Scientific Research Publishing

International Journal of Clinical Medicine, 2023, 14, 389-401
https://www.scirp.org/journal/ijcm
ISSN Online: 2158-2882
ISSN Print: 2158-284X

Relationship of High Sensitivity C-Reactive Protein with Cardiovascular, Diabetic, and Hepatic Biomarkers

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How to cite this paper: Krishnamurthy, H.K., Reddy, S., Jayaraman, V., Krishna, K., Song, Q., Rajasekaran, K.E., Wang, T.H., Bei, K. and Rajasekaran, J.J. (2023) Relationship of High Sensitivity C-Reactive Protein with Cardiovascular, Diabetic, and Hepatic Biomarkers. *International Journal of Clinical Medicine*, **14**, 389-401.
https://doi.org/10.4236/ijcm.2023.149035

Received: March 29, 2023
Accepted: September 4, 2023
Published: September 7, 2023

Abstract

Biomarkers are early predictors of various disorders, circulating level of C-reactive protein is a sensitive biomarker of systemic inflammation and may also be associated with the development of diabetic, hepatic, and cardiovascular diseases. In the present study, we aimed to investigate the association between circulating levels of high sensitive C-reactive protein (hs-CRP) and various biomarkers for hepatic, diabetic, and cardiovascular health. The retrospective analysis included 438 individuals who were tested for these panels simultaneously at Vibrant America Clinical Laboratory. The study population included free-living individuals without any preexisting clinical conditions. Among the cardiovascular markers, a positive correlation and significant association was found between high levels of hs-CRP and serum levels of triglycerides ($r = 0.0964$, $p < 0.0428$). Quantitative analysis also exhibited a negative correlation of HDL ($r = -0.1423$, $p < 0.0027$) and Apo A ($r = -0.1216$, $p < 0.0105$) with circulating levels of hs-CRP. Among all the diabetic markers, glucose ($r = 0.1547$, $p < 0.0011$) and glycated serum protein ($r = 0.1725$, $p < 0.0003$) were positively correlated with circulating hs-CRP. In the hepatic panel, AST, a transaminase that plays a vital role in amino acid metabolism, was found to have a strong positive correlation with hs-CRP ($r = 0.2139$, $p < 0.0001$). In conclusion, the results clearly show the association of hs-CRP with diabetic, hepatic, and cardiovascular risk factors indicating its central value as a key marker for several lifestyle-associated disorders.

Keywords

High Sensitive C-Reactive Protein, Systemic Inflammation, Cardiovascular Disorders, Diabetes, Triglycerides

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1. Introduction

Vascular disorders are one of the most important public health problems. Macrovascular diseases such as coronary artery disease, cerebrovascular disease, and peripheral artery diseases complicate and increase the chances of myocardial infarction and stroke [1]. Microvascular diseases such as nephropathy, neuropathy, and retinopathy may also result in lethal effects such as chronic kidney disorders, amputation of limbs, and loss of vision [2]. The levels of systemic vascular inflammation can be measured by the serum levels of C-reactive protein (CRP) and recent studies have proven that inflammation plays a pivotal role in the clinical pathogenesis of cardiovascular diseases. It's hypothesized that the correlation between CRP and cardiovascular diseases is indirect, the circulating CRP is produced by the liver and can be measured as the extent of any acute phase reaction in response to a nonspecific stimulus. The elevated levels of circulating CRP are related to an increased risk of congenital heart disease, myocardial infarction, and related deaths [3] [4] [5].

Serum amyloid A protein, fibrinogen, and CRP are some of the systemic markers of inflammation, but among them, CRP is the most promising sensitive and systemic biomarker [6]. Several prospective studies have proved that CRP can independently predict the future risk of coronary heart disease in non-diabetic subjects and have also found a two to four-fold increased risk of CHD in patients with type 2 diabetes. The early detection of high levels of CRP and identification of factors associated with increasing CRP play a crucial role in preventing severe CVD and other related vascular disorders [7] [8].

