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Original Research Article

To study the association of high sensitivity C-reactive protein with metabolic syndrome

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ABSTRACT

Background: Metabolic Syndrome is a constellation of dyslipidemia (elevated triglycerides, low high-density lipoproteins (HDL)), elevation of arterial blood pressure (BP), dysregulated glucose homeostasis, and increased abdominal obesity.
Methods: We studied the association of high sensitivity C-reactive protein with metabolic syndrome by case-control method in our tertiary care hospital in West U.P.
Results: The mean age of cases and controls was 52.6 ± 7.7 and 51.4±7.0 years, respectively. There were 25 (50%) male and 25 (50%) female in case groups, and 27 (54%) males and 23 (46%) females in control group. Our analysis revelaed that there was a significant association between hs-CRP and the central obesity when compared in case-control group (3.57 vs 0.96 mg/L) (p value <0.001). There was no significant association between hs-CRP and high triglycerides, hypertension, diabetes, and reduced high density lipoprotein cholesterol.
Conclusions: Raised hsCRP level can be considered as a surrogate marker of chronic inflammation in patients with metabolic syndrome.

Keywords: Dyslipidemia, hsCRP, Metabolic syndrome, Obesity

INTRODUCTION

Metabolic Syndrome is a cluster of interconnected factors that directly increase the risk of coronary heart disease (CHD), other forms of cardiovascular atherosclerotic diseases (CVD), and diabetes mellitus type 2.

Its main components are dyslipidemia (elevated triglycerides and low high-density lipoproteins (HDL)), elevation of arterial blood pressure (BP), dysregulated glucose homeostasis, and increased abdominal obesity.[1]

Besides the many components and clinical implications of metabolic syndrome, there is still no universally accepted pathogenic mechanism or universally defined diagnostic criteria. High sensitivity C reactive protein (hsCRP) is an acute phase reactant protein that the liver makes, when there is inflammation in the body and a sensitive marker of systemic inflammation, and has been found to be raised in the conditions like diabetes mellitus, cardiovascular disease, peripheral vascular disorders etc.[2-4]

METHODS

The present study was undertaken at Subharti Medical College and hospital, Meerut, Uttar Pradesh, India between June 2015 and March 2017.

Study was carried out to determine the correlation between highly sensitive C-reactive protein and metabolic syndrome. Patient aged more than 18years, 50 cases (Metabolic syndrome) and 50 controls, from both Out-patient department and in-patient department of medicine, were enrolled. It was a case-control study. The components of metabolic syndrome were defined according to the International Diabetes Federation (IDF) 2005 for South Asians.[5] Height and weight were measured. Waist circumference was measured using a non-elastic measuring tape at the highest level of iliac crest with the patient standing with feet 1 foot apart. Systolic and diastolic blood pressure was measured by sphygmomanometer. Individuals reporting a history of hypertension and current antihypertensive medication use were defined as having hypertension regardless of the blood pressure values measured at the time of evaluation.

In all the patients, a peripheral venous blood sample was drawn in the morning after 12hours of fasting, to measure venous fasting plasma glucose, serum total cholesterol, serum high density lipoprotein (HDL) cholesterol, and serum triglyceride levels. Serum glucose was measured by the glucose oxidase method; plasma triglycerides, total cholesterol and HDL-cholesterol were measured by enzymatic colorimetric assay using autoanalyser.

Serum hs-CRP levels were determined by particle enhanced immune-turbidometric assay using autoanalyser with dedicated reagents.

The measured parameters were expressed as Mean ±Standard deviation. The data generated were compared using student 't' test/ANOVA test at 5% level of significance. Correlations between the parameters were done using Pearson's correlation coefficient test at 5% level of significance. The data were analysed using SPSS version 15 (SPSS Inc.). The median hs-CRP levels were compared in patients with or without various components of metabolic syndrome using Mann-Whitney U test.

RESULTS

Their mean age was 52.6±7.7years for cases and 51.40±7.9years for controls. Fifty patients satisfying the criteria for metabolic syndrome and Fifty Control were studied. There were 25 (50%) male and 25 (50%) female in case groups and 27 (54%) males and 23 (46%) females in control group. Out of 50 cases studied, 41 (82%) had raised fasting glucose, 38 (76%) had hypertension, 44 (88%) had raised serum triglycerides, and 30 (60%) had low serum HDL levels (Table 1).

Table 1: Components of metabolic syndrome in different genders in case group.

Variable	Elevated Fasting Glucose (%)	Hypertension (%)	Obesity (%)	High serum Triglycerides (%)	Low serum High density Lipoprotein Cholesterol (%)
Males (n =25)	23 (88)	20 (80)	25(100)	22 (88)	14 (56)
Females (n= 25)	18 (72)	18 (72)	25(100)	22 (88)	16 (64)
Overall (n=50)	41 (80)	38 (76)	50(100)	44 (88)	30 (60)

In 41 diabetic patients, the mean hsCRP was 3.62mg/L as compared to 9 non-diabetic patients, mean hsCRP was 3.34mg/L which was insignificant (p value =0.44) (Table 2). In 38 hypertensive patients the mean hs-CRP was 3.68 compared to non-hypertensive group where the mean hs-CRP was 3.23mg/L (p value=0.17) (Table 2).

