Inside Out: C-reactive Protein (CRP) as Clinical Biomarker with Lipid Profile and Lactate Dehydrogenase in Metabolic Syndrome

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Abstract

Objective: To evaluate and compare the levels of C-reactive protein (CRP) and its correlation with lactate dehydrogenase (LDH) and abnormal lipid profiles in patients with metabolic syndrome versus healthy control.

Material and Methods: This was a case-control study and was conducted at the pathology laboratory of Jinnah Medical and Dental College from May 27, 2023 to December 27, 2023, receiving approval from the Ethical Review Committee of Sohail University in Karachi. Involved 300 participants, comprising 150 individuals diagnosed with metabolic syndrome and 150 healthy controls, representing the elderly age group and both genders. Following the acquisition of informed consent, demographic information and anthropometric measurements were documented, and blood samples were collected after an overnight fast to assess fasting blood sugar, lipid profiles, lactate dehydrogenase (LDH), and C-reactive protein (CRP) utilizing Bioscience and Oet-N10 kits, respectively.

Results: The results obtained in this study were compared between metabolic syndrome and control samples. Using the students't-test, the positive correlation was found between CRP and LDH in patients with metabolic syndrome with dyslipidemia as compared to healthy controls. The statistically significant difference was noted in BMI, WC, HC and WHR ratio between metabolic syndrome patients and controls,

Conclusion: This current study found that individuals with metabolic syndrome had higher basal metabolic rates, along with elevated CRP and LDH levels, which were independently associated with metabolic syndrome; Clinical monitoring and public health interventions are needed to reduce metabolic syndrome and its associated complications.

Keywords: C-reactive protein (CRP), lactate dehydrogenase (LDH), metabolic syndrome, body mass index (BMI), Basal metabolic rate (BMR)

How to cite: Inside Out: C-reactive Protein (crp) as Clinical Biomarker with Lipid Profile and Lactate Dehydrogenase in Metabolic Syndrome Comparison of the Efficacy of Gabapentin with Loratadine in Patients of Chronic Kidney Disease with Uremic Pruritus. Esculapio - JSIMS 2025;21(01): 168-173

DOI: https://doi.org/10.51273/esc25.251321130

Introduction

Metabolic syndrome a complex cluster of interconnected risk factors, is characterized by dyslipidemia, hypertension, insulin resistance, systemic inflammation, as reflected by elevated C-reactive protein (CRP), and abdominal obesity.[1] A cluster of metabolic issues dramatically escalates CVD risk. This interconnectedness raises the probability of metabolic syndrome and its complications.[2] The combined impact of these factors, including dysregulated lipid metabolism, elevated blood pressure, and impaired glucose homeostasis, elevates the likelihood of serious cardiovascular events such as peripheral arterial disease, coronary artery disease, and stroke in individuals with Metabolic syndrome.[3] Elevated CRP levels in Metabolic syndrome patients and LDH are documented as a significant predictor of adverse cardiovascular outcomes.[4] There is a crucial link

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Submission Date: 14-10-2024
1st Revision Date: 19-01-2025
Acceptance Date: 09-03-2025

found between Metabolic syndrome and a state of chronic, subtle inflammation.[5] C-reactive protein (CRP) has long been established as a reliable biomarker for systemic inflammation, with elevated levels indicating an increased risk for a wide range of chronic conditions, including diabetes mellitus, CVD, cancer, and other degenerative diseases, even in the absence of overt clinical symptoms.[6,7] In recent years, studies have begun to highlight the potential synergistic role of lactate dehydrogenase (LDH) alongside CRP in assessing cardiovascular risk in the context of Metabolic Syndrome.[8] Elevated LDH, a marker of tissue damage and cellular stress, alongside increased CRP, indicating systemic inflammation, strongly suggests heightened metabolic stress and elevated cardiovascular risk.[9,10] Notably, Metabolic syndrome patients with dyslipidemia, characterized by elevated triglycerides and low high-density lipoprotein (HDL) cholesterol, commonly exhibit elevated CRP levels, further underscoring the strong association between lipid abnormalities and systemic inflammation.[11] Given the established link between Metabolic syndrome, abnormal lipid profiles, elevated CRP, and potential tissue damage signaled by LDH, there is a clear and compelling need to further elucidate the intricate relationship between these biomarkers in predicting and managing cardiovascular complications.[12]