Elevation of CRP has been shown to be associated with an increased risk for type 2 diabetes development in patients with metabolic syndrome. The risk of fatal CVD is most common among patients with diabetes. Additionally, CRP levels are shown to be associated with fatty liver irrespective of the visceral fat volume [9]. Obesity, fatty liver disease, metabolic syndrome, diabetes, cardiovascular disease, and other lifestyle-associated disorders have all been shown to have an underlying inflammatory mechanism. In this context, it is important to study how levels of hs-CRP are correlated to biomarkers of cardiovascular, hepatic, and diabetic health [10] [11].

Traditional testing of CRP is in the range of 10 - 1000 mg/L while hs-CRP is measured in the range of 0.5 - 10 mg/L [12]. Given the association of systemic inflammation and its proven role in several chronic lifestyle diseases, we attempted to find the co-relations between this central inflammatory marker with key biomarkers of cardiovascular, diabetic, and hepatic health.

2. Material and Methods

2.1. Study Population

The study population was selected from the subjects who have been addressed to the Vibrant America Laboratory for cardiovascular, diabetic, and hepatic panels between July 2009 and November 2011. The retrospective analysis was completed

using the deidentified clinical data and test results from a total of 438 subjects and hence the study was exempted from the formal ethical review by Western IRB (Washington USA). The mean age (±SD) of the subjects was 48 ± 15 years with a female to the male ratio of 1:1 (50% female, 50% male).

2.2. Cardiovascular Markers

Blood samples were processed for the separation of serum and further analyzed for a cardiovascular panel comprised of lipids (total cholesterol, LDL, HDL, and triglycerides), apolipoproteins (Apo A1, Apo B), and a lipoprotein marker lipoprotein (A). Total cholesterol was measured by the cholesterol dehydrogenase method via the Beckman Coulter AU680 analyzer. Serum levels of LDL, HDL, and triglycerides were measured by an enzymatic-colorimetric method using the Beckman Coulter AU680 clinical chemistry analyzer. Other cardiovascular markers such as Apo A1, Apo B, and Lp(A) were also measured by a particle-enhanced immunoturbidimetric assay via Roche Cobas 6000 c 501 chemistry analyzer.

2.3. Diabetic Markers

Peripheral blood was obtained from the subjects and immediately processed for serum separation. All samples were subjected to measurement of various diabetic markers such as glucose, insulin, ferritin, hemoglobin A1C, glycated serum albumin, and adiponectin. Separated serum samples were processed for analysis within 2 h, serum samples may be refrigerated at 2˚C - 8˚C for 8 days if required.

Serum levels of glucose were measured by the enzymatic reference method in which the phosphorylation of glucose to glucose-6-phosphate catalyzed by hexokinase with consumption of ATP. The glucose-6-phosphate is further oxidized into gluconate-6-phosphate by glucose-6-phosphate dehydrogenase in the presence of NADP. The glucose concentration is measured photometrically as the rate of NADPH formation during the reaction. The invitro quantitative determination of serum insulin and ferritin was estimated by electrochemiluminescence immunoassay (ECLIA) analyzed using Elecsys and Cobas E analyzers.

The HbA_{1c} determination is based on the turbidimetric inhibition immunoassay (TINIA) for hemolyzed whole blood. The glycohemoglobin in the samples reacts with an anti-HbA_{1c} antibody to form a soluble antigen-antibody complex. Upon the addition of polyhaptens, the excess anti-HbA_{1c} reacts with the polyhaptens to form an insoluble antibody-polyhapten complex. The complex is further measured turbidimetrically using Roche/Hitachi Cobas c systems.

Serum levels of glycated serum protein are estimated by an enzymatic reaction catalyzed by proteinase K to digest GSP into low molecular weight glycated protein fragments (GPFs). The oxidative degradation of GPF is catalyzed by Diazyme's specific fructosamine to yield peptide fragments of amino acids, glucosone, and H_2O_2. The amount of H_2O_2 released is calorimetrically measured at 546 - 600 nm and is directly proportional to the concentration of glycated serum

protein present in the sample.

