

Article

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Homocysteine, vitamin B₁₂ and folic acid levels in metabolic syndrome

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Abstract

Background: Metabolic syndrome (MeS) is a risk factor for cardiovascular disease, chronic lung disease, fatty liver disease and kidney disease. Elevated serum homocysteine level is an independent risk factor for cardiovascular disease and lung disease. Vitamin B₁₂ and folic acid deficiency causes hyperhomocysteinemia. **Objective:** To measure serum homocysteine, vitamin B₁₂ and folic acid levels in metabolic syndrome. **Methods:** This cross sectional study was conducted in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka from March 2019 to February 2020. Total 30 female metabolic syndrome patients aged 25 to 45 years and 30 age and sex matched apparently healthy female subjects were enrolled for this study. The patients were selected from the outpatient department of Endocrinology of BSMMU. Fasting plasma glucose, lipid profile, serum creatinine, serum alanine aminotransferase levels were measured by autoanalyzer and serum homocysteine, vitamin B₁₂ and folic acid levels were measured by Chemiluminescent immunoassay. For statistical analysis, independent sample 't' test was done. **Results:** In this study, the mean value of serum homocysteine level was significantly higher in MetS than those of control group (p value <0.05). In addition, 16.67% MetS patients had hyperhomocysteinemia. **Conclusion:** From this study, it may be concluded that elevated homocysteine is associated with MetS.

Key words: Metabolic syndrome, homocysteine, vitamin B₁₂, folic acid.

Introduction

Metabolic syndrome and its various name Cardiometabolic syndrome or Insulin resistance syndrome or Syndrome X has been defined by World Health Organization (WHO), European Group for the study of Insulin Resistance (EGIR), National Cholesterol Education Program- Adult Treatment Panel III (NCEP-ATPIII) and International Diabetes federation (IDF). MeS has been characterized by several features including waist circumference ≥ 90 cm for men or ≥ 80 cm for women of South Asia plus 2 or more of the following criteria: triglyceride ≥ 150 mg/dL (1.7 mmol/L), HDL cholesterol < 40 mg/dL (1.03 mmol/L) in men, < 50 mg/dL (1.29 mmol/L) in women, blood pressure (systolic BP ≥ 130 or diastolic BP ≥ 85 mm Hg), fasting plasma glucose: FPG- ≥ 100 mg/dL (5.6 mmol/L).¹ Multiple metabolic impairment in metabolic syndrome are independent risk factors for cardiovascular disease, kidney disease, chronic lung disease and fatty liver disease.² Around the world about one quarter (20-25%) of adult population have metabolic syndrome.¹ In Bangladesh overall prevalence of metabolic syndrome is slightly higher (30%). It is higher in female (32%) in comparison with male (25%).³

Homocysteine is a toxic, nonproteogenic sulfur containing amino acid synthesized from dietary methionine in the liver and is metabolized either via trans-sulfuration or remethylation pathway. About half of the intracellular homocysteine remethylated to methionine by methionine synthase. Vitamin B₁₂ and folic acid are required for this reaction. Other half of homocysteine trans-sulfurated to cysteine with the help of cystathionine synthase which require vitamin B₆ as a cofactor. The cysteine ultimately converted to sulfate and cleared from the body via urine.⁴⁻⁶ Hyperhomocysteinemia has been associated with several disorders including atherosclerosis, thrombosis, stroke and various neurological and

psychiatric disorder, chronic kidney disease, bone tissue damage, gastrointestinal disorders, cancer and congenital disorder.⁷ Elevated serum homocysteine level is a sensitive marker of vitamin B₁₂ and folic acid insufficiency.⁸

Previous studies reported higher level of homocysteine and/or lower level of vitamin B₁₂ and folic acid in metabolic syndrome.⁹⁻¹¹ Whereas, others found no significant changes in homocysteine, vitamin B₁₂ and folic acid level in this group of patients.¹²⁻¹³

