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Research Article

ASSOCIATION OF SERUM FERRITIN AND HS-CRP LEVELS WITH METABOLIC SYNDROME.

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ABSTRACT

Ferritin is one of the key proteins regulating iron homeostasis and is a widely available clinical biomarker of iron status. Some studies suggest that prevalence of atherosclerosis and insulin resistance increases significantly with increasing serum ferritin. Metabolic syndrome is known to be associated with increased risk of atherosclerosis as well as insulin resistance. The metabolic syndrome (MetS) also called syndrome X is a major and increasing public health and clinical challenge worldwide in the era of urbanization, because of increasing obesity and sedentary life habits. To measure the levels of hsCRP and ferritin in metabolic syndrome patients and age and sex matched controls and to compare the association of hsCRP and ferritin between the two groups and association with metabolic syndrome components. Serum ferritin and hsCRP levels with measured in 60 metabolic syndrome patients and60 controls and results were compared. From this study, we can conclude that the assessment of these novel risk factors [hs-CRP, Lp(a), and MetS] may be used for the risk estimation and can help to prevent future mortality and morbidity due to CVD.

Keywords:- Metabolic Syndrome, Ferritin, Hscrp, Diabetes Mellitus, Cardiovascular Disorder

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INTRODUCTION

The metabolic syndrome is a cluster of metabolic and cardiovascular symptoms that are strongly associated with type II diabetes mellitus. In this kind of diabetes, rather than prolonged high levels of glycemia, there is insulin resistance with secondary hyperinsulinemia, both very frequently associated with, hypertension, dyslipemia, atherosclerosis, and, most importantly, obesity Diabetes Mellitus (DM) is a disorder characterized by persistent hyperglycemia due to insulin resistance. Insulin is a pleiotropic hormone which signals a number of cellular processes such as glucoregulation, lipid metabolism, and protein synthesis in multiple tissues. In patients with DM, these actions of insulin are reduced. Consequently, there is an increase in free fatty acids which promote oxidative stress, endothelial dysfunction, vascular damage, and atheroma formation. The clinical results are high BP, HDL suppression, and high triglycerides (TGL) additionally, DM is associated with macrovascular (myocardial infarction, stroke) and microvascular (retinopathy, neuropathy, renal disease) problems which interfere with blood and nutrient delivery to multiple tissues throughout the body. DM is a crucial factor in Metabolic Syndrome (MetS) and is highly predictive of Cardiovascular Disease (CVD) risk

The amount of ferritin in circulation normally reflects the amount of iron stored in the body in healthy individuals. However, serum ferritin is a positive acute phase response protein which is elevated in case of acute inflammation4. However, elevated serum ferritin (SF) concentrations have recently been implicated in the pathogenesis of many chronic inflammatory diseases including the metabolic syndrome (MetS).

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Elevated iron stores may induce diabetes through a variety of mechanisms, including oxidative damage to pancreatic beta cells, impairment of hepatic insulin extraction by the liver, and interference with insulin's ability to suppress hepatic glucose production. Raised serum ferritin may possibly be related to the occurrence of long term complications of diabetes, both micro vascular and macro vascular [1].

C reactive protein (CRP) represents the classical acute- phase protein produced by the liver in response to inflammatory stimuli, and the plasma levels of CRP provide a sensitive marker of increased inflammatory activity in the arterial wall [1]. Elevated CRP constitutes.

Material and Methods:

The Present study was carried out in the department of Biochemistry, Sri Lakshmi Narayana Institute of Medical Sciences, Puducherry. A cross sectional study was carried out from subjects who fulfill inclusion and exclusion criteria who were admitted and .the study was approved by the institutional ethical committee of Sri Lakhsmi Naryana Institute of Medical Sciences, Puducherry according Helsiniki 1975 human ethical guidelines. All the data were collected in a prescribed perform and obtained informed consent form.

Sample size:

60 (30 cases and 30 controls).

Inclusion criteria: Cases:

30 patients of metabolic syndrome between age group of 30-60.

Controls: 30 age and sex matched non metabolic syndrome individuals.

