Original Research Article

ASSOCIATION OF INFLAMMATORY MARKERS WITH METABOLIC SYNDROME AMONG PRE & POST-MENOPAUSAL WOMEN

ABSTRACT

Background: Metabolic Syndrome (MetS) comprises of an array of clinical, physiological, metabolic and biochemical disturbances; associated with a systemic inflammatory response. The debilitating condition entails high morbidity and mortality and thus it is important to identify and resolve it timely; a goal which may be achieved with the help of biomarkers. Highly sensitive C-reactive protein (hsCRP) and fibrinogen are acute phase reactants and indicate underlying inflammatory state and thus may be relevant to MetS.

Objectives: To determine the association of inflammatory markers with metabolic syndrome among pre & post-menopausal women.

Methodology: This cross-sectional analysis was carried out on a sample of 278 women (aged at or above 25 years) presenting to the Outpatient Department of General Medicine and the Obstetrics – Gynecology at Liaquat University Hospital (Hyderabad) with collaboration of Department of Physiology, University of Sindh and Diagnostic & Research Laboratory, LUMHS from February 2020 to October 2020. Data was collected using a structured interview-based questionnaire containing inquiries pertaining to basic biodata, sociodemographic details, and

biochemical analysis (CRP, DLC and fibrinogen and insulin measurement). Data was analyzed using SPSS v. 21.0.

Results: In this study a cumulative MetS prevalence was found out to be 63.7% and 57.6% according to IDF (WC80 diagnostic criteria) and NCEP ATP-III classifications, respectively. Subjects with MetS had higher CRP (4.07 ± 1.72 vs. 2.09 ± 0.98 mg/L, P : 0.0006); and fibrinogen levels (336 ± 77 vs. 193 ± 43 mg/dl, P < 0.001) than controls. CRP and fibrinogen levels increased with number of metabolic abnormalities. CRP level of 2.6 mg/L predicted the MetS with sensitivity, specificity and accuracy of 71%, 78% and 75% respectively. Subjects with MetS have increased inflammatory markers compared to healthy controls.

Conclusion: It can be concluded that both inflammatory markers (CRP and prothrombin) are positively associated with body mass index, body fat mass, percent body fat, and all parameters of MetS, except HDL with which only fibrinogen was negatively associated.

Keywords: Metabolic Syndrome, Inflammatory Marker, CRP, Prothrombin and Leucocytes.

INTRODUCTION

Metabolic syndrome is a cluster of clinical, physiological, metabolic, and biochemical features that are strongly related with an enhanced risk of occurrence of Type 2 diabetes mellitus and cardiovascular diseases and atherothrombotic complications. [1, 2] Metabolic syndrome leads to hormone resistance that alters normal endocrine function. Leptin resistance in these patients leads to ineffective appetite suppression and thus allows accumulation of excessive calories as visceral fat. Moreover, increased number of fat cells leads to increased production of adipokines that causes chronic inflammation. This inflammation forms the basis of several concurrent manifestations. [3, 4]

Increased oxidative and inflammatory stress are recognized as playing an important role in the initiation and progression of many clinical conditions, including those that occur concurrently with MetS (such as atherosclerotic vascular disease and obesity). [5, 6] Obesity is associated with increased circulating markers of oxidative stress and low-grade inflammation. [7] The MetS which

often accompanies obesity, has also been independently linked with increased oxidative stress and inflammatory burden. [8]

MetS is associated with a pro-inflammatory state in which the role of visceral obesity is thought to be central. Inflammatory cytokines, in particular interleukin (IL)-1, tumor necrosis factor, and IL-6, are the main inducers of the acute phase response. Two important acute-phase proteins, highly sensitive C-reactive protein (hsCRP) and fibrinogen have IL-6 response elements in the promoter regions of their genes. [9, 10]

Numerous studies have now confirmed that CRP levels are elevated in subjects with MetS. [11 - 15] CRP levels were shown to be strongly associated with insulin resistance calculated from the HOMA model, blood pressure, low HDL, and triglycerides. [14] There is a linear relationship between the number of metabolic features and increasing levels of hsCRP. [16 - 18] The strongest associations were observed between CRP levels, central adiposity, and insulin resistance. [19, 20]

Collectively, all of these studies support the hypothesis that an increased hsCRP in the setting of MetS confers an increased risk of future CV events. [11, 12] Hence, we studied inflammatory markers to confirm that those established associations are also present within the population of Indian subjects with MS.

OBJECTIVES

To determine the association of inflammatory markers with metabolic syndrome among pre & post-menopausal women.

METHODOLOGY

This cross-sectional, comparative analysis was carried out on a sample of 278 (147 premenopausal & 131 postmenopausal) women (aged at or above 25 years) presenting to the Outpatient Department of General Medicine and the Obstetrics – Gynecology at Liaquat University Hospital (Hyderabad) with collaboration of Department of Physiology, University of Sindh and Diagnostic & Research Laboratory, LUMHS from February 2020 to October 2020. Data was collected using a structured interview-based questionnaire containing inquiries pertaining to basic biodata, sociodemographic details, and biochemical analysis (CRP, DLC and

fibrinogen and insulin measurement). All anthropometric measurements along with visceral & body fat level were calculated using measuring tape & OMRON BfF508. Data was analyzed using SPSS v. 21.0.

