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A Biochemical Study of Acute Phase Response in Metabolic Syndrome

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Abstract

Background: Metabolic syndrome (MS) is associated with the risk of developing cardiovascular disease (CVD) and type 2 diabetes mellitus. The preferred clinical approach to cardiovascular prevention is to treat all the metabolic risk factors.

Objective: The Objectives is Study of Acute Phase Response in Metabolic Syndrome.

Materials & Methods: This study was conducted on 250 subjects and controls at Government Medical College & Associated Group of Hospitals Kota, Rajasthan from oct.2019 to sept.2021.The study group had 125 MS cases and an equal number of healthy controls. Their serum status of Insulin were estimated by Electro-Chemiluminescence immunoassay (ECLIA). Iron, Glucose were estimated by spectrophotometry and CRP measured by immunoturbidimetric method. TIBC (using iron and UIBC) and Insulin resistance (by HOMA IR score) were calculated.

Results: We observed a significant rise in Glucose, Insulin, Iron, TIBC and CRP in MS cases when compared to control subjects, HOMA score was found to be elevated in subjects with MS.

Conclusion: In our study we have found increased level of serum Iron, TIBC, Glucose, Insulin and CRP in patients with MS. In this study we have concluded that Acute Phase Response should be assessed as it may be an underline cause of metabolic syndrome and further development of CVD. Hence, all the metabolic risk factors should be treated to prevent CVD

Keywords: Acute Phase Response, Metabolic Syndrome, Insulin Resistance

Introduction

Metabolic Syndrome (MS) also known as "insulin resistance syndrome," is defined as constellation of abnormalities associated with increased risk for the development of type 2 diabetes mellitus and atherosclerotic cardiovascular disease (e.g., heart disease and stroke). Metabolic Syndrome is a disorder of energy distribution and storage, fat accumulation which progresses to type 2 diabetes mellitus and cardiovascular disease. In 2002, the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) devised a definition for the metabolic syndrome [1]. According to the NCEP ATP III definition, metabolic syndrome is present if three or more of the following five criteria are met: waist circumference over 40 inches (men) or 35 inches (women), blood pressure over 130/85 mmHg, fasting triglyceride (TG) level over 150 mg/dl, fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dl (men) or 50 mg/dl (women) and fasting blood sugar over 100 mg/dl. [1][2]

The NCEP ATP III definition is one of the most widely used criteria of metabolic syndrome. It

incorporates the key features of hyperglycemia/insulin resistance, visceral obesity, atherogenic dyslipidemia and hypertension.

An acute-phase reactant is one whose level increases by 25% of the standard value during inflammation[3]. Since metabolic syndrome is considered as chronic mild inflammatory state hence the levels of acute-phase reactants are usually elevated among patients with it [4] Increased Iron Stores is also a risk factor for occurrence of type 2 diabetes mellitus in patients with hemochromatosis [5]. The free iron which carries unstable electrons produces hydroxyl radicals, are powerful pro-oxidants that lysis the lipid cellular membrane, damages protein structural configuration, and displaces nucleic acids in genes [6,7]. Moderate increase in serum iron stores concentrations may reflect systemic inflammation and contribute to cause MS.

TIBC (Total iron binding capacity), indicator for the transferrin activity is the sole iron trafficking index. Ferritin is a key protein regulating iron homeostasis. In healthy individuals, ferritin value in blood reflects the iron stored in the body. However, elevated serum ferritin concentrations have been involved in the pathogenesis of several chronic inflammatory diseases including the metabolic syndrome (MS).The purpose of the study is to evaluate association of Acute phase response, insulin resistance with MS.

Materials And Methods

This study was conducted on 250 subjects and controls in Government Medical College and Associated Group of Hospitals, Kota, Rajasthan.

The study group was constituted by 125 newly diagnosed cases of patients with Metabolic Syndrome as confirmed by using The National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) criteria of metabolic syndrome.

