A STUDY ON ASSOCIATION OF SERUM FERRITIN AND hs-CRP LEVELS WITH METABOLIC SYNDROME

General Medicine

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ABSTRACT

Background: The metabolic syndrome is considered as a clustering of components that reflects the expanding waist lines of the world. hsCRP and ferritin participate in common pathophysiological processes, including oxidative stress and lipid peroxidation, which are important to the pathogenesis and development of insulin resistance and the metabolic syndrome.
Objectives: 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.
Materials and methods: Serum ferritin and hsCRP levels with measured in 30 metabolic syndrome patients and 30 controls and results were compared.
Results: Serum ferritin and hsCRP levels were significantly elevated in metabolic syndrome. Serum ferritin also correlated with the HbA1c levels.
Conclusion: Though there are various criterias to diagnose the syndrome, comparing other various parameters like hsCRP and ferritin with metabolic syndrome and its components may help in assessing the severity or prognosis of the condition.

KEYWORDS

Metabolic syndrome, ferritin, hsCRP.

INTRODUCTION

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[1]. "It is a constellation of interconnected physiological, biochemical, clinical and metabolic factors that directly increases the risk of cardiovascular disease (CVD), type 2 diabetes mellitus (T2DM) and cause increased mortality"[2]. Insulin resistance, visceral obesity, atherogenic dyslipidemia, genetic susceptibility, endothelial dysfunction, elevated blood pressure, hypercoagulable state and chronic stress factors all contribute to the pathogenesis of the syndrome[1].

"MetS is a state of chronic low grade inflammation as a consequence of complex interplay between genetic and environmental factors"[1]. It is characterized by production of abnormal adipocytokines such as tumor necrosis factor alpha (TNF-alpha), interleukin 1 (IL-1), IL-6 and adiponectin[3]. The interaction between various components of clinical and biological phenotype of the syndrome which contributes to the development of a proinflammatory state and further resulting in chronic, subclinical vascular inflammation which modulates and results in atherosclerotic processes[1].

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 inflammation[4]. However, elevated serum ferritin (SF) concentrations have recently been implicated in the pathogenesis of many chronic inflammatory diseases including the metabolic syndrome (MetS). 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[5].

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 wall6. Elevated CRP constitutes an independent predictor of advanced plaques in dyslipidemic subjects. Evidence points to strong relationships among obesity, inflammatory markers, metabolic syndrome and the risk of CVD. There is increasing evidence supporting the addition of elevated CRP to the list of characteristics of metabolic syndrome[7].

AIMS AND OBJECTIVES OF THE STUDY
1. To measure the levels of hsCRP and ferritin in metabolic syndrome patients and age and sex matched controls.
2. To compare the association of hsCRP and ferritin between the two groups and association with metabolic syndrome components.

MATERIALS AND METHODS
Source of data: A cross sectional study was carried out from subjects who fulfill inclusion and exclusion criteria who were admitted in SDMCMS & H Dharwad.Ethical committee clearance was taken prior to the study.

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)
            <50mg/dL (female)
4. Blood pressure: >130/85mmHg
5. 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.

Method of collection of data: A pretested proforma meeting the objectives of the study was prepared. The cases for the study were

selected in accordance with the above mentioned inclusion and exclusion criteria, the purpose of the study is explained to the patients and informed consent was obtained. The data was collected according to the proforma in terms of detailed history, clinical examination including abdominal waist, blood pressure measurement and the necessary investigations.

The following investigations was carried out:
• Hemoglobin level with peripheral smear, ESR
• FBS, PPBS, HbA1c.
• Serum ferritin.
• hsCRP.
• Serum triglycerides, HDL
• Renal function and liver function tests.

OBSERVATIONS AND RESULTS
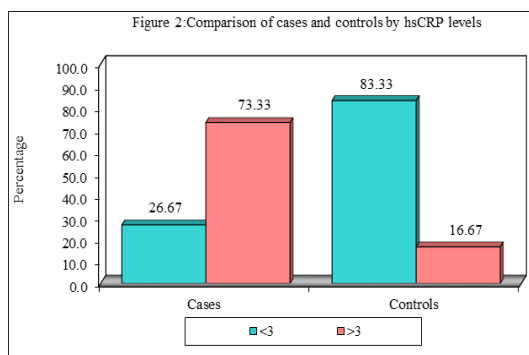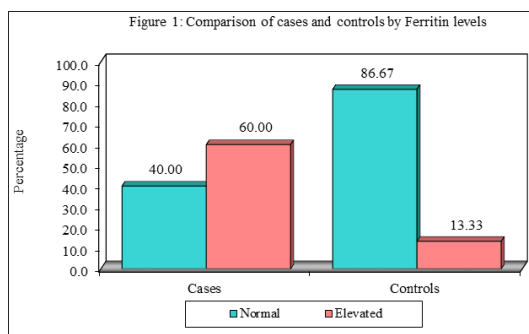Following are the observations and results of our study:

Figure 1: Comparison of cases and controls by Ferritin levels

Figure 2:Comparison of cases and controls by hsCRP levels

Table 1: Multiple logistics regression analysis of cases

Variables	Odds Ratio	Std. Err.	Z-value	p-value	95%CI lower	95%CI Upper
Age (<50 vs. >50)	3.89	2.55	2.0700	0.0390*	1.07	14.09
Gender (Male vs. female)	1.52	1.32	0.4900	0.6270	0.28	8.34
Ferritin (Normal vs. abnormal)	2.01	2.12	0.6600	0.5060	0.26	15.82
hsCRP (<3 vs. >3)	2.13	1.77	0.9100	0.3620	0.42	10.85

*p<0.05

Multiple logistics regression analysis of cases showed patients aged >50years had 3.89 times more odds of developing metabolic syndrome than patients <50 years. Females had 1.52 times more odds of developing metabolic syndrome than females. Also metabolic syndrome patients had 2.01 times elevated ferritin level odds compared to controls and 2.13 times elevated hsCRP level odds.

DISCUSSION
The study was conducted in SDMCMS & H, Dharwad 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. 12 out of 30 cases i.e. 40% of patients had diabetes of less than 5 years duration whereas 18 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 30 cases, 13 patients i.e. 43.33% had hypertension for less than 5 years whereas 17 patients i.e. 56.67% 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. 13 patients had HbA1c of less than 9 i.e. 43.33% and 17 patients had HbA1c of more than 9 i.e. 56.67%. Mean HbA1c was 9.97.

Comparison of ferritin between the groups
Serum ferritin was measured in both cases and controls. It was significantly elevated in the case group. 18 patients out of 30 cases i.e. 60% had elevated ferritin levels compared to only 4 patients out of 30 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 al8 and Sumesh Raj et al[9]. The mean ferritin value among cases was 225.62 whereas it was 108.22 among controls with significant p value of 0.0004.

Comparison of hsCRP between groups
hsCRP was measured in both case and control groups. It was significantly elevated in cases. 22 patients among 30 cases i.e. 73.33% had elevated hsCRP compared to 5 patients among 30 controls i.e. 16.67% 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.

SUMMARY AND CONCLUSION
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. 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 2.01 times elevated ferritin level odds compared to controls and 2.13 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.

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. Further studies are required in this approach.

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