

ASSOCIATION BETWEEN C - REACTIVE PROTEIN AND FASTING BLOOD GLUCOSE IN TYPE 2 DIABETES MELLITUS PATIENTS

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Received : 18/12/2022
Received in revised form : 14/01/2023
Accepted : 27/01/2023

Keywords:

Type 2 diabetes Mellitus, C - reactive protein, Fasting Blood Glucose Atherosclerosis.

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DOI: 10.47009/jamp.2022.5.1.137

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2023; 5 (1); 653-656



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Abstract

Background: Type 2 Diabetes Mellitus (T2DM) is associated with a marked increase in atherosclerotic micro and macrovascular diseases involving cardiac, cerebral and peripheral large vessels. Sub clinical systemic inflammatory marker C-reactive protein (CRP) may positively be associated with atherosclerotic risk of future coronary artery disease, cerebrovascular disease or peripheral arterial disease. This study was conducted to see the association between serum CRP and fasting blood glucose in T2DM patients. This case control study was conducted in the Department of Hospital Lab Services, ELMCH, Era University Lucknow during the period of Sep 2020 to Sep 2021, and total 80 subject were included. In this study the age range from 30 to 60 years of both sexes. Among them 40 were cases of type 2 diabetes mellitus patients having fasting blood glucose level >7.0 mmol/L without micro and macro vascular complication and 40 were age matched healthy control having fasting blood glucose <6.0 mmol/L. Venous blood was collected and fasting blood glucose & serum CRP were estimated by spectrophotometrically. Unpaired 't' test and Pearson Correlation coefficient test were done as the tests of significance. In this study serum CRP level was significantly ($p < 0.05$) higher in T2DM patients as compared to healthy control. Highly significant ($p < 0.001$) positive correlation was found between serum CRP and fasting blood glucose level in T2DM patients. Therefore, it was assumed from this study that chronic high serum CRP level may be an indicator of risk for development of Type 2 Diabetes Mellitus which can further act as a risk factor for atherosclerosis.

INTRODUCTION

Type 2 Diabetes mellitus (T2DM) is a complex condition combination of resistance to the action of insulin in liver and muscle together with impaired pancreatic β -cell function leading to relative insulin deficiency.^[1] Type 2 DM is affecting more than 3% of all adults and more than 10% of older than 65 years, making it 8 to 10 times more common than type 1 diabetes and accounts for over 90% of diabetes cases worldwide.^[2] The prevalence of type 2 diabetes mellitus in Bangladesh is 4.3%.^[3] Type 2 DM is associated with marked increase in atherosclerotic macrovascular diseases involving cardiac, cerebral and peripheral large vessels.^[4] The patients with type 2 DM and no prior history of

coronary heart disease have an equivalent risk of developing a myocardial infarction as non-diabetics with a prior myocardial infarction.^[5] Type 2 DM is associated with two to four fold excess risk of coronary heart disease, a five fold increase in risk of fatal stroke and a significantly increased risk of atherosclerosis-induced gangrene of lower limbs as compared to non-diabetic individuals. The increased atherosclerosis risk is attributed to the high prevalence of several predisposing factors like obesity, hypertension, insulin resistance and dyslipidemia in these patients. More than 3 out of 4 diabetic patients die of causes related to atherosclerosis, in most cases because of coronary artery disease.^[7] Type 2 DM is now recognized as an inflammatory condition associated with insulin

resistance and abnormal endothelial vascular reactivity. It is an increasingly prevalent risk for atherosclerotic macro and microvascular disease.^[8] The pathogenesis of atherosclerosis in diabetes is complex, but serum lipids are frequently abnormal and likely contribute to the risk of Coronary artery disease.^[9] Diabetes is not only a well-known risk factor for atherosclerosis but is also associated with increased levels of sensitive marks of sub clinical systemic inflammation like C- reactive protein (CRP).^[10] CRP is an acute phase reactant protein produced in the liver and important in the non-specific host defense against inflammation. Chronically increased serum CRP concentrations are positively associated with a risk of future coronary artery disease, cerebrovascular disease or peripheral arterial disease. Possible mechanism of atherosclerosis by CRP to enhance expression of local endothelial cell surface adhesion molecules Monocyte chemoattractant protein-1, endothelin-1, and endothelial plasminogen, activator inhibitor-1; reduce nitric oxide bioactivity increase the induction of tissue factor in monocytes and LDL-C uptake by macrophages and co-localize with complement membrane attack complex within the atherosclerotic lesions.^[11] There is a strong and independent association between even slightly elevated concentrations of CRP and cardiovascular events in initially healthy subjects and in patients with manifested atherosclerosis.^[12] CRP is a more powerful predictor of cardiovascular risk than traditional risk factor such as LDL-C.^[13] The impact of LDL-C on the risk of CVD is augmented by the presence of an inflammatory marker such as CRP. The combination of elevation of both has more ominous implications than elevations of either alone. The impact of combination of elevated LDL-C accompanied by increased serum CRP is also an acute- phase reactant as well as a thrombogenic risk factor.^[14] The Systematic inflammation among pupil with impaired insulin mediated glucose homeostasis result in atherosclerosis. CRP was elevated in clinical and sub clinical atherosclerosis process.^[15] In newly diagnosed or established type 2 DM patient serum CRP level are elevated more when compared with non-diabetic subject.^[16] About more than 3 out of 4 individuals with diabetes, die of atherosclerosis and its communication. The high level of serum CRP possibly predispose to development of atherosclerotic disease. The present case control study was aimed to explore the association with serum CRP and fasting blood glucose in type 2 DM patients.

