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Serum Calcium, Magnesium and C-reactive protein levels in female Metabolic Syndrome patients

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Abstract

Background: Metabolic syndrome (Mets) is a risk factor for cardiovascular, chronic lung, liver and kidney diseases. Hypercalcaemia, hypomagnesaemia and elevated C-reactive protein (CRP) produce various complications such as cardiac arrythmia, renal stones, atherosclerosis, Diabetes Mellitus, Obesity etc. Some researchers suggested that hypercalcaemia, hypomagnesaemia and elevated CRP occur in Metabolic syndrome patients. **Objectives:** To measure serum calcium, magnesium and CRP levels in Metabolic syndrome patients. **Methods:** This cross sectional study was conducted from March 2019 to July 2020 in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University(BSMMU), Shahbag, Dhaka. For this study, 30 female metabolic syndrome patients aged 25 to 45 year, from the Outpatient department of Endocrinology of BSMMU were selected. For comparison, 30 age and gender matched apparently healthy female subjects were control. Serum calcium and magnesium were measured by Colorimetric method and serum CRP was measured by Immuno-turbidimetric method. Independent sample't' test was performed for serum calcium and Mann-Whitney U test was performed for serum magnesium and CRP. **Results:** Mean serum calcium ($p \leq 0.05$ and median value of serum CRP ($p \leq 0.01$) were significantly higher, median value of serum magnesium was lower ($p > 0.05$) but not significant in Metabolic syndrome patients than that of control. **Conclusion:** This study may conclude that elevated serum calcium and CRP levels are associated with metabolic syndrome patients.

Key words: Metabolic syndrome, IDF, calcium, magnesium, CRP, Bangladesh.

Introduction

Metabolic syndrome was previously known as Insulin resistance syndrome or Syndrome X.[1] International Diabetes Federation (IDF) characterized this syndrome for both research and clinical purposes.[1] According to IDF definition, a person must have central obesity (defined as waist circumference ≥90 cm for men or ≥80 cm for women) with two or more of the following criteria to be diagnosed as MetS patient– (1) Hyperglycaemia (Fasting plasma glucose ≥100 mg/dl) or previously diagnosed type-2 Diabetes (2) Hyper-triglyceridaemia (≥150 mg/dl) or specific treatment for this lipid abnormality (3) Low high density lipoprotein cholesterol (<40 mg/dl in men and <50 mg/dl in women) or specific treatment for this lipid abnormality (4) Hypertension (Systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥85 mm Hg) or treatment for previously diagnosed Hypertension.[1] Multiple metabolic disorders in MetS create risk of cardiovascular, pulmonary, renal and hepatic diseases.[2] Around the world, about 20-25% of adult populations are suffering from MetS.[1] Its prevalence is slightly higher (30%) in Bangladesh than worldwide prevalence and it is higher in female (32%) than male (25%).[3] MetS presentation is different in male and female and changes with age. [4] In younger women, the most prevalent MetS combinations are elevated waist circumference (WC), high level of triglyceride (TG) and low level of high density lipoprotein (HDL) cholesterol. Anthropometric measures of obesity especially WC is significantly associated with all-cause of mortality risk in younger adults which is higher in women compared to men.[4]

Calcium is one of the essential minerals of the body which is required for smooth muscle contraction, nerve signal transmission, intracellular signaling and hormonal secretion etc.[5] Researchers found hypercalcaemia in MetS patients.[6-8] Hypercalcaemia causes hypertension (HTN), cardiac arrythmia, renal stones, Depression etc.[5]

Magnesium which is the second most abundant intracellular cation can activates more than 300 enzymes and plays a pivotal role in many enzymatic energy production reactions involved in carbohydrate and lipid metabolisms.[9] Researchers found hypomagnesaemia in MetS patients.[9-10] Hypomagnesaemia alters blood lipid composition. Thus it is involved in the pathogenesis of atherosclerosis.[11] It can produce cardiac arrhythmia, Obesity, HTN, Diabetes Mellitus (DM), Osteoporosis and can trigger low grade chronic inflammation.[5,11]

C-reactive protein (CRP) is the best characterized and well proved biomarker of inflammation.[12] It is an acute phase reactant protein which is important in the nonspecific host defense against inflammation, especially infection.[12,13] It also increases in chronic inflammatory conditions such as autoimmune and cardiovascular diseases.[14] It is produced mainly in the liver[12]. The production is controlled by interleukin-6 secreted from leucocytes, fibroblast, adipocytes and endothelial cells.[13] CRP level remains chronically elevated in MetS patients,[15-17] which may play important roles in atherogenesis, HTN and DM.[13]

Previous studies reported higher calcium, lower magnesium and elevated CRP levels in MetS patients compared to control.[6-10,15-17] One study result revealed no significant elevation of CRP in Mets patients.[18] Though there is some evidences of altered calcium, magnesium and CRP levels in MetS patients in separate studies of different countries in the world, there is no informed published data available in reproductive age group female in Bangladesh. Therefore, this study has been designed to assess serum calcium, magnesium and CRP status in a small cross section of female MetS patients in Bangladesh. It is desired that the outcome of this study may alert the clinicians to monitor serum calcium, magnesium and CRP levels in MetS patients in our country so that early detection of any specific change in these variables may help to prevent complications in this group of patients.

