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ORIGINAL ARTICLE

Role of Fibrinogen, hs-CRP, serum amyloid A protein (SAA), D Dimer in cardiovascular risk assessment

Shemy A S[1], * Arun B[2], DanielAbraham[3]
[1]Research Scholar, School of Health Sciences, Kannur University, Palayad Kerala 670661, India
[2]Assistant professor, Department of Life Sciences, Kannur University, Palayad, Kerala 670661, India
arunb@kannuruniv.ac.in*
[3]Vocational Teacher in MLT, Government VHSS, Kannur Kerala 670661, India

ABSTRACT
Inflammatory mechanisms are involved in the development and progression of vascular disease. Current risk prediction models based on conventional risk variables can estimate the long-term CV risk of several people. Extensive research is now being conducted to uncover novel risk variables that may increase our capacity to forecast CV risk reliably, identify new therapeutic targets, and enhance existing prognostic algorithms. Thus, the current investigation aimed to evaluate the influence of novel biochemical markers such as hs-CRP, fibrinogen, serum amyloid A protein, and D dimer on inflammatory indicators in cardiovascular disease. 100 healthy volunteers and members of the test population were chosen, and their details were recorded. The measurement of inflammatory markers followed standard procedures. Inflammatory indicators, including hs-CRP, fibrinogen, serum amyloid A protein, and D dimer, are associated with an elevated risk of coronary heart disease. In conclusion, our data indicate that elevated levels of inflammatory markers are connected with a high risk of heart disease and may thus be exploited for the early detection of coronary heart disorders.
Keywords: *Inflammatory markers, coronary heart disease, hs-CRP, fibrinogen, serum amyloid A protein, D Dimer.*

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INTRODUCTION

"Cardiovascular diseases (CVDs) encompass coronary heart disease, cerebrovascular disease, peripheral arterial disease, rheumatic heart disease, congenital heart disease, deep vein thrombosis, and pulmonary embolism. CVD is the leading cause of mortality for men and women in developed and developing nations. By 2030, cardiovascular disease is anticipated to be the leading source of global disease burden" [1]. Plaque buildup within the arteries causes CVD. A variety of elements found in the blood are what make up plaque. Over time, plaque builds up and causes arteries to stiffen and constrict, reducing blood flow to the heart muscle. A blood clot may grow on the surface of a plaque if it eventually ruptures. If the clot becomes big enough, it might prevent oxygen-rich blood from reaching the heart muscle region supplied by the artery. Angina and heart attacks might arise from this. CVD may damage the heart muscle over time, resulting in heart failure and arrhythmias. High blood pressure, high cholesterol levels, diabetes, metabolic syndrome, and chronic renal disease are the leading causes of death from cardiovascular disease, followed by a family history of CVD and other risk factors such as smoking and obesity. Atherothrombosis and the first signs of cardiovascular disease all begin with inflammation. The innate immune system interacts with atherosclerosis, as proven by advances in vascular biology [2]. Clinical investigations have linked chronic inflammation to future CV events, and it is hypothesized that new biomarkers of inflammation may enhance the identification of asymptomatic people at risk [3].

There is no evidence that inflammation is a crucial factor in the development and progression of atherosclerosis. Histopathological and immunochemical observations suggest that active inflammatory processes may cause plaque to break and increase the risk of coronary thrombosis, which can lead to a clinical ischemic event [4]. After a localized response, an acute phase reaction may start to happen. Some systemic inflammatory indicators may show how harmful the inflammation is, and high levels of these

indicators have been linked to heart disease. Before, fibrinogen was considered a separate risk factor for coronary heart disease (CHD). Now, it is seen as both a coagulation component and a marker for inflammation. In prospective population studies, C-reactive protein (CRP), another type of acute-phase reactant, was found to be a risk factor for cardiovascular disease on its own. However, fibrinogen and CRP are products of the acute phase response, and since their amounts can change after transcription, they may only be some of the essential inflammatory effectors. If inflammatory biomarkers can be used to diagnose CVD risk early, the global population can control a significant health issue and cut healthcare costs. Thus, the current investigation aimed to evaluate the influence of novel biochemical markers such as hs-CRP, fibrinogen, serum amyloid A protein, and D dimer on inflammatory indicators in cardiovascular disease.

