MONITORING OF HIGH SENSITIVITY C-REACTIVE PROTEIN IN TYPE 2 DIABETES MELLITUS PATIENTS MAY REDUCE THE MORTALITY

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ABSTRACT

The present study was conducted in Tripura, High sensitivity C-Reactive Protein (hs-CRP) has been assayed for 150 number of Type 2 Diabetes Mellitus (T2DM) patients (85 males and 65 females) aged above 45 years. It is observed that 7.33% of T2 DM patients have cardiac involvement in ECG with a marginal high value of hs-CRP. It is also observed that cardiac involvement is higher with the period of DM and age. The higher value is independent of sex (p value - male 0.0037, female 0.0074), serum lipid profile and renal status. Patients of hypertension or any other diseases were not included in the study. So these patients are at higher risk than those of normal hs-CRP. By screening the diabetic patients with moderately high levels of hs-CRP group can be isolated and proper treatment can reduce the mortality and morbidity.

KEYWORDS

Hs-CRP (High Sensitivity C-Reactive Protein), T2DM (Type 2 Diabetes Mellitus), Lipid profile, CAD (Coronary Artery Disease).

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INTRODUCTION

C-reactive protein is an acute phase protein present in the blood of acutely ill patients. It consists of five identical non-glycosylated polypeptide subunits non-covalently bound to form a disk shaped cyclic polymer with a molecular weight of about 115 KDa.¹ This alpha globulin is synthesized in the liver under the control of interleukin-6. Formation of fatty streak on endothelial cells on any grade of infection cause recruitment of leukocytes triggered by inflammatory cytokines, such as interleukin-1 and tumor necrosis factor-alpha. The primary pro-inflammatory cytokines such as CD-40 influence the expression of messenger cytokines such as interleukin-6, which travel from local sites of inflammation to the liver where a change in the programme of protein synthesis of the acute phase response occur.^{2,3}

This acute phase protein binds with the cell wall C-polysaccharide of *Streptococcus Pneumoniae* and agglutinate the organism and so named as C-Reactive Protein (CRP). CRP acts as nonspecific host defense, especially against infection and inflammation.¹ Elevated value of CRP is found in wide range of acute or chronic illness like gram positive and gram negative infection, trauma, rheumatoid arthritis, tuberculosis etc. In acute stage of infection CRP level increases to peak within 48 hours as much as 1000 folds.¹ Normally, its level ranges from 0.068 to 8.2mg/L.³

Chronic inflammation is an important factor for the development and progression of atherosclerosis. Different studies have revealed the fact that there is a strong positive association of CRP with the risk of future coronary events like coronary artery disease, peripheral artery disease and cerebrovascular disease.^{4,5,6} It requires the use of high sensitivity CRP (hsCRP) assay having detection limit less than 0.03 mg/L.⁷

Association of cardiovascular events with type-2 Diabetes Mellitus is an established fact and they have 2-4 fold high risk for CHD. The present study aimed at finding the relation of the hsCRP with the type-2 Diabetes Mellitus in Tripura state. Low grade chronic infection leads to moderate rise in hsCRP levels. Diabetic patients are more susceptible in this regard. Atherogenesis has also got a positive correlation with the chronic infection. Elevated levels of hsCRP predict not only cardiovascular events, but also the onset of type-2 diabetes mellitus, probably because hsCRP levels correlate with several components of metabolic syndrome including those not easily measured in clinical practice such as insulin sensitivity, endothelial dysfunction and hypofibrinolysis.^{8,9,10} In major studies from the United States and Europe, hsCRP levels predicted subsequent risk better than LDL-cholesterol levels.^{11,12} According to Adult Treatment Panel (ATP III), hsCRP levels less than 1, 1 to 3 and greater than 3 mg/L define as low, moderate and high risk groups respectively for future vascular events. Mortality rate increases when hsCRP levels is more than 3mg/L. Therefore, hsCRP could be a predictor of the risk factor of cardiovascular events.

