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## CORRELATION OF THE LEVELS OF HIGH SENSITIVITY C-REACTIVE PROTEIN (hs-CRP) IN PATIENTS DIAGNOSED WITH METABOLIC SYNDROME

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### Keywords:

International diabetes federation, Diabetes mellitus, Hypertension, Metabolic syndrome, High sensitivity C-reactive protein

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**ABSTRACT: Objectives:** Metabolic syndrome (MetS) is a cluster of several metabolic disorders including hyperglycemia, reduced high density lipoprotein cholesterol (HDL-C), raised triglyceride level in serum, hypertension and abdominal obesity. The independent risk factors of high sensitivity C-reactive protein (hs-CRP) levels may have a significant impact on evaluating the prevalence of MetS components in both men and women. **Methods:** The present study was conducted at Shri Ramkrishna Institute of Medical Sciences and Sanaka Hospital, Durgapur, West Bengal. The study includes 100 patients with MetS as a case and 100 healthy volunteers as a control. MetS was diagnosed according to international diabetes federation. **Results:** In our study the level of hs-CRP is high in metabolic syndrome patients (4.88  $\mu\text{g/ml}$ ) compared to control group is (1.699  $\mu\text{g/ml}$ ) A statistically highly significant difference was observed among two groups ( $p < 0.000$ ). **Conclusions:** The level of hs-CRP maybe used as a surrogate marker of chronic inflammation in metabolic syndrome patients and higher levels of the inflammatory marker hs-CRP are correlated with rise risk for development of cardiovascular disease and diabetes mellitus.

**INTRODUCTION:** Metabolic syndrome (MetS) is a group of signs and symptoms which include abdominal obesity, elevated blood pressure (BP) and insulin resistance (IR). It is related to increased risk of Type 2 Diabetes Mellitus (DM), chronic kidney disease, cardiovascular disease (CVD) is an important cause of mortality<sup>1</sup>. CVD is the most common cause of death globally and a significant contributor to morbidity, accounting for 17.8 million deaths worldwide, 330 million years of life lost, and 35.6 million years of disability<sup>2</sup>.

Persons with MetS are two times more at risk to die and three times more at risk to suffer from a heart attack or stroke<sup>3</sup>. Early diagnosis of the MetS is desirable as lifestyle interventions and adequate treatment of risk factors associated with the MetS can prevent CVD. Previous research showed that an increased waist circumference (WC) was a reliable first step in detecting individuals with the MetS and was easy to perform<sup>4</sup>.

The independent risk factors of hs-CRP levels may have a significant impact on evaluating the prevalence of MetS components in both men and women. Moreover, research has shown that there is a correlation between BMI and the increase in hs-CRP levels in adults<sup>5</sup>. Expanded adipose tissue also leads to the overproduction of proinflammatory cytokines, including C-reactive protein

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(CRP), interleukin-6 (IL-6) and tumor necrosis factor alpha (TNF), by monocyte-derived macrophages in adipose tissue. Several studies have shown that hs-CRP is positively associated with fasting insulin, IR and MetS. Previous studies have also indicated that hs-CRP positively correlates with many chronic diseases, such as hypertension (HTN), DM and dyslipidemia. Lifestyle can also have an impact on hs-CRP levels. Furthermore, lifestyle factors, such as smoking and drinking, can elevate the hs-CRP level<sup>6</sup>. Inflammation plays a pivotal role both in the development of IR and MetS<sup>7</sup>. There are suggestions to include hs-CRP as one of the diagnostic criteria for metabolic syndrome<sup>8</sup>.

### AIMS & OBJECTIVES:

1. Selection of the MetS patients and control subjects.
2. Measurement of systolic and diastolic BP, and WC in MetS patients and control subjects.
3. Assay of fasting blood sugar, lipid profile, C-reactive protein in MetS and control subjects.

**MATERIAL AND METHODS:** The study has been conducted between November 2022 to August 2023.

**Study Area:** The present study was conducted in the department of Biochemistry in collaboration with department of Medicine, Shri Ramkrishna Institute of Medical Sciences and Sanaka Hospital, Durgapur, West Bengal, India.

### Diagnosis of Metabolic Syndrome according to International Diabetes Federation (IDF)<sup>9</sup>:

- Waist circumference (WC)  $\geq 90$  cm for men and  $\geq 80$  cm for women) along with presence of any two of the following.
- Increased triglyceride:  $\geq 150$  mg/dl.
- Decreased high density lipoprotein cholesterol (HDL-C):  $< 40$  mg/dl in men,  $< 50$  mg/dl in women.
- Systolic blood pressure (SBP)  $\geq 130$  mm Hg or diastolic blood pressure (DBP)  $\geq 85$  mm Hg.
- Increased fasting blood Sugar (FBS)  $\geq 100$  mg/dl.

### Study Population:

**Group 1:** 100 subjects with MetS (diagnosed according to IDF criteria).

**Group 2:** 100 healthy Volunteers controls (age and sex matched) without MetS.

Informed consent has been taken from the participants in the study.