Although there is abundant evidence for altered homocysteine, vitamin B₁₂ and folic acid levels in MetS from separate studies but there is less published data available regarding these parameters in MetS patients of Bangladesh. All disease risk factors demonstrated substantial geographical ethnic and socioeconomic variation. It is imperative to evaluate this risk factor in the perspective of Bangladesh. Therefore, this study has been designed to assess serum homocysteine, vitamin B₁₂ and folic acid levels in female MetS patients. It is expected that the result of this study may aware the clinicians of serum homocysteine, vitamin B₁₂ and folic acid levels in MetS patients in this country and thus, early detection of any specific alteration may ensure better management of this group of patients.

Methods

This cross sectional study was carried out in the Department of Physiology, BSMMU, Dhaka from March 2019 to February 2020. The research work was carried out after obtaining ethical clearance from Institutional Review Board (IRB) of BSMMU. For this study, 30 MetS female patients of 25 to 45 years of age were enrolled from the Out Patient Department of Endocrinology of BSMMU. For control, 30 age matched apparently healthy female subjects were selected from the colleagues, relatives, attendant of the patients, hospital staffs and through personal contacts. Purposive sampling technique was used for sample collection.

All the subjects were free from respiratory disease, cardiac disease, renal disease, chronic liver disease, thyroid disorders, malignancy, menopause and on nutritional supplement like multivitamins (within 120 days) were excluded from the study. After selection of the subjects, a detail dietary, family, medical and menstrual history were recorded, thorough physical examination including anthropometric measurements were done and documented. With aseptic precaution, 6 ml of venous blood was collected from all subject after overnight fasting for biochemical tests. Fasting plasma glucose, fasting lipid profile, serum creatinine, serum alanine aminotransferase were measured by autoanalyzer and serum homocysteine, vitamin B₁₂ and folic acid were measured by Chemiluminescent immunoassay in the laboratory of Department of Biochemistry and Molecular Biology, BSMMU. All data were

expressed as mean±SD and percentage. For statistical analysis Independent sample 't' test was done by using SPSS for windows version 16. In the interpretation of results, p value <0.05 was considered as statistically significant.

Results

In this study all MetS patients were comparable to control by age. But WC, FPG, TG, SBP, DBP were significantly higher (p<0.001) and HDL-C was significantly lower (<0.05) in MetS compared to control (Table I). In addition, serum homocysteine was significantly higher (<0.05) but serum vitamin B₁₂ and folic acid levels were lower than control though these were statistically non significant (p>0.05) (Table II). Moreover, hyperhomocysteinemia was found in 16.67% MetS patients (Figure 1). None of control had elevated level of homocysteine.

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

| Variables | MetS (n=30) | Control (n=30) | p value |
|---------------|---------------|----------------|----------|
| Age(years) | 38.73±6.03 | 35.97±6.22 | 0.086 |
| WC(cm) | 96.23±5.98 | 75.63±3.32 | 0.000*** |
| FPG(mmol/L) | 8.97±3.50 | 5.04±0.38 | 0.000*** |
| TG(mg/dL) | 226.33±108.68 | 97.53±30.14 | 0.000*** |
| HDL-C(mg/dL) | 39.00±7.47 | 44.93±9.97 | 0.012* |
| SBP(mm of Hg) | 134.67±11.67 | 116.33±7.06 | 0.000*** |
| DBP(mm of Hg) | 87.83±9.16 | 74.00±6.07 | 0.000*** |

Data were expressed as mean±SD. Statistical analyses were done by Independent sample 't' test; WC-waist circumference; FPG-fasting plasma glucose; TG-triglyceride; HDL-C-high density lipoprotein cholesterol; SBP-systolic blood pressure; DBP-diastolic blood pressure; *p<0.05; ***p<0.001; N=total number of subjects; n=number of subjects in each group.

