Original Research Article

Study of highly sensitive C-reactive protein in type 2 diabetes mellitus and prediction of cardiovascular risk with glycemic status

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ABSTRACT

Background: Inflammation plays a vital role in accentuating the formation of atherosclerotic plaque in diabetes mellitus. So, the measurements of inflammatory markers provide a method of assessing cardiovascular risk. Among the inflammatory markers, highly sensitive C-reactive protein (hs-CRP) is used to detect the low-level inflammation when it is within the normal range. Also, hs-CRP measurement may be useful for assessment of the risk of complication in diabetes patients. So, the present study is conducted to measure plasma hs-CRP level in T2DM and to determine adequate glycaemic control reduces hs-CRP level. The objectives of this study were to correlate HbA1c and hs-CRP in T2DM and predict cardiovascular risk with glycaemic status.
Methods: Authors took 50 diabetic patients. The investigation includes FBS, PPBS, hs-CRP and HbA1c. hs-CRP is measured by immunoturbidimetry method. The reports were collected and compared with normal reference range.
Results: The correlation between hs-CRP levels and HbA1c level after six months show a significant relationship where mean HbA1c values on day 1 and after 6 months were 8.088±1.219 and 7.518±0.693 respectively. The hs-CRP values were 2.508±1.050 on day 1 and 2.15±0.927 after 6 months proving that better glycaemic controls decrease hs-CRP thereby decreasing cardiovascular risk.
Conclusions: hs-CRP values are directly related to HbA1c and better glycaemic control reduces risk of CVD.

Keywords: CVD, Type 2 DM, HbA1c, hs-CRP

INTRODUCTION

Diabetes mellitus is a syndrome characterized by chronic hyperglycemia and disturbances of carbohydrate, fat and protein metabolism associated with absolute or relative deficiency of insulin secretion and/or insulin action.[1] The major risk factors associated with diabetes are positive family history, age, obesity, especially upper body adiposity, physical inactivity and insulin resistance. A close link exists between DM and cardiovascular disease (CVD). CVD is the most prevalent cause of mortality and morbidity in diabetic populations.[2] CVD death rates in the world 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) CV risk factors including obesity, hypertension and dyslipidemia are common in patients with DM, particularly those with T2DM oxidative stress, increased coagulability, endothelial dysfunction and autonomic neuropathy.[3,4] C-reactive protein is an acute phase reactant and nonspecific marker of inflammation, produced predominantly in hepatocytes as a pentamer of identical subunits in response to several cytokines.[5] Serum CRP levels are elevated in response to acute infection, inflammatory condition and trauma. In this situation, the serum CRP levels rise rapidly generally

beyond 10mg/l with concomitant elevation of ESR.[6] The high sensitivity assay techniques such as immunoturbidimetry and high sensitivity ELISA can detect CRP with a sensitivity range of 0.01 to 10mg/L. The high sensitivity assays help quantify low grades of systemic inflammation in the absence of overt systemic inflammatory or immunologic disorder.[7] Hs-CRP has been incorporated into the reynolds risk scoring system for global CVD risk prediction.[8] Numerous studies, both observational and randomized controlled trials published since the 1990s have established hs-CRP, as an independent predictor of CVD. Several RCTs like Prove-IT, TIMI 22, CARE, PRINCE and JUPITER.[9-12] Previously many studies have been done proving that hs-CRP as a predictor of CVD in diabetes mellitus. Not may have dwelled upon the effect of glycemic status on the levels of hs-CRP and progression of CVD. The aim of present study is to correlate the HbA1c with hs-CRP levels and to predict the cardiovascular risk with glycemic status.[2,3]

METHODS

Present study is cross sectional study with follow up. The sample size of patients is 50. Present study was conducted at Aarupadai Veedu Medical College and hospital, Puducherry, India from January 2015 to June 2016. The inclusion criteria are adult patients of type 2 diabetes mellitus diagnosed according to American diabetic association criteria 2015.[13]

Exclusion criteria

- The exclusion criteria are heart failure infection acute febrile illness, renal disorders, hepatic disorders, malignant disorders.
- Patients on hormone replacement therapy, statins, thiazolidinediones and anti-inflammatory drugs like NSAIDS, type 1 DM.

Investigation include complete blood count, urine albumin, renal function test, FBS, PPBS, HbA1c. The Quantia CRP-US was used for the measurement of hs-CRP. The American heart association and U.S. centers for disease control and prevention have defined risk groups as follows: Low risk: less than 1.0mg/L, average risk: 1.0 to 3.0mg/L, high risk: above 3.0mg/L.[14]

Statistical analysis

For statistical analysis SPSS version 22.0 was used to calculate the p value and x^2 value. MS word, MS excel have been used for generating graphs, tables etc.