**Inclusion Criteria:** Patients with MetS was diagnosed according to IDF criteria above 35 years of age.

### Exclusion Criteria:

1. Patients taking other hormonal therapy like steroids and thyroxine.
2. Patients with thyroid disorders.
3. Pregnancy.
4. Patients with hs-CRP  $\geq 10$   $\mu\text{g/ml}$  were excluded from the study group.

**Waist Circumference Measurement:** WC was measured with a tape in a horizontal plane, mid way between the inferior margin of the ribs and the superior border of the iliac crest.

**Ethical Approval:** The study was approved by the institutional ethics committee.

**Sample Collection:** 5 ml of blood sample was aseptically collected as per the standard guidelines and protocol. Serum was allowed to separate and subsequently analyzed for various parameters. FBS was assayed by glucose oxidase and peroxidase method, triglyceride by glycerol-oxidase peroxidase, and HDL-C by enzymatic assay method. Serum hs-CRP levels was measured by Chemiluminescence immunoassay (CLIA) method.

**Statistical Analysis:** Data obtained was analysed by using SPSS 23 version software and results was compared in cases and controls. P value  $< 0.05$  was taken as significant at 95% confidence intervals. Student's t-test was used to find the association between hs-CRP and various components of MetS (WC, FBS, SBP, DBP triglyceride, and HDL-C).

**RESULT:** The total number of patients in our study were 200 (100%) out of which 100 (50%)

were healthy controls subjects and 100 (50%) with MetS patients were considered.

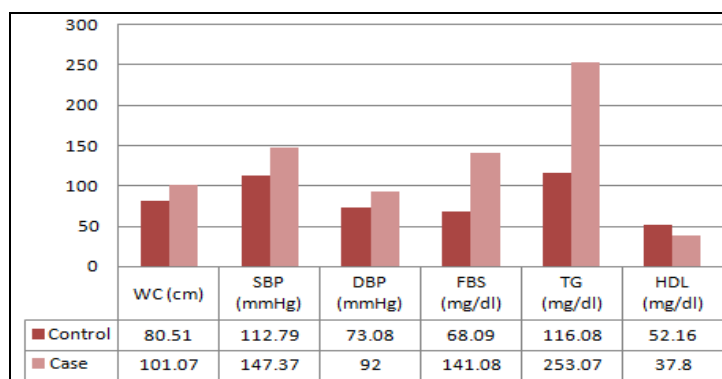
**TABLE 1: COMPARISON BETWEEN VARIOUS COMPONENTS OF METS PATIENTS AND CONTROL SUBJECTS**

Parameters	Control	Case	p-value
WC (cm)	80.51±4.68	101.07±8.0	<0.000
SBP (mmHg)	112.79±6.57	147.37±21.24	<0.000
DBP (mmHg)	73.08±5.38	92.0±10.96	<0.000
FBS (mg/dl)	68.09±6.05	141.08±56.02	<0.000
TG (mg/dl)	116.08±28.07	253.07±114.7	<0.000
HDL (mg/dl)	52.16±6.03	37.80±14.49	<0.000

WC: Waist circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FBS: Fasting blood sugar; TG: Triglyceride; HDL-C: High-density lipoprotein cholesterol; p<0.05 is considered significant.

**Table 1** shows that the mean and standard deviation (SD) of WC for control subjects is 80.51±4.68 cm and for MetS patients is 101.07±8.0 cm. A statistically highly significant difference was observed among two groups (p<0.000). The mean and SD of SBP for control subjects is 112.79±6.57

mmHg and for MetS patients, is 147.37±21.24 mmHg. A statistically highly significant difference was observed among two groups (p<0.000). The mean and SD of DBP for control subjects is 73.08±5.38 mmHg and for MetS patients is 92.0±10.96 mmHg. A statistically highly significant difference was observed among two groups (p<0.000). The mean and SD of FBS for control subjects is 68.09±6.05 mg/dl and for MetS patients is 141.08±56.02 mg/dl. A statistically highly significant difference was observed among two groups (p<0.000). The mean and SD of TG for control subjects is 116.08±28.07 mg/dl and for MetS patients is 253.07±114.7 mg/dl. A statistically highly significant difference was observed among two groups (p<0.000). The mean and SD of HDL-C for control subjects is 52.16±6.03 mg/dl and for MetS patients is 37.80±14.49 mg/dl. A statistically highly significant difference was observed among two groups (p<0.000).



