic syndrome, no significant relationship was observed between hs-CRP and HDL cholesterol or blood pressure in this cohort. These negative findings could be attributed to multiple factors, including the relatively small sample size, potential influence of unmeasured variables such as physical activity levels, dietary patterns, and genetic predisposition, or the possibility that mechanisms linking inflammation to HDL metabolism and blood pressure regulation are more complex and less direct compared to glucose and lipid pathways.[13,14] Another limitation is that the cross-sectional nature of the study precludes establishing a causal relationship between hs-CRP elevation and metabolic disturbances. It remains unclear whether elevated hs-CRP is a cause or consequence of metabolic derangements, necessitating longitudinal studies to clarify temporal associations.[15,16] Overall, our findings highlight hs-CRP as a simple, accessible biomarker that could aid early identification of obese individuals at heightened risk for insulin resistance and metabolic syndrome. Early detection could facilitate timely intervention, emphasizing the importance of incorporating inflammatory markers into routine metabolic evaluations in high-risk populations.

This study has several limitations that should be acknowledged. First, the cross-sectional design restricts the ability to establish causal relationships between elevated hs-CRP levels and the development of insulin resistance or metabolic syndrome; longitudinal studies would be more informative in confirming these associations over time. Second, the relatively small sample size and single-center setting may limit the generalizability of the findings to the broader Pakistani population. Third, potential confounders such as dietary habits, physical activity levels, socioeconomic status, and family history of

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metabolic disorders were not extensively controlled, which may have influenced the metabolic parameters and inflammatory status observed. Moreover, hs-CRP is a nonspecific marker of inflammation, and although exclusion criteria attempted to minimize confounding inflammatory conditions, subclinical or undiagnosed illnesses could not be completely ruled out. Moving forward, larger, multicenter, prospective studies are warranted to validate these findings across diverse population groups. Future research should also incorporate additional inflammatory markers, such as interleukin-6 and tumor necrosis factor-alpha, alongside hs-CRP to provide a more comprehensive assessment of the inflammatory milieu. Intervention studies examining whether lifestyle modifications or pharmacologic therapies targeting inflammation can effectively reduce hs-CRP levels and improve insulin sensitivity would offer valuable insights into potential preventive strategies for metabolic syndrome and related complications.

CONCLUSION

High-sensitivity CRP is significantly associated with insulin resistance and metabolic syndrome in obese individuals. hs-CRP could be a useful early marker for identifying high-risk patients in clinical practice.

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