RESULTS

Present study was conducted with the sample size of 50 patients. Who were from ages of 30 years and above with majority of them in 41-50 years. The sample consisted of 27 males and 23 females. Authors compared HbA1c value with hs-CRP on day 1 and followed them up after 6 months. During day 1, the patients with HbA1c values of <7 were 8, 7-8 were 20 and >8 were 22. The patients with hs-CRP values of <1 were 5; 1-3 were 32 and >3 were 13. The p values were statistically proving that both HbA1c and hs-CRP are significantly related and out of 22 patients with HbA1c >8, 10 had raised hs-CRP proving an increased CV risk. During our follow up after 6 months, the patients with HbA1c values in ranges of <7,7-8,>8 were 9, 32 and 9 respectively and number of pt for hs-CRP values of <1,1-3,>3 were 7, 36 and 7; proving our hypothesis that a glycemic value (HbA1c) have a direct influence on cardiovascular risk and good glycemic control reduces the cardiovascular risk significantly. Comparison between hs-CRP level and HbA1c on day 1 and follow up after a period of 6 months showed 78% cases had HbA1c level under control after 6 months and 22% cases had HbA1c not under control. 82% cases had decreased hs-CRP level and 18% had increased hs-CRP level. After 6 months also, there is significant correlation between hs-CRP level and HbA1c level. So, these values also suggest that adequate glycemic control can decrease the hs-CRP level.

DISCUSSION

Diabetes is a global pandemic causing substantial comorbidities affecting multiple system cardiovascular, cerebrovascular, respiratory system etc. The vascular co morbidities including atherosclerosis, accounts for virtually 80% death among diabetes.[15] Inflammation play a major role in formation of atherosclerotic plaques. The possible mechanisms are activated glycation products, reactive oxygen species and PKC activation.[16-18] Based on multiple epidemiological studies and interventional studies, increased concentration of hs-CRP are associated with future cardiovascular risk.[19] Many studies have investigated the relation between hs-CRP- DM and hs-CRP-CVD. As DM and inflammation play an important role in CVD development, present study aims to correlate HbA1c and hs-CRP to predict the cardiovascular risk with glycemic status.

Present study was conducted with 50 diabetic patients who were screened on day 1 and followed up after 6 months and results were compared providing the effect of glycemic status on hs-CRP. As our results suggested present study showed that patients in whom glycemic control was poor had 18% increased hs-CRP and patients with good glycemic control had 78% decreased hs-CRP which proves that good glycemic control reduces CVD risk substantially.

In previous study, according to Lui S et al, statistically significant positive association between dietary glycemic load and plasma hs-CRP.[20] The median hs-CRP concentration for the lowest quintile of dietary glycemic load was 1.9mg/L and for the highest quintile was 3.7mg/L; respectively (P for trend <0.01). Dietary glycemic load is significantly and positively associated

with plasma hs-CRP in healthy middle-aged women, independent of conventional risk factors for cardiovascular diseases. In present study, Asegaonkar S et al, showed elevated hs-CRP levels among cases compared to controls in T2DM.

According to hs-CRP levels, seven cases were in the low-risk (<1mg/l), 32 in the moderate-risk (1-3mg/l), and 21 in the high-risk (3-10mg/l) group. It showed that hs-CRP levels correlate with T2DM. This study also showed that increased HbA1c level correlate with hs-CRP.[21] According to Deepak et al, showed that hs-CRP is an independent marker of CVD. They found an association between hs-CRP and DM, metabolic syndrome and CAD. They found that standardized hs-CRP assays with adequate follow up duration are required to derive risk cut-off values for CVD in the Indian perspective.[22]

According to American heart association (AHA) and the centre for disease control and prevention (CDC) shows that hs-CRP is an independent marker of CAD and CVD risk and may be useful as a prognostic indicator for recurrent events in patients with acute coronary disease.[23] According to Mishra DP et al, this study found that hs-CRP levels correlated with HbA1c levels. Mean HbA1c levels were significantly higher in patients who had hs-CRP levels of 1 mg/L or more (p-value <0.001). Other factors such as age, blood pressure, BMI, LDL, serum creatinine was not correlated with hs-CRP level.[24]

All previous studies have concluded that diabetes is one of the risk factors for CVD and hs-CRP is a marker of low-grade inflammation in diabetic patients. So, high hs-CRP values increased cardiovascular risk if adequate glycemic status have not been achieved. Inpresent study also authors proved that hs-CRP values were high in poor glycemic status. Authors also proved that if adequate glycemic status is achieved, hs-CRP values can be decreased, and it decreases the cardiovascular risk.

Limitations of this study were authors have not included the BMI and lipid profile of patients, which could have a slight influence on the hs-CRP values. Few studies have been done which have found a significant influence of these factors on the hs-CRP values. If these factors could be included in future studies the outcome of predictability will be better.[7]

CONCLUSION

In present study concluded that hs-CRP level has a statistically significant correlation with high HbA1c levels (>8) and adequate glycemic control will decrease hs-CRP level.

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