The association between CRP and carotid atherosclerosis in individuals with type 2 diabetes has been well-documented.[13] The specific interplay between CRP, LDH, and dyslipidemia in patients with Metabolic Syndrome, and its implications for cardiovascular risk stratification and management, remains to be fully understood.[14] This knowledge gap underscores the importance of further investigation into the combined predictive power of these biomarkers. Therefore, this study aimed to comprehensively evaluate the correlation among serum CRP levels, LDH, and dyslipidemia in a cohort of patients with Metabolic Syndrome, with the overarching goal of better understanding their combined impact on cardiovascular mortality and morbidity. We hypothesized that a positive correlation between CRP and LDH would be observed in Metabolic Syndrome patients with dyslipidemia, suggesting an elevated inflammatory and metabolic ilness, and that this correlation would be associated with increased cardiovascular risk factors. Furthermore, we sought to determine if the combined measurement of CRP and LDH provides incremental prognostic value beyond traditional risk factors in this population.

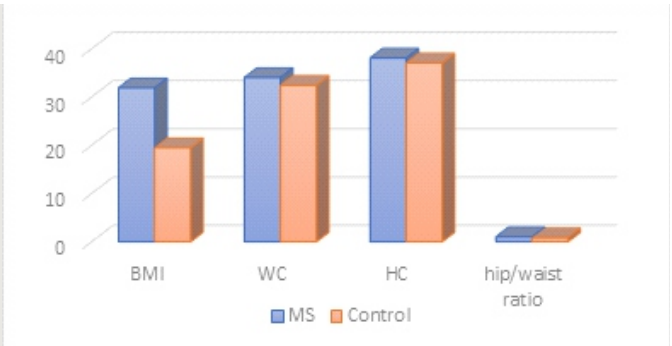
Material and Methods

This comparative case-control study was conducted in the pathology laboratory of Jinnah Medical and Dental College May 27, 2023, to December 27, 2023. Ethical approval was obtained from the Ethical Review Committee (ERC) of Sohail University, Karachi, Pakistan (Ref No: 000341/24, dated 27/05/2023). 150 participants aged 60-85 years, diagnosed with Metabolic Syndrome according to the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) criteria, served as cases. Waist circumference >102cm (males)/88cm (females), triglycerides ≥150mg/dL, HDL <40mg/dL (males)/50mg/dL (females), blood pressure ≥130/85mmHg, or glucose ≥100mg/dL. Control group of 150 healthy individuals without metabolic syndrome, age- and gender-matched participants. Exclusion criteria for both groups included: active infection, malignancy, autoimmune diseases, recent surgical procedures (within 3 months), and use of immunosuppressant medications. The sample size of 300 (150 cases and 150 controls) was determined based on a power analysis to detect a clinically significant correlation between CRP and LDH, with a power of 80% and a significance level of 0.05. Smoking status was recorded, and basic questions regarding diet and physical activity were asked to identify potential influences. All participants provided informed consent. Height, weight, waist circumference, and BMI were recorded, fasting blood samples (5mL) were collected for the estimation of fasting blood glucose, lipid profile, and lactate dehydrogenase (LDH) levels, quantified using enzymatic assays (Bioscience kits). Plasma CRP levels were measured quantitatively using kits provided by, using Oet-N10 multichannel analyzers. Data was analyzed using SPSS version 27. The student's t-test was used to compare means, and data were presented as means and percentages.

Results

In our study, 150 cases fulfilling the selection criteria for metabolic syndrome were included. Table 1 presents the descriptive analysis of metabolic syndrome patient (case) clinical and biochemical characteristics. The study included 50 (33%) males and 100 (67%) females, with a mean age of 68.44 years (range 60 to 85 years). Participants of both genders reported being on medication for diabetes, dyslipidemia, and cardiovascular disease. We analyzed the correlation of CRP with BMI, waist circumference, hip circumference, and waist-hip ratio. 42% of participants with abnormal waist and

