



A Study On Serum Ferritin And C-Peptide And Their Correlation With Metabolic Syndrome

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Abstract

Background : Metabolic syndrome (MetS) is a complex constellation of metabolic abnormalities, characterized by elevated serum glucose, hypertension, abdominal obesity, and dyslipidaemia . Various studies have generated evidence that MetS was associated with development of cardiovascular disease (CVD), kidney disease, and diabetes mellitus Studies have also demonstrated an association between high levels of acute phase reactant C-reactive protein (CRP), a sensitive marker of subclinical inflammation, and insulin resistance or MetS components . Ferritin, another acute phase reactant, has also been shown to be associated with insulin resistance

Aim And Objective:To look for association between serum ferritin and metabolic syndrome.To evaluate the relationship between serum C-Peptide and metabolic syndrome.

Methods: The patients admitted in Rajah Muthiah Medical College and Hospital between November 2019 to April 2021.are being screened for Metabolic syndrome on the basis of National Cholesterol Education Program: Adult Treatment Panel III2001 and harmonizing definition criteria. 70 Patients were randomly selected into the study based on the inclusion and exclusion criteria after getting informed consent.

Results:In our study, we observed type 2 diabetes mellitus in 63 (90%)patients, systemic hypertension in 57 (81%) patients, elevated triglycerides in 28 (40%) patients, decreased HDL cholesterol in 13 (19%) patients and central adiposity was seen in all of the patients. In this study we could come to the conclusion that serum ferritin which was elevated above average levels can be used as a marker for metabolic syndrome, and it can also be used as a prognostic indicator. In this study we could find that C-Peptide which was elevated can be used as a marker of insulin resistance for metabolic syndrome.

Conclusion:There is a positive association between elevated serum ferritin (above average levels) and metabolic syndrome indicating it is a pro inflammatory condition.There is a positive association between elevated C-Peptide and metabolic syndrome indicating it can be used as a marker for insulin resistance.

Keywords: Metabolic Syndrome (MetS), NCEP ATPIII 2001 (National Cholesterol Education Program: Adult Treatment Panel III 2001)

Introduction

Metabolic Syndrome (MetS) is cluster of physical conditions and metabolic abnormalities commonly found in association with increased risk for

development of type-2 diabetes mellitus (T2DM), cardiovascular disease (CVD) and other medical conditions.; according to National Cholesterol Education Program: Adult Treatment Panel III 2001

and harmonizing definition criteria, a person is identified as having metabolic syndrome if he/she has any three of the following:

- 1) Central obesity: waist circumference of > 102cm for males and >88cm for females.
- 2) Hypertriglyceridemia: Triglyceride level \geq 150mg/dL.

3) Low HDL cholesterol: < 40mg/dL for males and < 50mg/dL for females.

4) Hypertension: Blood pressure > 130mmHg systolic and/or > 85mmHg diastolic.

5) Fasting plasma glucose levels \geq 100mg/dl.

Harmonizing Definition:

Waist circumference (cm):

Men	Women	Ethnicity
>94	>80	Europid, sub Saharan African, Eastern and Middle Eastern
>90	>80	South Asian, Chinese, ethnic South and Central America
>85	>90	Japanese

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. In general, the prevalence of metabolic syndrome increases with age. Other risk factors include Overweight/Obesity, sedentary lifestyle, aging, Diabetes Mellitus, Coronary heart disease, lipodystrophy. Elevated serum ferritin levels can independently predict incidence of type 2 diabetes¹. Average levels of serum ferritin are 40 ng/ml for females and 100 ng/ml for males. Elevated ferritin levels have been associated with hypertension, dyslipidemia, elevated fasting insulin and blood glucose and central adiposity². The association between elevated iron stores and the metabolic syndrome is yet to be well established. Insulin and C-peptide are produced by the pancreas β -cells and released in equimolar amounts in response to plasma glucose concentrations. In review of decreased insulin action in MetS, plasma C-peptide concentrations have been better correlated with beta-cell function. Proinsulin(86 amino acids) gets cleaved into insulin and c-peptide. C-Peptide contains 31 amino acids with three “C_C” cystine bonds, it is secreted in equimolar ratio with insulin. $t_{1/2}$ of c-peptide is 3-4 times than that of insulin and undergoes renal excretion. It has been shown in many prospective studies that there is correlation between CRP and risk of diabetes, however only very less

studies are available showing the relationship of serum ferritin and c-peptide with metabolic syndrome. Within the past two decades, the biological importance of C-peptide has emerged as a regulator of low-grade inflammation³. Furthermore, the effect of C-peptide on metabolic syndrome development has just begun to be deduced. In a study of young Arab females, C-peptide was shown to moderately correlate with diastolic blood pressure, waist circumference, as well as high-density lipoprotein⁴.