Metabolic syndrome is explained by Adult Treatment Panel-3 as at least any three of the following:

1. Abdominal obesity: >90cm in men and >80cm in women
2. Serum triglycerides: >150mg/dL
3. Serum HDL: <40mg/dL (male)
4. <50mg/dL (female)
5. Blood pressure: >130/85mmHg
6. Fasting plasma glucose: >110mg/dL.

Exclusion criteria:

Patients with type 1 diabetes mellitus, gestational diabetes mellitus,Other states associated with altered serum ferritin or hsCRP levels,like hemochromatosis, hemosiderosis, thalassemia, recurrent,blood transfusion, iron deficiency anemia, patient on iron,supplementation, thiazide diuretics, antioxidant drugs, steroids, Patients with chronic infections, liver disease, renal disease, neoplastic condition, chronic alcoholics, smokers. Critically ill patients admitted in intensive care unit.

5ml of the blood samples which were taken for analysis were obtained from the antecubital vein. 5 ml of venous blood samples were collected from patients and controls. Blood samples were centrifuged and plasma was separated. The samples were then centrifuged at 3000 rpm for 15 minutes.

Statistical Analysis:

All values were expressed as mean ± standard deviation (SD). Independent samples't' test was used to test the significance of difference in means between study group and controls. For men and women, a student t-test or ANOVA test was used to compare between control and MetS participants normal or non-normal distribution, respectively. A P-value less than 0.05 were considered statistically significant. Statistical analysis was done by using Microsoft Excel and SPSS for windows version 11.5 (SPSS, Inc., Chicago).

Table 1: Multiple logistics regression analysis of cases
***p<0.05**

STAGE OF CKD	SERUM URIC ACID NORMAL	SERUM URIC ACID RAISED	p value
1	14 (16 %)	2 (1.5%)	<0.01
2	14(16 %)	2 (1.5%)	
3	16(17 %)	6 (10 %)	
4	22(25 %)	18 (30 %)	
5	24(26 %)	32 (57 %)	
TOTAL	90(100 %)	60 (100 %)	

Discussion:

The etiology of metabolic syndrome patients with CVD involves coronary atherosclerotic diseases, artery hypertension, left ventricular hypertrophy, diastolic dysfunction, endothelial dysfunction, coronary macro-vascular disease and autoimmune dysfunction diseases occurred [1-3]. MetS individuals seemingly are susceptible to other conditions notably polycystic ovary syndrome, fatty liver, cholesterol gallstones, asthma, sleep disturbance and some forms of cancer [4]. Abdominal

obesity is strongly associated with the MetS. It presents clinically as increased waist circumference (Men->40 inch-women>35inch) Obesity strongly associated with increased blood pressure in insulin–resistant persons. Increased CRP level, clinically observed in pro inflammatory persons with MetS [5]. Obesity is one of the causes for elevation of CRP levels due to excess adipose tissues release, inflammatory cytokines that may elicit higher CRP levels. Increased Plasma plasminogen Activator Inhibitor (PAI) and fibrinogen associated with the metabolic syndrome [6]. There are truly the scavengers of free radicals. The most important antioxidant enzymes are superoxide dismutase, catalase and glutathione peroxidase. Vitamin C (ascorbic acid), Vitamin E (tocopherol), Beta Carotene, Uricacid, Glutathione, Flavonoids, Ceruloplasmin, Caffeine, Ferritin, Transferrin, Bilirubin. The clustering of hypertension, dyslipidemia, glucose intolerance, insulin resistance, hyperinsulinemia, microalbuminuria, and obesity, particularly central obesity, has been termed the metabolic syndrome [7].

As per taking into account the inclusion and exclusion criteria as 30 cases and 30 controls. Out of 30 cases there were 16 males and 14 females and out of 30 controls there were 14 males and 16 females. So, there was no significant variation between the two groups. Among the cases we divided diabetics according the duration of diabetes of more than 5 years and less than 5 years. 24 out of 60 cases i.e. 40% of patients had diabetes of less than 5 years duration whereas 36 patients i.e. 60% had duration of more than 5 years. Mean duration of diabetes was 7.2 years. Similarly, hypertensives were divided according to the duration of hypertension as less than 5 years and more than 5 years. Out of 60 cases, 26 patients i.e. 43.30% had hypertension for less than 5 years whereas 34 patients i.e. 56.63% had hypertension of more than 5 years duration. Mean duration of hypertension was 5.67 years. Diabetics were also divided on the basis of HbA1c values of less than 9 and more than 9. 26 patients had HbA1c of less than 9 i.e. 43.31% and 34 patients had HbA1c of more than 9 i.e. 56.63%. Mean HbA1c was 9.92.

