High Sensitive C Reactive Protein in Diabetes Patients and its Correlation with Glycaemic Control

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Research Article

Abstract: **Background:** High sensive C reactive protein (hs–CRP) is found to be significant in people with diabetes. Hyperglycaemia is an associated factor to the increase of serum CRP levels. **Materials and methods**: The study conducted at SVS Medical College and Hospital, Mahabubnagar from August 2008 to July 2011. The subjects were the 200 randomly selected patients attending and/ or admitted to Medicine Out-patient and In-patient departments plus 100 age and sex matched healthy volunteers. Anthropometric measurements apartment blood sugars, blood urea, serum Creatinine, serum uric acid, and lipid profile and hs-CRP done in all 300 cases. .Data analyzed and statistically significance was sought. **Observations:** In comparison with non-diabetic subjects, the diabetic subjects were older ($P < 0.008$) and had higher BMI ($P<0.006$). They also had higher systolic blood pressure ($P<0.05$) and diastolic pressure blood pressure ($P<0.05$), fasting blood sugar ($P<0.0018$), post prandial blood sugar ($P<0.0016$) HbA1C % ($P<0.001$). hs-CRP levels were significantly higher among the male diabetic subjects with 4.88 ± 2.02 mg/L ($P<0.05$); the female diabetic patients showed levels of hs-CRP as 5.12 ± 2.14 mg/L for non-diabetic subjects with 1.24 ± 0.56mg/L. **Discussion and conclusions:** Anthropometric parameters were found to be high in diabetic subjects compared with non-diabetic subjects. The high hs-CRP levels in diabetic subjects were observed. Literature was reviewed accordingly. The results concluded that hs-CRP has strong association with diabetic individuals. The significance of hs-CRP in diabetic and non diabetic individuals was discussed.

Keywords: hs-CRP, -Insulin resistance, Diabetes mellitus, biochemical parameters, HbA1C.

Introduction

India has the distinction of having the highest number of T2D individuals worldwide, with a prevalence of 11.6% in urban populations (1, 2). Furthermore, Asian Indians are known to be at a high risk for T2D, CVD, and metabolic syndrome (3, 4). CRP, a pentameric protein produced by the liver has emerged as the 'golden marker for inflammation'. Among several markers of inflammation, hs–CRP is found to be significant in people with diabetes. Hyperglycaemia is an associated factor to the increase of serum CRP levels.**[5]** It is perceived that chronic low-grade inflammation as evidenced by elevated high-sensitivity C-reactive protein (hsCRP) might potentially be a cause underlying the etiology and manifestation of type 2 diabetes (T2D), although the exact mechanisms are still not well understood (6, 7). Additionally, hsCRP has also emerged as a powerful predictor of cardiovascular disease (CVD) (8). However, hsCRP levels are known to vary among populations, influenced by gender, age, and obesity (9). Elevated CRP appears to be better predictor of heart attack risk than an elevated cholesterol level.(10) The highest correlation between CRP and body mass index (BMI) was found, followed by the index of insulin resistance, fasting insulin and insulin sensitivity.(11) It was established that in persons with higher levels of CRP the possibility of diabetes to develop for the period of 3-4 years is greater than those with the normal values for CRP.(12) It was found that CRP is directly associated in atherosclerotic plaque formation. CRP induces the adhesion molecule expression in endothelial cells, stimulates monocyte chemo-attractant protein-1 production and induces complement activations. Binding to oxidized LDL-particles, CRP stimulates macrophage digestion.(13) hs-CRP (high sensitivity C-reactive protein) is the measurement of CRP level with greater accuracy. The lower limit of its measurement is 0.01 mg/L and the measurement is more than 100 times as sensitive as the usual CRP measurement (lower limit 5 mg/L). The median level of hs-CRP from blood samples of apparently healthy donors (median age of 32 years) is 0.3 mg/L.(14) Although hs-CRP levels >10 mg/L are often found in systemic inflammation. Levels <1, 1-3 and >3 mg/L respectively identify patients at low, intermediate and high risk for future cardiovascular events. The prognostic value of CRP level is independent and additive to lipid values.(15)

Materials nd Methods

The study conducted at SVS Medical College and Hospital, Mahabubnagar between August 2008 to July

2011. The subjects were the 200 randomly selected patients attending and/ or admitted to Medicine Out-patient and In-patient departments plus 100 age and sex matched healthy volunteers. A written and informed consent was taken from all the subjects. Ethical clearance was obtained from the Ethical committee of the College. After excluding subjects who smoked (current or within the past 6 months), had any acute infective illness (current or within the past 6 months), or had any chronic illness, a total of 200 subjects and 100 control group individuals were taken for the study. Weight and height measurements were obtained, using standardized technique.**[5]** The BMI was calculated as the weight (kg)/height squared (m)**²**. Blood pressure was recorded in the sitting position by using the right arm with a mercury Sphygmomanometer. Estimation of fasting blood glucose (FBG), post prandial Glucose (PPBG), blood urea serum Creatinine, lipid profile, HbA1c and hs-CRP were done on semi-autoanalyzer (Biotron BTR 830) in our clinical biochemistry laboratory. A Turbidimetric immunoassay for the high sensitive determination of C-reactive protein (hs-CRP) in human serum was used which was based on the principle of agglutination reaction. Measuring Range is 0.15 mg/L to 10 mg/L.

