

Original Article

Association of hs-CRP in Centrally Obese Patients with and without Metabolic Syndrome- A Clinical Study

Bhupinder Singh¹, Ashwani Kumar Sharma², Harsh Bala Gupta³, Hardeep Singh Nirman⁴, Simranjit Kaur⁵

^{1,3,4}Associate Professor, ²Professor, ⁵Junior Resident, Department of Medicine, G.M.C. Amritsar, Punjab, India

ABSTRACT:

Background: Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health. The present study has been designed to determine the correlation of hs-CRP in centrally obese patients with and without metabolic syndrome. **Materials & Methods:** The present study comprised of one hundred (100) obese patients, over 20 years of age. In all subjects, blood pressure and body weight was measured. Body Mass Index (BMI) and Waist circumference (WC) were measured. hs- CRP was performed with 'Dr. Turbichem hs-CRP diagnostic kit. **Results:** All the patients (100%) had central obesity. Out of the total, fifty 50 (50%) were fulfilling the criteria for metabolic syndrome. Fifty patients with metabolic syndrome comprised of 33 males (66%) and 17 females (34%), with male to female ratio as 1.94: 1. Most of the patients i.e. 29 (58%) were between 41 to 60 years of age. A significant difference in mean hs CRP value in subjects with different waist circumference, triglycerides (mg/dl), HDL cholesterol, blood pressure (mmHg), fasting glucose (mg/dl), number of criteria and presence or absence of metabolic syndrome. **Conclusion:** High sensitivity CRP can be used as surrogate marker of chronic inflammation in metabolic syndrome. There was a significant increasing trend in mean levels of hs-CRP as the components of metabolic syndrome increased, suggesting the fact that higher the number of components of metabolic syndrome in a patient, higher the risk of cardiovascular events.

Key words: Metabolic syndrome, Obesity, Triglyceridemia.

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Corresponding author: Dr. Hardeep Singh Nirman, Associate Professor, Department of Medicine, G.M.C. Amritsar, Punjab, India

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INTRODUCTION

Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health. A person with a BMI of 30 or more is generally considered obese. A person with a BMI equal to or more than 25 is considered overweight.¹ The prevalence of overweight and obesity among children and adolescents aged 5-19 has risen dramatically from just 4% in 1975 to just over 18% in 2016. The rise has occurred similarly among both boys and girls: in 2016, 18% of girls and 19% of boys were overweight.² In India obesity is emerging as an important health problem particularly in urban areas, paradoxically co-existing with under-nutrition. Almost 30-65% of adult urban Indians are either overweight or obese or have abdominal obesity.³ Among the numerous comorbidities of

obesity, central obesity hyperglycemia, hypertension and circulating hypertriglyceridemia (dyslipidaemia), cluster together to define metabolic syndrome.⁴ Clinical criteria for the diagnosis of Metabolic Syndrome according to three definitions, proposed by the various Health Organizations.⁵ (IGT- Impaired Glucose Tolerance, T2D- Type II Diabetes, IFG- Impaired fasting glucose), WHR (Waist Hip Ratio). The rise in C-reactive protein (CRP) as a response to the increase in the secretion of cytokines of adipose origin detected in obese individuals has been used as a marker of cardiovascular risk and diabetes in adults.

The difference between CRP and hs-CRP is contained in the "hs" abbreviation; "high sensitivity". CRP is traditionally measured down to concentrations of 3-5 mg/L, whereas hs-CRP measures down to concentrations around

0.3 mg/L. This improved sensitivity allows hs-CRP to be used to detect low levels of chronic inflammation. A Physicians' Health study indicated that the predictive value of hs-CRP was independent of other risk factors such as blood cholesterol and smoking. The results also suggested that hs-CRP was a better predictor of cardiovascular events than several other inflammatory biomarkers.⁶

AIM OF STUDY:

To determine the correlation of hs-CRP in centrally obese patients with and without metabolic syndrome and to study the correlation of hs-CRP with various components of metabolic syndrome.

MATERIALS & METHODS

The present study comprised of one hundred (100) obese patients, over 20 years of age presenting to the Department of Medicine, OPD & IPD of Guru Nanak Dev Hospital attached to Government Medical College Amritsar. Written, informed consent was obtained from all participants beforehand.

