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Research Article

STUDY OF ASSOCIATION OF INFLAMMATORY MARKERS WITH METABOLIC SYNDROME IN PREDIABETIC PATIENTS AT TERTIARY CARE CENTER OF RAJASTHAN, INDIA

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ABSTRACT

Objective: The objectives is study of acute-phase reactants in MS patients. Metabolic syndrome (MS) is associated with the risk of developing cardiovascular disease and type 2 diabetes mellitus. The preferred clinical approach to cardiovascular prevention is to treat all the metabolic risk factors.

Methods: This study was conducted on 250 subjects and controls at Government Medical College and Associated Group of Hospitals Kota, Rajasthan from October 2019 to September 2021. The study group had 125 MS cases and an equal number of healthy controls. Demographic characteristic of all participants noted including age, sex, weight, and height.

Results: We observed a significant rise in blood glucose, total cholesterol, S. triglyceride, S. low-density lipoprotein (LDL). S. Very LDL S. C-reactive protein (CRP), and ferritin level in MS cases when compared to control subjects, while serum high-density lipoprotein level found to be decreased in MS patients as compared to control group.

Conclusion: In this study, both CRP and ferritin level are increased as the number of components of MS increased. Therefore, these inflammation parameters could accurately and timely discriminate patients with MS, according to IDF criteria, who are at increased risk for future cardiovascular events. There was a significant correlation between inflammation and the diabetic complications.

Keywords: Acute-phase response, Metabolic syndrome, C-reactive protein, Ferritin.

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INTRODUCTION

Prediabetes means your blood glucose levels are higher than normal but not high enough to be diagnosed as diabetes. Prediabetes usually occurs in people who already have some insulin resistance or whose beta cells in the pancreas are not making enough insulin to keep blood glucose in the normal range. Without enough insulin, extra glucose stays in your bloodstream rather than entering your cells. Over time, you could develop type 2 diabetes [1]. 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 (CVD) (e.g., heart disease and stroke). MS is a disorder of energy distribution and storage, fat accumulation which progresses to type 2 diabetes mellitus and CVD. In 2002, the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III) devised a definition for the MS [2]. According to the NCEP ATP III definition, MS 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 <40 mg/dl (men) or 50 mg/dl (women), and fasting blood sugar (FBS) over 100 mg/dl [3,4].

The NCEP ATP III definition is one of the most widely used criteria of MS. 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 [5]. Since MS is considered as chronic mild inflammatory state; hence, the levels of acute-phase reactants are usually elevated among patients with it. Increased iron stores are also a risk factor for occurrence of type 2 diabetes mellitus in patients with hemochromatosis [6]. The free iron, which carries unstable electrons produces hydroxyl radicals, is powerful pro-oxidants that lysis the lipid cellular membrane, damages protein structural configuration, and displaces nucleic acids in genes [7,8]. Moderate increase in serum iron stores concentrations may reflect systemic inflammation and contribute to cause MS.

C-reactive protein (CRP) is a member of the short evolutionarily conserved pentraxin group of plasma proteins, consisting of five identical non-glycosylated peptide subunits which link to form a cyclic pentamer structure [9,10]. CRP is produced as a result of pro-inflammatory cytokine signaling primarily mediated by neutrophils and monocytes. CRP concentration is elevated during infection or inflammation as part of the innate immune response and alteration of CRP plasma concentration is dependent on the rate of CRP synthesis and the severity of infection.

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 MS. The purpose of the study is to evaluate association of acute-phase response, insulin resistance with MS.

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 MS as confirmed using the NCEP ATP III criteria of

MS. The case group (49.4±7.8 years) was compared with age- and sex-matched healthy controls (52.8±6.2 years) were included in the study.

Exclusion criteria

The subjects with acute and chronic inflammatory conditions such as 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.

Body mass index (BMI) calculated based on height and weight. This is weight in kilograms divided by the height in meters squared. In adults overweight, or pre-obesity, is defined as a BMI of 25–29.9 kg/m^2, while a BMI ≥30 kg/m^2 defines obesity. These BMI thresholds were proposed by a WHO expert report and reflect the increasing risk of excess weight as BMI increases above an optimal range of 21–23 kg/m^2, the recommended median goal for adult Caucasian populations (WHO/NUT/NCD, 2000).

Blood pressure of all participants was measured. Fating blood samples were obtained from all participants and unique ID was given to each participants to hidden the identity of the patients.