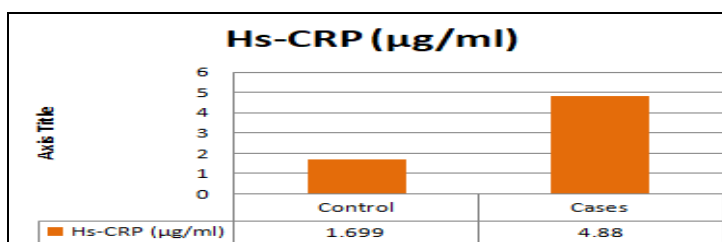
**FIG. 1: BAR DIAGRAM SHOWING RESULTS OF WC, SBP, DBP, FBS, TG AND HDL-C AMONG METABOLIC SYNDROME PATIENTS AND CONTROL SUBJECTS**

**TABLE 2: MEAN HS-CRP LEVEL IN METS PATIENTS AND CONTROLS GROUPS**

Hs-CRP (µg/ml)	Group	Mean	SD	P
	Case	4.88	0.61	<0.001
	Control	1.699	1.45	

**Table 2** shows that mean and standard deviation of Hs-CRP for control subjects is 1.699 µg/ml and for MetS patients is 4.88 µg/ml. A statistically highly

significant difference was observed among two groups (p<0.000).



**FIG. 2: BAR DIAGRAM SHOWING RESULT OF HS-CRP AMONG METABOLIC SYNDROME PATIENTS AND CONTROL SUBJECTS**

**DISCUSSION:** Metabolic syndrome is a very complex derangement in an emerging clinical challenge which is related with two times more chance to develop CVD risk and five times more chance to develop T2DM. In view to gain better insight into the interplay of insulin resistance, obesity and inflammation in the pathophysiology of MetS, CVD and diabetes mellitus. Our study was done, so that the information will facilitate the physician to develop enhanced treatment strategies for managing patients with MetS, CVD risk, and screening T2DM risk and thus improving the prognosis.

The present study was conducted in the department of Biochemistry in collaboration with department of Medicine, Shri Ramkrishna Institute of Medical Sciences and Sanaka Hospital, Durgapur, West Bengal, India. One hundred clinically diagnosed MetS patients according to IDF criteria with age range more than 35 years of either sex were selected to serve as subjects. One hundred subjects who did not meet IDF criteria for MetS were included as controls groups. In our study, the mean WC ( $101.07 \pm 8.0$ ) was significantly higher in MetS patients than in control group ( $80.51 \pm 4.68$ ) ( $p < 0.000$ ). Although central obesity seems to be the major determinant of elevated hs-CRP levels in the MetS, significant independent associations between hs-CRP and other components were found<sup>4</sup>.

The mean SBP ( $147.37 \pm 21.24$ ) was significantly higher in MetS patients than in control group ( $112.79 \pm 6.57$ ) ( $p < 0.000$ ); similarly, the mean DBP ( $92.0 \pm 10.96$ ) was significantly higher in MetS patients than in control group ( $73.08 \pm 5.38$ ) ( $p < 0.000$ ). In our study, the mean FBS ( $141.08 \pm 56.02$ ) was significantly higher in MetS patients when compared to control group ( $68.09 \pm 6.05$ ) ( $p < 0.000$ ). Two other studies also found an independent association between hs-CRP and fasting glucose<sup>4</sup>. The mean triglyceride ( $253.07 \pm 114.7$ ) was significantly higher in MetS patients when compared to control group ( $116.08 \pm 28.07$ ) ( $p < 0.000$ ). The mean HDL-C ( $37.80 \pm 14.49$ ) was significantly lower in MetS patients when compared to control group ( $52.16 \pm 6.03$ ) ( $p < 0.000$ ). Aronson et al. found an independent association between triglyceride level and hs-CRP. In addition they found associations between hs-CRP and glucose level and HDL

cholesterol<sup>10</sup>. The mean hs-CRP ( $4.88 \pm 0.61$ ) was significantly higher in MetS patients when compared to control group ( $1.699 \pm 1.45$ ) ( $p < 0.000$ ). 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 ( $p = 0.001$ )<sup>11</sup>. Anubha Mahajan et al also had similar results where hs-CRP values were significantly elevated in subjects with MetS compared to subjects without MetS ( $P = 2.1 \times 10^{-33}$  and  $1.1 \times 10^{-40}$  for men and women, respectively)<sup>12</sup>.

Likewise, CRP  $< 5$  mg/dl was shown to be associated with the presence of findings consistent with small-vessel obstruction in another study investigating 135 patients with presumed Myocardial infarction with nonobstructive coronary arteries (MINOCA)<sup>13</sup>. CRP  $> 10$  mg/dl for example, strongly suggested the presence of myocarditis in a pooled cohort of 556 patients regarded having MINOCA<sup>14</sup>.

**CONCLUSION:** In our study, it is evident that patients with metabolic syndrome have drastically higher levels of hs-CRP when compared with controls groups and the level of hs-CRP increased linearly with increase in number of metabolic syndrome components. Therefore the level of hs-CRP maybe used as a surrogate marker of chronic inflammation in metabolic syndrome patients and higher levels of the inflammatory marker hs-CRP are correlated with rise risk for development of cardiovascular disease and diabetes mellitus.

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**CONFLICTS OF INTEREST:** No conflict of interest.

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