MATERIALS AND METHODS

CRP has been measured with the detection level of 3mg/L, which is not sensitive enough to detect lower level value for prediction of cardiovascular risk. For this, high sensitive immunoturbidimetric method is used to detect the lower level near to 0.3mg/L. It is based on the light scattering properties of the antigen-antibody complex formed by the covalently coupling latex particles to a specific antibody and useful to detect very low level of CRP.⁸

The present study was conducted with 150 number of Diabetes Mellitus type-2 patients who have been suffering for more than 10 years. All of them are either under oral hypoglycemic drugs or Insulin. Their ages were 45 years and above. Equal number of persons were selected for study as control. Along with hs-CRP, lipid profile and Serum urea, Creatinine values were also estimated and the patients with their normal values were selected for the study.

RESULT

In this study serum of total 150 known type 2 diabetic patients were assayed for hs CRP by immunoturbidimetry method after observing all formalities. Equal number of normal

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persons were also taken for the estimation of hs-CRP. Estimation of lipid profile, urea and creatinine were done for all the patients and the normal individual. Among them 85(56.67% patients were male and 65(43.33% were female. The result has been divided into three groups – one group having hsCRP levels less than 1 mg/L, other group having hsCRP levels between 1.1-3mg/L and the group having CRP value 3.1-10 mg/L. In case of male patients, it shows that hsCRP value of 57 (67.06%) patients had less than 1mg/L, 23 patients (27.06) had 1.1-3mg/L and only 5 patients (5.88%) patients had in the range of 3.1-10mg/L. The mean value was 1.25+1.27 and p-value was 0.0037, which is very sensitive.

In case of females 42 (64.62%) patients had <1mg/L, 19 (29.23%) patients had in the range of 1.1-3mg/L and only 4 (6.15%) patients between 3.1-10mg/L. The mean value was 1.29+1.30 and p-value was 0.0074, which was again very sensitive. The hs-CRP value of total 66% of the patients had less than 1mg/L, 28% had 1-3mg/L and only 6% had 3.1-10mg/L with the mean value 1.29 + 1.30 and p-value 0.0001. It is highly sensitive.

It also shows that hs-CRP does not have any relation with the sex of the patients. So far the age is concern patients of 45-55 years of age group had no cardiac symptoms. All of those patients above 65 years with cardiac involvement were suffering from T2DM for more than 15 years. Total 7.33% of diabetic patients with high hs-CRP value showed cardiac involvement in ECG.

SUMMARY

The hs-CRP level of a person increases in all sorts of acute inflammatory and infectious cases which subsides when the acute phase is over. But persistent moderately higher level of hs CRP is found to be a risk factor for coronary heart disease. The present study in Tripura shows that 7.33% of T2DM. Patients had a marginal higher value of hs-CRP. The higher value is independent of sex, serum lipid profile and renal status, male (p value 0.0037) and female (p value 0.0074). Duration of T2DM and age of the patients had a positive correlation. The patients of 56-65 years of age group had 3.45% of cardiac involvement and the patients of T2DM with more than 15 years duration and above 65 years had higher cardiac involvement (44.44%). These patients are at higher risk than those of normal hs-CRP.

CONCLUSION

From this study in Tripura, it can be concluded that 7.33% of T2DM patients had a marginal higher value of hs-CRP and longer the duration of Diabetic Mellitus with the increased age (more than 65 years), higher is the cardiac involvement (44.44%). There is no relation with the sex, serum lipid profile and renal status of the patients in this regard. Therefore, hs-

CRP can be a marker of CAD for the patients of T2DM. If the hs-CRP is evaluated for the patients of in T2DM frequent intervals and those patients with higher hs-CRP can be screened and effective measures are taken, mortality and morbidity due to CAD can be controlled.