MATERIALS AND METHODS

The present case control study was carried out in the department of Hospital Lab Services, ELMCH, Era University, Lucknow from September 2020 to September 2021. Total number of 80 subjects were included in this study with age range from 30 to 60 years of both sexes. Among them 40 were cases of type 2 diabetes mellitus patients having fasting blood glucose level > 7.0 mmol/L and 40 were age-matched with healthy controls having fasting blood glucose <6.0mmol/L. All the cases of type 2 Diabetes mellitus patients without micro and macrovascular Complications were selected from the outpatient department. All the healthy control subjects were selected from persons attending with diabetic patients. All the study subjects were enrolled by convenient and purposive sampling technique. The objectives and benefits of the study were explained to all the study subjects to ensure their voluntary participation and informed written consent was taken from each subject prior to the study. Five (5) ml of Venous Blood was collected from the antecubital vein with all aseptic precaution. Blood was centrifuged at 3000 rpm and the serum was separated. Fasting blood glucose was measured as early as possible by enzymatic glucose oxidase method by spectrophotometer¹⁸. Serum CRP was measured by spectrophotometrically by dade behring¹⁹. All the data were expressed as mean + SD. Unpaired' test and Pearson correlation coefficient test were done as the tests of significance. The statistical analysis was done by using SPSS programme version 22. P value <0.05 was considered as level of significant.

RESULT

Mean + SD concentrations of fasting blood glucose in case and controls were 11.36 + and 4.99 + 0.96 mmol/L respectively. Fasting blood glucose level was significantly ($p < 0.001$) higher in case as compared to healthy control subjects. The concentrations of serum CRP in type 2 Diabetes patients and healthy controls were 7.27 + 5.02 and 5.40+0.49 mg/L respectively. In type 2 diabetes Mellitus Patients serum, CRP level was significantly ($p < 0.05$) higher than healthy control [Table-1]. Correlation Analysis showed highly significant ($p < 0.001$) positive correlation between serum CRP and fasting blood glucose in type 2 DM patients [Figure-1].

Table 1: Distribution and comparison of fasting blood glucose and serum CRP in study subjects

Biochemical parameter	Case (n=40)	Control (n=40)	"t" Value	"P" Value
Fasting blood glucose mmol/L (Mean + SD)	11.36 ± 4.39	4.99 ± 0.96	8.98	0.0001
Serum CRP Mg/L (Mean + SD)	7.27 ± 5.02	5.40 ± 0.49	2.34	0.022

DISCUSSION

Type 2 DM is responsible for the development of atherosclerotic diseases like coronary artery disease, cerebrovascular diseases and peripheral artery disease. Serum CRP is also an emerging risk factor for development of atherosclerosis. In our study the serum CRP level was significantly higher in type 2 DM patients in comparison to healthy controls subjects. These findings were consistent with the study by John.^[16] In the present study, highly significant positive correlation was found between serum CRP and fasting blood glucose in type 2 DM patients. Similar findings were reported in a study by others.^[15] Type 2 DM is now recognized as an inflammatory condition associated with insulin resistance and abnormal endothelial vascular reactivity. It is an increasingly prevalent risk for atherosclerotic micro and macro-vascular diseases.^[17] There is a strong and independent association between even slightly elevated concentrations of CRP and cardiovascular events in initially healthy subjects and in patients which manifest atherosclerosis in future.^[18]

There is insufficient data on the serum hs-CRP level of our normal non-diabetic population, however several studies by western writers have demonstrated that Asian people have a considerably greater level of CRP.^[19] CRP is a well-known inflammatory biomarker that is high in the blood of patients with severe inflammation and disorders such as T2DM and CVD. A Chinese population study found that CRP levels were greater in T2DM patients than in normal subjects,^[20] implying that CRP is an independent predictor of incident T2DM. Other studies have found that greater levels of CRP are connected with an increased risk of acquiring diabetes.^[21] Because of its relative stability in serum or plasma, accessibility of measurement, and availability of the international standard, CRP is a more usable and trustworthy sign in research and clinical settings than other inflammatory indicators such as cytokines.^[22] According to a European study, higher levels of CRP were more strongly and independently related with an elevated risk of T2DM in women than in men, and this did not change after stratification by age, smoking or drinking behaviour, obesity, or diabetes family history.^[23] We understand that these findings have far-reaching consequences for the development of insulin resistance, diabetes, and atherothrombosis therapy. We previously demonstrated that aspirin and statins are relatively more effective in lowering vascular risk among patients with elevated CRP level.^[24-26] and we predicted that CRP may have utility in the targeting of medications for the primary prevention of cardiovascular disease on that premise. Furthermore, a recent study reveals that rosiglitazone directly lowers CRP levels, which is an exciting finding given that this PPAR-inhibitor is already conventional therapy for type II diabetic patients.^[27]

CONCLUSION

In the present study serum CRP was significantly higher in type 2 Diabetes mellitus patients as compared to healthy control subjects. Highly significant positive correlation was found between serum CRP and fasting blood glucose in type 2 diabetes mellitus patients. Therefore, it is assumed from this study high serum CRP level is an indicator of risk for development of atherosclerosis. A large scale prospective base line study should be carried out to establish that the serum CRP is an independent risk for atherosclerosis.

Conflicts of interest: There is no conflict of interest.

Financial support: Nil

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