Original Article

Association of Lipid Profile Parameters with High-Sensitive C–reactive Protein (hsCRP) in Patients with Dyslipidemia

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Abstract

Dyslipidemia & local inflammation are the two major determinants of cardiovascular disease (CVD). Atherosclerosis leads to inflammation which is triggered by dyslipidemia. In this study we have tried to find out a correlation between lipid profile parameters & hsCRP, which is a very sensitive marker for inflammation. In this study hsCRP and the Lipid profile parameters were estimated in fifty two patients who visited the medicine OPD of College of Medicine & JNM Hospital, Kalyani. The results obtained indicate a strong significant positive correlation of total cholesterol (p value <0.001) and triglycerides (p value=0.032) with hsCRP and a negative correlation of HDL (p value=0.36) with the same. These results indicate that there may be a role for hsCRP in screening and risk stratification of atherosclerosis.

Keywords: Dyslipidemia; Subclinical inflammation; High-density lipoprotein cholesterol; High sensitive C-reactive protein; Lipid profile; Atherosclerosis

Introduction

The number of cases of cardiovascular diseases (CVDs), the leading causes of death at any age group intheworld is rising rapidly now-a-days.[1] Disorder in lipid metabolism is one of the main determinants of cardiovascular risk. It is widely accepted that increased levels of low-density lipoprotein cholesterol (LDL-C), triglycerides (TGs), total cholesterol (TC) and decreased levels of high density lipoprotein cholesterol (HDL-C) are associated with atherosclerosis. The primary target of lipid management is to achieve lowering of low -density lipoprotein cholesterol (LDL-C).[2] Beside lipid parameters, high sensitive C-reactive protein (hsCRP) – 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.[3-7] 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 (ACS). Even though both hsCRP and Lipid Profile parameters have a role in initiation and progression of atherosclerosis, no data is currently available regarding the correlation between them. Therefore the present study is conducted to find out the correlation between hsCRP levels with the lipid profile parameters.

Methodology

This is a Hospital based cross sectional descriptive epidemiological type of study that was conducted at medicine OPD of COMJNMH in collaboration with the department of Biochemistry, COMJNMH. The study included total 52 cases among which 30 were males and 22 were females. A Pilot study was conducted before starting the current study. Sample size calculation was done according to standard methods available. Statistical analysis was done using SPSS17 software.

Inclusion criteria

Newly diagnosed Patients with dyslipidemia, not taking any medications (neither hypolipidemic drugs nor any other drugs like thiazide diuretics, glucocorticoids etc. that can alter the lipid profile) were included in the study.

Exclusion criteria

Patients with infection, stroke, myocardial infarction, major surgery, mal-absorption, severe allergy, cancer, severe illness, liver dysfunction, chronic kidney disease (CKD), pregnancy, edema, oral contraceptive users and steroid or Non-steroidal anti-inflammatory drugs (NSAID) users were excluded from the study.

Parameters to be measured

- Total Cholesterol by CHOD/PAP method (ERBA system pack of TRANSASIA Biomedical).
- Triglycerides by GPO/PAP method (ERBA system pack of TRANSASIA Bio-medical).
- Direct HDL-cholesterol estimation by PEG Precipitation method (ERBA system pack of TRANSASIA Bio-medical).

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Table 1: Correlation of hsCRP with the lipid profile parameters.

Parameters	r -value	p-value
Triglyceride	0.22	0.032*
Total Cholesterol	0.48	<0.001*
HDL-C	-0.12	0.36
LDL-C	0.27	0.02*

*Statistically significant (p-value <0.05), r=Correlation coefficient

- LDL-cholesterol (Calculated by Fried Wald's formula).
- hsCRP by sandwich ELISA technique using hsCRP kit.

Results

Total 52 dyslipidemic subjects were included in this study to find out the correlation between lipid profile parameters & hsCRP. All the patients were newly diagnosed, prior to treatment [Table 1].

Discussion

This study showed a strong and significant positive correlation between the serum hsCRP Levels with the total serum cholesterol ($p<0.001$, $r=0.48$) and significant positive correlation of triglycerides with hsCRP ($p=0.032$, $r=0.22$). A statistically non-significant and weak negative correlation is seen between the serum hsCRP levels and HDL-C ($p=0.36$, $r= -0.12$). On the other hand, LDL-C showed a statistically significant positive correlation with serum hsCRP level ($p=0.02$, $r=0.27$).

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. Low-grade 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. [8] 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 hsCRP 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. Due to inadequacy of funds the authors were not able to estimate the above mentioned parameters.

Studies have shown levels of LDL-C, triglycerides and total cholesterol are associated with development and progression of atherosclerosis. [9] 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. [10] 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. [11] 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. These 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.

In rodent models of glucose metabolism, the *in vivo* infusion of human recombinant IL-6 has been shown to induce gluconeogenesis, subsequent hyperglycemia, and compensatory hyperinsulinemia. Similar metabolic responses have been observed in humans after administration of subcutaneous recombinant IL-6. The possible explanation is altered endothelial permeability and diminished peripheral blood flow which may limit insulin delivery and promote insulin resistance in metabolically active tissues. [12] Other potential mediators of insulin resistance deriving from adipose stores include tumor necrosis factor α, leptin, free fatty acids, and resist in. [13-18]

The data obtained from the study therefore supports the theory

that serum LDL-C, total cholesterol and triglycerides were higher and HDL-C was lower in individuals with higher hsCRP level suggesting a low grade systemic inflammation. These results indicate that there may be a role for hsCRP in screening and risk stratification of atherosclerosis.

As a categorical variable, hsCRP has potential as a marker of future cardiovascular disease risk. However, the influence of age and gender should be taken into account in its application to the prediction of cardiovascular disease risk.

Conclusion

Thus screening of patients with dyslipidemia for elevated blood hsCRP 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.

Limitations

Due to scarcity of funding it was not possible for the authors to estimate IL-1, IL-6, TNF-α, HOMA-IR and sIL-2R which would have made the study more relevant and conclusive

Conflict of Interest

All authors disclose that there was no conflict of interest.

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