Methods

Study design, setting and participants

After obtaining ethical clearance from Institutional Review Board (IRB) of BSMMU, Dhaka our cross sectional study was conducted in the Department of Physiology, BSMMU from March 2019 to July 2020. For this purpose, thirty (30) female, age ranging from twenty five to fourty five (25 to 45) year suffering from MetS, diagnosed according to International Diabetes Federation (IDF) criteria[1] were selected from the Outpatient Department of Endocrinology in BSMMU. For comparison, thirty (30) apparently healthy females of almost same age range were selected from the colleagues, hospital stuffs and patient's attendance in their proliferative phase of menstrual cycle to avoid hormonal influences.

Sampling

Subjects were collected by purposive sampling technique.

Exclusion criteria

Subjects suffering from renal, liver and thyroid disorders were excluded by taking history and biochemical tests (serum creatinine, serum alanine aminotransferase and thyroid stimulating hormone). Cardiac diseases, menstrual abnormalities, malignancy, chronic inflammations such as Rheumatoid arthritis, Chron's disease were excluded only by taking history. Subjects suffering from acute bacterial, viral or fungal infections (excluded by taking history of fever, sore throat, abdominal pain, burning sensation in urine and by measuring temperature, palpating lymph nodes) were also excluded. Menopausal females and females having history of recent major surgery, females on calcium and magnesium supplementations, taking hormonal contraceptives were also excluded from our study.

Data collection procedure

After taking written informed consent, histories about family, menstruation, medical and diet were recorded. Complete physical examinations including pulse rate, blood pressure, anthropometric measurements- WC, height and weight were measured and documented. With all aseptic precautions, 10 ml of 11-12 hours fasting venous blood was collected from all the subjects for estimation of fasting plasma glucose, fasting lipid profile, serum creatinine, alanine aminotransferase, thyroid stimulating hormone and albumin using automated analyzers in the laboratory of the Department of Biochemistry and Molecular Biology of BSMMU. Serum calcium and magnesium were measured by Colorimetric method and high sensitive CRP assay was performed by Immuno-turbidimetric method using an automated analyzer in the department of Biochemistry and Molecular Biology of BSMMU. Then adjusted or corrected total calcium (mg/dl) was manually calculated as,= total calcium (mg/dl) + 0.8 x [4 – albumin (gm/dl)].[5] Values ranging 8.5 to10.5 mg/dl for serum calcium[19], 1.7 to 2.4 mg/dl for serum magnesium[5] and cutoff value up to 5mg/l for serum CRP[19] were taken as normal reference range.

Statistical analysis

All data were not normally distributed even after log transformations. Then, Independent sample't' test was performed to compare means of normally distributed quantitative data, Mann-Whitney U test was performed to compare medians of quantitative data with skewed distribution by applying Statistical Package for Social Science (SPSS) for windows version 16. *p* value ≤0.05 was considered as statistically significant during result interpretation.

Results

All subject's baseline general characteristics are shown in table I. In this study, age was comparable and matched between MetS and control groups. According to IDF's MetS criteria[1], we found significantly higher (p=0.000) WC, SBP, DBP, FPG, TG and significantly lower (p-0.03) HDL-C in MetS patients in comparison to healthy controls (Table I).

Table I: Baseline characteristics of subjects in two groups (N=60)

Characteristics	MetS (n=30)	Control (n=30)	*p* value
Age (years)[a]	37.43±5.45	34.63±5.93	0.062
WC (cm)[b]	91.50	74.0	0.000
SBP (mm of Hg)[b]	135.0	110.0	0.000
DBP (mm of Hg)[b]	90.0	70.0	0.000
FPG (mmol/l)[b]	6.5	5.15	0.000
TG (mg/dl)[b]	174.0	82.50	0.000
HDL-C (mg/dl)[a]	42.00±8.17	47.90±12.35	0.033

Data were expressed as mean ± SD (a) and median (b). Statistical analysis were done by independent sample't' test (a) and Mann-Whitney U test (b); MetS-Metabolic syndrome; WC-waist circumference; SBP-systolic blood pressure; DBP-diastolic blood pressure; FPG-fasting plasma glucose; TG-triglyceride; HDL-C-high density lipoprotein cholesterol; N=total number of subjects; n=number of subjects in each group.

