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An Association of Lipid Abnormalities with High-Sensitivity C – reactive Protein (hsCRP) in Patients with Dyslipidemia: A Teaching Hospital Based Study

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Abstract

Background: High sensitive C-reactive protein (hs-CRP) is an acute phase protein whose levels are shown to be elevated in inflammation. Dyslipidemia & local inflammation are the two major determinants of cardiovascular disease (CVD). Atherosclerosis leads to inflammation which is triggered by dyslipidemia. **Subjects and Methods:** This present study we tried to find out the correlation between lipid abnormalities & hs-CRP. Sixty five subjects were selected purposively from the out-patient department of HIMS, Varanasi according to inclusion-exclusion criteria. **Results:** This study showed the strong and statistically significant positive correlation in between High-Sensitive C–reactive Protein (hsCRP) and Total Cholesterol with ($p<0.012$). Statistically significant positive correlation between High-Sensitive C–reactive Protein and Triglycerides ($p<0.01$). LDL-C also showed a statistically significant positive correlation with High-Sensitive C–reactive Protein ($p<0.02$). A statistically non-significant and weak negative correlation is seen between the serum hsCRP levels and HDL-C ($p=0.38$, $r= -0.14$). **Conclusion:** Patients with dyslipidemia for elevated blood hs-CRP levels may be done to identify those patients with an increased risk for future development of atherosclerosis as well as bad cardiovascular events at earlier stages so that they can changes their life style, food habit etc. to resist the further aggravation of dyslipidemic status as well as catastrophic cardiovascular events.

Keywords: Dyslipidemia, lipid abnormalities, hs-CRP.

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Introduction

Dyslipidemia & local inflammation are the two major determinants of cardiovascular disease (CVD). Atherosclerosis leads to inflammation which is triggered by dyslipidemia. The number of cases of cardiovascular diseases (CVDs), the leading causes of death at any age group in the world is rising rapidly now-a-days.[1] Lipid metabolism Disorder is one of the main determinants of cardiovascular risk. It is widely accepted that increased levels of low-density lipoprotein cholesterol, triglycerides, total cholesterol and decreased levels of high density lipoprotein cholesterol are associated with atherosclerosis. The primary target of lipid management is to achieve lowering of low -density lipoprotein cholesterol.[2] Beside lipid parameters, high sensitive C-reactive protein (hs-CRP), an inflammatory cytokine is an excellent biomarker for acute-phase response and has proved to be an important and characteristic predictor of future cardiovascular diseases and metabolic abnormalities in overtly seen healthy men and women.[3,4-7] LDL-C is known to activate a cascade of local inflammation which can lead to formation of atherosclerotic plaques, ultimately leading to cardiovascular disease or acute coronary syndrome. Even though both hs-CRP and Lipid Profile parameters have a role in initiation and progression of atherosclerosis, no data is currently available regarding the correlation between them. In this study we have tried to find out a correlation between lipid abnormalities & hs-CRP, which is a very sensitive marker for inflammation.

Subjects and Methods

This present study was carried out in the department of Medicine, Heritage institute of medical sciences, Varanasi, Uttar Pradesh, India in collaboration with the department of Clinical Biochemistry during the period from February 2017 to January 2018. (65) Sixty five subjects were selected purposively from the out-patient department of HIMS, Varanasi according to inclusion-exclusion criteria. Blood samples were obtained from the antecubital vein with the

subject sitting comfortably in a chair in a quiet room and transfused into vacuum tubes containing EDTA in the morning after an overnight fasting period. After separation, blood samples were centrifuged for 10 minutes at 3000 rpm to obtain serum. Then serum was aliquoted into two microtubes, one preserved for lipid profile measurements and another was preserved at -20oC for hsCRP estimation. Following biochemical parameters to be studied.8

1. Total Cholesterol 2. Triglyceride 3. HDL-Cholesterol 4. LDL-Cholesterol by Friedewald's formula. LDL-c = Tc-HDL-c(TG/5) and 5. hs-CRP levels were analyzed by sandwich ELISA technique using hsCRP kit.

We used student t-test and pearson's correlation coefficient to find the statistical significance. A P-value <0.05 was to be considered statistically significant.

Results & Discussion

This study showed the strong and statistically significant positive correlation in between High-Sensitive C–reactive Protein (hsCRP) and Total Cholesterol with ($p<0.012$). Statistically significant positive correlation between High-Sensitive C–reactive Protein and Triglycerides ($p<0.01$). LDL-C also showed a statistically significant positive correlation with High-Sensitive C–reactive Protein ($p<0.02$). A statistically non-significant and weak negative correlation is seen between the serum hsCRP levels and HDL-C ($p=0.38$, $r= -0.14$).

