ORIGINAL RESEARCH PAPER

Volume-8 | Issue-4 | April-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ASSOCIATION OF SERUM FERRITIN LEVELS WITH METABOLIC SYNDROME IN YOUNG ADULTS

General Medicine

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ABSTRACT

MetS is a complex web of factors that is associated with two fold risk of cardiovascular diseases and five fold risk of diabetes. Ferritin, an intracellular protein and key regulator of iron homeostasis, elevated body iron stores could promote oxidative stress.

The aim of this study was to establish the relationship between serum ferritin and metabolic syndrome (MetS), to study the relation between the number of components of metabolic syndrome and serum ferritin levels and also the comparison of serum ferritin with Body Mass Index (BMI) was made.

54 patients who had metabolic syndrome as diagnosed by the International Diabetes Federation (IDF) criteria and 54 healthy individuals as controls within the age limit between of 20 - 40 yrs were included.. Anthropometric measurements like height, weight, waist circumference were measured , blood pressure was measured and blood investigations were sent for lipid profile , fasting blood glucose levels and serum ferritin .following which data was analysed . The mean serum ferritin was 316.04 ± 355.92 and 78.4 ± 62.8 ng/ml amongst metabolic syndrome patient and controls respectively which was significantly high. Also serum ferritin levels were higher in subjects with higher number of components of metabolic syndrome.

KEYWORDS

metabolic syndrome, serum ferritin, waist circumference, hypertension, HDL

INTRODUCTION

India is experiencing an epidemiologic transformation, from infectious diseases and nutritional deficiencies to non-communicable disease and has become global burden. Non-communicable disease is easily preventable, and the essence lies in the identification and reduction of it.[1]

The hallmark of management of Non-communicable diseases (NCD) is Primary and Secondary prevention. The essence of prevention lies in risk factor identification and reduction. [1].It is estimated that by 2020, CVD will be the largest cause of disability and death in India, with 2.6 million Indians predicted to die due to CVD.[2]

Metabolic syndrome (MetS) is a constellation of various cardiovascular risk factors promting atherosclerotic cardiovascular diasease (CVD). It is consist of an 'atherogenic dylipidemic (i.e " low High Density Lipoprotein Cholesterol" (HDL-C), 'elevated triglycerides' (TG) , increased blood glucose levels , hypertension(HTN) or elevated blood pressure and proinflammatory and prothrombotic states..The reason might be due to the population migration from rural to urban areas with change in dietary habits and move from an active healthy lifestyle to an increasing sedentary lifestyle.[3]

Ferritin, an intracellular protein and key regulator of iron homeostasis, is a clinical measure of body iron stores. Elevated body iron stores could promote oxidative stress, and in this manner affect the pathogenesis of insulin resistance. Cross-sectional studies have found an association between metabolic syndrome (MetS) and serum ferritin levels.[4]

With this background, the aim of this study was to investigate and establish the relationship between changes in serum ferritin and metabolic syndrome (MetS and to compare the serum ferritin levels between the cases and control , to study the relation between the number of components of metabolic syndrome and serum ferritin levels and the comparision of serum ferritn with Body Mass Index (BMI) was made.

MATERIALAND METHODS

The "Association of Serum Ferritin Levels with Metabolic Syndrome in Young Adults" is a case-control study which was conducted in Medicine OPD of Padmashree Dr. D. Y. Patil Medical College, Hospital and Research Centre, Pimpri, Pune from 1st October, 2016 to 30th September, 2018. Data entry was done in MS Excel data sheet. Collected data was analyzed

Group A of 54 cases of Metabolic syndrome in young adults and Group B of 54 Normal healthy adults.