Serum levels of adiponectin are determined by the latex enhanced immunoturbidometric method. The serum samples were treated with anti-Adiponectin-coated latex and the formation of the antigen-antibody complex is characterized by the increase in the turbidity, which is measured photometrically at 570 nm. The concentration of adiponectin in the samples was determined by constructing a standard curve from the absorbance of the standards.

2.4. Hepatic Markers

The assay panel includes the estimation of most vital liver enzymes such as alkaline phosphatase (ALK), aspartate transaminase (AST), alanine transaminase (ALT), and other hepatic markers such as albumin, total bilirubin, and total protein. The serum levels of hepatic enzymes by colorimetric analysis using Roche/Hitachi Cobas c auto analyzers.

Serum levels of AST are determined by a two-step enzymatic reaction in which the AST present in the sample catalyzes the transfer of amino group between L-aspartate and 2-oxoglutarate resulting in the formation of oxaloacetate and L-glutamate. Further, the oxaloacetate oxidizes the NADH in the presence of malate dehydrogenase to form NAD. The oxidation rate of NADH is directly proportional to the catalytic activity of AST which is measured as the decrease in the absorbance. The enzyme activity of ALT is determined by the catalytic activity between L-alanine and 2-oxoglutarate. The reduction of pyruvate by NADH in a reaction catalyzed by lactate dehydrogenase results in the formation of L-lactate and NAD. The oxidation rate is directly measured as the catalytic activity of ALT and measured photometrically as the decrease in absorbance. Alkaline phosphatase is measured by the ability of phosphatases to cleave the p-nitrophenyl phosphate onto phosphate and p-nitrophenol in the presence of magnesium and zinc. The enzyme activity is directly proportional to the amount of p-nitrophenol released and measured as the increase in absorbance.

Serum levels of albumin are measured by the development of a blue-green complex between the cationic serum albumin and anionic bromocresol green at an ideal pH of 4.1. The color intensity of the blue-green complex is directly measured as the concentration of albumin. The total bilirubin is determined by a colorimetric diazo method in which the serum bilirubin readily solubilizes and forms a red azo dye complex with 3,5-dichlorophenyl diazonium. The color intensity of the complex is photometrically measured and directly proportional to the amount of total bilirubin. The total protein is estimated by divalent copper which reacts with the protein peptides which forms a characteristic purple-colored biuret complex. The color intensity of the complex is directly proportional to the concentration of protein.

2.5. High Sensitivity C-Reactive Protein

Serum hs-CRP levels were measured using a particle-enhanced immunoturbidimetric method, which measures the agglutinates of hs-CRP with latex particles

coated with anti-CRP monoclonal antibodies. The concentration of hs-CRP is measured turbidimetrically on Roche Cobas c 311 analyzers. The functional sensitivity is the lowest hs-CRP concentration that can be reproducibly measured with an inter-assay coefficient of variation of <10%.

3. Statistical Analysis

Clinical data were subjected to retrospective analysis from de-identified subjects using Java for windows version 1.8.161. Non-parametric Mann-Whitney U test was used to compare the serum levels of hs-CRP with normal and altered levels of various serum markers. Pearson's correlation was carried out to analyze the univariant relationship between serum biomarkers with hs-CRP at $p < 0.05$ significance. All statistical analysis was performed using GraphPad Prism Version 7.00 and a descriptive statistic was used to define the continuous variables (mean ± SD, and median, minimum and maximum).

4. Results

The baseline clinical characteristics of the study population were detailed in Table 1. The subjects were categorized based on the serum levels of various biomarkers such as cardiovascular, diabetic, and hepatic markers. Association of serum levels of hs C-Reactive proteins with selected cardiovascular, diabetic, and hepatic markers was evaluated.

