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Serum Ferritin as a Biomarker for Diagnosis of Metabolic Syndrome: A Cross-Sectional Study

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KEYWORDS

Metabolic syndrome, Serum ferritin, Biomarkers, Dyslipidemia, Hypertension, Insulin resistance

ABSTRACT:

Background: Metabolic syndrome comprises a cluster of conditions, including insulin resistance, hypertension, dyslipidemia, and central obesity, that collectively increase the risk of cardiovascular diseases and type 2 diabetes.

Aim: To investigate the association between serum ferritin levels and metabolic syndrome to determine whether serum ferritin can serve as a reliable biomarker for the early detection and diagnosis of metabolic syndrome.

Methods: An observational cross-sectional study was conducted from June 2022 to June 2024 at Aarupadai Veedu Medical College, Puducherry. A total of 128 participants aged 18 to 65 years were included, divided into two groups: 64 individuals with metabolic syndrome and 64 without metabolic syndrome, based on the International Diabetes Federation (IDF) criteria. Serum ferritin levels and other metabolic markers were analyzed using SPSS v26. Nonparametric statistical tests were employed due to the non-normal distribution of the data.

Results: No significant age difference was observed between the groups; however, a notable gender disparity was identified, with a higher proportion of males in the case group. Significant differences in metabolic parameters were noted, with the case group exhibiting higher waist-to-hip ratios, total cholesterol, LDL cholesterol, triglycerides, systolic and diastolic blood pressure, and fasting blood glucose levels. Serum ferritin levels were significantly elevated in the case group (123.39 ± 113.83 ng/mL) compared to the control group (18.45 ± 9.68 ng/mL), with a Mann-Whitney U test statistic of -7.167 ($p = 0.001$), indicating a strong association with metabolic syndrome.

Conclusion: Elevated serum ferritin levels are significantly associated with metabolic syndrome, suggesting their potential as a biomarker for early detection. While the correlations with individual components of metabolic syndrome were weak, serum ferritin offers valuable diagnostic insights. Further research is warranted to enhance its clinical applicability.

Introduction

Metabolic syndrome is characterized by a cluster of conditions that collectively elevate the risk of developing cardiovascular diseases and type 2 diabetes. These conditions include insulin resistance, hypertension, dyslipidemia, and central obesity.(1) Early identification of biomarkers that facilitate timely diagnosis and management of metabolic syndrome is critical, as early intervention can significantly mitigate the risk of

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associated complications. This syndrome represents a major global public health challenge, marked by increased waist circumference, abnormal cholesterol levels, hypertension, insulin resistance, and hyperglycemia.(2, 3) Prompt and accurate diagnosis is essential to guide the implementation of treatment and preventive strategies aimed at reducing its health implications.(4)

Serum ferritin, a blood protein responsible for iron storage, is well-recognized for its dual role in cellular iron regulation and acute-phase inflammatory responses. It serves as an indicator of both systemic iron stores and inflammation. Beyond its established use in diagnosing iron overload and deficiency, emerging evidence suggests that serum ferritin may play a role in non-hematological conditions, including metabolic syndrome.(5)

Elevated serum ferritin levels have been investigated as a potential biomarker for metabolic syndrome. While ferritin levels primarily reflect iron storage, increased levels may also indicate underlying inflammation or metabolic disturbances. Recent studies suggest that elevated serum ferritin levels are associated with components of metabolic syndrome, such as insulin resistance and obesity.(6) However, caution is warranted when using serum ferritin as a diagnostic biomarker for metabolic syndrome due to these overlapping roles.

Metabolic syndrome is a complex interplay of metabolic, diabetic, and cardiovascular risk factors that significantly contribute to global morbidity and mortality. Current diagnostic criteria for metabolic syndrome involve assessments of blood pressure, triglycerides, HDL cholesterol, waist circumference, and fasting glucose. Despite their utility, these criteria may lead to misdiagnoses or underestimation of potential health risks. Identifying alternative biomarkers, such as serum ferritin, could enhance diagnostic accuracy and facilitate earlier therapeutic interventions.(7)

Investigating the potential relationship between elevated serum ferritin levels and the presence or severity of metabolic syndrome offers a promising avenue for improving diagnosis. This approach requires careful consideration of confounding variables, including age, sex, dietary iron intake, and other medical conditions that may influence ferritin levels.(8) Expanding knowledge of serum ferritin's role in metabolic syndrome may inform clinical practice and public health strategies, enabling the adoption of more evidence-based approaches to managing this widespread and debilitating condition.(9)

This study aims to explore the relationship between serum ferritin levels and metabolic syndrome. By reviewing existing literature and analyzing new research, it seeks to quantitatively assess correlations between serum ferritin and various metabolic markers. The study also aims to clarify the potential of serum ferritin as a biomarker for early diagnosis, laying the groundwork for future research and clinical applications.(10)

Materials and Methods

The present observational cross-sectional study was conducted from June 2022 to June 2024 in the outpatient and inpatient departments of the Department of General Medicine at Aarupadai Veedu Medical College, a tertiary care center in Puducherry. The primary objective of the study was to investigate the relationship between serum ferritin levels and metabolic syndrome. Written informed consent was obtained from all participants prior to their inclusion in the study. Ethical approval was granted by the Institutional Human Ethics Committee of Aarupadai Veedu Medical College and Hospital, Kirumampakam, Puducherry, under approval number IHEC No.AV/IHEC/2022/090.