The case group (49.4 ± 7.8 years) was compared with age & sex-matched healthy controls (52.8 ± 6.2 years) were included.

Exclusion Criteria: The subjects with acute and chronic inflammatory conditions like infections, chronic liver disease, chronic blood transfusions for thalassemia syndromes, chronic anemia, and chronic kidney disease, known case of Diabetes Mellitus, other systemic illness, Congestive heart disease, taking anti inflammatory and lipid lowering drugs were excluded from the study.

About 5 ml of blood was collected by venipuncture in the plain vial as per the standard protocols.

The fluoride Plasma was used for Fasting glucose estimation and serum was used for Insulin, Iron, and C-Reactive Protein (CRP).

Method employed for estimation of serum Insulin was Electrochemiluminescence immunoassay (ECLIA) and serum Iron, UIBC were measured by spectrophotometry.

Serum CRP was estimated by immunoturbidimetric method.

Total iron binding capacity (TIBC in µg/dl) is sum of serum iron (µg/dl)and unsaturated iron binding capacity(UIBC in µg/dl) Insulin Resistance (IR) was measured using the formula based on homeostasis model assessment (HOMA) method. It is the product of fasting glucose and insulin levels divided by a constant 405. (IR=Fasting Glucose (mg/dl) x Fasting Insulin (mIu/ml)/405)

Patient recruitment and study design were according to the institutional ethical committee (IEC) recommendations. Samples were run in triplicates and the mean results obtained are represented as mean ± SD. We have used a nonparametric statistical tool, the student *t*-test for comparing one variable between two independent samples (or groups). A *p*-value <0.05 was considered to be significant and a *p*-value of<0.01 was considered to be highly significant for a given hypothesis testing. All the statistical analysis were performed using Graph Pad PrismVer.6.0 (Graph Pad Software, Inc., CA, USA) and Microsoft Excel, MS office2013 (Redmond, WA, USA).

Results

Total 250 samples along with age and sex matched controls were measured in this study. **(Fig 1: A).** Mean age of study group was (49.4 ± 7.8 years) and that of control group was (52.8 ± 6.2 years). There were 81 males and 44 females in study group and 75 males and 50 females in control group.

The serum Iron level **(Fig. 2: A)** in MS (126.85 ± 10.04 µg/dl) was significantly high (*p*-value <0.01) when compared to that of control group (98.58 ± 16.12 µg/dl).

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The serum TIBC level **(Fig. 2: B)** in MS (565.87 ± 88.85µg/ml) also showed significant variation (*p*-value <0.02) when compared to that of the control group (515.81± 115.84 µg/dl).

The serum CRP level **(Fig. 2: C)** in MS (5.29 ± 1.85 mg/dl) also showed significant variation (*p*-value <0.02) when compared to that of the control group (2.23± 1.02 mg/dl).

