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Research Article

SERUM HIGH SENSITIVITY C-REACTIVE PROTEIN IN PATIENTS OF CORONARY ARTERY DISEASE (CAD) WITH TYPE 2 DIABETES MELLITUS

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ABSTRACT
Coronary Artery Disease (CAD) appears to be common in the Indian population of different geographical origins, religions and languages. Type 2 diabetes mellitus is a strong risk factor for coronary heart disease (CHD). Measurement of lipid fractions and ratios are widely recommended for risk assessment. High sensitivity C-Reactive protein is an established prognostic marker of cardiovascular disease risk (CVD) in diabetic subjects. The objectives was to find the significance of non-HDL cholesterol, LDL-c/HDL-c ratio and serum hs-CRP level in CAD patients. In this study, we included fifty CAD patients as subjects and an equal number of controls. Both subjects and controls were assessed for anthropometric, physiological and biochemical parameters. The present study showed significant increased levels of total cholesterol, TAGs, HDL, LDL and non-HDL cholesterol. LDL-c/HDL-c ratio in CAD patients (subjects) was also significant when compared to controls. Hs-CRP levels in CAD patients were increased. Serum hs-CRP, TC/HDL and LDL/HDL ratios could be regarded as objective markers, in association with existing atherogenic dyslipidemia in patients with CAD.

***Keywords*:** *Coronary Artery Disease, Serum hs-CRP, Type 2 Diabetes Mellitus, Lipid Fractions and Ratios*

INTRODUCTION
Dambal1 *et al.,* (2013), Vepsalainen *et al.,* (2011) reported that the inflammation plays a major role in the pathogenesis of artherosclerosis. The predictors of atherosclerotic disease are cytokines and acute-phase proteins (CRP, ceruloplasmin, Alpha-1 antitrypsin, alpha-2 macroglobulin).Vasudevan *et al.,* (2014) on the above mentioned acute phase protein high sensitive C-reactive protein (hs-CRP) is also called ultra sensitive CRP. Hs-CRP is synthesized in liver in response to cytokine production (IL-6, IL-1) during tissue injury, inflammations. Evidence shows that it is a best marker for risk of atherosclerosis and cardiovascular disease (CVD) especially coronary artery disease (CAD) and it is used as a predictor of future myocardial infarction. Damball *et al.,* (2013) Strong risk factor of coronary heart disease is type 2 diabetes mellitus, which in turn it is the leading cause of death worldwide. Vasudevan *et al.,* (2014) 80% of the total diabetic mortality is due to the cardiovascular disease. Evaluation of hs-CRP gives more information about patients who are at risk and may need medical treatment. Nearly half of the heart attacks happen in patients who do not have high levels of cholesterol in their blood. Luigi *et al.,* (2009) CVD is not only due to lipid factors, but also due to inflammations. The aim of the present study is to determine hs-CRP in diabetic CAD patients and normal subjects.

MATERIALS AND METHODS
Data was collected from fifty CAD patients as subjects and an equal number of controls based on the inclusion and exclusion criteria. The study was conducted at Sri Lakshmi Narayana Institute of Medical Sciences (SLIMS), a tertiary healthcare institution in Puducherry, after obtaining clearance from institutional human ethics committee.
Informed consent from the subjects was obtained. 100 subjects were patients suffering from CAD with the history of type 2 diabetes mellitus from past 2 years (Group A) and 100 were normal subjects (Group B). Patients with history of endocrinological disorders ischemic heart disease, smokers, patients with acute infections who were likely to have acute phase response and patients on drugs 00like hypolipidemics were excluded from the study. A standard questionnaire was designed to record

demographic data and personal habits including age, sex, other co morbid conditions, duration of T2DM, history of medication and any complication. Systolic and diastolic blood pressure was recorded from all the study subjects.

For anthropometric measurements we recorded weight (kilograms), height (cms), waist circumference (cms). Then we calculated body mass index (BMI), as weight (kilograms/Height^2) as a measure of obesity. After overnight fast 5ml of venous blood samples were calculated for various biochemical assays. Serum were separated and assayed for estimation of serum cholesterol (TC), triglycerides (TG), HDL, LDL levels and hs-CRP were analysed by auto-analyser and IFCC approved methods.

Statistical Analysis

To compare the means of subjects and controls unpaired Student't test was used by using SPSS 20 version software.

RESULTS

The mean and standard deviation of anthropometric and physiological measures of controls and subjects are depicted in Table 1.

Table 1: Anthropometric and physiological measures of controls and subjects (CAD)

Parameter	Controls (Mean ± SD)	Subjects (Mean ± SD)
W.C (cm)	39.68 ± 4.31	42.62 ± 7.71*
SBP (mmHg)	131.5 ± 19.55	140.3 ± 17.9***
DBP (mmHg)	73.96 ± 9.56	91.56 ± 13.3*

Data expressed as mean ± SD. (Significant, highly significant***) W.C, Waist Circumference; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure.*

Fasting Lipid Profile Levels in Controls and CAD Patients

Table 2 shows the comparison of mean, standard deviation of fasting lipid profile between controls and subjects. This study showed the significance of total cholesterol, low density lipoprotein (LDL), high density lipoprotein (HDL) and triacylglycerol (TAGs).

