

Association of High Sensitive C- Reactive Protein with Female Metabolic Syndrome Patients in Bangladesh

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Abstract

Background: Raised level of high sensitive C-reactive protein (hsCRP) is found in Metabolic Syndrome patients (MS).

Objective: To observe association of serum hsCRP with Metabolic Syndrome in female patients.

Methods: This cross-sectional study was conducted from March 2019 to July 2020 in the Department of Physiology, Bangladesh Medical University (BMU), Shahbagh, Dhaka, Bangladesh. Female (n=30, 25 to 45 year) were diagnosed with MS in the study according to the criteria of International Diabetes Federation (IDF). Apparently healthy female (n=30, age matched) were included in the study as control. Serum hsCRP level was measured by Immuno-turbidimetric method and Chi-square test was done to observe associations of serum hsCRP with MS.

Results: Median value of hsCRP was found significantly higher (p value ≤ 0.01) in MS patients than that of control subjects. Around 53.3% of MS patients were found to have elevated level of hsCRP.

Conclusion: This study may conclude that elevated hsCRP was associated with MS.

[Shaheed Syed Nazrul Islam Med Col J 2026, Jan; 11 (1):87-93]

DOI: <https://www.doi.org/10.69699/ssnimcj.2026.11.1.12>

Keywords: Metabolic syndrome (MS), High sensitive C-reactive protein (hsCRP), Female, Bangladesh.

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Introduction

Metabolic syndrome (MS) is a cluster of several metabolic disorders such as abdominal obesity, insulin resistance, hyperinsulinaemia, dyslipidaemia and hypertension.¹ These multiple metabolic disorders are risk factor for cardiovascular disease, chronic lung disease, kidney disease, and fatty liver changes.² Compared to healthy persons, MS patient have three times more chance of heart attack or stroke.¹

International Diabetes Federation (IDF) characterized MS for both research and clinical purposes.¹ According to IDF definition, a MS patient must has central obesity (waist circumference ≥ 90 cm for men or ≥ 80 cm for women in South Asia) with two or more of the following criteria– (1) Hyperglycemia (Fasting plasma glucose ≥ 100 mg/dl) or previously diagnosed as type-2 diabetes, (2) Hypertriglyceridaemia (≥ 150 mg/dl) or specific treatment for this lipid abnormality, (3) Low HDL cholesterol (< 40 mg/dl in men, < 50 mg/dl in women) or specific treatment for this lipid abnormality, (4) hypertension (Systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg) or treatment for previously diagnosed HTN.¹

About 20-25% of adult population have MS around the world.¹ MS prevalence is slightly higher (30%) than worldwide prevalence in Bangladesh.³ Mainly MS affects the middle-aged and elderly citizens but its prevalence is increasing in younger generation^{1,4}. Its occurrence is higher in female (32%) than that of male (25%) in this country.³ Increased waist circumference (WC), high triglyceride (TG) and low high density lipoprotein (HDL) cholesterol are the mostly prevalent MS combinations in younger women in the world.⁵ Increased WC or visceral adiposity is seen significantly associated with all-cause of mortality risk in younger adult women compared to men.⁵ Furthermore, DM,

inflammation, atherothrombosis- these three are strictly interrelated disorders of immune system.⁶ BMI and insulin resistance are considered as the strongest determinants of the inflammatory state.⁷

hsCRP is routinely monitored as an indication of infection, inflammation (both acute & chronic) and autoimmune diseases.^{7,8,9} hsCRP is synthesized in the hepatocyte.^{7,8,9} It is also synthesized in adipocytes, smooth muscle cells of artery, lung, kidney, neurons and leucocytes.^{7,8,9} The production is controlled by interleukin-6 which is secreted from leucocytes, fibroblast, adipocytes and endothelial cells.^{7,8,9} The researcher found that CRP is positively correlated with WC, BP, TG, total cholesterol, LDL-C, plasma glucose, fasting insulin and negatively correlated with HDL-C.¹⁰ It was found high in women with MS when compared to women without MS.¹¹ It is found to be increased with the number of metabolic features increased.^{12,13,14} Elevated hsCRP levels are predictive of myocardial infarction, stroke, diabetes and hypertension and a prognostic marker for cardiovascular events.¹⁵

Previous studies reported elevated CRP level that was found to be associated with MS.^{12,14,16,17} One study result revealed no significant association of CRP with Ms.¹³ Though there is some evidences of altered CRP levels in MS patient in separate studies of different countries in the world, there is no informed published data available in the reproductive age group female patients in Bangladesh. Therefore, this study has been designed to observe association of CRP level with MS in female reproductive age group in this country. All disease risk factors showed considerable geographical, ethnic and socioeconomic variations. So, identify the hsCRP as a risk factor of MS in Bangladesh is justifiable. It is desired that the outcome of this study may aware of the clinicians to

observe increased level of CRP in MS female patients in this country. Furthermore, measurements of the hsCRP may provide therapeutic approaches to modulate the inflammatory responses and thereby alter disease progression.

