



Original Article

Liver Enzyme Correlated with C-Reactive Protein as a Biomarker of Metabolic Syndrome in Elderly Patients

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ABSTRACT

Metabolic syndrome is a multifactorial disease with various risk factors that arise from insulin resistance associated with obesity, diabetes, hypertension, and dyslipidemias. **Objective:** To investigate the association between C-Reactive Protein and various risk factors related to CVS and metabolic health in elderly adults. Increased levels of various liver enzymes were found to be indicative of the progression of metabolic syndrome. **Methods:** In this study, total of 150 individuals with diagnosed metabolic syndrome were included, and they were compared to an equal number of control cases. The participants were selected from individuals visiting the Pathology and Molecular Biology Laboratories in Karachi for lab investigations. before collecting blood samples, basic vital signs, blood pressure, height, and waist circumference measurements were recorded to determine the participants' body mass index. The blood samples were then taken to assess liver enzyme levels and CRP. **Results:** The study examined and compared the levels of inflammatory marker and liver enzymes in both cases of metabolic syndrome (MetS) and the control group. The findings revealed a significant association (p-value of 0.001) between metabolic syndrome and elevated levels of liver enzymes and CRP. Specifically, the suspected cases of metabolic syndrome showed strong correlations with alanine aminotransferase, gamma-glutamyl transferase, and aspartate aminotransferase. However, alkaline phosphatase did not show substantial differences between the two groups. **Conclusions:** Our research revealed correlation between metabolic syndrome, liver enzymes and CRP. These findings indicate that high levels of liver enzymes and CRP can be indicative of cardiovascular functional abnormalities in elderly patients with metabolic syndrome.

INTRODUCTION

Obesity, hyperglycemia, hypertriglyceridemia, hypertension, and decreased levels of high-density lipoprotein are all symptoms of the metabolic syndrome. The diagnosis of MetS requires three of the following five factors: an increase in waist circumference, an increase in triglycerides, a decrease in HDL, an increase in blood pressure, and an increase in fasting glucose [1, 2] An increased risk of chronic diseases, such as type 2 diabetes

and cardiovascular problems, is linked to metabolic syndrome (MetS). Numerous research studies have demonstrated the significant impact of sex and age on the development of metabolic syndrome. These factors play a crucial role in determining the likelihood of MetS emergence in different populations [3] The serum enzymes alanine and aspartate aminotransferase, alkaline phosphatase (ALP), and gamma-glutamyl transferase

(GGT) are those that are frequently used in monitoring liver function [4], according to a study carried out in Bangladesh in 2021 [4]. Contrarily, the normal thresholds for liver enzymes frequently mislead the diagnosis of persons with metabolic syndrome and related non-alcoholic fatty liver disease. Obesity is one of the main MetS risk factors associated with non-alcoholic fatty liver disease (NAFLD). Cardiovascular disease may be more likely to occur as a result of a group of illnesses known as MetS that develop concurrently [5, 6]. Recent studies indicate that elevated levels of alanine aminotransferase and aspartate aminotransferase serve as key indicators of liver damage. However, CRP and GGT levels show an inverse correlation with metabolic disorders and other diseases [7, 8]. It is worth noting that patients with non-alcoholic fatty liver disease (NAFLD) who also have a high body mass index tend to exhibit increased levels of AST, ALT, and GGT, which are liver enzymes associated with liver damage [9, 10]. These findings highlight the complex association between liver enzymes, metabolic disorders, and NAFLD in individuals with high BMI [11]. In individuals with non-alcoholic fatty liver disease, the most common liver abnormality observed is an elevation in serum alanine aminotransferase, while alkaline phosphatase and gamma-glutamyl transferase tend to be less elevated. Previous investigations have identified other inflammatory markers, but it has been shown that C-reactive protein plays a significant role in the elevation of liver enzymes [12]. Numerous literatures reported that ALT and other liver indicators accurately predict the likelihood of developing type 2 diabetes mellitus [13, 14]. The current understanding of NAFLD progression revolves around a metabolic imbalance in the body. It has been proposed that inflammatory processes in the liver contribute to the systemic inflammation that characterizes metabolic syndrome [15]. Obesity and metabolic syndrome are associated with chronic inflammation, which is characterized by aberrant cytokine production, increased acute phase reactants, and activated inflammatory signaling pathways. Recent research has demonstrated a substantial correlation between high CRP levels and a number of metabolic syndrome symptoms. Adipose tissue is being implicated in a growing body of research as a key regulator of chronic low-grade inflammation in people with the metabolic syndrome.

