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Association of high sensitivity C reactive protein and Glycemic status with type 2 Diabetes mellitus

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Abstract:

Back ground and objective: High sensitivity C-reactive protein (hsCRP) has been associated with metabolic syndrome (MetS) and its components. Several studies have suggested hsCRP to be used as a marker for the primary prevention of cardiovascular diseases. So, we aimed to evaluate the association between hsCRP levels and the components of Metabolic Syndrome in type 2 diabetic and non-diabetic population.

Methods: This case control study was carried out in the clinical biochemistry laboratory in Saveetha Medical College and hospital with 50 type 2 Diabetes mellitusand 50 age and sex matched controls. The investigation include hs-CRP and HbA1c. The sample was processed in Vitros 5600 automated dry chemistry analyser. The reports were collected and compared with normal reference range. Data was analysed and there seemed to be correlation between chronic inflammatory protein hs-CRP and HbA1Clevels.

Results:hsCRP and HbA1c were significantly higher in T2DM subjects when compared with controls. As the number of the components of Metabolic Syndrome increased, there was a linear increase in hsCRP levels in whole study population (p trend <0.001), diabetic subjects (p trend <0.001), as well as in controls (p trend <0.001). Mean hs-CRP levels in type 2 diabetics was 6.59±2.88 mg/l which was significantly higher compared to mean hs-CRP levels of normal healthy controli.e1.32±0.34 mg/l. Correlation coefficient (r values)were used to study the association of hs-CRP and HbA1C levels.

Conclusion: There was significant positive correlation observed between hs-CRP levels and HbA1C levels. Diabetic patients having poor control of glycemic status are in more active inflammatory state. Chronic inflammation may have a role in vascular toxicity resulting in endothelial damage in type 2 diabetic patients. Thus better glycaemic control reduces risk of Cardio vascular diseases.

Keywords: C reactive protein, Glycemic status, Metabolic syndrome, type 2 Diabetes mellitus and non diabetes.

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 DM and is 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 concominant 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. [11] 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 glycemicstatus.[2,3]

METHODS

Present study is cross sectional study with follow up. The sample size of patients is 100, 50 diabetic and 50 non diabetic patients. Present study was conducted at Saveetha Medical College and Hospital, Chennai, India from November 2019 to March 2020. The inclusion criteria are elderly patients of type 2 diabetes mellitus diagnosed according to American diabetic association criteria 2015.

Exclusion criteria

- The exclusion criteria are heart failure, infection, acute febrile illness, renal disorders, hepatic disorders and malignant disorders.
- Patients on hormone replacement therapy, statins, thiazolidinediones and anti-inflammatory drugs like NSAIDS and 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 x2 value. MS word, MS excel have been used for generating graphs, tables etc.

The data was first tabulated in Microsoft Excel worksheet. They were analysed using online software. Continuous variables were presented as mean±SD. Discrete variables were expressed as absolute number and percentages. Correlation was calculated using Pearson Correlation Coefficient. Student's t-test was used to find significance of difference of the mean. P value <0.05 was considered significant.

RESULTS

We had a total of 100 patients in our study. The mean age of the study group was 51.06 ± 11.36 years and the control group 55.16±11.29 years (Table 1). Mean hs-CRP in the study group was 6.59±2.88 mg/l which was significantly higher than the control group (1.32±0.34 mg/l,[p <0.001]

A positive correlation was observed between hs-CRP and HbA1c in the study group [Figure 1]

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. Correlation had been figured out in graph. [Figure : 1]

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 plays 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.

Table 1: Distribution of patients according to age in study (n=50) and control group (n=50)

Age range	Study group	Percentage	Control group	Percentage
30-40	11	22	8	16
41 – 50	14	28	10	20
51 – 60	15	30	12	24
61 – 70	10	20	20	40
Range	30 - 70		30 - 70	
Mean ± SD	51.06±11.36		55.16±11.29	