The American Heart Association and US Centers for Disease Control and Prevention have defined risk groups as follows:

Low risk: <1.0 mg/L

Average risk: 1.0 to 3.0 mg/L

High risk: > 3.0 mg/L

Statistics

The results were statistically analyzed with students't' test. The results are expressed as Mean ± Standard deviation (S.D.); $P < 0.05$ was considered statistically significant. To correlate between various parameters, Pearson's correlation coefficient was used.

Observations

The clinical and biochemical characteristics in relation to hs-CRP of the study group were shown in the table-1. In comparison with non-diabetic subjects, the diabetic subjects were older ($P < 0.008$) and had higher BMI ($P<0.006$). They also had higher systolic blood pressure ($P<0.05$) and diastolic pressure blood pressure ($P<0.05$), fasting blood sugar ($P<0.0018$), post prandial blood sugar ($P<0.0016$) HbA1C % ($P<0.001$). hs-CRP levels were significantly higher among the male diabetic subjects with 4.88 ± 2.02 mg/L ($P<0.05$); the female diabetic patients showed levels of hs-CRP as 5.12 ± 2.14 mg/L for non-diabetic subjects with 1.24 ± 0.56mg/L. When the study subjects were characterized as high risk using hs-CRP cut –off >3.0 mg/L , the subjects with abnormal hs-CRP (hs-CRP>3.0 mg/L) were older ($P<0.008$) , and also had higher body mass index ($P<0.006$), systolic pressure ($P<0.05$) than the subjects with normal hs-CRP (hs-CRP < 3.0 mg/L). Fasting plasma glucose ($P<0.001$) and HbA1c ($P<0.05$) were also higher in subjects with abnormal hs-CRP than the subjects with normal hs-CRP.

Table 1: Clinical and Biochemical Characteristics of Study Subjects

Parameter	Study group (n=200)	Control group (n=100)	'p' value
Age (years)	51 ± 08	48 ± 12	0.078
Female (%)	46	41	0.076
BMI (Kg/M^2) Males	25.2 ± 4	20.2 ± 3.6	0.045 *
BMI (Kg/M^2) Females	26.45 ± 4.32	20.92 ± 2.8	0.042*
WC (cm) Males	88.86 ± 10.14	84.36 ± 8.84	0.048*
WC(cm) Females	91.34 ± 9.86	86.20 ± 7.88	0.049*
WHR Males	1.0 ± 0.24	0.86 ± 0.46	0.043*
WHR Females	1.0 ± 0.42	0.88 ± 0.56	0.042*
Fasting blood sugar (mg%)	128 ± 16	80 ± 14	0.034*
Post-prandial blood sugar (mg%)	202 ± 24	108 ± 10	0.025*
Hb A_1C (%)	8.6 ± 1.2	4.5 ± 2.0	0.029*
Blood Urea (mg%)	38.68 ± 14.34	20.56 ± 10.60	0.048*
Serum Creatinine (mg%)	1.6 ± 0.8	0.8 ± 0.6	0.046*
Serum Uric acid (mg%)	5.24 ± 0.88	4.78 ± 1.56	0.052
Total Cholesterol (mg%)	218.86 ± 24.56	168.24 ± 14.42	0.042*
LDL Cholesterol (mg%)	138.58 ± 25.02	94.68 ± 25.68	0.041*
HDL Cholesterol (mg%)	22.68 ± 14.00	36.46 ± 12.68	0.051
Triglycerides (mg%)	184.24 ± 18.46	124.46 ± 15.68	0.038*
Systolic blood pressure (mmHg)	142 ± 09	118 ± 16	0.044*
Diastolic blood pressure (mmHg)	88.8 ± 18.04	78 ± 12	0.042*
hs-CRP (mg/L) Males	4.88 ± 2.02	1.22 ± 0.46	0.0064**
hs-CRP (mg/L) Females	5.12 ± 2.14	1.24 ± 0.56	0.0058**

"p" value less than 0.05 is significant

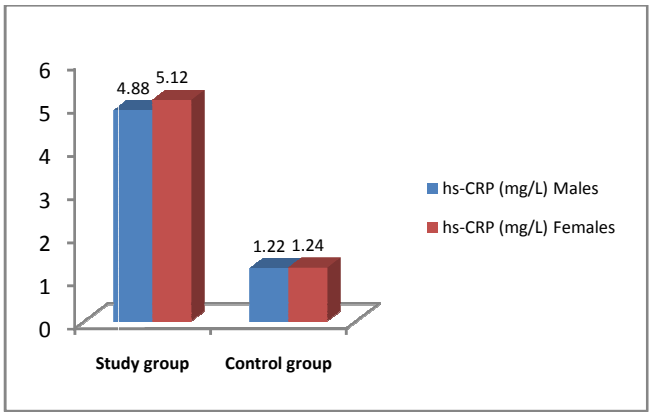

***Figure 1*:** showing the mean hs-CRP levels in the present study

The Odd ratio was zero which showed significant association in the levels of low risk hs-crp between diabetic and healthy control group. Also by applying the chi-square test we found significant association ($p<0.0001$) in each category of hs-CRP in diabetic cases and healthy controls. SE of the difference of mean was 0.2704 and 95% confidence interval for the difference of mean- 3.5535 to 4.6265 with the lower limit was 0.105 and upper limit was 0.308. The correlation between hs-CRP and HbA1c and hs-CRP and anthropometric parameters has been checked by Pearson's correlation coefficient.