MATERIAL AND METHODS

100 patients with cardiovascular disease diagnosed by a cardiologist were selected as the test population. Moreover, 100 healthy individuals with no history of CVD, hypertension, diabetes, renal disease, or another systemic disease will be included as Controls. The subjects should not have liver or renal involvement, autoimmune diseases, cancer, or chronic or acute infections. Age and sex-matched controls fulfilling the above criteria will be included. Neither the patients nor the Controls should be suffering from acute or chronic illness or on prolonged medication for other purposes. Subjects above the age of 80 and below 30 will be excluded. Physical activity grading was recorded based on standard validated techniques. The participants' dietary habits were also evaluated by recording the intake of Fat, Sodium, Fruits, vegetables, Wholegrain cereals, Fish, and Alcohol using a questionnaire. The BMI was measured by using the height and weight of the patient. The habit of Smoking/ Tobacco use was recorded. The systolic and diastolic blood pressure was measured per the JNC 8 criteria, and the Glycated Hemoglobin (HbA1c) was also measured using standard procedure. The hs-CRP was evaluated by turbidimetry method on Beckman Coulter AU480 automated clinical chemistry analyzers. The fibrinogen estimation was carried out by turbidimetry method on Beckman Coulter AU480 automated clinical chemistry analyzers. D Dimer was estimated by the FPIA method on bioMerieux VIDAS automated analyzers. Serum amyloid A protein (SAA) and Oxidised LDL were evaluated by the ELISA method on an ELISA analyzer.

RESULTS AND DISCUSSION

One hundred healthy volunteers were selected as the control group; 78% were males, and 22% were females. A total of 97 % of the control population were married, and the mean age of the control group was 61.48 ±10.99. The test population was selected based on the inclusion criteria: 79 % were males, and 21 % were females. A total of 96 % of the test population were married. The mean age of this group was 61.45 ±11.64. There was no significant difference in age and sex match between the groups. There was no significant difference in the height of the control group (163.9± 5.956) and the test group (163.4± 6.666). A significant difference was noticed in the weight of the control (62.34+±5.236) and weight of the test population (68.33 ± 9.168), waist of control (33.73±1.705) and test group (36.48±1.514).

	Control group	Test Group
BMI	23.31±2.614	25.56±3.177
Cholesterol	153.5±27.57	207.9±48.71
Systolic BP	113.5±7.8883	142.7±26.93
Diastolic BP	76.5±4.794	82.9±10.94
HbA1C	4.997±0.3161	5.593±0.642

The test population shows a significant change in the BMI, Cholesterol, HbA1C, systolic and diastolic BP. In the general population, a higher body mass index (BMI) has been identified as a risk factor for cardiovascular disease [5]. Patients with type 1 diabetes have a roughly fourfold increased risk for myocardial infarction; however, there is conflicting information about the effect of BMI on this risk [6]. Several studies indicate that decreasing blood pressure reduces cardiovascular risk [7]. AHA and ACC recommendations [8] also indicate the significance of lowering total cholesterol in reducing cardiovascular risk. There is abundant evidence that decreasing LDL cholesterol after reducing CV risk is beneficial [8].

Variable	CATEGORY	Total Count	Mean	St. Dev
Fibrinogen (mg/dL)	Control	100	253.50	34.83
	MI	100	309.77	57.27
hs-CRP (mg/L)	Control	100	0.5406	0.2581
	MI	100	4.924	2.038
SAA (mg/L)	Control	100	1.8487	0.6583
	MI	100	4.759	1.380
Ox LDL (mg/dL)	Control	100	107.45	31.57
	MI	100	458.9	110.4
D Dimer (ng/mL)	Control	100	240.1	131.4
	MI	100	757.6	238.8

Fibrinogen (mg/dL), hsCRP (mg/L), SAA (mg/L), Ox LDL (mg/dL), D Dimer (ng/mL)

Fibrinogen

Fibrinogen plays a role in the coagulation cascade and controls blood viscosity. Its acute-phase levels may rise by 100–200% over baseline [9], demonstrating its sensitivity to inflammatory stimuli. However, the inflammatory system and the hemostatic system work together closely. Activation of the inflammatory response may stimulate the coagulation system, downregulate proteins critical to the regulation of the coagulation response, and inhibit fibrinolysis. Ischaemic heart disease (IHD) risk and atherosclerosis degree are correlated with plasma fibrinogen concentration [9].