Inclusion criteria

Centrally obese individuals fulfilling the modified NCEP ATP III criteria for metabolic syndrome.

Exclusion criteria

1. Critically ill patients.
2. Patients of acute & chronic Liver, kidney and thyroid dysfunction
3. Pregnant females.

After thorough history including personal, occupational, & family history, complete physical examination was done in all subjects to exclude any significant systemic illness. Blood pressure and body weight was measured. Body Mass Index (BMI) was calculated as weight in kg/height in m². Waist circumference (WC) to the nearest 0.1 cm was measured. Other investigations included haemoglobin, total leukocyte count (TLC), differential leukocyte count (DLC), fasting and Random blood glucose levels, renal profile- blood urea, S. creatinine, lipid profile- cholesterol, triglycerides, HDL and LDL. hs-CRP was performed with 'Dr. Turbichem hs-CRP diagnostic kit for determination of high sensitivity C reactive protein. Results were tabulated and subjected to statistical analysis. P value less than 0.05 was considered significant.

RESULTS

Table I Distribution of subjects

| Total- 100 | | |
|-----------------|-------------------------|----------------------------|
| Central Obesity | With Metabolic Syndrome | Without Metabolic Syndrome |
| Number | 50 | 50 |

Table I shows that all the patients (100%) had central obesity. Out of the total, fifty 50 (50%) were fulfilling the criteria for metabolic syndrome.

Table II Age & Gender distribution of the patients

| Assoc. of Met. S | Age Group | Male | Female | Sub-total | Total |
|--------------------------|-------------|------|--------|-----------|------------|
| With Met. S (n=50) | <40 yrs. | 04 | 03 | 07 (14%) | |
| | 41- 60 yrs. | 21 | 08 | 29 (58%) | |
| | >61 Yrs. | 08 | 06 | 14 (28%) | |
| Total | | 33 | 17 | 50 (100%) | 50 (50%) |
| Without Met. S (n=50) | <40 yrs. | 04 | 04 | 08 (16) | |
| | 41- 60 yrs. | 17 | 13 | 30 (60%) | |
| | >61 Yrs. | 06 | 06 | 12 (24%) | |
| Total | | 27 | 23 | 50 (100%) | 50 (50%) |
| Grand Total | | | | | 100 (100%) |

Table II shows that fifty patients with metabolic syndrome comprised of 33 males (66%) and 17 females (34%), with male to female ratio as 1.94: 1. Most of the patients i.e. 29 (58%) were between 41 to 60 years of age. The maximum number of male patients (21) was between 41 to 60 years of age and 8 were more than 61 years of age. Only 4 male patients were less than 40 years of age.

Table III Patients fulfilling the criteria of metabolic syndrome

| BP: >130/85 | FBS: >100 mg% | Low HDL M<40, F<50 | Triglycerides: >150 mg% |
|-------------|---------------|-----------------------|-------------------------|
| 26 | 28 | 18 | 19 |

Table III shows that all the fifty (50) patients were centrally obese. Of them, 26 (52%) had high blood pressure, 28 (56%) had raised fasting blood sugar levels (hyperglycaemia), 18 (36%) had low levels of high Density Lipoproteins (HDL) and 19 (38%) were having high levels of triglycerides.

Table IV Mean adjusted values of hs-CRP

| Parameters | No. of subjects | Mean hs-CRP | P-Value |
|--|-----------------|-------------|---------|
| Waist circumference | | | |
| >102cm in men and 88 cm in women | 100 | 1.58 | <0.0001 |
| <102 cm in men and 88 cm in women | | | |
| Triglycerides (mg/dl) | | | |
| >150 | 39 | 3.74 | <0.001 |
| <150 | 61 | 0.92 | |
| HDL cholesterol | | | |
| <40 mg/dl in men and 50 mg/dl in women | 23 | 4.18 | <0.001 |
| ≥40 mg/dl in men and 50 mg/dl in women | 77 | 1.20 | |
| Blood pressure (mmHg) | | | |
| >130/85 | 51 | 3.03 | <0.001 |
| <130/85 | 49 | 0.81 | |
| Fasting glucose (mg/dl) | | | |
| >100 | 48 | 3.16 | |
| <100 | 52 | 0.84 | <0.001 |
| Number of Criteria | | | |
| 1 | 31 | 0.54 | <0.001 |
| 2 | 19 | 1.07 | |
| 3 | 20 | 2.59 | |
| 4 | 18 | 3.90 | |
| 5 | 12 | 5.75 | |
| Metabolic syndrome | | | |
| Yes | 50 | 3.63 | <0.001 |
| No | 50 | 0.70 | |