Methods

Study design, setting, participants

The cross-sectional study was conducted in the Department of Physiology, BMU, Shahbag, Dhaka from March 2019 to July 2020. The study aims were to measure serum calcium, magnesium and hsCRP levels and to observe their associations with MS in 25 to 45 year old female patients (n=30). Age matched 30 healthy females with regular menstrual cycle were taken as control. The protocol was approved by the Institutional Review Board (IRB) of BMU.

Sampling

The patients were enrolled from the outpatient department of Endocrinology, BMU by purposive sampling and the control subjects were recruited by personal contact.

Exclusion criteria

Exclusion criteria of the patient includes presence of any acute infections, various organ diseases, malignancy and history of recent major surgery. Pregnant, menopausal women and women taking hormonal therapy were excluded in the study.

Data Collection procedure

Informed written consent was taken from each subject after briefing about the study. Detailed personal and medical history were recorded. Height, weight, waist circumference (WC), pulse rate, blood pressure were

measured and documented. Fasting blood sample was collected from all the subjects with all aseptic precautions for estimation of serum hsCRP. In the department of Biochemistry and Molecular Biology of BMU, Dhaka, hsCRP assay was performed by Immuno-turbidimetric method using an automated analyzer. Cutoff value up to 5mg/l for serum CRP¹⁸ were taken as normal reference range.

Data analysis

Data of 30 MS patients and 30 apparently healthy subjects were used in data analysis. Even after log transformations, data of hsCRP were found skewedly distributed. So, Mann-Whitney U test was performed to compare medians of hsCRP. Chi-square test was performed to observe association of serum hsCRP with MS by using SPSS for windows version 22. p value ≤ 0.05 was considered as statistically significant.

Results

In this study, age was matched between MS and control groups. According to IDF's MS criteria,¹ significantly higher ($p \leq 0.001$) waist circumference, systolic blood pressure, diastolic blood pressure, fasting plasma glucose, triglyceride levels and significantly lower ($p \leq 0.05$) HDL-C levels were found in female MS patients than that of control in this study. Median value of serum hsCRP was found significantly higher ($p = 0.002$ and $p \leq 0.01$) in MS (5.16 mg/l) than that of control (1.66 mg/l). Furthermore, about 53.3% of MS patients (Figure 1) had elevated hsCRP levels whereas only 10% of controls had elevated serum CRP levels (Figure 2) which was found to be significantly associated with MS (Table I).

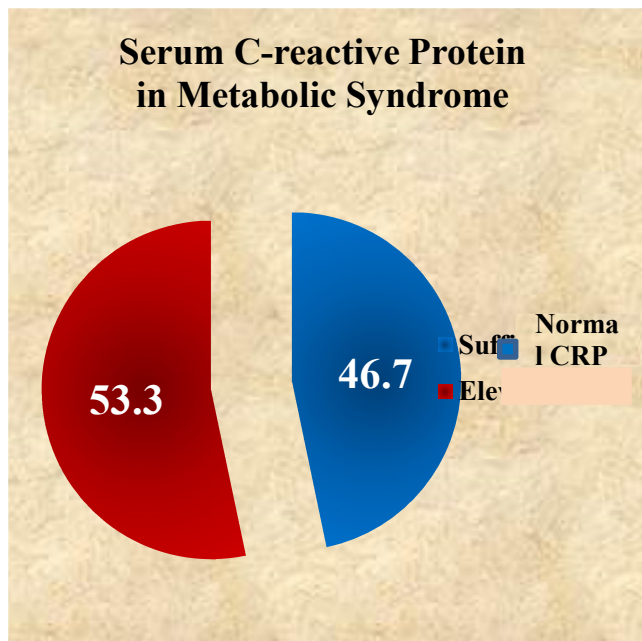


Figure 1. Frequency distribution of serum C-reactive protein in metabolic syndrome (n=30). Data were expressed in percentage.