Comparision between the groups as Serum ferritin was measured in both cases and controls. It was significantly elevated in the case group. 36 patients out of 60 cases i.e. 60% had elevated ferritin levels compared to only 8 patients out of 60 controls i.e. 13.33% had elevated ferritin levels. This was statistically significant with p value of 0.0001. This was comparable with the results of Dong Wei et al [8] and Sumesh Raj et al [9]. The mean ferritin value among cases was 225.68 whereas it was 108.28 among controls with significant p value of 0.0003. Comparision between the groups as hsCRP was measured in both case and control groups. It was significantly elevated in cases. 44 patients among 60 cases i.e. 73.37% had elevated hsCRP compared to 10 patients among 60 controls i.e. 16.62% had elevated hsCRP. This was statistically significant with p value of 0.0001. This was comparable to the results of Mukesh G Gohel et al [10] and Seyyed MR Kazemi-Bajestani et al[11]. The mean hsCRP among cases was 18.07 whereas it was 2.83 among controls with significant p value of 0.0010.

Metabolic syndrome being a common condition encountering in medical practice, it is important to study the correlation of various components of metabolic syndrome with various parameters. In our study, serum ferritin levels and hsCRP was studied. Both were significantly elevated in cases compared to controls. While correlating these two parameters with various components of metabolic syndrome, it is shown that serum ferritin levels significantly correlated with HbA1c levels whereas there was no correlation between ferritin levels with either duration of diabetes or hypertension. Abdominal obesity is strongly associated with the MetS. It present clinically as increased waist circumference (Men->40 inch-women>35inch) Obesity strongly associated with increased blood pressure in insulin–resistant persons. Increased CRP level, clinically observed in pro inflammatory persons with MetS [12]. Obesity is one of the causes for elevation of CRP levels due to excess adipose tissues release, inflammatory cytokines that may elicit higher CRP levels. Increased Plasma plasminogen Activator Inhibitor (PAI) and fibrinogen associated with the metabolic syndrome [13]. On the other hand hsCRP levels show no correlation with duration of diabetes or hypertension not even to HbA1c levels. It shows that serum ferritin levels are directly correlated with the glycemic control. Multiple regression analysis showed metabolic syndrome patients had 2.03 times elevated ferritin level odds compared to controls and 2.16 times elevated hsCRP level odds. Compared to earlier studies, our study also showed serum ferritin and hsCRP levels rise in metabolic syndrome patients. But unlike some of the earlier studies it was not directly correlating with the duration of diabetes or hypertension. Elevated serum ferritin levels might reflect systemic inflammation in addition to increased body iron stores. It has been observed that inflammation regulates expression of ferritin mRNA & protein levels and its secretion. Excessive iron deposits produce hydroxyl radicals which cause lipid peroxidation. This leads to DNA fragmentation and tissue damage. Therefore, one of the mechanisms involved in progression of MetS to CVDs and Type II DM is inflammation and oxidative stress mediated through ferritin.

Metabolic syndrome, as the same suggests is a syndrome which has signs and symptoms or various components to diagnose it. Though there are various criteria to diagnose it as discussed earlier, these parameters may be used as an add-on. Also it may also predict the severity and prognosis of metabolic syndrome. So more research is needed to differentiate the effects of major

serum antioxidant on MetS and complications. Further studies are required in this approach.

Conclusion:

From the findings of our study we can conclude that metabolic syndrome is associated with significantly increased serum ferritin though in the normal limits. These increased serum ferritin levels may be one of the key elements that progresses the journey of metabolic syndrome to Type II DM and other cardio metabolic derangements. In this study, we found a significant association of novel risk factors namely MetS and levels of hs-CRP and Lp(a), which stated that they have high prevalence of developing CVD. Thus, we can conclude that assessment of these novel risk factors may be used for the risk estimation of CVD and can help to prevent future mortality and morbidity due to CVD.Further studies are required to investigate the pathophysiological mechanism of increased ferritin levels in patients with insulin resistance syndrome.

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