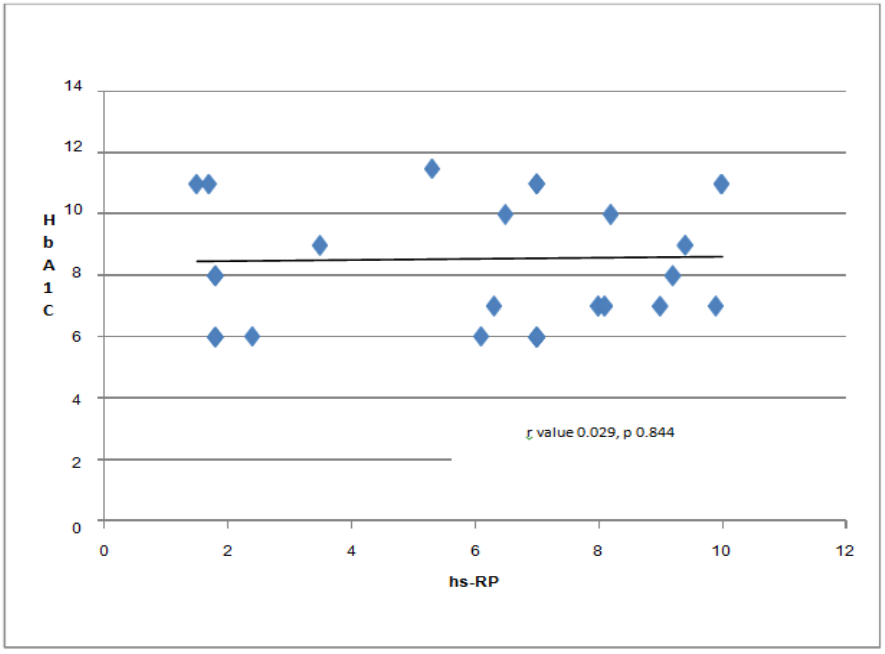

Figure 1: Correlation of HS-CRP With Hba1c Among Diabetics

In our hospital based study we found high hs-CRP values in Diabetic subjects who did not have their blood sugarlevel in control. hs-CRP values showed significant correlation with HbA1C. [12] Cardiovascular events are increased inType 2 DM subjects due to a complex combination of various traditional and non-traditional risk factors that havean important role to play in the beginning and in the evolution of atherosclerosis from endothelial dysfunction toclinical events. DM2 might induce inflammation by increasing advanced glycation end products that may activatemacrophages and increase oxidative stress and interleukin -6 synthesis, resulting in production of CRP.[9]

Arterialinflammation induced due to toxic effects of inflammatory proteins has emerged to be central in initiation andprogression of atherosclerosis. [13] In people with diabetes, high hs-CRP levels (> 1 mg/l) were associated with increasein CV mortality after adjusting for age, sex and glucose tolerance tests.[10] It is reported that relative cardiovascularrisk categories for serum hs-CRP levels are: low risk < 1.0 mg/L, average risk 1.0-3.0 mg/L, high risk 3.0-10.0 mg/Land unspecific elevation being >10mg/l and needs to be evaluated for acute inflammatory conditions.[10]In the present study the hs-CRP values are significantly higher in diabetics who had no complicationscompared to controls (p <0.001)

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

According to Deepak et al,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) 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, 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 increase cardiovascular risk if adequate glycemic status have not been achieved.