C-peptide is used as a measure of insulin secretion in humans. Because serum insulin level is affected by various factors like exogenous insulin administration and significant amount of secreted insulin undergoes hepatic extraction before it appears in the peripheral blood⁵, while secreted C-peptide undergoes only minimal change and its level in the peripheral blood equals to that of in the portal blood.

Methods: The patients admitted in Rajah Muthiah Medical College and Hospital between November 2019 to April 2021. are being screened for Metabolic syndrome on the basis of National Cholesterol Education Program: Adult Treatment Panel III 2001 and harmonizing definition criteria. 70 Patients were randomly selected into the study based on the inclusion and exclusion criteria after getting informed consent.

Inclusion Criteria:

- 1) Central obesity: waist circumference of > 102cm for males and >88cm for females
- 2) Hypertriglyceridemia: Triglyceride level ≥ 150mg/dL.

- 3) Low HDL cholesterol: < 40mg/dL for males and < 50mg/dL for females.
- 4) Hypertension: Blood pressure > 130mmHg systolic and/or > 85mmHg diastolic.
- 5) Fasting plasma glucose levels ≥ 100mg/dl.

Harmonizing definition:

Waist circumference (cm):

Men	Women	Ethnicity
>94	>80	Europid, sub Saharan African, Eastern and Middle Eastern
>90	>80	South Asian, Chinese, ethnic South and Central America
>85	>90	Japanese

Exclusion Criteria:

- 1) Anemic individuals (Hemoglobin <10g/dL).
- 2) Patients who have received transfusion in the past 3 months.
- 3) Persons who has donated blood in the past 4 months.
- 4) Acute febrile illness.
- 5) Total Leucocyte count > 11,000/cu mm (or) < 3000/cu mm.
- 6) Chronic kidney disease of eGFR < 60ml/min/1.73m²

[By using MDRD formula (Modification of Disease in Renal Disease)]

$$eGFR \text{ (ml/min/1.73m}^2\text{)} = 186.3 \times Pcr(e)^{-1.154} \times age(e)^{0.203} \times 0.742(\text{if female}) \times 1.212 \text{ (if black)}$$

If Male (black): eGFR is calculated by below formula

$$eGFR \text{ (ml/min/1.73m}^2\text{)} = 186.3 \times Pcr(e)^{-1.154} \times age(e)^{0.203} \times 1.212(\text{if black})$$

If Male (non-black): eGFR is calculated by below formula

$$eGFR \text{ (ml/min/1.73m}^2\text{)} = 186.3 \times Pcr(e)^{-1.154} \times age(e)^{0.203}$$

If Female (black): eGFR is calculated by below formula

$$eGFR \text{ (ml/min/1.73m}^2\text{)} = 186.3 \times Pcr(e)^{-1.154} \times age(e)^{0.203} \times 0.742(\text{if female}) \times 1.212(\text{if black}).$$

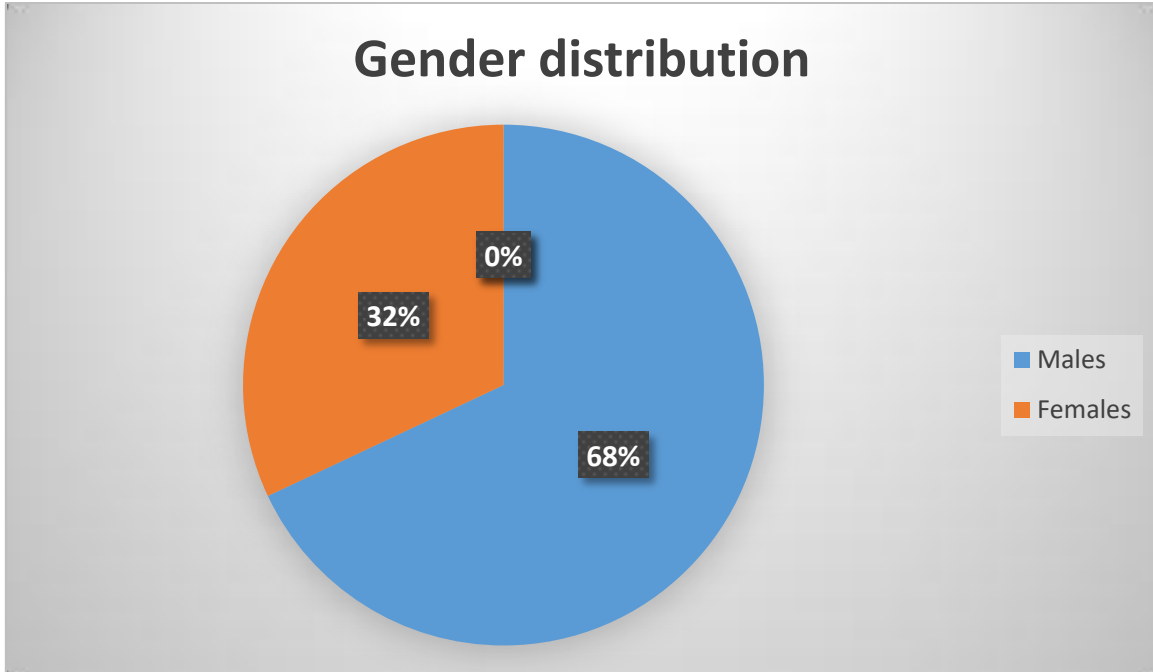
If Female (non-black): eGFR is calculated by below formula

