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Research Article

ASSESSMENT OF METABOLIC SYNDROME: ROLE OF SERUM FERRITIN

PREETI SHARMA[1]*, PRADEEP KUMAR[1], RACHNA SHARMA[2], KISHORE K[3], SHARMA G[3]

[1]Department of Biochemistry, Santosh Medical College and Hospital, Santosh University, Ghaziabad, Uttar Pradesh, India. [2]Department of Biochemistry, TSM Medical College and Hospital, Lucknow, Uttar Pradesh, India. [3]Department of Medicine, Santosh Medical College & Hospital, Santosh University, Ghaziabad, Uttar Pradesh, India. Email: prcdri2003@yahoo.co.in

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ABSTRACT

Objective: The aim of the study is to explore the association between serum ferritin level and metabolic syndrome and its components.

Methods: Serum ferritin level and metabolic syndrome and its components were measured among 100 study subjects with respect to 25 healthy controls at Santosh Medical College and Hospital, Ghaziabad. Fasting and post-prandial blood sugar level was estimated by using glucose oxidase-peroxidase (POD) method. Total cholesterol, triglycerides, and high-density lipoprotein cholesterol were estimated by using cholesterol oxidase (CHOD)-POD method, glycerol-3-phosphate oxidase-phenol aminophenazone method, and Phosphotungustate/CHOD-POD method, respectively. Low-density lipoprotein cholesterol was estimated by using Friedewald's equation. Serum concentration of ferritin was estimated by using Micro ELISA test kit. Cases and controls were compared using Chi-square test and unpaired Student's t-test and p values were calculated.

Results: Significant relationship was observed between serum ferritin level and components of metabolic syndrome. Body mass index, blood sugar level, and lipid profile were significantly (<0.05) different between the groups. Serum concentration of creatinine and urea was not significantly (>0.05) different between the groups. Serum ferritin level was elevated in case group with metabolic syndrome and this difference was extremely significant (<0.01) between the groups.

Conclusion: Serum ferritin, key regulator of iron homeostasis, can be used as indicator of progressing risk of metabolic syndrome.

Keywords: Dyslipidemia, Ferritin, Insulin resistance.

INTRODUCTION

Ferritin is a ubiquitous intracellular globular protein complex made up of 24 protein subunits and is essentially a iron storage protein both in prokaryotes and eukaryotes [1]. Studies have indicated that increased accumulation of iron affects the synthesis and secretion of insulin thereby compromising insulin action in target tissues [2]. Metabolic syndrome is closely linked to insulin resistance and increases the risk of cardiovascular diseases (CVD) [3,4]. A number of studies were conducted between various components of metabolic syndrome [5a] and ferritin level. Given that metabolic syndrome is a major risk factor for type 2 diabetes [5b], it is critical to clarify whether the association between ferritin and risk of type 2 diabetes is mediated through metabolic syndrome. However, most previous studies evaluated only individual components of metabolic syndrome rather than the clustered condition of metabolic syndrome. Therefore, the aim of our study is to evaluate the ferritin concentration association with metabolic syndrome and its multiple components.

MATERIALS

The cross-sectional study was conducted at the Department of General Medicine, in Santosh Medical College and Hospital, Ghaziabad, for 1-year. A written informed consent was taken from the patients inducted into the study. The patients attending the OPD of the Medicine Department were included into the study. Patients included were adults of either sex having metabolic syndrome. The 100 study subjects and 25 controls between the age group 31-80 were taken into the study. Patients of metabolic syndrome were diagnosed on the basis of IDF criteria for diagnosis of metabolic syndrome. This study was ethically approved by the Institutional Ethical Committee of Santosh Medical College and Hospital, Ghaziabad.

Exclusion criteria

Subjects who are anemic, donated blood in last 3 months, suffering from hamochromatosis or adult onset still's disease, having raised inflammatory markers, i.e., CRP, patients with gastrointestinal diseases, thyroid disorders, and oncological disorders were not included into the study. Patients and control were undergone following investigations:

1. Complete blood count with peripheral blood smears
2. Blood glucose level both in fasting and post-prandial state
3. Lipid profile including total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), very low-density lipoprotein (VLDL), triglycerides (TG)
4. Kidney function test including blood urea and serum creatinine
5. Urine routine and microscopy
6. C- reactive protein
7. Serum ferritin.

METHODS

Serum cholesterol was estimated by cholesterol oxidase-peroxidase enzymatic colorimetric method [6], HDL was measured by enzymatic clearance assay using phosphotungstate method [7] for *in vitro* quantitative determination, TG by glycerol-3-phosphate oxidase-phenol aminophenazone (GPO-PAP) method of enzyme colorimetry [8]. VLDL was estimated by Friedwald's WT formula [7], LDL by Friedwald's formula [7], blood glucose by GPO-PAP enzymatic colorimetric method [9] both in fasting and post-prandial state. Serum ferritin was estimated by MICRO ELISA using human ferritin enzyme immunoassay test kit [10].

Statistical analysis

All the variables were expressed in mean±standard deviation. All variables were statistically analyzed using statistical software IBM SPSS version 20.0. An unpaired Student's t-test and Chi-square test were used to analyze the different parameters between the case and control group. A $p<0.05$ was used as statistically significant.