Table II: Serum homocysteine, vitamin B₁₂ and folic acid levels in two groups (N=60)

| Variables | MetS(n=30) | Control(n=30) | p value |
|------------------------------------|----------------------------------|----------------------------------|---------------------|
| Homocysteine (µmol/L) | 10.89±4.01 (5.19-22.98) | 8.91±2.85 (5.07-14.82) | 0.031* |
| Vitamin B ₁₂ (pg/mL) | 396.90±150.52 (166.00-878.00) | 462.50±143.17 (311.00-925.00) | 0.089 ^{ns} |
| Folic acid (ng/mL) | 8.77±2.29 (4.00-14.10) | 8.81±3.90 (3.50 -17.30) | 0.961 ^{ns} |

Data were expressed as mean±SD. Values in parentheses indicate ranges; Statistical analyses were done by Independent sample 't' test; *p<0.05; ns-non significant (p>0.05); N=total number of subjects; n= number of subjects in each group.

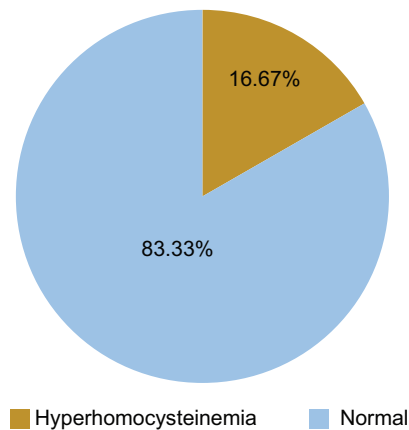


Figure 1: Frequency distribution of hyperhomocysteinemia in MetS patients

Discussion

In this study, significantly higher serum homocysteine level in MetS patients compared to control agrees reports of some previous studies.^{9,11} Again, the current study revealed that serum vitamin B₁₂ and folic acid were lower in metabolic syndrome patients than those of control group but these were statistically non-significant. But some researchers reported significantly lower value of vitamin B₁₂ and folic acid level in MetS patients.⁹⁻¹¹ In this study a substantial number MetS patients demonstrated hyperhomocysteinemia. This result agrees to other investigators reporting hyper-homocysteinemia in MetS.^{9,11} In contrast normal homocysteine level in MetS patients has also been reported.¹²⁻¹³

It is obvious from the above facts that hyperhomocysteinemia is associated with MetS. Literature review suggested that hyper-homocysteinemia occur due to vitamin B₁₂ and folic acid deficiency as vitamin B₁₂ and folic acid are involved in remethylation pathway of homocysteine.^{4-5,11} In the present study, lower vitamin B₁₂ and folic acid level in MetS support this trend of hyperhomocysteinemia in this group of patients.

Obesity has been recognized as the core factor of the pathophysiology of MetS¹⁴⁻¹⁵. High carbohydrate and fat and low protein intake in obese person causes vitamin B₁₂ deficiency.¹⁶ Food-bound vitamin B₁₂ separates from protein in the presence of acid and pepsin in stomach and this release vitamin B₁₂ combines with haptocorrin (R-protein). After releasing vitamin B₁₂ from R- protein it binds with an intrinsic factor in the small intestine where it is absorbed by binding with carrier protein.¹⁷ Helicobacter pylori infection is more common in obese patient, it may cause food cobalamin malabsorption (FCM).¹⁸⁻¹⁹ FCM is the inability to split cobalamin from food or other binders.¹⁷ Also obesity may cause increase catabolism and sequestration of vitamin B₁₂ in adipose tissue.²⁰ All these mechanisms ultimately causes deficiency of vitamin B₁₂ in obesity. Folic acid deficiency in metabolic syndrome may occur due to obesity. Cytochrome P450 activity increases in obesity and this Cytochrome P450 uses folic acid as a substrate.²¹

Conclusion

After analyzing the results of the study, it is concluded that elevated homocysteine is associated with MetS.

Conflict of interest None

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