Cholesterol, LDL, HDL, triglycerides, Apo A, Apo B, and lipoprotein are the vital cardio markers involved in the study. Pearson correlation analysis between the serum levels of selected cardio markers with serum levels of high sensitive C-reactive protein (hs-CRP) exhibited a positive correlation with serum levels of triglycerides ($r = 0.0964$, $p < 0.0428$) (Figure 1). The serum levels of HDL ($r = -0.1423$, $p < 0.0027$) and Apo A ($r = -0.1216$, $p < 0.0105$) (Figure 1) were found to have a negative correlation with hs-CRP (Table 2). Further, the significance of varying serum levels of lipids and lipoproteins with serum hs-CRP was studied by the Man-Whitney U test. The results showed a strong association of high levels of hs-CRP with triglycerides ($p < 0.0001$) (Table 3), while the high levels of hs-CRP do not have any significant impact on other cardiovascular markers.

The diabetic panel in the present study includes 6 vital markers such as insulin, ferritin, hemoglobin A1c, glucose, adiponectin, and glycated serum protein. Using Pearson correlation analysis (Table 2) among all the tested diabetic markers, glucose ($r = 0.1547$, $p < 0.0011$) (Figure 2) and glycated serum protein ($r = 0.1725$, $p < 0.0003$) (Figure 2) were found to have a strong positive correlation with circulating levels of hs-CRP. The high levels of circulating hs-CRP were found to have a strong significant association with circulating levels of insulin ($p < 0.0001$) by Mann Whitney U test (Table 3).

Being a hepatic origin protein, studies on the relation between the C-reactive protein and its effects on liver enzymes are surprisingly rare. The present study

Table 1. Baseline clinical characteristics of the study population.

	n = 438	Frequency (n)	Mean ± SD
	Male	220	48.8 ± 14.4
	Female	218	48.0 ± 15.5
High sensitivity C-reactive protein	Low	-	-
	Normal	365	1.0 ± 0.8
	High	73	11.5 ± 12.2
Cardio marker			
Cholesterol ≤199 mg/dL	Low	-	-
	Normal	389	181.4 ± 33.0
	High	49	263.9 ± 27.8
Low-density lipoprotein ≤99 mg/dL	Low	-	-
	Normal	263	99.9 ± 20.6
	High	175	158.3 ± 24.4
High-density lipoprotein ≥56 mg/dL	Low	53	35.4 ± 5.3
	Normal	385	58.4 ± 14.9
	High	-	-
Triglyceride ≤149 mg/dL	Low	-	-
	Normal	405	88.9 ± 35.3
	High	33	313.3 ± 107.5
Apolipoprotein A1 ≥120 mg/dL	Low	50	117 ± 12.9
	Normal	388	173.9 ± 31.5
	High	-	-
Apolipoprotein B ≤89 mg/dL	Low	-	-
	Normal	367	89.5 ± 17.6
	High	71	137.9 ± 17.4
Lipoprotein (A) ≥30 mg/dL	Low		
	Normal	273	14.0 ± 6.4
	High	165	69.8 ± 31.4
Diabetic marker			
Insulin 30 - 230 ml U/L	Low	15	1.8 ± 0.4
	Normal	387	8.6 ± 4.9
	High	36	43.2 ± 24.6
Ferritin Male: 30 - 400 ng/mL Female: 13 - 150 ng/mL	Low	06	16.0 ± 3.1
	Normal	372	125.2 ± 90.3
	High	60	367.6 ± 3
Hemoglobin A1c 5.7 - 6.4 (%)	Low	-	-
	Normal	416	5.3 ± 2.6
	High	21	5.3 ± 2.7
Glucose 101 - 126 (mg/dL)	Low	06	60.5 ± 3.0
	Normal	384	92.3 ± 9.8
	High	48	151.1 ± 71.9