Calculated Parameters of Lipid Profile Levels in Controls and CAD Patients

The results in Table 2 show mean and standard deviation of Non-HDL Cholesterol, LDL/HDL ratio and TC/HDL ratio between controls and subjects. From the study, it's clear that LDL/HDL ratio, TC/HDL ratio and Non-HDL Cholesterol have significant difference between Subjects
(CAD patients) and Controls group.

Table 2: Biochemical parameters in controls and study subjects (CAD)

Parameter	Controls (Mean ± SD)	Subjects (Mean ± SD)
Total cholesterol (mg/dl)	155.48 ± 24.68	181.68 ± 52.43*
TAGs (mg/dl)	100.48 ± 27.04	130.34 ± 44.93***
HDL (mg/dl)	41.91 ± 6.92	38.02 ± 6.65*
LDL (mg/dl)	104.72 ± 24.72	122.10 ± 35.66**
Non-HDL (mg/dl)	113.57 ± 22.54	139.66 ± 51.25***
LDL/HDL	2.60 ± 1.02	2.89 ± 0.99**
Hs-CRP	0.74±0.45	3.56±1.2***

Data expressed as mean ± SD. (Significant, highly significant***) T.C, Total Cholesterol; TAGs, Triacylglycerols; HDL, High Density; Lipoprotein; LDL, Low Density Lipoprotein*

Fasting Serum hs-CRP Level in Controls and CAD Patients

Table 2 depicts the mean and standard deviation of serum hs-CRP levels (fasting) between controls and subjects. The study depicted a significant difference in serum hs-CRP levels among CAD patients and controls.

DISCUSSION

American heart association and the centers of disease control and prevention (CD) have made several recommendations for the use of hs-CRP in cardiovascular risk assessment. Defined risk groups of hs-CRP are as follows levels <1.0mg/L are low risk, levels of 1.0 to 3.0 mg/L are average risk, >3.0 mg/L are high risk Shishehbor *et al.,* (2003). We found that hs-CRP concentrations are higher in type 2 diabetic CAD patients (3.56±1.2) when compared to normal subjects (0.74±0.45). Mirza *et al.,* (2013) study also reported that hsCRP values are significantly higher in diabetics with complications (3.55±0.86mg/L). Several other studies also reported that serum hs-CRP values significantly high in patients with type 2 diabetes mellitus. Mohan *et al.,* (2005) study shows that the 150 subjects selected from population of Chennai urban rural epidemiology study (CURES), have similar findings that the CAD diabetic patient had higher hs-CRP levels when compared to diabetic subjects without CAD and control subjects. Minna *et al.,* (2006) 7-year follow up period on 45 to 65 years aged diabetes patients resulted that the mean hs-CRP levels were significantly higher in men who died of CHD.

We have evaluated lipid parameters along with hs-CRP on both type 2 diabetic CAD and normal subjects, we found that Total cholesterol(TC), Triacylglycerol (TAG), low density lipoprotein (LDL) were significantly high in diabetic CAD patients. High density lipoprotein (HDL) was significantly low in diabetic CAD patients mean value (38.02 ± 6.65) when compared to normal subjects mean value is (41.91 ± 6.92). Misra *et al.,* (2004) studies have been reported that HDL-C levels are decreased in patients with CAD. Cuchel (2006) Evidence presented that HDL-C is inversely related to total body cholesterol.

Other calculated parameters are non-HDL-c, LDL/HDL ratio also shows significantly high in study subjects when compared to healthy volunteers. Hence, recently lipid ratios, such as TC/HDL-C, LDL-C/HDL-C and TAG/HDL-C have gained attention. Lloyd-Jones (2010) Changes in these ratios have been shown to be better indicators of successful CAD risk reduction than changes in absolute levels of lipids or lipoproteins. In Rana *et al.,* (2012), Libby (2005), Manninen *et al.,* (1992) the LDL-C/HDL-C and TC/HDL-C ratios help initiating lipid-lowering therapy. The current *NCEP guidelines* recommend levels of LDL-C and HDL-C that represent a ratio of about 2.5. This study reports that LDL-C/HDL-C and TC/HDLC ratios in CAD patients were significantly high compared to controls (Table 2). LDL-C/HDL-C ratio could be a useful tool to assess the risk of complications in CAD and also to monitor the patients who are on treatment. In the present study, there was an increased LDL-C level. Real *et al.,* (2001) study showed that LDL-C/HDL-C ratio and TC/HDL-C ratio also correlate with cardiovascular disease. Participants in our study had increased levels of Non–HDL-C in CAD (Table 2) similarly; Rana *et al.* (2011) have reported an increased level of non-HDL-C that was an independent risk in patients with CAD.

In the present study, an effort was made to study the lipid fractions, *viz* serum total cholesterol, triacylglycerols, LDL, HDL, LDL/HDL ratio, Non-HDL-C and serum hs-CRP levels in subjects having CAD. The results were compared with control samples. Since elevated levels of hs-CRP and lipid fractions in CAD patients proved that it is an independent predictor of CAD patient. Hs-CRP is highly significant in CAD patients when compared to the normal subjects.

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