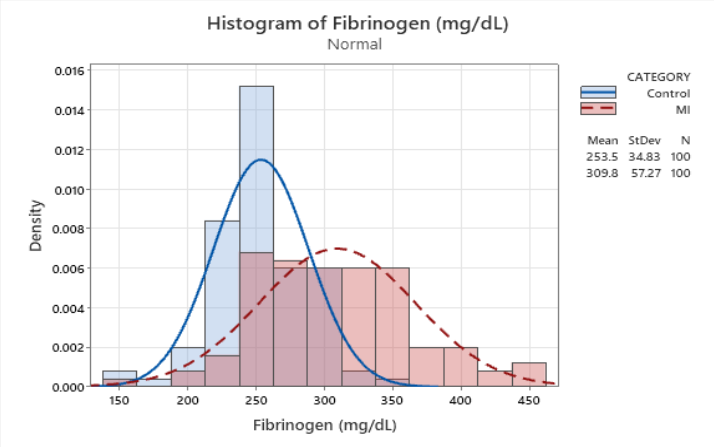

Figure 1: Comparison of Fibrinogen (mg/dL) between the test and control Population.

The present study shows a significant difference (t=-8.39, p<0.001) in the Fibrinogen (mg/dL) level between the tests (309.8 ± 57.3) and control (253.5 ± 34.8) population. An elevated fibrinogen level in the plasma has been linked to increased cardiovascular risk since it supposedly represents an inflammatory state in the arterial wall. Different studies by Danesh et al. [10], Tracy et al. [11], and Yano et al. [12], were also reporting the same.

High-sensitive C-reactive protein

C-reactive protein (CRP) is a molecule that belongs to the pentraxin superfamily. The liver is responsible for most of its synthesis as an acute phase reactant. Following acute infection, inflammation, or trauma, serum CRP levels rise [13]. These clinical conditions are characterized by a rapid increase in serum CRP levels, often over ten mg/l, and an accompanying rise in erythrocyte sedimentation rates.

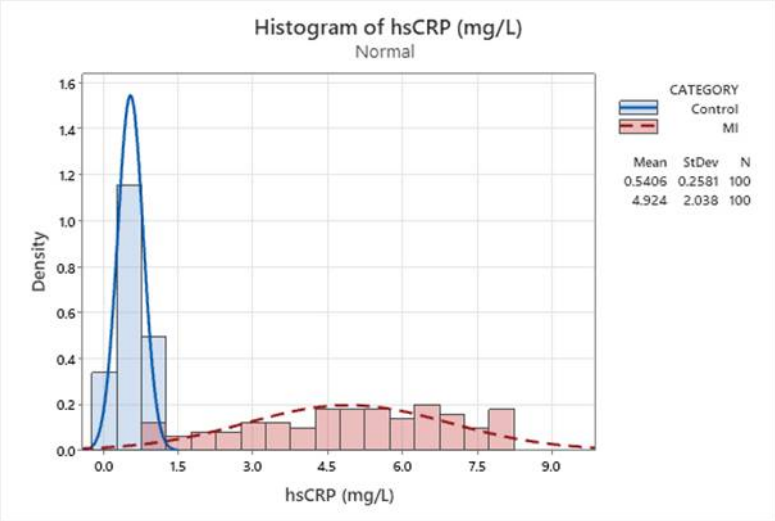

Figure 2: Comparison of hs-CRP (mg/L) between the test and control Population.