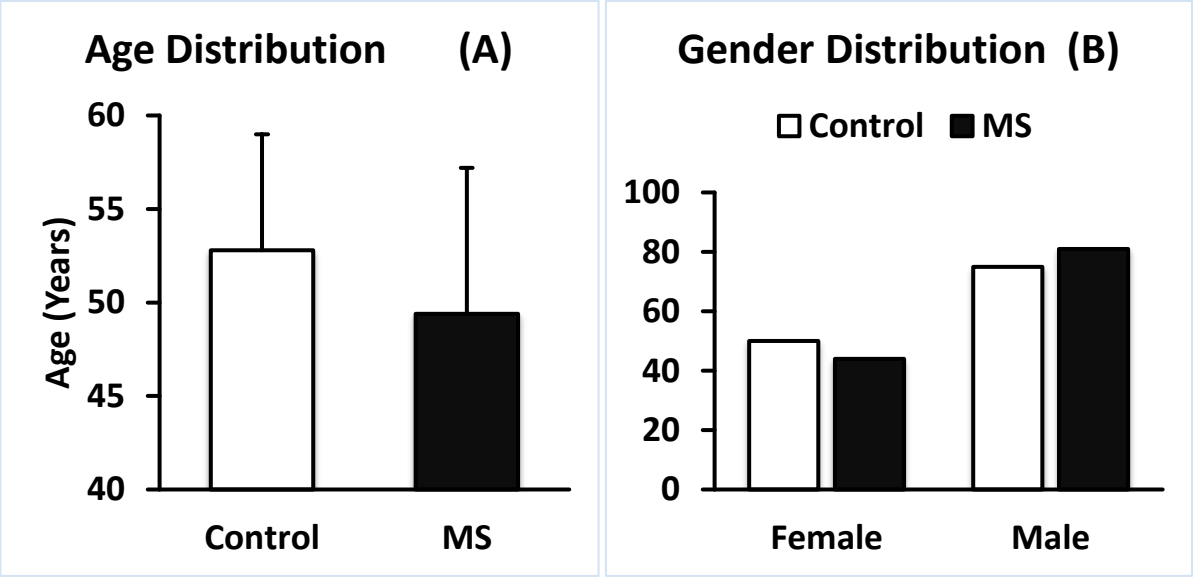

Fig. 1:(A) Age distribution between cases and controls. **(B)** Gender distribution between cases and controls.

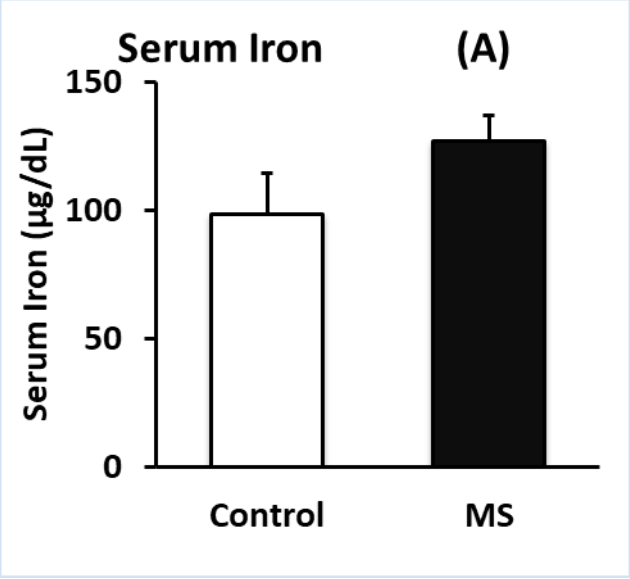

Fig. 2:(A) Comparison of serum Iron level

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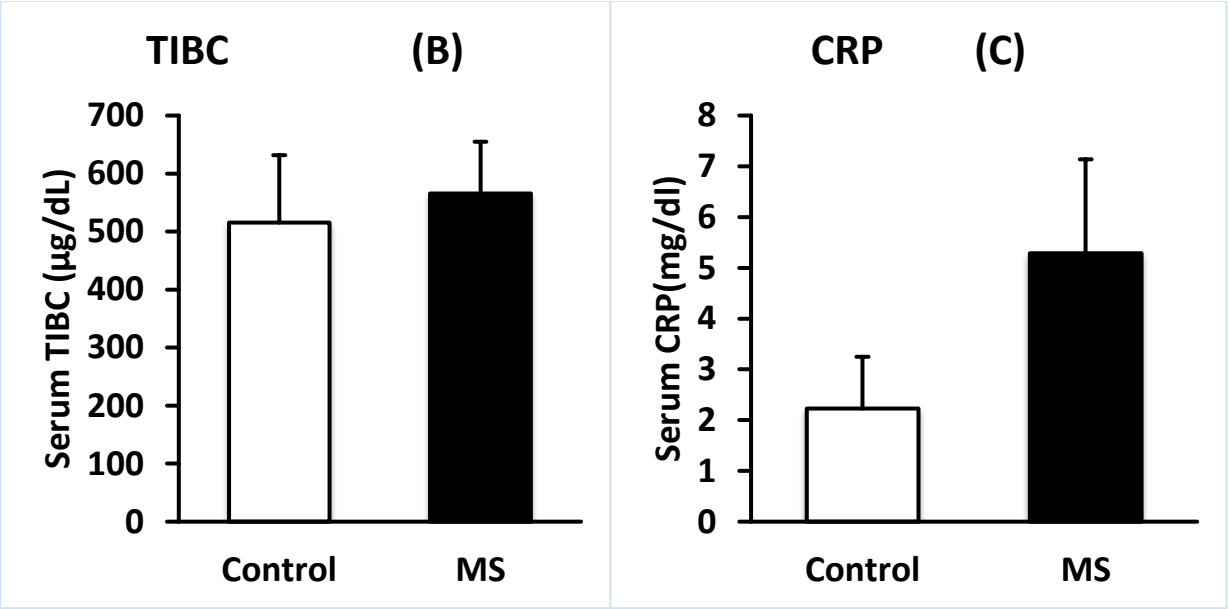