The following investigations were performed from all samples.

1. Serum Lipid profile – by spectrophotometry method
2. FBS – by spectrophotometry method
3. S.CRP – by immunoturbidimetric method
4. Serum Ferritin – Electrochemiluminescence immunoassay.

FBS level between 100 and 125 mg/dl considered as a prediabetic as per ADA criteria.

MS was defined if central obesity was combined with at least two of the following factors: TG level ≥150 mg/dl or specific treatment for this abnormality, HDL cholesterol <40 mg/dl or specific treatment for this abnormality, systolic/diastolic blood pressures ≥130/85 mmHg or treatment of previously diagnosed hypertension, and fasting plasma glucose ≥100 mg/dl or previously diagnosed type 2 diabetes.

The patient recruitment and study design were according to the Institutional Ethical Committee recommendations. Results obtained are represented as mean±SD. All the statistical analysis was performed using GraphPad PrismVer.6.0.

RESULTS

A total 250 samples along with age- and sex-matched controls were measured in this study (Fig. 1a). Mean age of the 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 the control group (Fig. 1b).

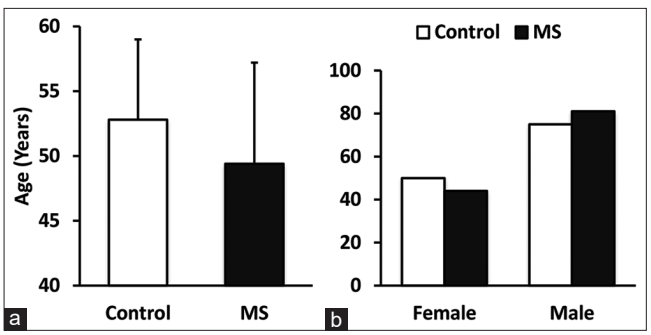

Fig. 1: (a) Age distribution between cases and controls. (b) Gender distribution between cases and controls

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

The Fasting Plasma Glucose level (Fig. 3) in MS (124.21±10.21 mg/dl) was significantly high (p<0.01) when compared to that of the control group (86.52±15.66 mg/dl).

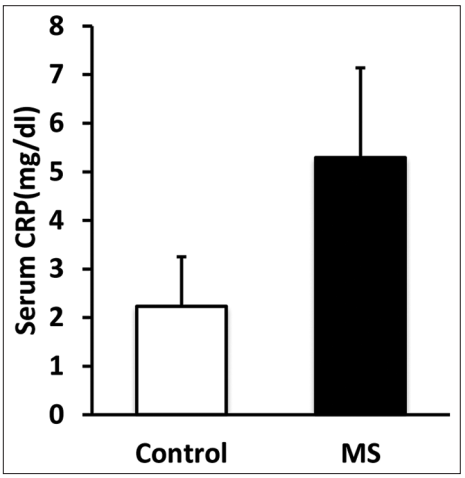

Fig. 2: Comparison of serum CRP level **p*-value <0.01

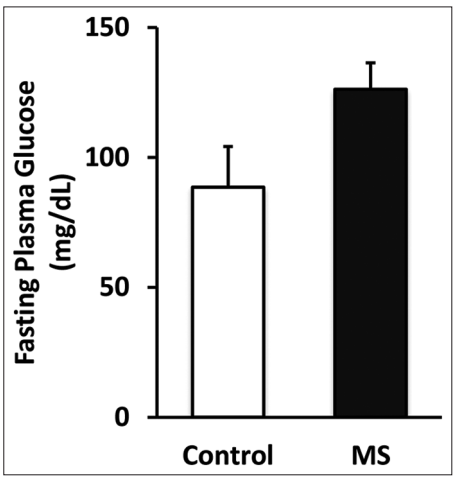

Fig. 3: Comparison of fasting plasma glucose level

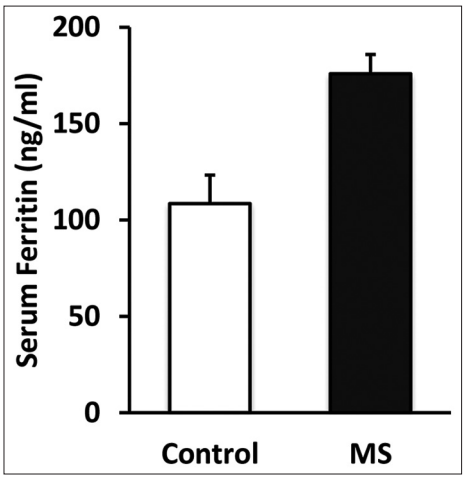

Fig. 4: Comparison of serum ferritin level **p<0.01

Table 1: Comparison of various biochemical parameter between case and control group