Inclusion criteria

- Participants between 20 – 40 years of age who were diagnosed as MetS under IDF crietria

Cases: Metabolic syndrome is defined in accordance with International Diabetes Federation (IDF).[5]

Waist Circumference: Waist circumference >90 cm (Male), >80 cm (Female) in the South Asian individuals and two or more of the following:

- Hypertriglyceridemia: Triglycerides >150mg/dl or specific medication.
- Low HDL cholesterol: <40 mg/dl and <50 mg/dl, respectively for male and female or specific medication.
- Hypertension: Blood pressure >130mmHg systolic or >85mmHg diastolic or specific medication.
- Fasting plasma glucose ≥100mg/dl or specific medication or previously diagnosed Type 2 diabetes.

Controls: Normal healthy adults of 20 -40 years of age.

Who did not have metabolic syndrome by IDF criteria

Exclusion criteria

- Patients with history of Cardiac, renal, hepatic, endocrinological abnormalities, haemochromatosis and other systemic diseases
- Anemia –Hemoglobin levels <13g/dl in males and<12g/dl in females.[6]
- H/O blood transfusion, iron or any supplementary therapy in last six months
- H/O drug abuse
- Any Acute illnesses or current evidence of infective, inflammatory diseases will be excluded

After the Scientific and Ethical Committee of the Institution approved the study protocol. A well written informed consent was taken from each patient and strict confidentiality was maintained about each patient. Questionnaire included information regarding age, gender, and detailed physical and clinical examination of all patients. A detailed history of regarding the history and duration of HTN, T2DM, dylipidaemia were asked to the patient and any prior history of CVD and regarding lifestyle and habits .

Anthropometric measurements like height, weight, waist circumference were measured using standard techniques.Waist circumference was measured by measuring tape around the waist. The blood pressure of patients was measured in right arm supine position using a sphygmomanometer and two readings were recorded.

Body mass index (BMI) was calculated using the expression:
BMI = weight (kg) / height ^{2} (m).

Biochemical parameters were sent for. The fasting lipid profile (FLP) i.e total cholesterol , TG , HDL , LDL was estimated using COBAS 311 using Roche reagents by approved enzymatic method after centrifugation followed by serum seperation.

Two ml fasting serum and plasma samples used for measurement of blood glucose by spectrophometric Glucose oxidase per oxidase (GOD-POD) method which is enzymatic, specific, accurate and rapid method of measurement of true blood glucose using COBAS 311 analyzer.[7]

Estimation of serum ferritin was done by using automated Chemiluminescence Immunoassay system (CLIA) with desirable levels in males are 29-248 ng/ml and females 10-150 ng/ml.[8] The working principle is based on non-competitive chemiluminescence Immunoassay stating that upon mixing monoclonal biotinylated antibody, the enzyme-labeled antibody and a serum containing the native antigen, reaction results between the native antigen and the antibodies, without competition or stearic hindrance, to form a soluble sandwich complex.[9] The serum was seperated using centrifugation method and the analysis was carried out using an automated clinical analyzer of , COBAS 411 machine.

Data entry was done in MS Excel data sheet for preparation of 'Master Chart.' Data analysis was done using Epi-info software. The categorical variables were assessed using Pearson chi-square. The test was considered significant only if the p value comes out to be less than 0.05.

RESULTS

There were 31 males amongst cases 28 males in controls while 23 and 26 females amongst the case and control group respectively. the mean age was 33.48 ± 4.66 yrs in patients with metabolic syndrome and 33.07 ± 4.49 yrs amongst controls. It was observed that all 54 patients had 3 components, 43 patients had 4 components and 15 patients had all 5 components of metabolic syndrome.

In metabolic syndrome group 14 (25.9) cases had History of Diabetes Mellitus, 24 (44.4) cases had History of Hypertension, 10 (18.5) cases History of Dyslipidaemia , and 18 (33.3) cases had Family history of Metabolic syndrome while amongst the control group 4 (7.4%) had positive Family history of Metabolic syndrome.

It was seen 39 patients were hypertensive, 45 patients were diabetics, 35 patients had high triglyceridaemia and 17 patients had low HDL. It was observed that the mean waist circumference 96± 4.08 cms and 82.8 ± 5.26 cms, HDL was 38.68 ± 8.94 and 44.8 ± 7.62 mg/dl, triglycerides was 182.66 ± 63.8 mg/dl and 142.3 ± 41.1mg/dl amongst the metabolic syndrome and control group respectively which was statically significant. The mean BMI was 27.08 ± 2.789 for the cases as compared to 25.2 ± 3.45 for controls which was significant.