In 44 cases with high triglyceride and 6 cases without these criteria, the mean hsCRP values were 3.66 and 2.9mg/L, which were insignificant (p value 0.07).

In 14 males with low HDL and 11 males with normal HDL, the mean hs-CRP values were 3.92 and 3.30mg/L respectively, which was insignificant (p value=0.14). (Table 2). In 16 females with low HDL and 9 females with normal HDL, the mean hs-CRP values were 3.31 and 3.83mg/L respectively, which was insignificant (p value=0.16) (Table 2).

In 50 cases having abnormal waist circumference criteria, the mean hsCRP was 3.56mg/L, compared with patients having normal waist circumference whose mean hsCRP was 0.96mg/L, which was highly significant (p value <0.001) (Table 3). The metabolic syndrome patients were further grouped in terms of number of criteria satisfied. Out of 50 cases, 11 (22%) were satisfying 3 criteria, 25 (50%) 4criteria and 14 (28%) five criteria.In the minimal 3 criteria group (which is required for the metabolic syndrome as per IDF) mean hsCRP was 2.81mg/L. We measured the hs-CRP levels with increasing components of metabolic syndrome. With minimum three components of metabolic syndrome, the mean value was 2.81mg/L; with 4 components, the mean value was 3.76mg/L; and with all the five components, the mean value was 3.80mg/L, showing an increase in mean hsCRP values with increasing component of metabolic syndrome (Figure 1).

Table 2: comparison of hsCRP levels between patients with and without various components of metabolic syndrome in cases.

Metabolic syndrome component in cases	Mean hs-CRP ±SD (mg/l)	P-value
Male (n=25)	3.65± 1.11	
Female(n=25)	3.50±0.85	0.59
Diabetes		
Yes (n=41)	3.62±0.96	
No (n= 9)	3.34±1.09	0.44
Hypertension		
Yes (n= 38)	3.68±1.2	0.17
No (n=12)	3.23±0.9	
High TG		
Yes (n= 44)	3.66±0.96	
No (n=6)	2.90±0.91	0.07
Low HDL		
Male		
Yes (n=14)	3.92±1.16	
No (n=11)	3.30±0.99	0.14
Female		
Yes (n=16)	3.31±0.88	0.16
No (n=9)	3.83±0.72	

hs-CRP = C-reactive protein; HDL = high density lipoprotein cholesterol; TG = serum triglycerides; BP = blood pressure

Table 3: Association of central obesity (abdominal circumference) with mean hsCRP in cases and control.

Parameters	Cases (mean ±SD)	Controls (mean ±SD)	P value
ABD (cm)	94±6.0	71±8.01	<0.001
hsCRP (mg/l)	3.57±0.98	0.96±0.44	

Table 4: Distribution of each component of the metabolic syndrome in various published studies.

Study (reference)	Elevated Fasting Glucose (%)	Hypertension (%)	Obesity (%)	High TG (%)	Low HDL (%)
Bo et al[17] N = 1877	18	66	36	30	8
Florez et al[14] N = 190	31	70	80	32	46
Ramachandran et al[18] n = 475	26	55	31	45	65
Present study N = 50 cases	82	76	100	88	60

Mean age in case group was 52.6years while in control group it was 51.4years. While the mean hsCRP in case group was 3.57 while in control group it was 0.96mg/L, showing a definite increased in case group, which was significant (p value<0.001). Comparative analysis reveals mean age in case group was 52.6years while in control group it was 51.4years. While the mean hsCRP in case group was 3.57 while in control group it was 0.96mg/L, showing a definite increased in case group (Figure 2).

DISCUSSION

The distribution of each component of the metabolic syndrome according to the modified NCEP-ATPIII criteria for metabolic syndrome in other published studies and our study is depicted in (Table 4). Bo et al concluded in their study that hypertension (66%) was more prevalent among metabolic syndrome patients while Florez et al concluded maximum prevalence of hypertension (70%) and obesity (80%) in their study.

Our study revealed maximum prevalence of raised triglycerides (88%) followed by raised blood sugar (82%) and hypertension (76%). Obesity was present in all cases as part of IDF criteria for diagnosing metabolic syndrome.

In adults in the United States participating in the third National Health and Nutrition Examination Survey (NHANES III) prevalence of metabolic syndrome was 22

per cent, with an age dependent increase (6.7%, 43.5%, and 42% for ages 20 to 29, 60 to 69, and >70years, respectively).[6] Similar observations were reported by Gupta et al in their population based study.[7] This is due to the increasing prevalence of diabetes, hypertension, and dyslipidaemia in the ageing population.