Continued

Adiponectin ~58.5 (ug/mL)	Low	24	3.2 ± 0.76
	Normal	412	16.2 ± 9.5
	High	02	-
Glycated serum protein ~300 (umol/L)	Low	-	-
	Normal	407	228.1 ± 34.8
	High	31	415.0 ± 140.5
Hepatic marker			
Alkaline phosphatase (ALK) Male: ~130 (U/L) Female: ~105 (U/L)	Low	06	35.5 ± 3.2
	Normal	413	68.3 ± 16.2
	High	19	134.4 ± 36.6
Aspartate transaminase (AST) Male: ~40 (U/L) Female: ~32 (U/L)	Low	-	-
	Normal	399	21.2 ± 5.3
	High	39	66.7 ± 62.4
Alanine transaminase (ALT) ~42 (U/L)	Low	-	-
	Normal	381	19.9 ± 7.1
	High	57	65.2 ± 37.6
Albumin ~5.2 (g/dL)	Low	-	-
	Normal	431	4.6 ± 0.2
	High	7	5.3 ± 0.1
Total bilirubin ~1.3 (mg/dL)	Low	-	-
	Normal	424	0.5 ± 0.2
	High	14	1.6 ± 0.5
Total protein ~8.7 (g/dL)	Low	03	5.8 ± 0.1
	Normal	419	7.1 ± 0.3
	High	16	8.3 ± 0.7

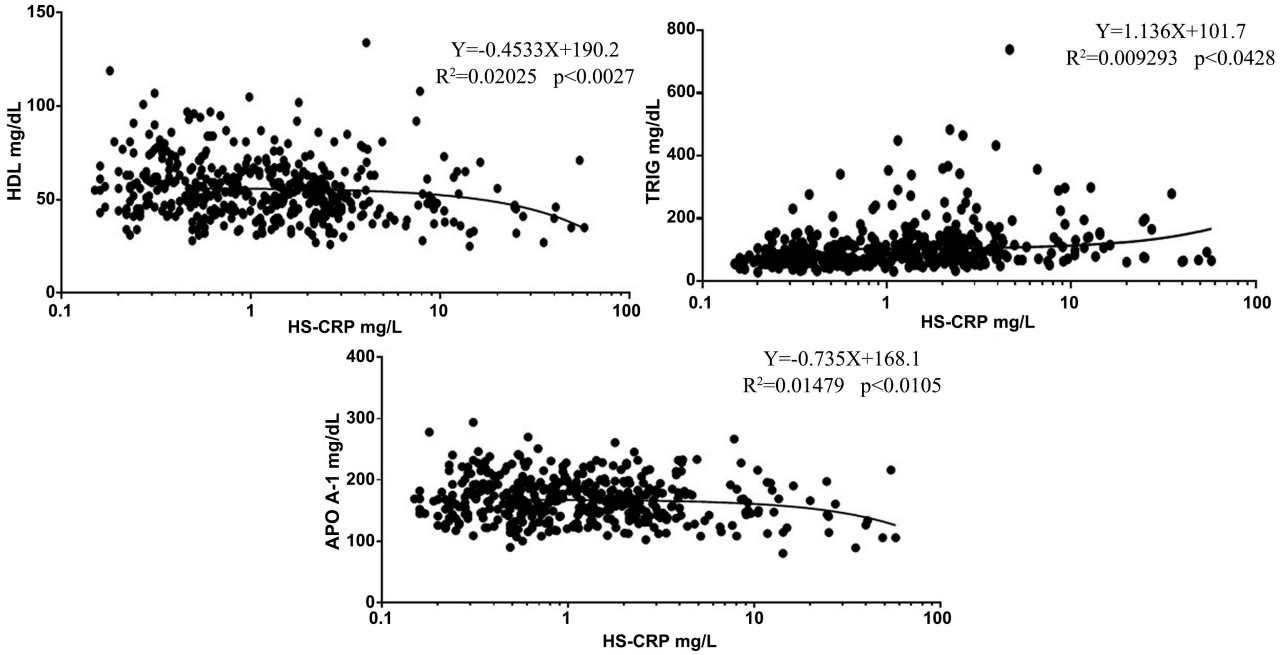

Figure 1. Log-log$_{10}$ graph showing the linear regression and correlation between serum HS-CRP with lipids.