Table 1: Correlation between lipid abnormalities with hs-CRP with the in dyslipidemic patients

Parameters	Correlation coefficient (r)	p-value
Total Cholesterol	0.34	0.012
Triglycerides	0.44	0.01
Low density lipoprotein-C	0.28	0.02
High density lipoprotein -C	-0.14	0.38*

*Statistically significant ($p<0.05$); r=Correlation coefficient

These findings support the hypothesis that dyslipidemia can induce an inflammatory reaction at blood vessels which is a hall mark feature for development of atherosclerosis. Lowgrade inflammation is a novel risk factor in all stages of atherosclerosis and acute coronary syndrome. CRP is an acute phase protein which is generated shortly after an inflammatory stimulus from the liver cells. Several cytokines like IL-1, IL-6 and TNF-α that are secreted locally in the area of the damaged tissue regulate the production of CRP.9 Cardiovascular diseases, metabolic syndrome, Type-2 diabetes mellitus and obesity are associated with low grade of systemic inflammation and in these conditions, as inflammation is subclinical or low grade, hence CRP level does not increase at a greater amount as seen in severe systemic infections rather its increment is small so that highly sensitive method is needed to estimate that small amount of CRP in blood, there for hs-CRP estimation have been emerged in the field of medical sciences. This in part suggests that the associations of CRP concentrations with fasting insulin, fasting glucose, and HOMA-IR could be due to the presence of a chronic systemic sub-clinical inflammation. Disease like Dilated cardiomyopathy (DCM) is associated with increased inflammatory response reflected among other markers in high sensitivity C-reactive protein (hsCRP) and soluble interleukin-2 receptor (sIL-2R) levels. There was a significant correlation between sIL-2R and hsCRP levels in dyslipidemic patients but not in normo-lipidemic patients Therefore estimation of IL-1, IL-6 and TNF-α along with HOMA-IR and sIL-2R was also essential for identification of other cardiovascular disease in immune-mediated inflammatory diseases. Above findings support the hypothesis that dyslipidemia can induce an inflammatory reaction at blood vessels which is a hall mark feature for development of atherosclerosis. Low grade inflammation is a novel risk factor in all stages of atherosclerosis and acute coronary syndrome. This present study has shown levels of LDL-C, triglycerides and total cholesterol are associated with development and progression of atherosclerosis.10 The transport vehicle of cholesterol and other lipids in body is low density lipoprotein cholesterol (LDL-C). Once oxidized, LDL-C is called small dense LDL which can trigger a low grade local inflammation leading to cytokine release. Phagocytosis of oxidized LDL by monocytes transforms them into foam cells with a lipid core which is the beginning of atherosclerotic plaque formation. Moreover, the storage site of triglycerides is mainly adipose tissue which was earlier considered to be a passive organ is now known to express the pro-inflammatory cytokines like IL-6. Excess loading of triglycerides in adipose tissue as seen in obesity can cause release of IL-6 by adipose tissue which can be involved in induction of low grade systemic inflammation as well as inflammation at blood vessels.11 High serum level of high density lipoprotein cholesterol (HDL-C) on the other hand is associated with reduced risk for development of atherosclerotic disease as it is involved in reverse cholesterol transport. HDL-C particle are therefore believed to be anti-atherogenic and antagonized pathways of inflammation, thrombosis and oxidation of LDL-C. Serum amyloid A (SAA) is transported predominantly on HDL and levels of this protein increase markedly during acute and chronic inflammation in both animals and humans. Increased SAA levels predict the risk of cardiovascular disease in humans. There are evidences, showing that secretory phospholipase A2, an HDL-associated protein, and platelet-activating factor acetylhydrolase, a protein associated predominantly with LDL in humans and HDL in mice, might also play roles both as markers and mediators of human atherosclerosis. In contrast to positive acute-phase proteins, negative acute-phase proteins have received less attention. The level of Apo lipoprotein A-I (apoA-I), the major apolipoprotein of HDL, decreases during inflammation. Recent studies also indicate that HDL is oxidized by myeloperoxidase in patients with established atherosclerosis. T hese alterations

may limit the ability of apoA-I to participate in reverse cholesterol transport. Paraoxonase-1 (PON1), another HDL-associated protein, also decreases during inflammation. PON1 is atheroprotective in animal models of hypercholesterolemia. Controversy over its utility as a marker of human atherosclerosis may reflect the fact that enzyme activity rather than blood level (or genotype) is the major determinant of cardiovascular risk. Thus, multiple lipoprotein-associated proteins that change in concentration during acute and chronic inflammation may serve as markers of cardiovascular disease. High serum level of high density lipoprotein (HDL) on the other hand is associated with reduced risk for development of atherosclerotic disease. HDL particle are believed to be anti atherogenic and antagonized pathways of inflammation, thrombosis and oxidation.12 The data obtained from the study therefore supports the theory higher and HDL-C was lower in individuals with higher hs-CRP level suggesting a low grade systemic inflammation. These results indicate that there may be a role for hs-CRP in screening and risk stratification of atherosclerosis.

Conclusion

In conclusion, the patients with dyslipidemia for elevated blood hs-CRP levels may be done to identify those patients with an increased risk for future development of atherosclerosis as well as bad cardiovascular events at earlier stages so that they can changes their life style, food habit etc. to resist the further aggravation of dyslipidemic status as well as catastrophic cardiovascular events.

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