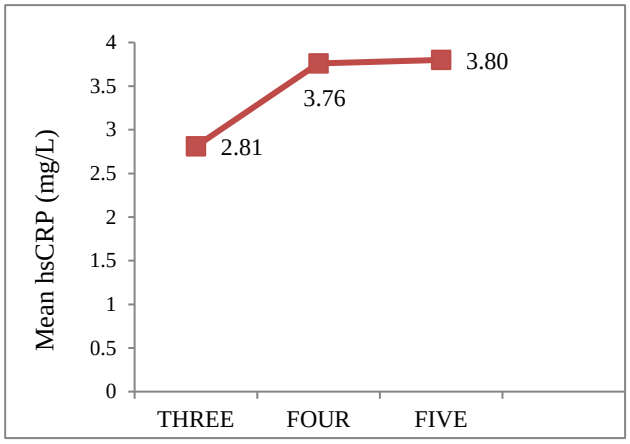

Figure 1: Relation of mean hsCRP with increasing components of metabolic syndrome.

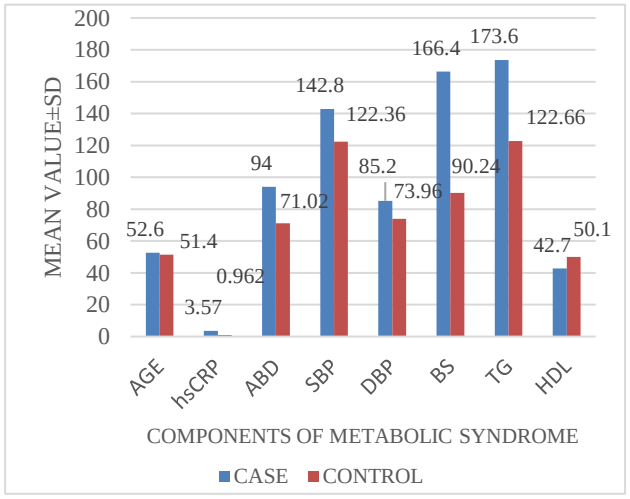

Figure 2: Age-matched comparison of various components of metabolic syndrome and hsCRP in cases and controls.

In Korean population, it was observed that in participants aged 40-69years, the mean hs-CRP level increased according to age and was observed to be 1.2, 1.5 and 1.6mg/L for the age groups 40-49, 50-59, and 60-69 years, respectively.[8] The hs-CRP value increases with age, presumably reflecting the increasing incidence of sub-clinical inflammation as the age advances.

When we compared the mean hs-CRP levels of each of the age groups, (<50, and >50years), it was found to be 3.72 and 3.45mg/L, which was insignificant (p value= 0.34), probably because of the small sample size (n=50) of our study population and increased mean value of components of metabolic syndrome in age-group less than 50years.

Our study group had higher prevalence of various components of metabolic syndrome when compared with other studies (Table 4). This was because ours was a hospital-based study while all others were population-based studies.

Our analysis revealed that there was a significant association between hs-CRP and the central obesity when compared in case-control group (3.57 vs 0.96 mg/L) (p value <0.001). Several studies have showed that central obesity is associated with high hs-CRP levels.[9] In some other studies, it was observed that diabetes mellitus was associated with elevated hs-CRP levels.[10,11] A positive association between high blood pressure and elevated hs-CRP was noted in some studies but our study did not show any association between hypertension and elevated hs-CRP level.[12,13]

In our study, central obesity is shown to have the highest association with high hs-CRP levels (p<0.001). Florez et al also found that abdominal obesity was the single most important component associated with increased hsCRP levels in 190 subjects with metabolic syndrome (p = 0.001).[14,15] In the Insulin Resistance Atherosclerotic Study (IRAS), a strong association was found between hs-CRP and measures of body fat (p = 0.0001).[15] It is well documented that the synthesis of CRP in the liver is under the control of interleukin-6 and tumour necrosis factor alpha (TNF-α), cytokines that are released or induced by adipose tissue, which could be the link between obesity and the elevation of CRP levels.[16] Hence, the most important determinant of the systemic chronic low-grade inflammation is probably central obesity.

In our study, we also found that there was higher mean concentration of hs-CRP with increasing number of components of the metabolic syndrome. Patients satisfying 3, 4, and 5 criteria had a mean hs-CRP of 2.81, 3.76, and 3.80mg/L respectively. As expected there was positive association with increasing number of abnormal components of the syndrome. Bo et al also found similar findings, the mean hs-CRP for those with 0, 1, 2, 3, 4, 5 components of the metabolic syndrome were 1.9, 1.8, 2.9, 4.1, 4.1, and 5.3 mg/L (p = 0.001).[17,18] This suggests the fact that higher the number of components of metabolic syndrome in a patient, higher the risk of cardiovascular events.

CONCLUSION

There is highly significant correlation present between central obesity and hsCRP. There is increase in hsCRP with increasing number of metabolic syndrome components. The addition of hsCRP to the present definition of the metabolic syndrome may help identify patients at high risk for future diabetes and cardiovascular

disease. Hence, raised hsCRP level can be considered as a surrogate marker of chronic inflammation in patients with metabolic syndrome.

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