Risk of Ischemic Heart Disease due to Hyperglycemia: A Independent Marker CRP

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Abstract
Background: One of the major complication of diabetes mellitus (DM) is cardiovascular disease, which is the main cause of death in patients of north Indians. Hyperglycemia leads to the risk of inflammation as well as vascular damage through various mechanisms. This study was being conducted to evaluate the role C-Reactive Protein (CRP) as as inflammatory marker in type 2 DM with IHD and type 2 DM without IHD patients.

Methodology: A comparative study was conducted. The present study were assessed the fasting blood glucose and C-reactive protein levels in two groups. Group A comprised of 50 diabetic patients with Ischemic heart disease (IHD) , Group B consist of 50 diabetic patient without IHD. All the patients were selected from Govt. Medical College, Amritsar.

Result: The mean of CRP and Fasting blood glucose (FBS) were significantly (P<0.05) high in type 2 diabetic patient with IHD as compared to type 2 diabetic patient without IHD .

Conclusion: It is concluded that there is significance association between the level of serum CRP and FBS. Moreover, positive correlation between CRP and FBS has been shown that inflammatory marker is the main indicator of insulin resistance which is observed in type 2 DM without IHD patients and with IHD patients. CRP can be used as a marker for diagnosis of early stages of the risk of IHD in type2 diabetic patients.

Keywords: C-Reactive Protein, Diabetes Mellitus, Ischemic heart disease, Fasting blood sugar.

Introduction
Diabetes Mellitus is not a single disease entity, but rather a group of metabolic disorders sharing common features of hyperglycemia. Hyperglycemia in diabetes results from defects in insulin secretion, insulin action or most commonly both. The chronic hyperglycemia and metabolic disregulation may be associated with secondary damage in multiple organ systems, especially the kidneys, eyes, nerves and blood vessels. Diabetes mellitus is one the strongest risk factors for cardiovascular disease and, in particular, for ischemic heart disease (IHD)1. CVD is the most prevalent cause of mortality and morbidity in...
diabetic populations\(^2\). C-Reactive Protein (CRP) concentration is a significant predictor of diabetes in middle-aged people independent of classic and clinically employed risk factors such as BMI, fasting triglycerides and glucose\(^3\). Oxidative stress might be implicated in promoting a state of low-grade inflammation indicated by marker such as CRP with elderly type 2 diabetes\(^4\). A recent study that investigated the association between CRP and metabolic syndrome pointed to the direct harmful effect of CRP on vessel walls which may alter endothelial permeability and eventually lead to insulin resistance\(^5\). CVD death rates in the United States are 1.7 times higher among adults (> 18 years) with DM than those without diagnosed DM, largely due to an increased risk of stroke and myocardial infarction (MI)\(^6\). Thus, the risk of cardiovascular disease in diabetics can be reduced by improving the glycemic control.

In our study, it is observed by the fact that low-grade inflammation by CRP, to be an independent and strong early indicator of IHD in patients of type 2 diabetes.

**Methodology**

The present study was undertaken in the Department of Biochemistry, Govt. Medical College, Amritsar. A comparative study was performed among the O.P.D. and indoor patients of medicine department, Guru Nanak Dev Hospital, Amritsar. We divide patients into two groups. 50 diabetic patients in the age group 30 to 70 years, diagnosed on the basis of history and clinical symptoms were selected for the study. The patients suffering from Ischemic Heart disease, liver disease, tuberculosis, cancer, rheumatoid arthritis, collagen disorders, gout, thyroid disorders were excluded from the study (Group B). Compared with another 50 diabetic patients with Ischemic Heart Disease with age and sex matched individual from the same population (Group A).

5ml of venous blood was taken with a dry disposable syringe under aseptic conditions by vein puncture in antecubital vein in a disposable vial for biochemical analysis of FBS, TC, TG, LDL, VLDL, HDL and CRP. FBS and Lipid profile were estimated by enzymatic method on semiautoanalyser. Serum C-Reactive Protein was estimated by Latex method. Analysis of data was done on spss version 15. Data was expressed as mean SD. Student’s t was applied to compare variables between groups. The Pearson correlation coefficient values was used to detect the association amongst different variables.

**Result**

To evaluate relationship between serum level of CRP and Fasting blood sugar in type 2 diabetic patients with IHD (group A), DM without IHD, 50 patients in both groups were selected.

1) Biochemical analysis of all these parameters have shown significantly high in both groups, depicted in Table 1

2) The Fasting blood glucose levels of patients in group B in northern Indian population was found to be with mean ± S.D of 144.02 ± 49.2mg/dl as compared to 171±69.4mg/dl in group A

3) The Serum C-Reactive Protein levels of patients in group B in northern Indian population was found to be with mean ± S.D of 6.44±1.51mg/l as compared to 37.4±53.7 mg/l in group A.