Inclusion criteria

1. Consenting individuals
2. Aged 25 years and above

Exclusion Criteria

1. Women on hormone replacement therapy
2. Pregnant or lactating women
3. Women suffering from secondary hypertension
4. Women with artificial/induced menopause
5. Women taking any medicine for HTN, DM, contraception or endocrinological disorders.

Statistical Analysis

Data was collected and recorded in excel software and then transferred and analyzed (SPSS, version 23 for analysis). Chi square test was applied to check difference of variables between groups. Levene's test was used for homogeneity of variance. The results were said to be significant if the p-value was <0.05.

RESULTS

Total 278 participants were selected. In this study a cumulative MetS prevalence was found out to be 63.7% and 57.6% according to IDF (WC80 diagnostic criteria) and NCEP ATP-III classifications, respectively. Differences among women with MetS from those without MetS on various important aspects, are tabulated below.

Table 1: Differences among women with MetS from those without MetS

Variables	With MetS	Without MetS	P-value

	n= 160	n= 118	
Age (years)	*45.50 ± 9.91*	*38.80 ± 10.07*	*< 0.01*
WC (cm)	*99.26 ± 9.39*	*87.69 ± 9.29*	*< 0.01*
BMI (kg/m^2)	*31.79 ± 4.11*	*26.58 ± 4.26*	*< 0.01*
WHR	*0.91 ± 0.05*	*0.88 ± 0.04*	*< 0.01*
Body fat (%)	*43.79 ± 6.72*	*34.98 ± 8.25*	*< 0.01*
Visceral fat	*8.91 ± 1.75*	*6.83 ± 1.52*	*< 0.01*
HDL (mg/dl)	*42.31 ± 9.46*	*48.20 ± 8.64*	*< 0.01*
LDL (mg/dl)	*131.44 ± 38.32*	*107.03 ± 29.80*	*< 0.01*
Triglycerides (mg/dl)	*195.10 ± 63.37*	*124.7 ± 44.04*	*< 0.01*

Subjects with MetS have increased inflammatory markers compared to healthy controls. E.g., subjects with MetS had higher CRP (4.07 ± 1.72 vs. 2.09 ± 0.98 mg/L, P: 0.0006); and fibrinogen levels (336 ± 77 vs. 193 ± 43 mg/dl, P < 0.001) than controls. CRP and fibrinogen levels increased with number of metabolic abnormalities.

Table 2: Inflammatory markers compared to healthy controls

Variables	With MetS n= 160	Without MetS n= 118	P-value
CRP Level (Mean)	*4.07 ± 1.72*	*2.09 ± 0.98*	0.0006
Fibrinogen Level (Mean)	*336 ± 77*	*193 ± 43*	< 0.001

CRP level of 2.6 mg/L predicted the MetS with sensitivity, specificity and accuracy of 71%, 78% and 75% respectively.

DISCUSSION

In this study, the prevalence of MetS was found to be 59.9%. According to literature review the highest prevalence of MetS in Asian countries was found in urban Pakistan (49.0%). [21] Another

study conducted in India showed prevalence of Mets to be 47.2% in female population. [22] yet another study conducted in the urbanized areas of Karachi, [23] showed the prevalence of METS at 34% and 49% according to IDF and NCEP ATP III criteria, the same study shows significantly higher prevalence in old female subjects, that coincides with this study.

Our study shows higher prevalence of METS than another study [24] conducted in Pakistan that showed that the prevalence of METS to be around 57% in females. Our study was partly in contrast to the study of Gupta *et al*. [25] in which they found the maximum prevalent component to be hypertension (51%), followed by waist circumference (34%), triglycerides (33%), and diabetes (17%). Our research on the other hand showcased all variables to be significant with the most markedly including the aforementioned and BMI, LDL and HDL (among others).

Subjects with MetS had significantly higher level of CRP and fibrinogen than controls. This supports the hypothesis that MS is a pro-inflammatory state. [26, 27] Higher levels of CRP and fibrinogen in MS compared to controls have been reported in most of the studies in the literature. [5, 6] There was no difference in hsCRP level between sexes in this study, but one study reported higher hsCRP level in women. [28]

Both markers were positively associated with BMI, body fat mass and percent body fat, cholesterol, LDL, HOMA-IR and negatively with basal metabolic rate. Vikram et al. [29] made similar observation about relation between CRP and BMI, and WHR; but found no relation between CRP and lipid parameters in Indian young teenagers. Lower levels of CRP have been reported in Japanese [30] and Chinese [19] than Caucasians and Indians; however relation with metabolic syndrome persisted within population.

Among various parameters of MetS, both markers were positively associated with WHR and hypertension. Festa et al. [14] from the Insulin Resistance and Atherosclerosis Study showed that CRP was positively correlated with BMI, waist circumference, blood pressure, triglycerides, cholesterol, LDL cholesterol, plasma glucose, and fasting insulin and inversely correlated with HDL cholesterol and insulin sensitivity index.

Conclusion

It can be concluded that both inflammatory markers (CRP and prothrombin) are positively associated with body mass index, body fat mass, percent body fat, and all parameters of MetS, except HDL with which only fibrinogen was negatively associated.

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