Table 5: Spearman's correlations analysis of HbA1c with descriptive characteristics, lipid profile and hs-CRP levels

	Age	**BMI**	**HbA1C**	**TG**	**TC**	**HDL**	**LDL**	**hs-CRP**
Age	1.000	0.054	-0.004	-0.154	-0.162	-0.165	-0.148	-0.098
BMI		1.000	0.346	0.056	-0.064	-0.054	0.046	0.326**
HbA1C			1.000	0.265*	0.109	0.108	-0.122	0.308**
TG				1.000	0.368*	0.128	0.072	0.201
TC					1.000	0.262	0.296**	0.169
HDL						1.000	0.116	0.188
LDL							1.000	0.068
hs-CRP								1.000

*Correlation is significant at the 0.05 level; **Correlation is significant at the 0.01 level.

Discussion

Diabetes mellitus (DM) is characterized by clustered metabolic abnormalities including hyperglycaemia, elevated triglycerides, low HDL cholesterol, and central obesity. Levels of high-sensitivity (hs) C-reactive protein (CRP) are significantly elevated in individuals with DM and are associated with measures of adiposity. The predominant role of adiposity on the regulation of the inflammatory response is not surprising. Adipose tissue is in itself a source of CRP and a major producer of interleukin-6, a key stimulator of CRP secretion. In obesity, adipose tissue contains an increased number of resident macrophages and T cells, which interact closely with adipocytes to modulate the inflammatory response.**[17]** The C-reactive protein derives from the fact that it reacts with capsule polysaccharide of streptococcus pneumonia. It is an acute phase response protein markedly increased in both inflammatory and infectious diseases. It plays an important role in innate immunity.**[3]** In vivo release of interleukin-6, linked closely to CRP pathway which is related to insulin resistance, has been reported in human subcutaneous adipose tissue (SAT). The relatively large SAT mass (truncal and peripheral SAT) in Asian Indians, may generate relatively more CRP and preferentially drive this pathway rather than the insulin resistance pathway, although both appear to be interlinked.**[18]** Persistent and mild elevations in hs-CRP levels in Asian Indians residing in India could be due to increased exposure to repeated infections.[18] Thus, a single value of an elevated CRP level may not have adequate predictive importance for Diabetes mellitus. Diabetic subjects have higher Body Mass Index3 (BMI) which was also proved by our results. BMI have the positive correlation with the obesity which leads to DM.**[19]** Cosin Aguilar from his study state that the obese patients showed higher prevalence of diabetes.**[20]** Higher CRP levels in Asian Indians than white Caucasians, may contribute to a high prevalence of DM in this ethnic group. High CRP concentrations significantly correlate with insulin resistance and the metabolic syndrome in adults.**[18]** In the present study, serum hs-CRP levels were positively related to anthropometric variables such as Body Mass Index (BMI) and Systolic and Diastolic blood pressure which is in relation to other similar previous studies.**[21]** Hb1Ac was higher in the diabetic subjects than normal subjects. The

present study showed the significance increase of hs-CRP in subjects with diabetes mellitus. Also the correlation of hs-CRP with fasting plasma glucose and HbA1c observed is similar to the previous study. Another interesting observation was the relationship of hs-CRP with glycemic control could influence inflammation. In diabetic subjects hs–CRP was positively correlated with HbA1c. Similar results were found in earlier studies.**[22,23, 24, 25, 26, 27]** The present study showed that hs-CRP has a strong association with diabetes mellitus in Central Rural India population. It is also concluded that age and body mass index has strong association with diabetic individuals. It is very well understand that the levels of hs-CRP significantly associated with age, BMI, systolic and diastolic pressure. Also the conclusion has been drawn that elevated hs-CRP level significantly different with different age groups of diabetes mellitus individuals. A limitation of this study was the cross-sectional design. We only performed measurements at one time point. hs-CRP is a sensitive marker for acute phase inflammation and has a high within-subject variability. The findings of this investigation need to be confirmed in a larger number of Asian Indians of both genders, and the clinical significance of the correlations observed in this study need to be evaluated in prospective studies. However, hs-CRP is likely to remain the standard for assessing inflammation because of the availability and ease of use of this assay.

Conclusion

Thus the study concluded that HbA1c, hs-CRP has a strong association with diabetes mellitus in the population of Central Rural India. The present analysis is exploratory in nature, but serves to add clinical insight on the inflammatory burden of the populations residing in our region.

Disclosure

There is no conflict of interest in this work, not funded by any agency or any pharmaceutical firm.

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