It was observed that serum ferritin was significantly increased amongst metabolic syndrome patient as compared to control group. The mean serum ferritin was **316.04 ± 355.92** and 78.4 **± 62.8 ng/ml** amongst metabolic syndrome patient and controls which was statistically significant but there was no statiscal significance when serum ferritin levels were compared amongst male and female patients with metabolic syndrome .

Table 1 : Comparison of the diagnostic characteristics of cases and controls

		Cases	Control	p Value
Mean age		33.48 ± 4.66	33.07 ± 4.49	0.66
Gender	Male	31 (57.4)	28 (51.9)	0.54
	Female	23 (42.6)	26 (48.1)	
Waist circumference	**Male**	97.17 ± 3.38	86.4 ± 4.2	0.001
	Female	96.23 ± 4.92	78.4 ± 4.8	
Height (cm)		172.8 ± 6.64	170 ± 7.52	0.06
Weight (kg)		80.86 ± 9.22	74.8 ± 8.36	0.001
Mean BMI (m/kg2)		27.08 ± 2.789	25.2 ± 3.45	0.001
Systolic BP (mmHg)		148 ± 19.05	118 ± 13.6	0.001
Diastolic BP (mmHg)		88.4 ± 6.18	74 ± 7.2	0.001
Fasting glucose (mg/dl)		152.8 ± 66.06	92.2 ± 32.4	0.001
Cholesterol (mg/dl)		258.2 ± 78.9	184.3 ± 39.5	0.001
Triglyceride (mg/dl)		182.66 ± 63.8	142.3 ± 41.1	0.001
HDL (mg/dl)		38.68 ± 8.94	44.8 ± 7.62	0.001
LDL (mg/dl)		72.52 ± 17.64	62.2 ± 12.5	0.001
Serum ferritin(ng/ml)		**316.04 ± 355.92**	**78.4 ± 62.8**	**0.001**

Table 2 : Distribution of cases according to BMI

BMI	Metabolic syndrome	Control
Undernutrition (≤18.49)	0	3 (5.6)
Normal (18.50-24.99)	12 (22.2)	20 (37.0)
Overweight (25.00-29.99)	34 (63.0)	27 (50)
Obese 1 (30.00-34.99)	6 (11.1)	4 (7.4)
Obese 2 (35.00-39.99)	2 (3.7)	0
Total	54 (100)	54 (100)

Table 3 : Comparison of Serum ferritin level with 3, 4 and 5 components of metabolic syndrome

Variables	Metabolic syndrome
3 components	316.04 ± 355.92
4 components	392.0 ± 326.5
5 components	542.3 ± 464.4

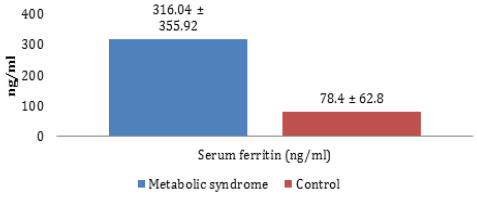

Fig 1 : Comparison of Serum ferritin level among the case and control

It was observed that amongst cases mean serum ferritin with normal BMI (18.5 – 24.99) was 177.60 ± 145.16ng/ml, overweight BMI (25.0 – 29.99) was 278.43 ± 293.05 ng/ml, obese 1 BMI (30.0 – 34.99) was 352.6 ± 247.8 ng/ml and obese 2 BMI (35.0 – 39.99) was 1500ng/ml as shown in table 4.

Table 4: Serum ferritin level in grades of BMI

BMI	N	Mean	SD
18.50-24.99	12	177.60	145.16
25.0-29.9	34	278.43	293.05
30.0-34.9	6	352.66	247.82
35.0-39.9	2	1500.00	-
Total	54	316.0400	355.92885

DISCUSSION

In the present study the findings indicates significant increase in concentration of serum ferritin in metabolic syndrome as compared to the control group.