The present study shows a significant increase (t=-21.34, p<0.001) in the level of hs-CRP (mg/L) in the test population (4.92 ± 2.04) when compared to the control population (0.541 ± 0.258). This was in accidence with previous studies conducted by Rajeshwar et al. [14], who report hs-CRP levels may help to predict ischemic stroke, Goswami et al. [15], and Guruprasad et al. [16] report hs-CRP is an independent predictor of CAD. Rao et al. [17] performed prospective cohort research and found that high-sensitivity C-reactive protein (hs-CRP) significantly predicted future coronary events. So far, the hs-CRP has undergone more research than any other biomarker in the search for a perfect biomarker for worldwide CVD risk prediction. Obesity, type 2 diabetes mellitus, metabolic syndrome, increased carotid intima-media thickness, stable coronary artery disease, first acute coronary event, and recurrent cardiovascular disease events were all shown to be independently predicted by hs-CRP [18].

Serum amyloid A (SAA)

Emerging indicators of inflammation include the serum amyloid A proteins, which belong to the family of apolipoproteins typically seen in HDL. Coronary artery disease (CAD) has higher SAA levels, and these levels predict a worse prognosis for CAD.

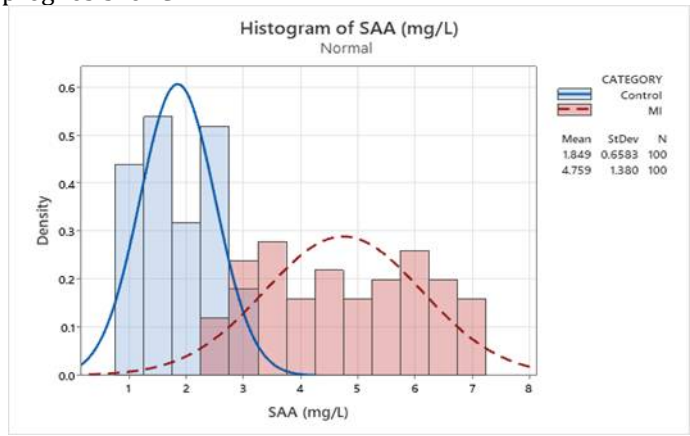

Figure 3: Comparison of SAA (mg/L) between the test and control Population.

The present study shows a significant difference (t=-19.04, p<0.001.) between the SAA (mg/L) level of tests (4.76 ± 1.38) and the control population (1.849 ± 0.658). According to Kosuge et al. [19] research elevated SAA levels were connected to cardiovascular events but unrelated to CRP concentrations. Thus, these findings suggested that SAA was a more accurate predictor of these patients' outcomes than CRP. In addition, SAA levels were significantly correlated with coronary artery disease and the likelihood of experiencing a cardiovascular event. There is a mountain of epidemiological evidence connecting SAA to CVD, and more SAA is related to death from CVD [20].

Ox LDL

Atherosclerosis is initiated and progresses in large part due to oxidative stress. Oxidized low-density lipoprotein (ox-LDL) is an indicator of oxidative stress. It is still debatable whether or not systemically detected oxLDL is associated with coronary heart disease, despite its participation in all phases of

atherosclerosis, from the formation of fatty streaks to the onset of plaque instability and rupture. Foam cell production is thought to be induced by ox-LDL, a preliminary but essential stage in the progression of atherosclerosis [21]. Additionally, oxLDL inhibits NOS expression, promotes the production of metalloproteinases, and causes apoptosis in human coronary endothelial cells [21].

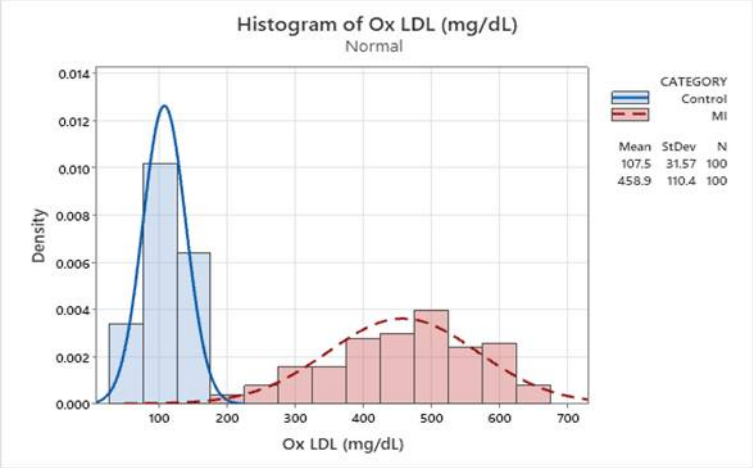

Figure 4: Comparison of Ox LDL (mg/dL) between the test and control Population.