REFERENCES

- David R Claus, Alexander P, Osmand and Henry Gewurz: Radioimmunoassay of human C-reactive protein and level in normal sera, J Lab Clin Med Vol 87, No. 1, Jan 1978:120-128.
- Dixon JS, et al.: C-reactive protein in the serial assessment of disease activity in rheumatoid arthritis. Scand J Rheum, 13:39-44, 1984.
- Shine B, de Beer FC and Pepys MB: Solid phase radioimmunoassay for human C-reactive protein. J Lab Clinica Chimica Acta 117:13-23, 1981.
- Dowling P and Cook S: Immune events in demyelinating disease in Wolfgang E, Ellison GW, Stevens JG and Andrew JM (eds): Multiple Sclerosis. Academic Press Inc New York. 269-277, 1972.
- Kushner I: "C-reactive protein in rheumatology." Arthritis Rheum 34:1065-1068, 1991.
- Boekholdt SM, Hack CE, Sandhu MS, et al.: C-reactive protein levels and coronary artery disease incidence and mortality in apparently healthy men and women: The EPIC-Norfolk prospective population study 1993-2003. Atherosclerosis 187:415, 2006.
- Schultz DR and Arnold PI: "Properties of four acute phase proteins: C-reactive protein, serum amyloid A protein, glycoprotein and fibrinogen." Seminars in Arthritis and Rheumatism 20:129-147, 1990.
- "Clinical Guide to Laboratory Test." Edited by NW Tietz, 3rd Edition. WB Saunders Company, Philadelphia, PA. 19106 (1995).
- Ridker PM, Buring JE, Shih J, et al.: Prospective study of C-reactive protein and risk of Cardiovascular events among apparently healthy women, Circulation, 1998;98:731-733.
- Soinio M, Marniemi J, Laakso M, et al.: High Sensitivity C-reactive protein and coronary heart disease mortality in patients with type-2 diabetes. A 7 years follow-up study. Diabetes Care. 2006;29:329-331.
- Pradhan AD, Manson JE, Rifai N, et al.: C-reactive protein, interleukin-6 and risk of developing type-2 diabetes mellitus. JAMA 286:327, 2001.
- Ridker PM: Clinical application of C-reactive protein for cardiovascular disease detection and prevention. Circulation 107:363, 2003.

Age (In years)	Controls N (%)	Known Diabetics [N=150]		
		Non-cardiac N (%)	Cardiac N (%)	Total N (%)
45 - 55	48 (32)	45 (100)	-	45 (30)
56 - 65	67 (44.67)	84 (96.55)	3 (3.45)	87 (58)
66 and above	35 (23.33)	10 (55.56)	8 (44.44)	18 (12)
Total	150 (100)	139 (92.67)	11 (7.33)	150 (100)
Table 1: Age distribution of study subjects (diabetic non-cardiac and cardiac patients) and gender matched healthy controls				

Gender	Total N (%)	hs-CRP Level - Diabetics [N=150]			hs-CRP [Mean $\pm$ SD]		P value
		< 1mg/L	1-3 mg/L	3.1-10 mg/L	Diabetics [N=150]	Control [N=150]	
Male	85 (56.67)	57 (67.06)	23 (27.06)	5 (5.88)	1.25 $\pm$ 1.27	0.87 $\pm$ 0.24	0.0037
Female	65 (43.33)	42 (64.62)	19 (29.23)	4 (6.15)	1.33 $\pm$ 1.34	0.91 $\pm$ 0.29	0.0074
Total	150 (100)	99 (66)	42 (28)	9 (6)	1.29 $\pm$ 1.30	0.89 $\pm$ 0.26	0.0001

Table 2: Gender distribution and hs-CRP level among study subjects and controls

(Student's T-test for 2 independent means, one-sided p value, 95% confidence interval)

Fig. 1: Correlation of age (In years) and hs-CRP (In mg/L) among study subjects ($R^2=0.235$) [N=150]