4) Table 2 shows the comparison of CRP and FBS levels in different age group of group A and Group B

5) Comparison of Fasting blood glucose and Serum C-Reactive Protein levels according to fasting blood glucose levels in patients of diabetes mellitus type-2 without IHD of northern Indian population showed a highly significant increase. Thus, this depicts that serum C-Reactive Protein and Fasting Blood Glucose have a positive correlation with each other. As shown in Table No. 3
### Table 1: Demographic biochemical parameters of Group A and Group B

| Parameter    | Groups | P-value |
|--------------|--------|---------|
|              | A      | B      |
|              | Mean ±SD | Mean ±SD |       |
| FBS (mg/dl)  | 171.9±69.4 | 144.0±49.2 | P <0.02 |
| CRP (mg/l)   | 37.4±53.7  | 10.8±6.35 | P<0.01  |
| TC (mg/dl)   | 213.3±40.6 | 168.4±32.3 | P<0.01  |
| TG (mg/dl)   | 204.3±69.2 | 171.1±53.5 | P<0.02  |
| LDL (mg/dl)  | 136.3±33.3 | 101.8±28.6 | P<0.05* |
| HDL (mg/dl)  | 40.2±31.7  | 42.8±32.5 | P<0.02  |
| VLDL (mg/dl) | 40.4±12.5  | 34.2±8.0  | P<0.01* |

HS – highly significant, S – significant

### Table 2: Comparison of CRP and FBS levels in different Age group of Group A and Group B

| Sr.No | Age in yrs. | Group A | | Group B | |
|-------|-------------|---------|-----------|---------|
|       | CRP (Mean±SD) | FBS (Mean±SD) | CRP (Mean±SD) | FBS (Mean±SD) |
| 1     | 62.4±90.5 | 192.6±67.7 | 6.8±0.99 | 120.9±33.7 |
| 2     | 34.4±32.8 | 171.8±44.8 | 10.9±6.56 | 154±34.7 |
| 3     | 32.8±5.8  | 156.8±71.7 | 10.7±5.3  | 147±57.5 |

1-P< 0.05  2-P<0.01  3-P<0.01( in case of FBS)
1-P< 0.05  2-P<0.01  3-P<0.05( in case of CRP)

### Table 3: Comparison of CRP levels in different groups distributed according to FBS in type 2 DM without IHD

| Sr.No | Group | No. of Cases | FBS | CRP | P <value |
|-------|-------|--------------|-----|-----|---------|
|       |       | Range | Mean | Range | Mean | |
| 1     | a     | 34     | <150 | 117.2 | 0.6-1.6 | 0.77 | 0.01 |
| 2     | b     | 10     | 150-200 | 173.4 | 0.8-1.6 | 1.28 | 0.01 |
| 3     | c     | 6      | >200 | 247   | 0.8-3.2 | 2.0  | 0.01 |

### Comparison of FBS and CRP in Group A (Diabetic patients with IHD) and Group B (Diabetic patients without IHD)
**Discussion**

Diabetes mellitus is one of the commonest diseases in the modern era. Diabetes is a long term disease with variable clinical manifestations and progressions. Hyperglycemia in diabetes leads to a number of complications. These are cardiovascular, renal, neurological, ocular and other such as inter current infections. The high mortality rates in Africa due to ischemic heart disease appear to be related to the high prevalence of hypertension, hyperglycemia, and hypercholesterolemia. In Southern Asia, the high mortality rates due to ischemic heart disease appear to be related to the high prevalence of diabetes and hypercholesterolemia. Recently, inflammation and inflammatory cytokines have been postulated to be important additional pathogenetic factors in the development of insulin resistance and type 2 diabetes.

The perception of cardiovascular disease, CRP as an inflammatory marker play a role in the pathogenesis of diabetes, in addition genetic variation in CRP was associated with the level of CRP and the risk of diabetes.

In our study we found that there is positive correlation between FBS and CRP, moreover it is observed that with increasing level of FBS in type 2 diabetic (Group B) patients also have shown the increase level of serum CRP levels in same patient as shown in table no. 3.

Recent cross sectional studies have also demonstrated clear association of serum CRP level with obesity and insulin resistance. These findings suggest that the inflammatory state illustrated by elevated CRP concentration is associated with hyperglycemia and diabetes through obesity or increase insulin resistance. However epidemiological findings concerning this issue are controversial. Several studies have reported a significant positive association between elevation in CRP levels and the future risk of diabetes even after adjustment of BMI.

Thus there is increasing evidence to suggest that insulin resistance is a chronic low grade inflammatory state. The high CRP manifested the characteristic so called metabolic syndrome, which is a tendency towards elevated blood glucose, insulin, BMI, triglycerides and decreased HDL cholesterol levels. The monitoring and evaluation of inflammatory markers alongside the metabolic risk factors will enable better understanding of metabolic disease prevention and progression. In fact, taking into account CRP may represent a important tool to identify people at risk of cardiovascular, especially in type 2 diabetes mellitus patients.
Conclusion
Hence, taken into account of the above facts it can be said that serum C-reactive protein levels were raised in type-2 diabetes mellitus without IHD patients, but were lower than diabetes mellitus type-2 with IHD patients. Thus, CRP is an independent predictor of heart disease in patients of diabetes mellitus type-2. CRP has a positive correlation with Fasting blood glucose levels and increases when the blood glucose levels increases. Thus, in conclusion, our study establishes a correlation of CRP and fasting blood glucose in type-2 diabetics and also used as a diagnostic tool for screening of diabetic patient for the development of IHD, so that it can be prevented earlier.

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