Biochemical parameter	Control (n=125)	Case (MS patients) (n=125)	p
Serum cholesterol (mg/dl)	145.50±10.5	172.60±15.5	<0.01
Serum triglyceride (mg/dl)	135.40±9.6	155.40±9.6	<0.01
Serum HDL (mg/dl)	48.5±5.0	43.5±6.0	<0.05
Serum VLDL (mg/dl)	27.08±3.90	31.5±4.0	<0.05
Serum LDL (mg/dl)	69.92±5.20	97.60±4.20	<0.01
FBS (mg/dl)	86.52±15.66	124.21±10.21	<0.01

P<0.05 considered as a significant. FBS: Fasting blood sugar, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, VLDL: Very low-density lipoprotein, MS: Metabolic syndrome

The serum ferritin level (Fig. 4) in MS (175.84±9.98 ng/ml) was also significantly high (p<0.01) when compared to that of the control group(108.5±14.85 ng/dl).

DISCUSSION

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

Among study group (n=125), MS 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).

Prediabetes represents an elevation of plasma glucose above the normal range but below that of clinical diabetes. Prediabetes can be identified as either impaired fasting glucose (IFG) or impaired glucose tolerance (IGT). The latter is detected by oral glucose tolerance testing. Both IFG and IGT are risk factors for type 2 diabetes, and risk is even greater when IFG and IGT occur together. Prediabetes commonly associates with the MS. Both, in turn, are closely associated with obesity. The mechanisms, whereby obesity predisposes to prediabetes and MS, are incompletely understood but likely have a common metabolic soil. There have been two major criticisms of the ADA's change in definition of prediabetes based on fasting glucose levels.

First, a high proportion of the population becomes "medi-calized," and second, persons with fasting glucose levels of 100–110 mg/dl convert to diabetes with a lower frequency than do those with levels of 110–125 mg/dl. Regarding the latter, compared with individuals with fasting levels of 100–110 mg/dl, those in the range of 110–125 mg/dl have a 2- to 6-fold higher risk for developing diabetes. In addition to hyperglycemia, dyslipidemia and hypertension, as originally described by Reaven [11], abdominal obesity, proinflammatory and prothrombotic states have now been included as key features of the MS.

Research shows that adipocytes produce bioactive substances, known as adipocytokines or adipokines. While each of the individual components of the MS is clearly associated with increased CVD risks, the presence of the MS greatly augments CVD morbidity and mortality. A number of large population and prospective studies have demonstrated significantly increased risk of all-cause mortality, and CVD mortality and morbidity, in association with the presence of the MS. Accumulation of adipocytes leads to the dysregulated production of adipokines, which contributes to the development of MS. The list of these dysregulated adipokines and cytokines is constantly growing and is a reflection of the heterogeneity of adipose tissue due to the number of resident cell types [12].

Halle *et al.* (1997) reported 3.26 times higher risk for developing type 2 diabetes and 2.8 times higher risk for developing MS for individuals with the highest serum ferritin quartile compared with those of the lowest [13]. Pedro *et al*. (2005) stated that chronic subclinical inflammation may be one of the pathophysiological mechanism explaining the increased risk of diabetes subsequently MS and other complications associated with obesity. Adipose tissue expresses inflammatory cytokine and stimulates the release of inflammatory markers such as CRP [9].

Gillum *et al*. [10] (2001) and Piperno *et al*. [14] (2002) stated that elevated serum high sensitive CRP and serum ferritin levels with MS 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 CVD.

Jaspinder *et al*. (2014) concluded that MS is associated with the risk of developing CVD and prediabetes [12]. Barbagallo *et al*. (2007) and Felizola and Saulo (2015) explained that in the USA, about a quarter of the adult population have MS, and the prevalence increases with age, with racial and ethnic minorities being particularly affected [15].

CONCLUSION

In this study, both CRP and ferritin level are increased as the number of components of MS increased. Therefore, these inflammation parameters could accurately and timely discriminate patients with MS, according to IDF criteria, who are at increased risk for future cardiovascular events. There was a significant correlation between inflammation and the diabetic complications.

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