Table 2. Pearson correlation coefficient for serum levels of hs-CRP with various serum markers.

	r	p
Cardiovascular markers		
Cholesterol	−0.06344	0.1831
LDL	0.004295	0.9283
HDL	−0.1423	0.0027
Triglyceride	0.0964	0.0428
Apolipoprotein A	−0.1216	0.0105
Apolipoprotein B	0.04545	0.3405
Lipoprotein (A)	0.06239	0.1905
Diabetic markers		
Insulin	0.1725	0.0003
Ferritin	0.05868	0.2182
Haemoglobin A1c	0.07513	0.1164
Glucose	0.1547	0.0011
Adiponectin	−0.07922	0.0962
Glycated serum protein	0.01408	0.7678
Hepatic markers		
Alkaline phosphatase (ALK)	0.2139	<0.0001
Aspartate transaminase (AST)	−0.02081	0.6626
Alanine transaminase (ALT)	0.01883	0.6929
Albumin	−0.106	0.0259
Total bilirubin	−0.09518	0.0455
Total protein	0.06007	0.2075

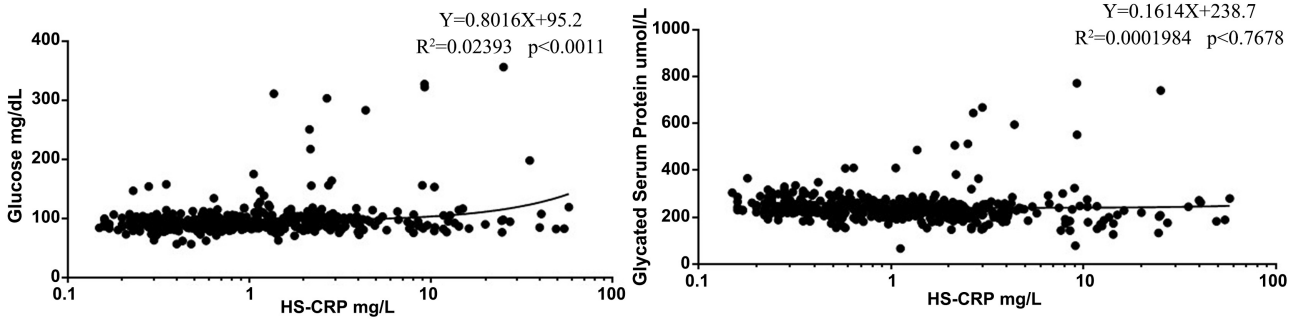

Figure 2. Log-$\log_{10}$ graph showing the linear regression and correlation between serum HS-CRP with diabetic markers.

highlights the association of 6 important hepatic markers as alkaline phosphatase (ALK), aspartate transaminase (AST), alanine transaminase (ALT), albumin, total bilirubin, and total protein with hs-CRP. AST was found to have a strong positive correlation ($r = 0.2139$, $p < 0.0001$) with the circulating hs-CRP (Table 2). Aspartate transaminase (AST) is the most vital phosphate-dependent

Table 3. Mann-Whitney U test results for the significant association of serum levels of hs-CRP.