In the present study, we proved that hs-CRP values were high in poor glycemic status. we 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, we 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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Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Power AC. Diabetes mellitus: Diagnosis, classification and pathophysiology. In: Chapter 417 in Harrisons principles of internal medicine; Kasper DL, Fauci AS, Hauser SL, Lomgo DL, Jameson JL, Loscalzo J, eds. USA; McGrew- Hill: 19th ed; 2015;2:2399.
2. Centers for disease control and prevention. National diabetes statistics report: Estimates of diabetes and its burden in the United States, 2014. Atlanta, GA: US Department of Health and Human Services; 2014.
3. Rivellese AA, Riccardi G, Vaccaro O. Cardiovascular risk in women with diabetes. NutritMetabol Cardiovasc Dis. 2010;20(6):474-80.
4. Duncan B, Schmidt M, Pankow J, Ballantyne C. Atherosclerosis risk in communities study. Low-grade systemic inflammation and the development of type 2 diabetes: the atherosclerosis risk in communities study. Diab. 2003;52:1799-05.
5. Libby P. Mechanisms of acute coronary syndromes and their 11. implications for therapy. N Engl J Med. 2013;368:2004-13.
6. Black S, Kushner I, Samols D. C-reactive protein. J Biol Chem. 2004;279:48487-90.
7. Roberts WL, CDC/AHA. CDC/AHA workshop on markers of inflammation and cardiovascular disease: application to clinical and public health practice: laboratory tests available to assess inflammation-performance and standardization: a background paper. Circul. 2004;110:e572-6.
8. Ridker PM, Buring JE, Rifai N, Cook NR. Development and validation of improved algorithms for the assessment of global cardiovascular risk in women: the Reynolds risk score. JAMA. 2007;297(6):611-9.
9. Ridker PM, Morrow DA, Rose LM, Rifai N, Cannon CP, Braunwald E. Relative efficacy of atorvastatin 80mg and pravastatin 40 mg in achieving the dual goals of low-density lipoprotein cholesterol <70mg/dl and C-reactive protein <2mg/l: an analysis of the prove-it timi-22 trial. J Am Coll Cardio. 2005;45(10):1644-8.
10. Ridker PM, Rifai N, Pfeffer MA, Sacks F, Braunwald E. Long-term effects of pravastatin on plasma concentration of C-reactive protein. Circul. 1999;100(3):230-5.
11. Albert MA, Danielson E, Rifai N, Ridker PM, Prince investigators. Effect of statin therapy on C-reactive protein levels: the pravastatin inflammation/CRP evaluation (Prince): a randomized trial and cohort study. JAMA. 2001;286(1):64-70.
12. Ridker PM, Danielson E, Fonseca FA, Genest J, Gotto Jr AM, Kastelein JJ, et al. Rosuvastatin to prevent vascular events in men

and women with elevated C-reactive protein. New Eng J Med. 2008;359(21):2195.
13. American diabetes association. Erratum. classification and diagnosis of diabetes. Sec. 2. In standards of medical care in diabetes-2016. Diabetes Care. 2016;39(1):S13-22.
14. Yousuf O, Bibhu D, Martin S, Joshi H, Blaha J. High-sensitivity C-reactive protein and cardiovascular disease: J Am Coll Cardiol. 2013;62(5):397-08.
15. American Diabetes association. Consensus statement: role of cardiovascular risk factors in prevention and treatment of macrovascular disease in diabetes. Diab Care. 1993;16:72-8.
16. Brownlee M, Cerami A, Vlassara H. Advanced glycosylation endproducts in tissue and the biochemical basis of diabetic complications. N Engl J Med. 1988;318:1315-21.
17. Ikeda K, Higashi T, Sano H, Jinnouchi Y, Yoshida M, Araki T, et al. N ε-(carboxymethyl) lysine protein adduct is a major immunological epitope in proteins modified with advanced glycation end products of the Maillard reaction. Biochem. 1996;35(24):8075-83.
18. Reddy S, Bichler J, Wells-Knecht KJ, Thorpe SR, Baynes JW. N. epsilon-(carboxymethyl) lysine is a dominant advanced glycation end product (AGE) antigen in tissue proteins. Biochem. 1995;34(34):10872-8.
19. Pfutzner A, Forst T. High sensitivity C-reactive protein as cardiovascular risk marker in patients with diabetes mellitus. Diab TechnolTher. 2006;8(1):28-36.
20. Liu S, Manson J, Buring J, Stampfer M. Relation between a diet with a high glycemic load and plasma concentrations of high-sensitivity C-reactive protein in middle-aged women. Am J Clin Nutr. 2002;75:492-8.
21. Asegaonkar S, Marathe A, Tekade M, Cherekar L. High-sensitivity C-reactive protein: a novel cardiovascular risk predictor in type 2 diabetics with normal lipid profile. J Diab Complic. 2011;25:368-70.
22. Deepak Y, Denis X, Alben S. High sensitivity C-reactive protein and cardiovascular disease: An Indian perspective. Indian J Med Res. 2015;142:261-8.
23. David C, Paul M. Clinical significance of hs-CRP in cardio vascular disease. Biomarkers in Medicine. Circulation. 2007;2:229-41.
24. Mishra DP, Das S, Sahu P. Prevalence of inflammatory markers (high-sensitivity C-reactive protein, nuclear factor-κB, and adiponectin) in Indian patients with type 2 diabetes mellitus with and without macrovascular complications. Meta SyndrRelat Dis. 2012;10:209-13.