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Study of Serum Ferritin Level and its Correlation with Metabolic Syndrome

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Abstract
Introduction: *The metabolic syndrome (Syndrome X) consists of a group of metabolic abnormalities that confer increased risk of cardiovascular diseases (CVD) and Diabetes Mellitus (DM). Major features of metabolic syndrome include central obesity, hypertriglyceridemia, low High Density Cholesterol, hyperglycemia and hypertension.*
Aim: *The aim of the study is to explore the association between serum ferritin level and metabolic syndrome.*
Materials and Methods: *A total of 210 subjects between the age group 30-60 years were taken for the study. Patients of metabolic syndrome i.e. subjects were diagnosed on the basis of NCEP ATP III criteria. Evaluation of cases and controls was carried out covering four aspects- clinical, anthropometric, biochemical and nutritional. Venous blood samples were collected after a 12 hour fasting period into heparin, citrate and anticoagulant free BD vacutainer tubes. Serum concentration of ferritin were estimated by using micro ELISA test kits. Cases and controls were compared using Chi-square test and unpaired students test and p values were calculated.*
Result: *Significant relationship was observed between serum ferritin level and components of metabolic syndrome. There was a strong correlation between serum ferritin levels and metabolic syndrome with a p value <0.001. Individual components of the metabolic syndrome also showed positive association with the serum ferritin levels (p value <0.001).*

Introduction

The metabolic syndrome (Syndrome X) consists of a group of metabolic abnormalities that confer increased risk of cardiovascular diseases (CVD) and Diabetes Mellitus (DM). Major features of metabolic syndrome include central obesity, hypertriglyceridemia, low High Density Cholesterol, hyperglycemia and hypertension. Prevalence of the metabolic syndrome varies across the globe, in part reflecting the age and ethnicity of the populations studied and the diagnostic criteria applied. Asian Indians are a high risk population with respect to diabetes and CVD, the numbers are consistently on rise. The prevalence of metabolic syndrome in Asian Indians varies according to the region, the extent of urbanization, lifestyle patterns, and socioeconomic/ cultural factors. Recent data show that about one-third of the urban population in India's major cities have Metabolic syndrome.

Ferritin, one of the key proteins regulating iron homeostasis, is a widely available clinical

biomarker to evaluate iron status and especially important for detecting iron deficiency. Elevated serum ferritin levels independently predicted incident type 2 diabetes in prospective studies in apparently healthy men and women. Some studies demonstrate the strong associations between ferritin concentrations, obesity and inflammation, that contribute to the development of type 2 diabetes. Most of the previous studies have evaluated only the individual components of metabolic syndrome with serum ferritin levels rather than the clustered condition of metabolic syndrome. The aim of our study is to evaluate the ferritin concentration association with metabolic syndrome and its multiple components.

Materials and Methods

The prospective and cross-sectionalstudy was conducted in PG Department of General Medicine, Sarojini Naidu Medical College, Agra for 6 months from Aug 2018 to Feb 2019. A written informed consent were taken from the patients included in the study. The study population was patients of metabolic syndrome visiting outpatient department of the hospital.

National Cholesterol Education Program Adult Treatment Panel III (ATP III) criteria of Metabolic Syndrome consists of following components-

1) Central obesity: Waist circumference > 102cm for men or > 88 cm for women.
2) Hypertriglyceridemia: Serum triglycerides > 150mg/dl.
3) Low HDL cholesterol < 40 mg/dl for men or <50 mg/dl for women.
4) Arterial hypertension > 130/85 mmHg or patients on antihypertensive treatment.
5) Hyperglycemia: fasting plasma glucose=or > 110 mg/dl.

Patients with Diabetes Mellitus, hypertension, anemia, dyslipidemia, h/o hemochromatosis (S.Ferritin levels >200ng/ml), h/o blood transfusion, iron or vitamin therapies in last 6 months, raised inflammatory markers .i.e., CRP were excluded from our study. A total of 210 subjects between the age group 30-60 years were taken for the study. Patients of metabolic syndrome i.e. subjects were diagnosed on the basis of NCEP ATP III criteria.Evaluation of cases and controls was carried out covering four aspects- clinical, anthropometric, biochemical and nutritional. Venous blood samples were collected after a 12 hour fasting period into heparin, citrate and anticoagulant free BD vacutainer tubes.

