Original article

High sensitivity C-reactive protein (hsCRP) levels in type 2 Diabetes mellitus patients attending tertiary care academic hospital

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Abstract

Introduction: Diabetes mellitus (DM) is a chronic metabolic disease characterized by hyperglycaemia due to defects in insulin secretion, insulin activity or both. It is a leading cause of death worldwide and one of the main causes of long-term disability. Rapid diagnosis of complications play an important role in overall management of DM. C-reactive protein (CRP) is an example of one of these biomarkers.

Material and Methods: High sensitivity C-reactive protein (hsCRP) levels in type 2 DM patients were estimated.

Results: The mean hsCRP in control group was 0.63 mg/dl, in diabetic group 8.5 mg/dl. The hsCRP values were significantly raised in diabetic (case group) as compared to control group (P value < 0.0001).

Conclusion: hsCRP can be considered as an important biomarker in monitoring and preventing complications associated type 2 DM.

Keywords: Diabetes mellitus, biomarkers, high sensitivity C-reactive protein.

Introduction

Diabetes mellitus (DM) is a chronic metabolic disease characterized by hyperglycaemia due to defects in insulin secretion, insulin activity or both.[1] Retinopathy, nephropathy and cardiovascular symptoms are important long-term complications of DM. [1]In addition, the incidence of atherosclerotic cardiovascular, peripheral arterial, and cerebrovascular disease is also high in diabetic patients. [1]

The prevalence of DM among adults over 18 years of age has increased globally from 4.7% in 1980 to 8.5% in 2014. [2]A study conducted with an aim to estimate the global burden of DM from the year 1995 to 2025 has projected that, India will have maximum increase in DM cases.[3] Similarly various studies from different parts of India have reported increased prevalence of DM.

As per etiopathogenesis of DM, it is be broad classified into type 1 DM and type 2 DM. [1] Type 1 DM is caused due to absolute deficiency of insulin secretion whereas type 2 DM can be attributed to combination of insulin activity resistance and insufficient insulin secretion. [1] Type 2 is common as compared to type 1, occurring in approximately 90-95% of those with DM. [1]

Rapid diagnosis of complications play an important role in overall management of DM. As type 2 DM is associated with chronic low-grade inflammation, several biomarkers related to inflammation can be applied for its diagnosis, assessment of treatment and prognosis.[4] C-reactive protein (CRP) is an example of one of these biomarkers.

CRP is homo-pentameric acute-phase protein produced primarily in the liver by stimulation of adipocyte-derived pro-inflammatory cytokines, like interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α).[5] It was first discovered by Tillet and Francis (1930) while investigating the sera of patients with acute-stage of Pneumococcal infection. [5] The name CRP was derived due to its reaction with the capsular (C) polysaccharide of *Pneumococcus*. [5]

CRP is the most commonly measured circulating biomarker for sub-clinical inflammation. It is widely available with stable and standardised assays for measurement. High sensitivity C-reactive protein (hsCRP) is similar as conventional CRP.[6] Recent evidences suggest that hsCRP is a strong independent risk factor for subsequent development of stroke, myocardial infarction, peripheral vascular disease and DM. [7]

hsCRP levels can predict the first cardiovascular event in several populations. Its level, if measured prior to the onset of clinical disease may be an independent predictor of the DM. [7] But any contribution of CRP to pathogenesis of DM has received little attention. Therefore the present study was conducted in a tertiary level academic hospital of Maharashtra with an aim to estimate the hsCRP levels in type 2 DM patients.

Material and methods

The present cross-sectional study was carried out in the Department of Biochemistry, B J Government Medical College and Sassoon General Hospital, Pune, Maharashtra. The study period was from December 2015 to June 2017.

A total of 70 newly diagnosed type 2 DM patients aged between 40-60 years having blood glucose level >126 mg/dl in fasting and >200 mg/dl random blood glucose load were included in the study.

A signed informed consent was obtained as per the proforma from all the subjects or their legally responsible attendant. The protocol of the study was approved by Institutional Ethics Committee.

Following were the exclusion criteria:

1. Patients with recent clinical infection, chronic inflammatory condition or neoplastic diseases.
2. Bleeding disorders, cerebral haemorrhage of any etiology, autoimmune disorders.
3. Conditions mimicking stroke.
4. Patients with recent surgery or major trauma.
5. Patients with any major renal or hepatic disease.
6. Ongoing cardiac ischemia and known peripheral vascular disease.