METHODS

This case-control study was conducted on elderly-aged patients who were referred to Pathological and Molecular laboratories from various parts of Karachi for investigations of cardiovascular risk factors, diabetes and liver abnormalities. Out of 300 participants, 150 cases representing both genders who satisfied the MetS

diagnostic criteria and 150 controls were included. Detailed medical history was taken and BMI, blood pressure was measured. The study was approved by Ethical Review Committee (ERC), Sohail University, Karachi, Pakistan. Sample collection were done between January 2019 and December 2020. The consent was obtained from all participants. A total of 150 individuals with hypertension, diabetes, obese, and dyslipidemia were included in the study. General parameters such as blood pressure, height, and weight were noted. Blood pressure was measured using digital meter. Waist circumference was measured between the ribs and the iliac crest. Body mass index was calculated by dividing the weight in kilograms by the square of the height in meters. Fasting blood samples were collected to estimate the lipid profile and measure liver enzymes including ALT, AST, ALP, and GGT using kinetic methodology. All tests were performed following the protocols provided in the respective kits. Mindray Instrument was used to examine all biochemical parameters, and Innoline, France provided the kits. CRP was measured using Oet-N10 multichannel analyzers. This study comprised participants with high TG and LDL-C values, systolic blood pressure, and body mass index (BMI). All participants with known inflammatory or heart diseases, those who took medication for another conditions, or those who consumed alcohol four days a week were excluded from the study. Data analysis was done by using SPSS version-25.0 for quantitative investigation. The means, SDs, and correlation between the inflammatory marker and liver enzymes were used to analyze all of the categorical data. To ascertain the mean difference, a random sample t-test was performed. p-value < 0.05 was considered significant.

RESULTS

Out of the 300 individuals, 150 cases who met the MetS diagnostic criteria and 150 controls were included from both genders. The study's sample size was 50 men (33%) and 100 women (67%) with mean age of 72.50 years. The study participants who met the basic characteristics of the MetS were screened out for further biochemical investigations. The biochemical parameters were found considerably higher in MetS patients as compared to controls ($p < 0.001$ and $p < 0.01$). ALT and elevated ALP had a higher prevalence of positive criteria for all components of the metabolic syndrome result of present study showed elevated ALT, AST and GGT levels when compared with control. Compared to the control participants; CRP levels were found significantly higher in patients with metabolic syndrome. The outcomes of present study display significant association between liver enzymes and C-reactive proteins. Table 1 shows that the sample t test was

used to compare means between subjects having MetS and Controls.

Table 1: Case and Control Comparison of MetS Diagnostic Analysis Criteria.

Variables	Controls Mean ± SD	MetS Mean ± SD	P-value	Normal Ranges
Anthropometric Indices of Obesity				
Weight, kg	62.47±15.77	**85.48±11	< .01	50-89
Body Mass Index, kg/m ²	19.4±2.84	**28.67±5.84	< .01	18.5 to 24.9
Waist Circumference, cm	32.±9.89	***83.42±11.64	< .001	63.50-152.40
Waist-Hip Ratio	0.71±0.07	***0.97±0.08	< .01	0.69-1.23
Clinical Examination				
Systolic BP, mmHg	118±16.95	***182±17.61	< .001	100.0 - 180.0
Diastolic BP, mmHg	72±10.91	**96±12.55	< .01	60.0 - 120.0
Biochemical Estimations				
FBS, mg/dL	84.24±9.31	***115.36±36.27	< .001	59 - 277
Cholesterol, mg/dL	166.40±24.04	***254.00 ± 57.16	< .001	60 - 389
TG, mg/dL	112.08±29.89	***266.68±50.72	< .001	45 - 288
LDL, mg/dL	89.01±24.53	***149.21 ± 84.09	< .001	29 - 477.2
HDL, mg/dL	33.12±6.54	**51.42±25.89	< .01	24 - 126
ALT, U/L	25.33±6.39	***148.88 ± 54.80	< .001	upto-42
AST U/L	22.90±6.01	***132.81 ± 39.76	< .001	upto-37
GGT, U/L	28.91 ± 3.98	***69.72 ± 19.29	< .001	upto-40
CRP, mg/dL	3.97 ± 0.89	***23.02 ± 5.010	< .001	0-8

*p < .05, significant; **p < .01, very significant; ***p < .001, highly significant

The figure 1 shows comparison of correlated graph between ALT with CRP (r=0.664) AST with CRP (r=0.155) and GGT with CRP (r=0.583) in the metabolic syndrome cases.