Following investigations were carried out on both patients and controls-

Complete blood counts with peripheral blood smears, blood glucose levels in both fasting and post-prandial state, lipid profile including total cholesterol, high density lipo-protein, low density lipo-protein, very low-density lipo-protein, triglycerides, kidney function tests including blood urea and serum creatinine, urine routine and microscopy, CRP, Serum ferritin, TIBC.

Table 1: Age Distribution of Patients Studied

Age groups	Male		Female		Total	
	No.	%	No.	%	No.	%
31-40	16	17.02	30	17.02	46	21.9
41-50	42	44.68	44	44.68	86	40.95
51-60	32	34.04	32	34.04	64	30.48
61-70	2	2.13	4	3.45	6	2.85
71-80	2	2.13	6	5.17	8	3.81
TOTAL	94	100	116	100	210	100

Mean ± SD = 47.93 ± 12.03

There were 210 patients in this study. Majority of patients 86 (40.95%) were in their fifth decade of life in males (42) and females (44). There were only 6 patients between 61-70 yrs and only 8 patients above 70 yrs of age.

Table 2: Mean Values of the various Characteristics Studied in Male & Female

Variables	Male (n=94) Mean ±SD	Female (n=116) Mean ±SD
Waist circumference (cm)	93.2 ± 11.2	84.3 ± 9.3
BMI (kg/m2)	26.5± 2.23	26.42±2.52
Systolic BP mmHg	146.55± 8.92	146.25±7.82
Diastolic BP mmHg	91.57± 8.53	91.61± 5.8
Triglyceride mg/dl	166.2± 12.53	155.4± 9.4
HDL mg/dl	38.12± 8.23	42.2± 6.12
Fasting blood sugar mg/dl	134.12± 3.12	128.22± 4.12
PPBS mg/dl	204.8± 32.5	201.3± 22.3
S.Ferritinng/ml	142.4± 12.2	113.78± 11.39

The above table compares the mean values of various studied in males and females.The mean waist circumference was 93.2 ±11.2 cm and in female was 84.3 ± 9.3 cm.BMI in male was 26.5± 2.23 kg/m2 and in females it was 26.42±2.52 kg/m2.There is no significant difference in the diastolic and systolic blood pressure in male and female group.Triglyceride levels were higher in males (166.2 ± 12.5) mg/dl as compared to females (155±9.4) mg/dl.HDL levels were lower in males (38.12± 8.23) mg/dl as compared to females (42.2± 6.12)mg/dl.Fasting blood sugar was higher in males (134.12± 3.12) than females (128.22± 4.12).Serum ferritin levels were lower in females (113.78± 11.39) as compared to males (142.4± 12.2).

Table 3: Prevalence of Various Components of Metabolic Syndrome in the Study Group

Components of metabolic syndrome	Male (n=94)		Female (n=116)		Total (n=210)	
FBG > 100 mg/dl	84	89.4%	98	84.4%	182	86.6%
Systolic BP > 130/85 mmHg	74	78.4%	79	68.1%	153	72.8%
Diastolic BP > 85mmHg	78	82.98%	80	64.4%	158	74.2%
BMI > 24 mmHg	79	84%	106	91.3%	165	78.5%
Waist circumference , M > 90cm, F > 80 cm	70	74.4%	98	84.4%	158	75.2%
Triglyceride >150 mg/dl	70	74.4%	80	68.9%	150	71.4%
HDL, M <40 mg/dl, F< 50 mg/dl	54	57.4%	45	38.7%	99	47.1%
Diabetic on treatment	74	78,7%	92	79.3%	166	79%
Hypertensive on treatment	59	62.7%	76	60.5%	135	64.2%

The above table shows the prevalence of various components of metabolic syndrome in males and female patients of the study group. 84(89.4%) males and 98(84.4%) females had fasting blood sugar >100mg/dl.74 (78.4%) males and 79(68.1%) females had systolic BP>130 mmhg. Higher number of males 78 (82.98%) had diastolic BP >85 mmHg as compared to females 80 (68.4%). Larger percentage of female 106 (91.3%) had BMI>24 than male 79 (84%).

Central obesity was present in more females 98 (84.4%) in comparison to male 70 (74.4%). Triglyceride level was deranged in larger percentage of males 70 (74.4) than females 80 (68.9%). HDL levels were deranged higher percentage of males 54 (57.4%) as compared to females 45 (38.7%).74 (78.7%) male and 92 (79.3%) of female were taking treatment for diabetes. 59 (62.7%) males and 76 (60.5%) females were taking treatment for hypertension.