hip circumference had a BMI ≥25. Significant differences in BMI, waist circumference (WC), hip circumference (HC), and waist-hip ratio (WHR) were observed between the metabolic syndrome and control groups, as depicted in Figure 1. Basic biochemical parameters, including triglycerides (TG), LDL, and blood pressure, were elevated, while HDL was low in Metabolic syndrome patients compared to healthy controls ($p<0.001$, Table 2). Fig-2 presented the Pearson's correlation coefficient analysis between CRP and LDH in individuals with metabolic syndrome (Metabolic syndrome) and healthy controls. For Metabolic syndrome cases, a very weak positive correlation was observed, with a



coefficient of r=0.026. This indicates a minimal association between CRP and LDH levels in metabolic syndrome. In the control group, the correlation coefficient was r=0.0000153 indicating no significant correlation between these two markers. This suggests that the relationship between CRP and LDH, albeit very weak, is more pronounced in metabolic syndrome cases compared to controls.

Table 2: *Comparison of diagnostic criteria of metabolic syndrome between cases and controls.*

Parameters	Metabolic syndrome (n = 150)	Controls (n = 150)	P value
FBS, mg/dl	105.36 ± 36.27	88.24 ± 9.31	< .001***
TG, mg/dl	156.68 ± 50.72	117.08 ± 29.89	< .001***
HDL-C, mg/dl	34.12 ± 6.54	43.42 ± 25.89	< .001***
LDL-C mg/dl	148.53± 852.05	89.01 ± 24.53	< .001***
SBP, mmHg	168 ± 17.61	120 ± 16.95	< .001***
DBP, mmHg	90 ± 12.55	76 ± 10.91	< .001***

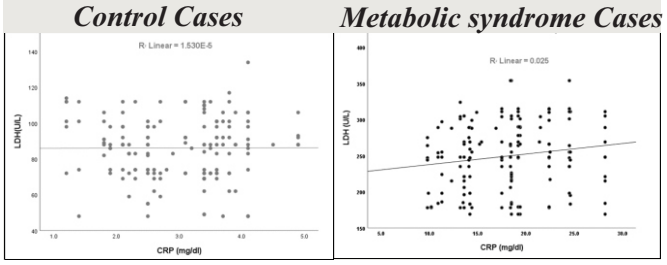


Table 1: *Descriptive Baseline analysis of clinical and biochemical analysis in the metabolic syndrome of Study Population N = 150*

	M ± *SD*	[95% CI]	Range
Age, years	67.13 ± 7.56	[67.52, 69.35]	60 – 90
Anthropometric Indices of Obesity			
Weight, kg	62.47 ± 15.77	[60.68, 64.26]	38 – 134
Body Mass Index, kg/m^2	23.67 ± 5.84	[23.24, 24.34]	15.90 – 50.40
Waist Circumference, cm	84.42 ± 11.64	[83.10, 85.74]	63.50 – 152.40
Waist-Hip Ratio	0.88 ± 0.08	[0.87, 0.89]	0.69 – 1.23
Clinical Examination			
Systolic BP, mmHg	131.91 ± 18.05	[129.30, 133.23]	100.0 – 180.0
Diastolic BP, mmHg	81.60 ± 12.26	[80.14, 82.81]	60.0 – 120.0
MAP, mmHg	98.07 ± 12.27	[96.67, 99.46]	76.67 – 136.67
Biochemical			
FBS, mg/dL	107.11 ± 38.68	[93.64, 99.96]	59 – 277
CHO, mg/dL	194.00 ± 57.16	[172.48, 184.03]	60 – 389
TG, mg/dL	158.02 ± 53.74	[131.65, 142.11]	45 – 288
LDL, mg/dL	149.21 ± 84.09	[111.10, 126.42]	29 – 477.2
HDL, mg/dL	34.71 ± 7.03	[36.56, 40.97]	24 – 126
AST	73.80 ± 56.95	[67.33, 80.27]	12 – 214
LDH, U/L	247.18 ± 47.87	[237.68, 256.68]	169-354
CRP, mg/dL	18.70 ± 5.34	[9.55, 11.44]	1.2 – 28.2

Figure 1: *Comparison of BMI, WC, HC and WHR of Metabolic syndrome patients and controls*

Figure 2: *The Pearson's correlation coefficient analysis between CRP and LDH in Metabolic syndrome cases (r=0.026) and control cases (r=1.530E-5).*