(B) Comparison of serum TIBC level.*p-value <0.02, (C)Comparison of serum CRP level * p-value <0.01

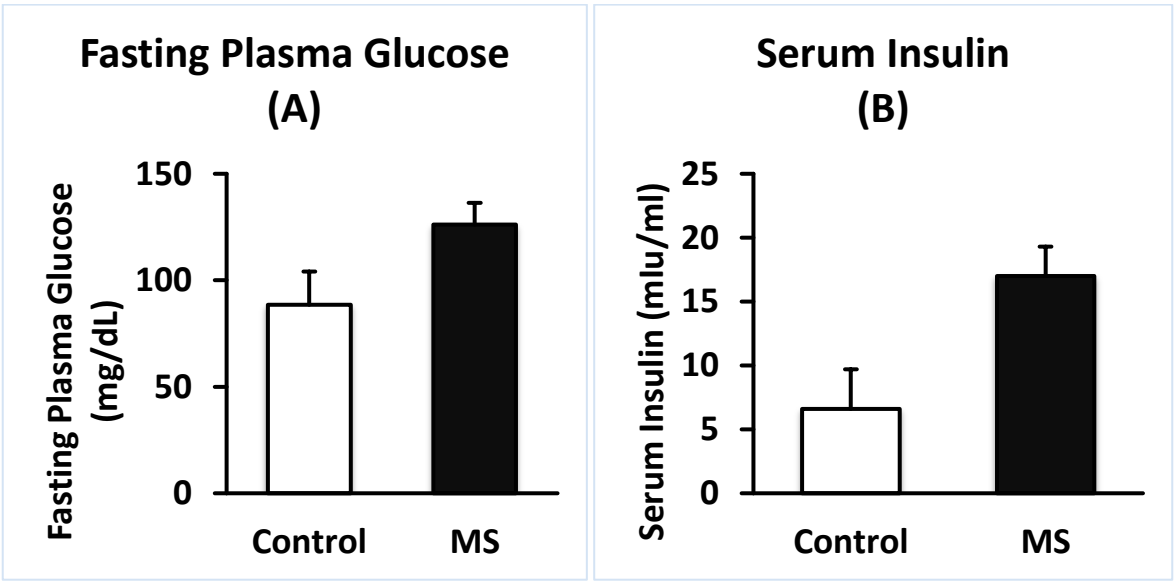

Fig. 3:(A) Comparison of Fasting Plasma Glucose level. (B) Comparison of serum Insulin level **p-value <0.01