$$eGFR \text{ (ml/min/1.73m}^2\text{)} = 186.3 \times Pcr(e)^{-1.154} \times age(e)^{0.203} \times 0.742(\text{if female}).$$

Patient were investigated with, Blood Urea, Serum creatinine, Fasting lipid profile, Complete blood count, Fasting blood sugar, Serum C-Peptide. Metabolic syndrome was diagnosed using NCEP: ATPIII 2001 and harmonizing definition criteria.

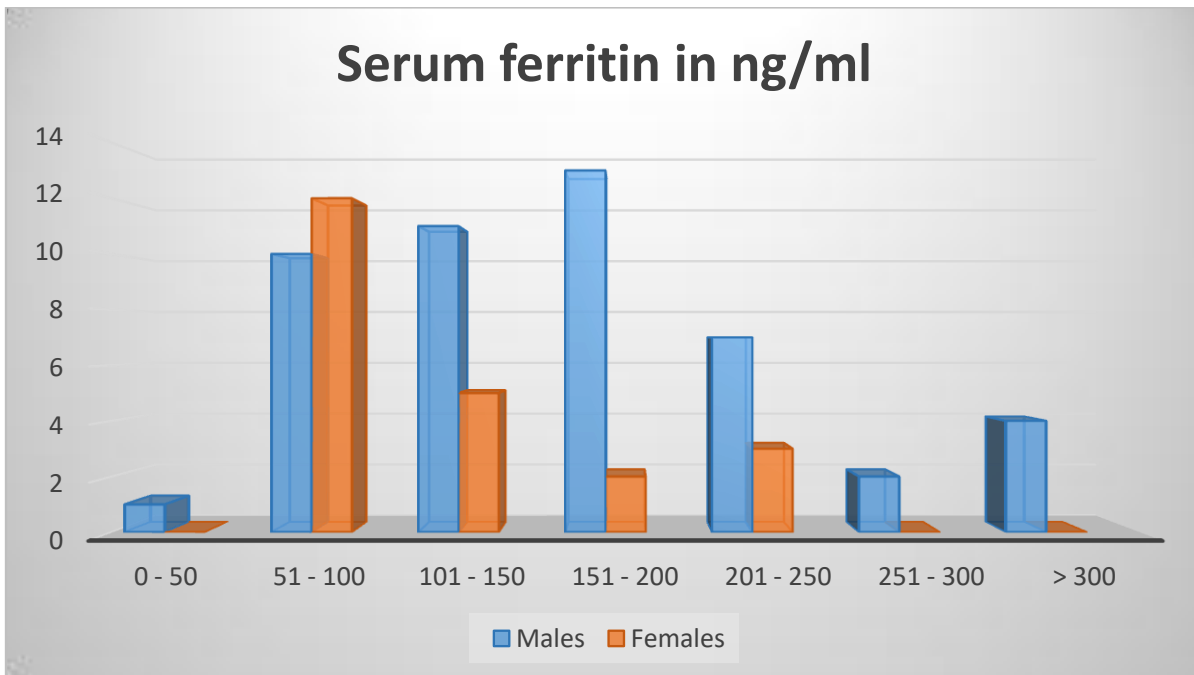
Results:

Graph :1 Gender distribution

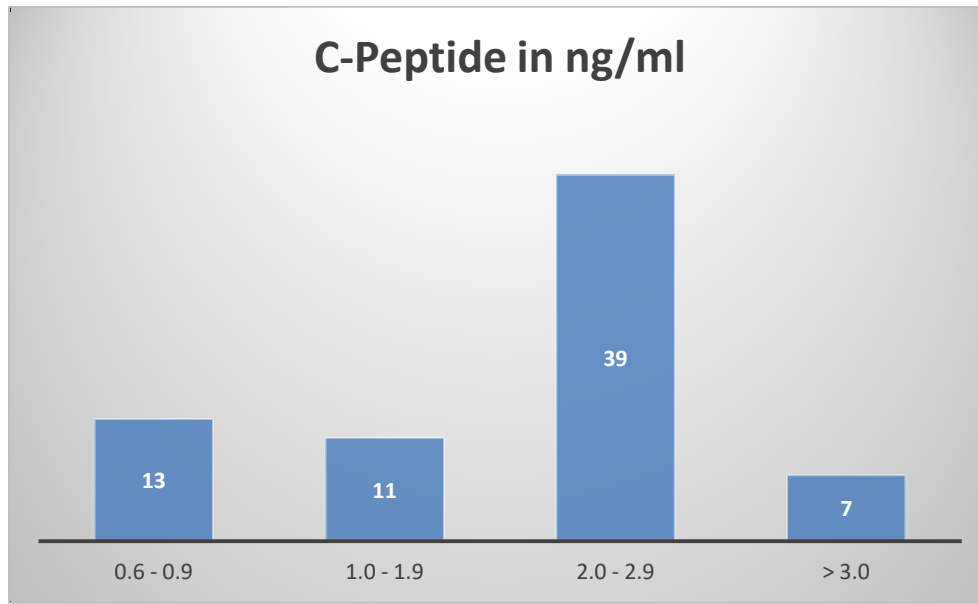


In this present study out of the 70 patients enrolled 48 were male and 32 were female.

Table :2 Serum ferritin values



Graph :3 Serum C-Peptide values



In this present study out of the 70 patients enrolled 48 (68%) were male and 22 (32%) were female.

In this study, we observed type 2 diabetes mellitus in 63 (90%) patients, systemic hypertension in 57 (81%) patients, elevated triglycerides in 28 (40%) patients, decreased HDL cholesterol in 13 (19%) patients and central adiposity was seen in all of the patients. The average serum ferritin in our study was 121 ng/ml for females and 161 ng/ml for males. The present study revealed that serum ferritin was elevated significantly in metabolic syndrome with $p=0.000001$ for females and $p=0.0000001$ for males. This has showed that elevated serum ferritin (above average levels) had a significant correlation with metabolic syndrome. The average C-peptide level in our study was 1.983 ng/ml. The present study revealed that C-Peptide was elevated significantly in metabolic syndrome with $p=0.028$. This has showed that elevated C-Peptide levels had a significant correlation with metabolic syndrome.

Discussion:

In this study it is seen that elevated serum C-Peptide levels would be more common in those with metabolic syndrome. Patients were evaluated with detailed history, meticulous examination and laboratory investigations. Laboratory investigations included fasting lipid profile, fasting blood sugar, complete blood count, renal function test, serum ferritin and serum C-Peptide. As serum ferritin is an acute-phase reactant there was possibility of

confounding if the patient has any associated infection or inflammation, thus we have minimized this by excluding the patients with associated high CRP and and suspected active infection and inflammation. Since metabolic syndrome is a pro inflammatory condition^{6,7}. Most of our patients were selected when they had come for treatment of diabetes and hypertension. Biqiang Li, Wein Lin et al also concluded in their study that serum ferritin increases the risk of metabolic syndrome factors. They stated that higher the serum ferritin levels, higher the metabolic disorder severity and more frequent the metabolic syndrome incidence rate⁸. The present study revealed that serum ferritin was elevated significantly in metabolic syndrome with $p=0.000001$ for females and $p=0.0000001$ for males. In this study we can see that C-Peptide was elevated significantly in metabolic syndrome with $p=0.028$. This has showed that elevated C-Peptide levels had a significant role in measuring the insulin resistance in metabolic syndrome.

Conclusion

There is a positive association between elevated serum ferritin (above average levels) and metabolic syndrome indicating it is a pro inflammatory condition. There is a positive association between elevated C-Peptide levels and metabolic syndrome indicating insulin resistance.

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