In addition, a total of 70 age and sex matched healthy individual without any major illness and not on any medication willing to give consent were included as controls. About 2 ml of blood samples were obtained from the ante-cubital vein of each subjects and control. The blood sample was transferred to a clean dry sterile plain vacutainer and allowed to clot for 30 minutes and then centrifuged.

The serum sample was used for estimation of hsCRP levels. The hsCRP assay is based on a latex enhanced immunoturbidimetric assay.

Results

Table 1 The age distribution of case and control.

	Control	Cases
Mean ±SD	50±5.8	50±6.2
Median	49	50
Minimum	40	40
Maximum	60	60

As shown in table 1, the mean age of distribution of cases and control was 50±6.2 and 50±5.8 years respectively. There was no significant difference observed between age distributions among two groups (Mann Whitney Test, P value>0.05).

In group I (controls) out of 70, 43 (61.4%) were males and 27 (38.6%) were females participants whereas in group II (cases) out of 70 type DM patients, 45 (64.2%) were males and 25 (35.8%) were females. There was no significant difference observed between gender distributions among two groups (Mann Whitney Test, P value>0.05).

The serum hsCRP levels and its comparison among study group is shown in table 2. The mean hsCRP in control group was 0.63 mg/dl, in diabetic group 8.5 mg/dl. The hsCRP values were significantly raised in Diabetic (case group) as compared to control group (P value 0.0001).

Table 2. The serum hsCRP levels and its comparison among study group.

Parameter	Mean ± SD		P value (level of significance-t test)
	Control	Cases	Control VS cases
hsCRP (mg/L)	0.63 ± 0.23	8.5 ± 1.33	0.0001

Discussion

DM is a leading cause of death worldwide and one of the main causes of long-term disability. In India, DM is a fast gaining status of a potential epidemic with more than 62 million currently diagnosed with the disease. In the year 2000, India (31.7 million) topped the world with highest number of people with DM followed by China (20.8 million) with the USA (17.7 million) in second and third place respectively.[8]

In this study, a total of 70 diabetic patients attending out patient service of Department of Medicine were studied along with age and gender matched 70 healthy controls. The age distribution of the patients in this study was between 40 and 60 years. Average mean age was 50.8 in case group 50.08 years in control respectively. The risk of Type II DM increases with increasing age.[4]

Although insulin resistance and insulin secretion dysfunction are the main physiological abnormalities associated with type 2 DM, the specific underlying determinants still remain unclear.[9, 10] In recent years, various studies have linked DM with numerous commonly coexisting conditions that originate through inflammatory mechanism. [11]

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The best strategy for reducing its burden is by targeting population at risk for primary prevention and risk factor management. Biomarkers which help in outcome prediction and therapeutic decision making are very important in the management of diabetic patients thereby reducing mortality rates.[12]

More recent study have highlighted IL-6 and CRP as sensitive physiological markers to be associated with hyperglycaemia, insulin resistance and overt type 2 DM. Pradhan *et al* (2001) reported that elevated IL-6 and CRP levels predict the development of type 2 DM and supported the role of inflammation in pathogenesis of DM.[11]

IL-6 is a major pro-inflammatory cytokine produced by variety of tissues including activated leucocytes, adipocytes and endothelial cells. [11] CRP is the main downstream mediator of the acute phase response derived via IL-6 dependent hepatic biosynthesis. As compared IL-6, laboratory procedure for estimation of CRP is quite simple and cost effective.[11]

In the present study, the hsCRP levels in type 2 DM patients were estimated and compared with those of healthy controls. Nakanishi *et al* (2003) reported that CRP may be a risk factor for development of DM independent of either obesity or insulin resistance.[13]

In this study, the mean hsCRP in DM patients was 8.5 mg/dl whereas for control group it was 0.63 mg/dl. The hsCRP values were significantly raised in Diabetic (case group) as compared to control group (p-value < 0.0001). Similar observation was noted by Mahajan *et al* (2009).[11] They observed that median hsCRP levels were significantly higher in both diabetic men and women compared to their non diabetic counterparts (*P* value 0.0001). [11]

Conclusion

The present study shows that hsCRP concentration is significantly increased in type 2 DM. It is further increased in diabetic patients with complications and poor glycemic control. hsCRP can be considered as an important biomarker in monitoring and preventing complications associated type 2 DM.

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