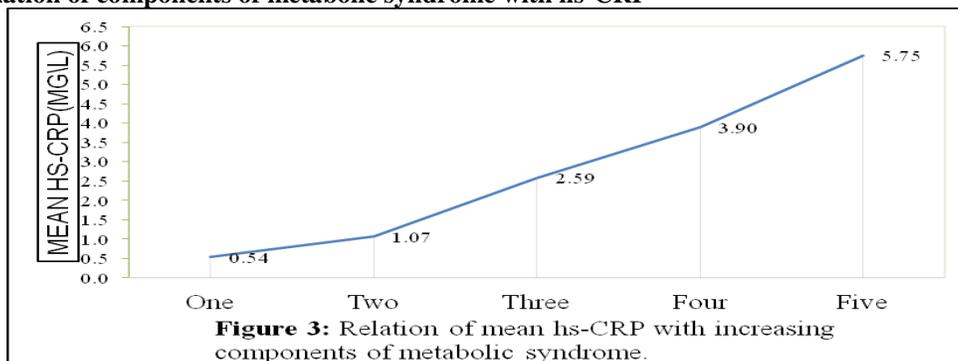
Table IV shows significant difference in mean hs CRP value in subjects with different waist circumference, triglycerides (mg/dl), HDL cholesterol, blood pressure (mmHg), fasting glucose (mg/dl), number of criteria and presence or absence of metabolic syndrome.

Table V Correlations between response variable and controlled variables

| Pearson Correlation coefficients (r) | hs-CRP | P-value |
|--------------------------------------|--------|---------|
| Triglycerides | 0.71 | <0.001 |
| High blood pressure | 0.70 | <0.001 |
| Fasting glucose | 0.62 | <0.001 |
| Waist circumference | 0.60 | <0.001 |
| HDL cholesterol | -0.62 | <0.001 |

Table V describes that the correlation between hs-CRP and triglycerides is 0.71, hs-CRP & high blood pressure is 0.70, hs-CRP & fasting blood glucose is 0.62 and hs-CRP & waist circumference is 0.60. It shows that these four relationships are significant (P<0.001).

Graph I Correlation of components of metabolic syndrome with hs-CRP



Graph I shows the correlation of components of metabolic syndrome with hs-CRP, depicts that with increasing components of metabolic syndrome, the levels of hs-CRP also increase.

Table VI Median hs -crp present of metabolic syndrome

| Present of Metabolic syndrome | Median of HS-CRP |
|--|------------------|
| Triglycerides | 3.8 |
| Triglycerides + High blood pressure | 4.1 |
| Triglycerides + High blood pressure + fasting glucose | 5.1 |
| Triglycerides + High blood pressure + fasting glucose +HDL | 6.0 |

Table VI shows that with minimum three components of metabolic syndrome i.e. Triglycerides + High blood pressure + Fasting glucose, the median value of hs-CRP was 5.1. With four components (Triglycerides + High blood pressure + Fasting glucose+ HDL), it was 6.0

DISCUSSION

The metabolic syndrome is a cluster of the heart attack risk factors: diabetes and pre-diabetes, abdominal obesity, high cholesterol and high blood pressure. It is estimated that around a quarter of the world's adult population have metabolic syndrome and they are twice as likely to die from and three times as likely to have a heart attack or stroke compared with people without the syndrome. In addition, people with metabolic syndrome have a fivefold greater risk of developing type II diabetes. The clustering of CVD risk factors that typifies the metabolic syndrome is now considered to be the driving force for a CVD epidemic.^{7,8}

The underlying cause of the metabolic syndrome continues to challenge the experts but both insulin resistance and central obesity are considered significant factors. Genetics, physical inactivity, ageing, a pro-inflammatory state and hormonal changes may also have a causal effect, but their role may vary depending on ethnic group. Various clinical studies affirm correlation of circulating markers of inflammation with propensity to develop cardiovascular events.