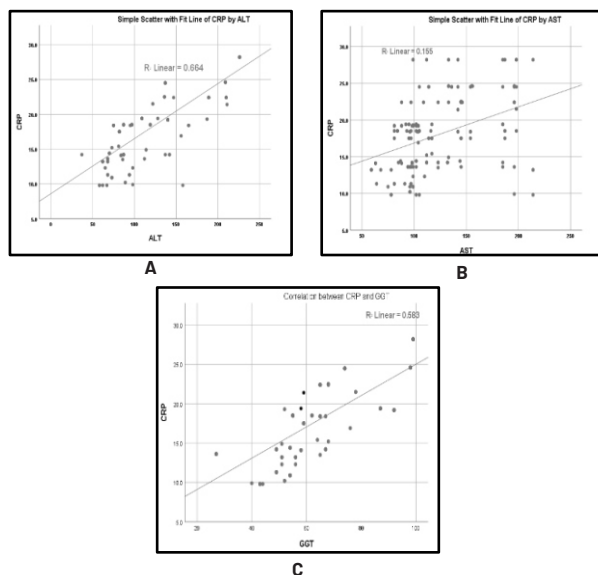


Figure 1: Correlation Between ALT with CRP, AST with CRP and GGT with CRP

On further analysis it was observed between ALT and ALP, and it was discovered that ALT was not significant with ALP (r=0.779) and when compared with control subjects as shown in graph b correlation between ALP and ALT (r=0.388) as shown in Figure 2.

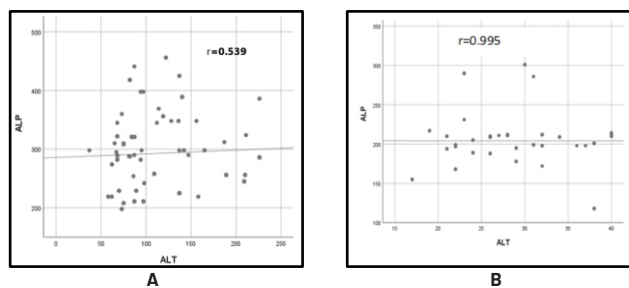


Figure 2: The figure shows comparison of correlated graph between ALT with ALP (r=0.539) in the metabolic syndrome cases and when compared with control subjects as shown in graph b correlation between ALP and ALT (r=0.995).

In this study it was noted that ALT and with AST were significant. It was also observed that all liver enzymes were significantly elevated with increased level of CRP between metabolic syndrome when compared with non-metabolic syndrome.

DISCUSSION

CRP is an acute-phase reactant produced by the liver in response to inflammation, and it serves as a marker of systemic inflammation. Chronic low-grade inflammation is believed to play a role in the pathogenesis of metabolic syndrome and its related complications. Inflammation can contribute to insulin resistance, endothelial dysfunction, and atherosclerosis, which are underlying mechanisms in the development of metabolic syndrome [16]. In present study increased levels of CRP and liver enzymes were observed in both the genders of study participants. Elevated levels of liver enzymes such as alanine transaminase (ALT), aspartate transaminase (AST) and gamma-glutamyl transferase (GGT) are often markers of liver dysfunction or injury. However, liver enzymes can also be influenced by factors such as obesity, insulin resistance, and fatty liver disease, which are components of metabolic syndrome. In present study we identified the relationship between ALT, AST, ALP, and GGT with CRP in MetS. The relevant findings were observed which include, all liver enzymes were elevated with elevated levels of CRP in MetS [17]. Secondly, in correlation analysis, all liver enzymes except ALP were significantly correlated with ALT and thirdly, the inflammatory marker was also significant with ALT in MetS. Correlation analysis on non-metabolic syndrome was also performed, and it was discovered that the correlations between ALT and AST and ALT and ALP were not significant. Similar studies were conducted, and the results were reported to be similar across different areas and countries [18]. The presence of elevated CRP levels and liver enzymes in individuals with metabolic syndrome may suggest a heightened state of inflammation and liver dysfunction. In a study conducted by Udenze et al., in 2021, it was found that elevated levels of liver enzymes

were associated with obesity, as well as increased levels of fasting insulin and CRP in individuals with metabolic syndrome (MetS). The study also suggested that dysmetabolism and an elevated cardiovascular risk were among the risk factors present in individuals with metabolic syndrome in the Nigerian population [19]. Another study revealed that serum alanine aminotransferase (ALT) was strongly linked to overall obesity, while gamma-glutamyl transferase (GGT) was associated with both overall and abdominal obesity [3]. Furthermore, a study conducted by Chen *et al.* in 2016 reported that liver enzymes, particularly ALT and GGT, were found to be within normal limits but significantly correlated with metabolic syndrome (MetS) [20].

CONCLUSIONS

In our study, we identified that elevated liver enzyme levels and C-reactive proteins are both a strong predictor of MetS and the risk of development of cardiovascular events in old aged persons. It is recommended from the present that doctors should completely assess the liver enzymes, inflammatory markers like CRP, metabolic abnormalities, and metabolic syndrome in older patients for comprehensive therapy and prevention of cardiovascular risk factors and morbidity.

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Authors Contribution

Conceptualization: RG

Methodology: RG, UN, FA, SZ

Formal Analysis: SE

Writing-review and editing: SPK, SE, FA

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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