The current study shows a significant (t=-30.61, p<0.001) increase in the mean of Ox LDL (mg/dL) of the tests (459 ± 110) than the control (107.5 ± 31.6). Several studies have shown compelling evidence [22] that acute coronary syndrome (ACS) is caused by the activation of an inflammatory process driven by the immune system and linked with atherothrombosis. Since oxidized LDL has been discovered in individuals with coronary heart disease plasma, it may play a crucial role in forming inflammatory processes in all stages of atherosclerotic lesions. It has also been shown that ox-LDL is implicated in the earliest and most essential functions of atherogenesis, including endothelial damage, production of adhesion molecules, leukocyte recruitment and retention, foam cells, and thrombus development [22].

D Dimer

D-dimer is a marker for hypercoagulability and thrombotic events formed from the cleavage of cross-linked, insoluble fibrin molecules. In individuals with vascular disease, somewhat increased levels of D-dimer are related to the risk of venous and arterial events. D-dimer concentrations within the normal range vary considerably from person to person among healthy persons.

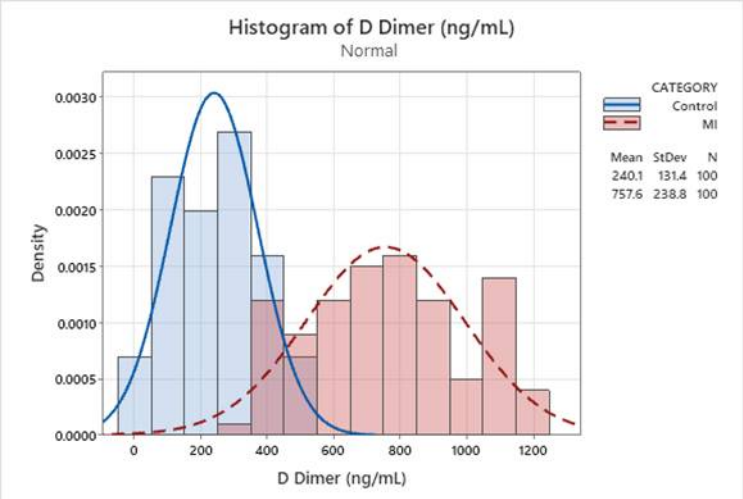

Figure 5: Comparison of D Dimer (ng/mL) between the test and control Population.

The present study reports a significant difference (t=-18.99, p<0.001) between the D Dimer (ng/mL) of the tests (758 ± 239) and the control (240 ± 131) population. D-dimer levels are elevated in diseases that stimulate the coagulation system, such as acute venous thromboembolism, ischemic cardiovascular disease, and cancer. An independent 1.7-fold more significant risk of coronary heart disease has been revealed by a meta-analysis [23] for those with the highest vs. the lowest third of D-dimer levels. D-dimer may signify the total procoagulant balance or hereditary variables, the amount of subclinical atherosclerosis, or the existence of underlying coagulation disorders predisposing to coronary

thrombosis in this setting. Moderately raised D-dimer levels suggest small increases in blood coagulation, thrombin production, and intravascular fibrin turnover, which may be necessary for coronary heart disease. D-dimer has been identified as one of the most significant indicators for predicting CVD events above conventional markers [24].

CONCLUSION

Inflammatory processes are now recognized as playing a central role in the pathogenesis of atherosclerosis and its complications. Although the part of the immune system and inflammatory pathways in the development of CVD is well established, inflammation has only recently been recognized as playing a central role in the pathogenesis of atherosclerosis and its complications. Plasma concentrations of several inflammatory indicators have been reported to correlate with future cardiovascular risk in various cardiovascular conditions. These indicators include hs-CRP, Fibrinogen, D Dimer, and serum amyloid A protein. In conclusion, our data imply that changes in the levels of newer inflammatory indicators, such as hs-CRP, Fibrinogen, D-Dimer, and serum amyloid A protein, are related to an elevated risk of coronary heart disease and may be regarded as a relevant marker of this risk.

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