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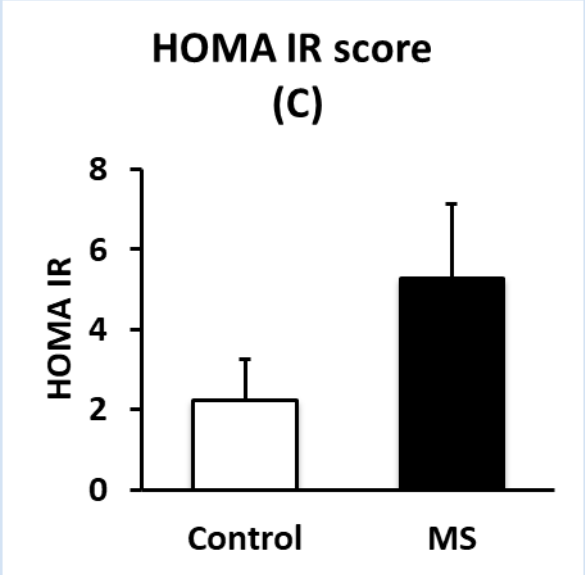

(C) Comparison of HOMA IR score. *p-value <0.01

The Fasting Plasma Glucose level (Fig. 3: A) in MS (126.21± 10.21mg/dl) was significantly high (p-value <0.01) when compared to that of the control group (88.52 ± 15.66 mg/dl). The serum Insulin level (Fig. 3: C) in MS (17.01 ± 2.28 mIu/ml) was significantly high (p-value <0.01) when compared to that of the control group (6.6 ± 3.09 mIu/ml). The HOMA IR score (Fig. 3: C) in MS (5.3 ± 1.04) was also significantly high (p-value <0.01) when compared to that of the control group (1.4± 0.9).

Discussion

The present case control study was conducted on 125 metabolic syndrome patients attended Department of Medicine in Government Medical College and Associated Group of Hospitals, Kota, Rajasthan.

Among study group (n=125) Metabolic syndrome found more in males(81) compared to that of females(44) when compared to equal number of age and sex matched healthy individuals (n=125). In this study, a significant increase in serum Iron, TIBC (*p*-value <0.02), Glucose, Insulin, CRP (*p*-value <0.01) was observed. This is in agreement of previous studies.

Wolff SP (1993) et al. concluded Elevated body iron may show an important role in the development of diabetic complications. Increased body iron may cause to metabolic abnormalities, which may increase free radicals formation. These radicals can take part in oxidative damage and lead to diabetic complications development.

Halle M et al, (1997) reported 3.26 times higher risk for developing type 2 diabetes and 2.8 times higher risk for developing metabolic syndrome for individuals with the highest serum ferritin quartile compared with those of the lowest. [8]Pedro VM et al.,(2005) stated that Chronic subclinical inflammation may be one of the pathophysiological mechanism explaining the increased risk of diabetes Subsequently metabolic syndrome and other complications associated with obesity. Adipose tissue expresses inflammatory cytokine and stimulates the release of inflammatory markers such as CRP. [9]

Gillum RF et al[10].,(2001),Piperno A et al[11].(2002) stated that Elevated serum high sensitive C reactive protein (hsCRP) and serum ferritin levels with metabolic syndrome and/ or insulin resistance tend to exhibit a certain degree of inflammation that, in one way or another, is likely to increase their risk of developing diabetes mellitus and/or cardiovascular disease.

Jaspinder K et al.,(2014) concluded that Metabolic syndrome is associated with the risk of developing cardiovascular disease and type 2 diabetes.[12]. Barbagallo, M. et al (2007) & Felizola, Saulo JA et al.,(2015) explained that In the USA, about a quarter of the adult population have metabolic syndrome, and the prevalence increases

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with age, with racial and ethnic minorities being particularly affected.[13]

Several cross sectional studies had previously examined showed the association between iron stores and individual metabolic cardiovascular risk factors, including hypertension and central obesity. In our study, the HOMA IR score was found to be elevated in MS (*p*-value <0.01) when compared to that of the control group

Conclusion

In our study we have found increased level of serum Iron, TIBC, Glucose, Insulin and CRP in patients with MS. In this study we have concluded that Acute Phase Response should be assessed as it may be an underline cause of metabolic syndrome and further development of CVD. Hence, all the metabolic risk factors should be treated to prevent CVD.

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