Discssion

In our study of 150 metabolic syndrome patients, females were predominantly affected (67%), consistent with literature suggesting a higher prevalence of metabolic syndrome in older women. The mean age of 68.44 years highlights the increased risk of Metabolic syndrome and its complications in the elderly population, as age is a significant factor in the syndrome's progression, all these findings in concondrance with other clinical researches . Besides that, it has also been correlated with various inflammation-provoking illnesses.[15]

Like this Current study exhibited a significant correlation was found between elevated BMI (≥25), waist circumference (WC), hip circumference (HC), and the waist-to-hip ratio (WHR) with C-reactive protein (CRP) levels was confirmed by one of a published study.[16] Obesity markers and their association with inflammation in metabolic syndrome have been well-documented suggesting that central obesity strongly contributes to systemic inflammation in metabolic syndrome patients as compared to healthy controls likewise confirmed in our study.[17,18]

In our research basic biochemical parameters, such as blood pressure, triglycerides (TG), and low-density lipoprotein (LDL), are significantly elevated in patients with metabolic syndrome, while high-density lipoprotein (HDL) is notably lower compared to healthy controls, with p-values <0.001. These findings underscore the metabolic abnormalities associated with Metabolic syndrome and align with previous research documenting similar dyslipidemia and hypertension patterns in Metabolic syndrome patients.[19] The persistence of elevated TG, LDL, and blood pressure in Metabolic Syndrome, as seen in our study and recent 2024 studies, underscores the importance of emerging biomarkers and novel therapies.[20] An array of factors, including a sedentary way of living, obesity, consumption of soft drinks, and insulin resistance, play a part in an increased risk of Metabolic syndrome.[21] Metabolic syndrome is a sequel of an intricate interaction of genetic and environmental variables that manifests as chronic low-grade inflammation.[22] This reported inflammation could be an alternative justification for raised serum LDH and mortality in those with Metabolic syndrome. To top it off, prior research found a compelling link among higher amounts of CRP and increased components of Metabolic syndrome ; greater odds of subsequent CVD events.[23]

In 2023, Zhang et al reported that metabolic-associated fatty liver disease (MAFLD) corresponded to overall plaque in the coronary arteries. Aside from general CHD risks, for instance, sex, age, smoking, hyperlipidemia, diabetes, and hypertension, MAFLD, still showed an independent correlation to noncalcified and mixed plaques.[24]

During our study, both CRP and LDH were elevated, Hence, a 2021 report attributed high LDH to a greater risk of CVD as well as CHD, cerebral infarction, cardiac failure, arrhythmias, and an overall worsened CVD-related mortality in Metabolic syndrome.[25]

These findings of our research suggested that CRP and LDH could potentially serve as useful biomarkers in clinical practice for identifying metabolic syndrome patients at elevated risk of cardiovascular disease, warranting closer monitoring and more aggressive intervention. CRP and LDH help identify high-risk metabolic syndrome patients for risk stratification, treatment monitoring, advanced testing, and post-intervention assessment.

However, as a single-center case-control study, our findings have limited generalizability and may be susceptible to selection and recall biases due to the lack of comprehensive dietary and activity data. Consequently, the causality between elevated LDH/CRP and metabolic syndrome's development cannot be determined. Future multi-center, prospective studies with detailed data collection are needed to validate these associations and elucidate the molecular mechanisms linking elevated LDH to mortality outcomes in this population, potentially solidifying LDH as a valuable biomarker for cardiovascular risk assessment.

Conclusion

Significantly elevated CRP levels in Metabolic syndrome patients, coupled with increased LDH, strongly suggest systemic inflammation and tissue damage, exacerbated by metabolic disruptions like high triglycerides, LDL, blood pressure, and low HDL. This CRP-LDH elevation links to heightened cardiovascular risk and mortality, underscoring its clinical importance. These findings suggest they could be used as biomarkers for identifying high-risk metabolic syndrome patients. Future research must pinpoint molecular mechanisms, identify specific biomarkers for early detection, explore targeted

therapies to reduce CRP and LDH, and conduct longitudinal studies to improve Metabolic syndrome management.

Conflict of Interest: *None*

Funding Source: *None*

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Authors Contribution

RG: Conceptualization of Project
UN: Data Collection
EA: Literature Search
SK: Statistical Analysis
MS: Drafting, Revision
ZS: Writing of Manuscript