Table 4: Number of Components of Metabolic Syndrome of Patients Studied

No. of component of metabolic syndrome	Male (N=94)		Female (N= 116)	
	No.	%	No.	%
3 components	32	34.04	38	32.76
4 components	34	36.17	42	36.21
5 components	28	29.79	36	31.03

There were 38 (32.7%) females and 32 (34.4%) males with 3 components of metabolic syndrome, 42 (36.21%) females and 34 (36.17%) males with 4 components and 36 females (31.04%) and 28 (29.79%) males with 5 components of metabolic syndrome.

Table 5: Mean Serum Ferritin according to number of Components of Metabolic Syndrome of Patients Studied

No. of components of MS	S.Ferritin	
	Male	Female
3 components	92.34±9.76	67.14±16.84
4 components	130.498±19.07	115.08±13.93
5 components	209.38±27.16	165.54±16.52
P trend	<0.001	<0.001

The above table correlates the severity of metabolic syndrome in the form of increasing components of metabolic syndrome with serum ferritin levels. It shows that mean serum ferritin levels rising significantly with increasing number of components of metabolic syndrome in both males and females (p trend<0.001)

Discussion

Iron plays a key role in many physiological processes, the harmful effect of iron is decreased through binding to proteins, such as ferritin which is involved in the iron homeostasis and acts as an iron storage protein[1]. Serum ferritin concentration is directly related to iron levels for this reason the evaluation of this protein in blood has been used in diagnosis indicator in iron overload related diseases[1,2]. However ferritin levels can also be altered in inflammation, in chronic renal insufficiency and by metabolic disorders. The relationship between serum ferritin and iron overload is still controversial while some studies indicate a causative relationship of the effects of iron overload in several metabolic syndrome complications[3,4]. In the present study there were 116(55.2%) females & 94(44.7%) males. This observation was in concordance with the observation reported by Ramachandran et al [5](2003)

Majority of patients 41% were in the 41-50 age group i.e in fifth decade and 30.4% patients were in 51-60 age group. There were only 16 patients above 60yrs of age. Mean age of the total patients was 47.35±8.03. This finding was comparable to the finding of Pemminati and Adikari[6](2010). In study done by BilgilliSebel et al[7] all subjects of metabolic syndrome had BMI>25 kg/m, mean BMI in our study was 26.39±5.78 kg/m, central obesity was more prevalent in females 98(84.4%) as compared to males 70(74.4%). This is in concordance with the study Ramchandranet al[5] which showed 48.6% prevalence in females and 22.3% in males. Trigylcerides levels were deranged in larger percentage of males 74.4%(70) then females 68.9% (80) and 54.4% (54) males had decreased HDL levels as compared to only 38.75% (45) females.This finding is concordant with the study by Jung suchanget al[8] which showed higher prevalence of deranged triglycerides and HDL in males.

Among the components of metabolic syndrome elevated blood glucose was the most frequently occurring criteria (83%).In our study we divided male and female patients into three groups (containing 3,4 and 5 components of metabolic syndrome) and studied the mean serum ferritin levels of each group in males and females

separately. In similar study conducted by Megan jehn[9] it was revealed that the highest prevalence of the metabolic syndrome occurred in those with the higher levels of serum ferritin.

The positive independent association between serum ferritin levels and presence of metabolic syndrome is biologically possible. Iron is involved in multiple cellular processes and is important for the activity of various enzymes but it can also be toxic and cause organic bio-molecular oxidation. Ferritin is a clinical measure of body iron stores. Elevated iron stores may promote oxidative stress that may contribute to cellular damage leading to insulin resistance and abnormal pancreatic beta cell function. Chronic oxidative stress is also associated with oxidation dysfunction of long chain fatty acids in mitochondria, which can lead to hypertriglyceridemia in circulation and excessive triglyceride accumulation in muscle and liver tissue.

In this study we observed a positive association between higher iron stores, measured by serum ferritin levels, and the increasing number of component of the metabolic syndrome. We also observed that individual components of the metabolic syndrome i.e central obesity, elevated blood sugar, hypertension and dyslipidemia correlated well with the increasing leveling of serum ferritin.

Conclusion

Metabolic syndrome was mostly prevalent in 41-50 year age group and was more common in females. Among the components of metabolic syndrome elevated blood glucose levels was the most frequently occurring criteria followed by central obesity then elevated blood pressure and dyslipidemia. There was a strong correlation between serum ferritin levels and metabolic syndrome with a p value <0.001. Individual components of the metabolic syndrome also showed positive association with the serum ferritin levels (p value <0.001).

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