In our study with 100 centrally obese persons, and fifty patients fulfilling the criteria of metabolic syndrome, males were 66% and females were 34%. It is a hospital based study and hence the number of males is likely to be high reflecting a social bias. In the study of Vidyasagar et al (2013)⁹, majority of the patients with metabolic syndrome (60.4%) were in the age group of 40-60 years, the next major group was patients of > 60 years (36.3%).

In our analysis, it has been revealed that there was a significant association between hs-CRP and various components of metabolic syndrome. It was more so with rising triglyceride levels (3.74 vs 0.92 mg/l, p<0.001) then with fasting glucose (3.16 vs 0.84 mg/l, p<0.001). Several studies have shown that central obesity is associated with high hs-CRP levels.¹⁰ In some other studies, it has been observed that diabetes mellitus is associated with elevated hs-CRP levels.¹¹

Our study included one hundred centrally obese patients who were assessed for other components of metabolic syndrome (hypertension, dyslipidemia, raised fasting blood sugar and low HDL). The findings revealed that there is a strong positive association between hs-CRP in centrally

obese patients and fasting hypertriglyceridemia, elevated levels of fasting blood sugar and high blood pressure.

Among 100 participants, 58% were males and 42 % were females. The mean age of the study population was found to be 53.49 ± 9.79 years. In this study 50% participants were with metabolic syndrome and 50% were without metabolic syndrome. A significantly higher mean hs-CRP levels were found in participants with high blood pressure (3.03 mg/l, P<0.001), triglycerides (3.74 vs 0.92 mg/l, P<0.001) and fasting glucose (3.16 vs 0.84 mg/l, P<0.001). Also, participants with low HDL cholesterol presented higher levels of hs-CRP (4.18 vs 1.20 mg/l, P<0.001), the difference is statistically significant.

Triglycerides are highly atherogenic important component of plasma lipids. They are commonly elevated among the type-2 diabetics, familial combined hyperlipidemia or overweight people especially those with metabolic syndrome, contributing to cardiovascular risk due to atherogenesis. Multiple research studies suggest that fasting triglycerides are considered to be independent risk factor for CAD but recently some researchers have laid more stress on non-fasting TG as strong predictor of CAD and death.¹¹

An increasing number of components of metabolic syndrome were associated with an increase in hs-CRP mean levels from 0.54 to 5.75 mg/l. Participants with metabolic syndrome, defined as an aggregate of any three or more of these components, presented with significantly higher adjusted mean levels of hs-CRP (3.63 vs 0.70 mg/l, P<0.001). Mugabo & Renier (2010)¹² suggested that Impaired glucose tolerance in centrally obese patients as shown by elevated fasting blood sugar closely correlates with increasing hs-CRP owing to interference in insulin action. Current evidence supports a central role of inflammation in the pathogenesis of atherosclerosis in diabetes. This alteration may contribute to the accelerated development of vascular disease in patients with type 2 diabetes. It suggests that marked clinical benefit can be obtained by aggressive management of fasting hyperglycemia in patients at risk of metabolic syndrome.

In model one, it is seen that the triglycerides and hs-CRP is highly significantly associated (p-value <0.001). hs-CRP was 4% increased by one unit increase of triglycerides. The predicted geometric mean value of hs-CRP is 0.005. In the

model two, high blood pressure also included and it was seen predicted geometric mean value of hs-CRP is increased 0.005 to 0.022 compared to model one.¹³ This suggests the fact that higher the number of components of metabolic syndrome in a patient, higher the risk of cardiovascular events. More recently it was considered that measurement of CRP should be added in the metabolic syndrome components as it was closely related with other components of the syndrome.¹⁴

CONCLUSION

High sensitivity CRP can be used as surrogate marker of chronic inflammation in metabolic syndrome. The findings revealed that there is a strong positive association between hs-CRP in centrally obese patients and fasting hypertriglyceridemia, elevated levels of fasting blood sugar and high blood pressure and a negative correlation between hs-CRP and HDL. There was a significant increasing trend in mean levels of hs-CRP as the components of metabolic syndrome increased, suggesting the fact that higher the number of components of metabolic syndrome in a patient, higher the risk of cardiovascular events. This insight into the role of inflammation in the pathobiology of cardiovascular events has initiated important new areas of direct clinical relevance.

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