In this study, serum calcium was significantly higher (p=0.031), serum CRP was significantly higher (p=0.002). Serum magnesium was lower (p=0.916) in MetS than that of control groups, but this difference was not statically significant (p=0.916) (Table II).

Again, in this study, about 53.3% of MetS patients had elevated CRP levels whereas only 10% of controls had elevated serum CRP levels (Table III). About 3.3% and 6.7% of MetS patients had hypercalcaemia and hypomagnesemia respectively. None of the controls had hypercalcaemia or hypomagnesaemia in this study (Table IV).

Table II : Serum total calcium, magnesium and CRP in two groups (N=60)

Variables	MetS (n= 30)	Control (n= 30)	*p* value
Serum calcium (mg/dl)[a]	9.22 ± 0.57 (8.24-10.52)	8.94 ± 0.36 (8.22-9.80)	0.031
Serum magnesium (mg/dl)[b]	1.90 (1.80-2.10)	1.95 (1.80-2.20)	0.916
Serum CRP (mg/l)[b]	5.16 (1.61-8.77)	1.66 (1.21-3.16)	0.002

Data were expressed as mean ± SD (range) (a) and median (interquartile range) (b). Statistical analysis was done by independent sample 't' test (a) and Mann-Whitney U test (b); MetS: metabolic syndrome; CRP=C-reactive protein; N=total number of subjects; n=number of subjects in each group.

Table III: Frequency distribution of serum CRP in two groups (N=60)

Variables	MetS	Control
Normal No. (%)	14 (46.7)	27 (90.0)
Excess No. (%)	16 (53.3)	03 (10.0)

Data were expressed as number. Values in parentheses indicate percentage; MetS: metabolic syndrome; N= total number of subjects; No=number of subjects in each group.

Table IV : Frequency distribution of serum calcium and magnesium in two groups (N=60)

	MetS(n=30)			Control(n=30)		
	Sufficient No. (%)	Excess No. (%)	Deficient No. (%)	Sufficient No. (%)	Excess No. (%)	Deficient No. (%)
Serum Calcium	26 (86.7)	1 (3.3)	3 (10.0)	27 (90.0)	0 (0)	3 (10.0)
Serum Magnesium	25 (83.3)	3 (10.0)	2 (6.7)	27 (90.0)	3 (10.0)	0 (0)

Data were expressed as number. Values in parentheses indicate percentage; N= total number of subjects; n=number of subjects in each group.

Discussion

In our study, we found significantly higher serum calcium and serum CRP levels in MetS patients compared to control subjects which were similar to some previous studies.[6-8,15-17] Though some researchers reported significantly lower magnesium level in MetS patients,[8-10] our study revealed low serum magnesium level which was not significant in MetS than that of control. In our study, hypercalcaemia and hypomagnesaemia only found in MetS patients. Again, in our study, 53.3% MetS patients had elevated serum CRP levels. Only 10% of control subjects had elevated serum CRP levels.

Several studies suggested that obesity is the core factor in the pathophysiology of MetS.[20,21] Adipose tissue is known as metabolically active endocrine organ. Increased weight and visceral obesity occurs when body gains positive energy balance. In this condition, adipocytes undergo hypertrophy, become hypoxic and necrosed.[20] They excessively secret adipocytokines of pro-inflammatory types– interleukin-6 (IL-6), tumor necrotic factor (TNF)- alpha. Catecholamine secretion also increases which causes lipolysis and increment of blood free fatty acid level. Increased pro-inflammatory adipocytokines and free fatty acid impair insulin signaling pathway, thus produce insulin resistance.[20,21]

Insulin resistance and/or hyperinsulinaemia may dysregulates parathyroid gland's hormone secretion. It increases parathyroid hormone secretion which may produce hypercalcaemia by increased bone resorption, intestinal calcium absorption and renal calcium reabsorption.[7] In our study, we also observed hypercalcaemia in MetS patients.

During periods of severe hyperglycaemia, the kidneys lose their ability to hold on to magnesium. Magnesium loss in urine increases which ultimately produces hypomagnesaemia.[22] In our study, we observed lower but not significant serum magnesium level in MetS patient. This may be due to our MetS patients had not too much glucose level (6.5 vs 5.15 mmol/l) in their serum.

IL-6 and TNF-alpha secretion increase excessively from hypoxic, necrosed, macrophage infiltrated adipose tissue of a MetS patient,[20] in response to which, liver starts to produce excessive amount of CRP that comes into circulation and elevates serum CRP level.[15-17]

The limitation of our study is that because of budget constraints serum PTH and Vitamin-D levels were not measured. Another limitation of our study is that it was a cross sectional study which could not establish cause-effect relationship of serum calcium, magnesium and CRP with MetS.

Conclusion

After analyzing the results of the study, it can be concluded that elevated serum calcium and serum CRP levels are associated with Metabolic syndrome patient.

Conflict of interest None

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