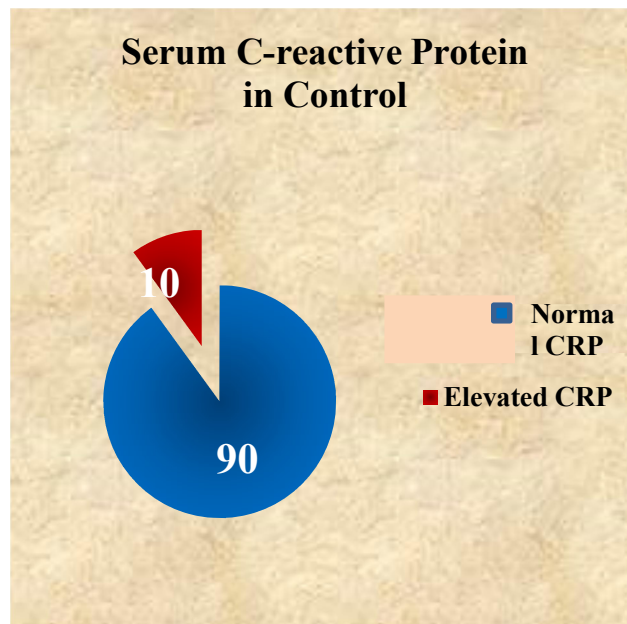


Figure 2. Frequency distribution of serum C-reactive protein in control (n=30). Data were expressed in percentage.

Table I: Association of elevated serum hsCRP with MS (N=60)

	Groups		Total	p value
	Normal hsCRP (<5.0 mg/l)	Elevated hsCRP (>5.0 mg/l)		
MS	14(46.7)	16(53.3)	30	0.000***
Control	27(90.0)	3(10)	30	
Total	41	19	60	

Data were expressed as number. Values in parentheses indicate percentage; Statistical analysis was done by Chi-Square test to observe association of serum hsCRP with MS; n: number of subjects; *** $p \leq 0.001$.

Discussion

In this study, significantly higher serum hsCRP level in MS patients compared to control corresponded with some previous studies.^{12,13,14,16,17} Among the subjects of MS and control group in this study, MS had elevated serum hsCRP than control. Elevated serum hsCRP was associated with MS in this study. Similar finding was also reported by other investigators.^{12,14,16,17}

Literature review suggested that obesity is the core factor in the pathophysiology of MS.¹⁵⁻²⁰ It is all known that, adipose tissue is a metabolically active endocrine organ.²¹ When the body gains positive energy balance, weight gain and visceral obesity occurs.²¹ In this condition, adipocyte undergoes hypertrophy and becomes dysfunctional.²¹ Secretions of adipocytokines (IL-6 and TNF-alpha) from dysfunctional adipose tissue are increased.¹⁹ Secretion of catecholamine also increases which causes lipolysis and rises

blood free fatty acid level.^{21,22} The excessive secretion of IL-6, TNF-alpha and free fatty acid impair insulin signaling pathway and produce insulin resistance.^{21,22}

In MS patients, IL-6 and TNF- alpha secretion increases excessively from their hypertrophied and dysregulated adipose tissue. In response to which, liver produces more CRP than normal. The excessively secreted CRP comes into circulation from hepatocyte and elevates blood CRP level in MS patients.^{12,16,17,20}

CRP plays a direct role in inflammatory process.²³ It involves in indirect opsonization by binding with C1q of the classical complement cascade.²³ It also involves in direct opsonization after binding with Fcg receptors.²³ CRP also regulates inflammatory progression.⁹

So, there may be a postulated hypothesis of creation of atherothrombosis in MS patients. Chronic low-grade inflammation is characteristic of the MS where CRP level increases.⁶ Researchers already know that chronic low-grade inflammation play an important role in atherogenesis and its progression by its inflammatory nature.⁹ Researchers identified critical role playing of chronic inflammation at all stages of the atherosclerotic process.²³ From development of endothelial dysfunction and plaque progression to development of plaque complications through plaque instability and rupture, CRP leads to clinical vascular events.²³

From above discussion, it is obvious that, a relatively high prevalence of MS is a worldwide phenomenon and MS has elevated CRP level which may produce cardiovascular risk and risk related to vascular diseases in various organ in this group of population. The findings in this study may predict that there is

possible role of inflammation as measured by hsCRP in the pathogenesis of development of MS complication.

One of the limitations of this study is that, it was a cross- sectional study which could not establish cause-effect relationship of serum hsCRP with MS. So, well-designed prospective studies will be necessary to clarify the effect of hsCRP on MS. Longitudinal studies will also need to establish the cutoff points for elevated hsCRP as a clinical assessment tool for MS among Bangladeshi women.

Conclusion

After analyzing the results of the study, it is concluded that elevated serum hsCRP is associated with MS at reproductive age group (25 to 45 years) female patients in Bangladesh which may play an important pathogenic role in atherothrombotic disease.

Acknowledgement

The authors of this study are grateful to the authority of the Department of Biochemistry and Molecular Biology, BMU, Dhaka for their kind cooperation they provided during study period.

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