RESULTS

Various clinical parameters were very well studied in this case–control study conducted at Santosh Medical College and Hospital, Ghaziabad. Table 1 shows the comparison of various parameters of study subjects and control samples. Except for creatinine, urea, hemoglobin, and LDL; all the parameters were significantly changed (<0.05) among metabolic syndrome patients. Table 2 shows that there were 100 (100%) cases whose mean serum ferritin (124.21±52.08) was compared to mean of controls (38.66±14.48). Statistically significant association (p<0.05) between control and subjects were observed. Moreover, ferritin level comparison between cases having triglyceride level >150 and control was found statistically significant, which is apparent in Table 3. Table 4 shows 100 cases having low HDL and whose serum ferritin (122.07±54.28) was compared to mean serum ferritin of control (38.66±14.48). The association was statistically significant. In Table 5, 86 blood pressure (BP) patients (BP>130/85) having serum ferritin level was 126.35±52.20 showed statistically significant association with control ferrritin level (38.66±14.48). Table 6 shows that there were 90 cases out of 100 having impaired glucose levels, whose mean ferritin 124.42±51.90 was compared to mean serum of the controls (38.66±14.48). The association between control and cases was statistically significant. In Tables 7-9 comparison between serum ferritin level of patients with number of components of metabolic syndrome and control has been done. We found statistically significant relationship between the subjects and controls.

DISCUSSION

Serum ferritin is an acute phase reactant and may be elevated in the presence of inflammation [11]. The present study was done to determine the association of serum ferritin in metabolic syndrome and also to determine the level of ferritin with components of metabolic syndrome. Though there is an apparent evidence that moderately raised level of iron storage, which are commonly found genetic heamochromatosis [11] and may cause adverse health outcome. Patients were meticulously examined with detailed history and laboratory examination. The laboratory investigations included fasting lipid profile, fasting blood glucose, post-prandial blood glucose, complete blood picture, and serum ferritin. The study revealed a significant increase in serum ferritin levels in cases (124.21±52.08) as compared to control (38.66±14.48) with p<0.001. Outcome of our study is in good match with the study done by Li *et al*. [12] and Park *et al.* [13]. They concluded moderately raised level of iron was associated with metabolic syndrome and insulin resistance [12,13]. Iron is a transition metal, has tendency to catalyze lipid peroxidation leading to the formation of oxidant species and free radicals, which induce tissue injury [14]. A number of researchers have postulated the role of oxidative stress and insulin resistance in the etiology of metabolic syndrome [3,15]. Hence, a high content of iron load may induce disorders of glucose metabolism. Under oxidative stress, elevated level of serum ferritin may contribute to cellular damage leading to insulin dysfunctions.

Our study also include relation of serum ferritin with each component of metabolic syndrome that is TG, low HDL, central obesity, BP, and fasting blood glucose. A positive correlation has been observed between serum ferritin and each component of metabolic component. Studies conducted by Halle *et al*. [16] and Li *et al.* [17] also concluded that there is a positive correlation between TG and serum ferritin. Serum ferritin level with low HDL (122.07±42.28) was when compared with mean serum ferritin of control (38.66±14.48), a positive relation has been observed (<0.001). Studies done by William *et al.* [18] also found similar relation. Ford and Cogswell [19] conducted research on ferritin level of of hyperglycemics and on comparing the level with ferritin level of control, significantly raised the level of ferritin was observed among study subjects. In our study also, we found the elevated level of serum ferritin in hyperglycemics. Kim *et al.* [20] also revealed that moderately increased iron stores are associated with

Table 1: Clinical parameter of both case and control group*

Serial number	Parameters	Control (n=25)	Case (n=100)	p value
1	Age (years)	36.76±7.84	57.40±8.18	<0.001
2	BMI (kg/m^2)	23.43±2.36	29.39±1.76	<0.001
3	Central obesity (cm)	81.76±7.91	99.11±6.72	<0.001
4	Fasting plasma glucose (mg/dl)	89.16±15.69	148.97±34.07	<0.001
5	Post-prandial blood sugar (mg/dl)	134.60±19.29	230.96±64.30	<0.001
6	Systolic blood pressure (mm Hg)	124.24±10.41	146.59±14.85	<0.001
7	Diastolic blood pressure (mm Hg)	79.12±6.88	92.22±10.29	<0.001
8	Heamoglobin (%)	14.02±1.03	13.89±0.94	0.551
9	Total cholesterol (mg/dl)	168.48±14.61	210.10±44.95	<0.001
10	Triglycerides (mg/dl)	128.72±26.14	162.09±26.78	<0.001
11	HDL (mg/dl)	45.84±4.96	38.54±5.56	<0.001
12	LDL (mg/dl)	112.84±18.01	128.63±32.73	0.022
13	Creatinine (mg/dl)	0.98±0.23	1.04±0.32	0.361
14	Urea (mg/dl)	37.52±35.76	31.89±8.92	0.158
15	Serum ferritin (mg/dl)	38.66±14.48	124.21±52.08	<0.001