	Greater than reference range (n = 73)		Within range (n = 365)		p ($p < 0.05$)
Cholesterol	190 ± 39.8	186 (92 - 285)	190.8 ± 42.0	190 (89 - 364)	0.9966
LDL	125.9 ± 31	120 (58 - 200)	122.8 ± 37.0	121 (32 - 289)	0.4003
HDL	52.1 ± 18.8	47 (25 - 134)	56.3 ± 15.2	55 (26 - 119)	0.0040
Triglyceride	**136.4 ± 104**	**106 (48 - 738)**	**99.7 ± 65.2**	**81 (28 - 483)**	**<0.0001**
Apolipoprotein A	159.3 ± 39.4	150.2 (80 - 266.7)	169.1 ± 33.8	166.2 (89.7 - 294)	0.0266
Apolipoprotein B	102.3 ± 22.0	103.6 (59 - 151.1)	96.3 ± 25.5	94.6 (40.4 - 198)	0.0237
Lipoprotein (A)	40.1 ± 38.2	21.9 (6.3 - 141.2)	34.0 ± 32.5	20.4 (5.4 - 156.8)	0.2055
Insulin	**18.5 ± 20.0**	**11.3 (2.5 - 124.7)**	**10.1 ± 10.1**	**7.5 (1.2 - 101.7)**	**<0.0001**
Ferritin	179.9 ± 190.7	111.3 (14.5 - 1148)	157.4 ± 154	116.8 (12.0 - 1279)	0.5811
Hemoglobin A1c	5.7 ± 1.6	5.2 (4.3 - 14.4)	5.4 ± 0.7	5.3 (4.3 - 11.5)	0.6664
Glucose	108.5 ± 55.5	94.9 (72.3 - 356)	96.3 ± 23.7	93 (56.7 - 310.8)	0.5643
Adiponectin	13.8 ± 8.2	11.5 (2.4 - 39.5)	16.1 ± 10.7	13.2 (0.87 - 78.7)	0.1248
Glycated Serum Protein	240 ± 114.1	219.3 (78.4 - 771.8)	241.7 ± 56.3	232.9 (66.0 - 668.4)	0.0056
Alkaline phosphatase (ALK)	**84.4 ± 31.3**	**83 (48 - 260)**	**67.9 ± 19**	**66 (31 - 187)**	**<0.0001**
Aspartate transaminase (AST)	23.2 ± 9.8	21.2 (9.3 - 67)	25.6 ± 24.9	21.1 (9.4 - 397)	0.5038
Alanine transaminase (ALT)	25.2 ± 17.7	20 (8.2 - 109)	26.0 ± 22.1	20.9 (6.7 - 192.9)	0.6895
Albumin	4.5 ± 0.3	4.5 (3.6 - 5.2)	4.6 ± 0.2	4.6 (3.7 - 5.7)	0.0005
Total bilirubin	0.50 ± 0.30	0.43 (0.17 - 1.83)	0.56 ± 0.31	0.50 (0.16 - 2.92)	0.0120
Total protein	7.2 ± 0.4	7.2 (5.6 - 8.6)	7.1 ± 0.4	7.1 (5.8 - 11.0)	0.0377

transaminase enzyme in amino acid metabolism which catalyzes the reversible transfer of a α-amino group between aspartate and glutamate. Alkaline phosphatase ($r = -0.106$, $p < 0.0259$) and serum bilirubin ($r = -0.09518$, $p < 0.0455$) were found to be weakly correlated with the hs-CRP (Table 2). The Man-Whitney U test showed a significant association of alkaline phosphatase (<0.0001) with high serum levels of hs-CRP (Table 3).

5. Discussion

Lifestyle-associated disorders have become the bane of human health. These comorbidities such as metabolic syndrome, diabetes, etc. affect the health of the general population and leave them vulnerable to a host of diseases, the higher risk of death with SARS-CoV2 infections is a case in point [13]. Earlier detection of chronic inflammation, diabetes, and cardiovascular risk and implementation of preventive strategies would have far-reaching effects in the domain of public health [14].

Detecting the circulating levels of various inflammatory markers such as C-reactive protein, serum amyloid A, plasma viscosity, ceruloplasmin, etc. can be an effective tool in predicting various disorders from metabolic syndrome to