The table below shows the various cross sectional studies on serum ferritin levels in metabolic syndrome patients in India, which shows significant elevated serum ferritin in metabolic syndrome patients

Table 5: comparison between various studies in serum ferritin and its association with metabolic syndrome

STUDY (place of study)	Serum ferritin level amongst cases	Serum ferritin levels amongst control
Preeti sharma et al., (U.P,india)	124.21 ± 52.08 ng/ml	38.66 ± 14.48 ng/ml
Sivasankari J et al., (Puducherry)	106.9 ± 28.39 ng/ml	59.75 ±16.89 ng/ml
A Wadhwa et al., (New Delhi, India)	279.33 ± 46.69 ng/ml	245.15 ± 56.94 ng/ml
Meghana et al.,	187.97 ± 35.95 ng/ml	88.10 ± 12.65 ng/ml
Present Study (pune , India)	**316.04 ± 355.92ng/ml**	**78.4 ± 62.8 ng/ml**

In a study conducted in Finland by Hämäläinen P et al., it was observed that elevated serum ferritin over a 6.5 year period was associated with development of MetS in both men and women. Whereas, lower increases in serum ferritin over the same timeframe are associated with resolution of hypertriglyceridemia in men and hyperglycemia in women. They also observed a positive correlation between waist circumference and serum ferritin levels in both the genders.[10]

In the study conducted by Preeti Sharma et al., mean serum ferritin in 3 components metabolic syndrome was 113.69 ± 48.82 ng/ml, 4 components metabolic syndrome was 116.45 ± 44.56 ng/ml, 5 components metabolic syndrome was 140.07 ± 58.37 ng/ml while mean serum ferritin in normal was 38.66 ± 14.48 ng/ml. The association between mean serum ferritin level among 3, 4 and 5 components of metabolic syndrome with normal cases was statistically significant.[11]

In the study conducted by Young Suk Shim et al., mean BMI of the cases in first quartile of serum ferritin was 23.20 ± 0.07 kg/m2, in second quartile of serum ferritin was 23.70 ± 0.07 kg/m2, in third quartile of serum ferritin was 24.16 ± 0.07 kg/m2 and in fourth quartile of serum ferritin was 24.59 ± 0.08 kg/m2.[12]

Iron in excess results in the generation of reactive oxygen species which causing increased oxidative stress by attacking cell membrane, increasing lipid peroxidation resulting in DNA fragmentation and tissue damage. Hence, iron overload aggravates IR by affecting the insulin receptor signaling, and as a result, there is impaired utilization of carbohydrates in the liver and the muscle.[13]

The ATP III recommends waist circumference as a marker of adiposity rather than BMI because abdominal obesity correlates more closely with metabolic risk factors and insulin resistance than an elevated BMI.[14]

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.[15]

LIMITATIONS:

1) A larger study will be needed for better results.
2) Follow up serum ferritin levels with treatment could not be done.

CONCLUSION

On the basis of the results, we conclude that

- Serum ferritin level was significantly higher in cases with metabolic syndrome than in normal healthy adults. .
- The association between mean serum ferritin level among patients who had 3, 4 and 5 components of metabolic syndrome as compared to controls, was directly proportional as the components increase.
- There is an increasing serum ferritin levels with increasing BMI.

Hence, serum ferritin can be used as marker for Metabolic Syndrome and clinical indicator for the severity of the disease.

ACKNOWLEDGEMENT:

Authors would like to thank my family and Dr. A.L. Kakrani, Head of Department, Department of Medicine, Dr. D.Y. Patil Medical College and Hospital, Pimpri, Pune and staff of the hospital and my friend Debojyoti Das

Funding: *No funding sources*
Conflicts of interest: *None declared*
Ethical Approval: *the Institutional Ethical Committee approved the study*

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