All the variables were expressed in mean±SD. *Unpaired Student's t-test. BMI: Body mass index, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, SD: Standard deviation

Table 2: Comparison of serum ferritin with obesity*

Central obesity	Cases	Serum ferritin	Controls	Serum ferritin	p value
Males>90, females>80	100	124.21±52.08	25	38.66±14.48	<0.001

All the variables were expressed in mean±SD. *Unpaired Student's t-test. SD: Standard deviation

Table 3: Comparison of serum ferritin with triglycerides*

Triglycerides (mg/dl)	Cases	Serum ferritin	Controls	Serum ferritin	p value
>150	66	126.76±52.82	25	38.66±14.48	<0.001

All the variables were expressed in mean±SD. *Unpaired Student's t-test. SD: Standard deviation

Table 4: Comparison of serum ferritin with HDL*

HDL (mg/dl)	Cases	Serum ferritin	Controls	Serum ferritin	p value
Males<40, females<50	78	122.07±54.28	25	38.66±14.48	<0.001

All the variables were expressed in mean±SD. *Unpaired Student's t-test. HDL: High-density lipoprotein, SD: Standard deviation

Table 5: Comparison of serum ferritin with blood pressure*

Blood pressure	Cases	Serum ferritin	Controls	Serum ferritin	p value
>130/85	86	126.35±52.20	25	38.66±14.48	<0.001

All the variables were expressed in mean±SD. *Unpaired Student's t-test, SD: Standard deviation

Table 6: Comparison of serum ferritin with fasting plasma glucose*

Fasting plasma glucose	Cases	Serum ferritin	Controls	Serum ferritin	p value
>100 or IGT	90	124.42±51.90	25	38.66±14.48	<0.001

All the variables were expressed in mean±SD. *Unpaired Student's t-test. IGT: Impaired glucose tolerance, SD: Standard deviation

Table 7: Serum ferritin with 3 components of metabolic syndrome*

Serial number	Variables	Cases (100)	Control (25)	p value
1	Cases with 3 components	27	25	<0.001
2	Serum ferritin	113.69±48.82	38.66±14.48	<0.001

Serum ferritin with components (central obesity, low HDL, and hypertriglyceridemia) of metabolic syndrome was expressed in mean±SD. *Unpaired Student's t-test. HDL: High-density lipoprotein, SD: Standard deviation

Table 8: Serum ferriin with 4 components of metabolic syndrome*

Serial number	Variables	Cases (100)	Control (25)	p value
1	Cases with 4 components	37	25	<0.001
2	Serum ferritin	116.45±44.56	38.66±14.48	<0.001

Serum ferriin with components (Central obesity, low HDL, hypertriglyceridemia, IGT) of metabolic syndrome was expressed in mean±SD. *Unpaired Student's t-test. IGT: Impaired glucose tolerance, HDL: High-density lipoprotein, SD: Standard deviation

Table 9: Serum ferritin with 5 components of metabolic syndrome*

Serial number	Variables	Cases (100)	Control (25)	p value
1	Cases with 5 components	36	25	<0.001
2	Serum ferritin	140.07±58.37	38.66±14.48	<0.001

Serum ferritin with components (central obesity, low HDL, hypertriglyceridemia, IGT, hypertension) of metabolic syndrome was expressed in mean±SD. *Unpaired Student's t-test. IGT: Impaired glucose tolerance, HDL: High-density lipoprotein, SD: Standard deviation

elevated fasting blood glucose. A positive association has also been found when serum ferritin of BP patients was compared with control. The results of our study are in concordance with studies done by Piperno *et al.* [4] and Mainous *et al.* [21]. Central obesity being the most noticed component of metabolic syndrome according to IDF criteria. In our study, we found significant relation between serum ferritin and central obesity. The mean value of ferritin of central obesity cases (124.21±52.08) was compared with the mean value of controls (38.66±14.48), and it showed significant results (p=0.001). Studies conducted by Aderbique *et al.* [22] also concluded the similar outcome.

In this study, we also analyzed the association of serum ferritin with each group containing 3, 4, and 5 components of metabolic syndrome according to IDF criteria. The mean serum ferritin with 3, 4, and 5 components of metabolic syndrome are 113.69±48.82, 116.45±44.56, and 140.07±58.37. This clearly indicates that serum ferritin was significantly increasing with increased number of components of metabolic syndrome. According to Li *et al*. [12] also, serum level of ferritin increases with increased number of components of metabolic syndrome. Hence, it can be concluded from our study that serum ferritin may be the predictor of metabolic syndrome.

CONCLUSION

The incidences of metabolic syndrome are increasing at a rapid pace all through the world. With clustering of risk factors, metabolic syndrome is a pathophysiological disorder which make a person prone to CVD and type 2 diabetes. Ferritin, an intracellular protein and key regulator of iron homeostasis. It measures body's iron stores. Elevated body iron stores could promote oxidative stress, and in this manner affect the pathogenesis of insulin resistance and thereby metabolic syndrome. Serum ferritin level can works as a follow-up and risk assessment measuring indicator in subjects with metabolic risk factors.

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