diabetes and cardiovascular risk [15]. In recent years, the detection of circulating levels of hs-CRP has become an effective biomarker for the prediction of a diverse class of diseases due to its accuracy, superior assay precision, and commercial availability [12]. While conventional testing measures CRP within the range of 10 to 1000 mg/L, hs-CRP is more effective in detecting inflammation at a much lower concentration ranging from 0.5 to 10 mg/L. Additionally, the existence of standards for proper calibration makes hs-CRP an analyte of choice in comparison to other existing acute phase reactants [16]. It is important to note, however, that markers of inflammation including hs-CRP are extremely nonspecific specific in nature and can be detected in various inflammatory conditions. A scientific statement by CDC/AHA reported the possible role of hs-CRP in originating atherosclerosis. An article by Life Extension magazine stated that CRP is the cause of inflammation rather than just a marker of inflammation [17]. Several reports have demonstrated hs-CRP as a strong, independent biomarker for inflammation and one of the most clinically acceptable predictors of cardiovascular risk (Emerging Risk Factors Collaboration 2010). There have been several pieces of evidence that proved the role of inflammation in various glucose-related disorders [18] [19]. The detection of inflammatory markers such as hs-CRP in the development of glucose-related disorders was found to appear in various modes of pathogenesis. For instance, antibodies against islet cells and glutamic acid decarboxylase are autoimmune inflammatory markers against β cells in nonobese adults without diabetes. Inflammatory markers such as tumor necrosis factor α, and decreased insulin sensitivity also help in predicting diabetes [20]. Various cross-sectional studies have proved elevated levels of inflammatory markers such as hs-CRP in subjects with diabetes when compared with subjects without diabetes [21]. Obesity is the most common reason for diabetes and associated cardiovascular diseases that are strongly associated with a chronic inflammatory response such as activation of inflammatory signaling pathways, uncontrolled cytokine production, and elevated levels of acute-phase reactants [22]. Similarly, metabolic syndrome includes multiple risk factors such as obesity, insulin resistance, type 2 diabetes, etc. Metabolic syndrome is associated with multiple inflammatory biomarkers such as hs-CRP, CD_{40} ligand, interleukin-6, P-selectin, etc. WHO defines metabolic syndrome as subjects with increased cardiovascular morbidity and mortality [23] [24]. In case of both obesity and metabolic syndrome, the implication of cholesterol and other lipids on adipose tissue turns it into a major regulator of chronic inflammatory responses that, in turn, triggers adipose tissue to produce interleukin-6, tumor necrosis factor-α, and various other pro-inflammatory cytokines that are considered as chief stimulators of hs-CRP in the liver [25]. Obesity and metabolic syndrome are widely accompanied by nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH) [26]. Several studies have shown the association of NAFLD and NASH with components of metabolic syndrome and it's also characterized by the elevation of alanine aminotransferase (ALT). It could be hypothesized that the elevated levels of liver-derived inflammatory markers particularly hs-CRP

might be involved in common liver abnormalities.

The present study is the first to demonstrate the association of a systemic inflammatory marker hs-CRP with three different classes of metabolic markers—cardiovascular, diabetic, and hepatic. In the current retrospective data of the healthy population, the baseline levels of hs-CRP were found to be normal in more than 50% of the population.

The data presented in the study has several diagnostic implications as hs-CRP thus far has been considered as an important marker primarily in the prediction of cardiovascular risk alone. The data presented here supports the hypothesis that hs-CRP is related to various glucose-related disorders and is also associated with altered levels of liver enzymes apart from cardiovascular disorders. This could also suggest that increased serum hs-CRP might be associated with most features of metabolic syndrome. Elevated levels of hs-CRP are independently associated with various clinical risk factors. Monitoring the circulating levels of hs-CRP might be a simple, practical, and potential tool for assessing the risk of developing cardiovascular diseases, glucose-related disorders, and liver health.

Data Availability

In order to access supporting data, contact the corresponding author.

Acknowledgements

We acknowledge Vibrant America LLC for supporting this research.

Authors' Contributions

Hari Krishnan Krishnamurthy, Karthik Krishna, and Tianhao Wang performed the research. Hari Krishnan Krishnamurthy, John J. Rajasekaran, Karenah E. Rajasekaran, and Vasanth Jayaraman designed the study. Qi Song, Kang Bei, and Swarnkumar Reddy analyzed the data. Hari Krishnan Krishnamurthy and Swarnkumar Reddy wrote the article.

Institutional Review Board Statement

The study comprises a retrospective analysis exempted by the Western Institutional Review Board.

Conflicts of Interest

Hari Krishnan Krishnamurthy, Vasanth Jayaraman, Karthik Krishna, Tianhao Wang, Kang Bei, and John J. Rajasekaran are employees of Vibrant Sciences LLC. Swarnkumar Reddy, Qi Song, and John J. Rajasekaran are employees of Vibrant America LLC. Vibrant America is a commercial diagnostic lab that could benefit from increased testing of micronutrients and cardiovascular biomarkers.

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