The study included male and female participants aged 18–65 years who exhibited features of metabolic syndrome, as defined by the International Diabetes Federation (IDF) guidelines. Exclusion criteria comprised the presence of renal or hepatic diseases, a history or clinical evidence of hemochromatosis (serum ferritin >500 ng/mL), endocrinological abnormalities, drug or alcohol abuse, anemia (hemoglobin <12 g/dL), recent blood transfusions or iron/vitamin therapies, and acute illnesses or infections.

A sample size of 128 participants (64 cases with metabolic syndrome and 64 control subjects without metabolic syndrome) was determined using consecutive sampling. The calculation was based on a study by Tran et al. (2022), which reported an expected mean difference in serum ferritin levels of 64.88 ng/mL and a standard deviation of 129.76 ng/mL. With a significance level of

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5% and a power of 80%, the sample size was estimated accordingly. Demographic data and patient histories were systematically recorded, and clinical assessments and laboratory investigations were performed. Data collection focused on variables associated with metabolic syndrome, including central obesity, hypertension, diabetes mellitus, low HDL cholesterol, hypertriglyceridemia, and serum ferritin levels.

Statistical analysis: Data were entered into Microsoft Excel and analyzed using SPSS software (IBM SPSS Statistics for Windows, Version 26.0; IBM Corp., Armonk, NY, 2019). Normality tests (Kolmogorov-Smirnov and Shapiro-Wilk) indicated that the data did not follow a normal distribution. Consequently, nonparametric tests were applied for statistical analysis. Descriptive statistics, including frequency, percentage, mean, and standard deviation, were calculated for the study variables. The Chi-square test was employed to evaluate categorical variables, while the Mann-Whitney U test was used to compare serum ferritin levels between the case and control groups. The significance level was set at 5% ($\alpha = 0.05$), and a p-value of <0.05 was considered statistically significant.

Results

Table 1 presents the distribution of age groups among patients with metabolic syndrome and normal individuals. Among individuals aged ≤35 years, 10.9% were patients with metabolic syndrome, compared to 17.2% of normal individuals. The 36–45 years age group accounted for 32.8% of the patients and 34.4% of the normal individuals, demonstrating a comparable representation in this category. The 46–55 years age group included 31.3% of the patients and 37.5% of the normal individuals, making it the most represented age group among the normal individuals. In the 56–65 years category, 18.8% of the patients were included, as opposed to 9.4% of the normal individuals. Lastly, the >65 years age group was the least represented, comprising 6.3% of the patients and only 1.6% of the normal individuals. Overall, the age distribution reveals a relatively balanced representation across the groups, with a slight predominance of older individuals in the patient group compared to the normal group.

The gender distribution of the participants revealed a statistically significant difference between the case and normal individual groups. Among the cases, 60.9% (39 participants) were male and 39.1% (25 participants) were female. Conversely, the normal individual group consisted of 43.8% (28 participants) male and 56.3% (36 participants) female participants. These findings suggest a gender-related disparity in the prevalence of metabolic syndrome, with a higher proportion of males in the case group and a greater prevalence of females in the normal individual group. This significant gender difference emphasizes the importance of considering gender as a potential influencing factor in the analysis and interpretation of the association between serum ferritin levels and metabolic syndrome.

The comparison of mean and standard deviation values for various measurable variables, as summarized in Table 2, demonstrates significant differences between the case and normal individual groups. Variables analyzed include age, waist-to-hip ratio (WHR), total cholesterol, LDL, HDL, triglycerides (TG), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting blood sugar (FBS), and serum ferritin levels. The mean age was slightly higher in the case group (48.54 ± 10.94) than in the normal individual group (44.34 ± 9.46), although this difference was not statistically significant. Significant differences were observed in all other variables. The case group exhibited a higher WHR (0.60 ± 0.22) compared to the normal group (0.37 ± 0.07), along with elevated levels of total cholesterol, LDL, TG, SBP, DBP, and FBS. Conversely, HDL levels were significantly lower in the case group. Notably, serum ferritin levels were substantially higher in the case group (123.39 ± 113.83) than in the normal individual group (18.45 ± 9.68). These findings suggest that individuals with metabolic syndrome exhibit worse cardiovascular and metabolic risk profiles, including significantly elevated serum ferritin levels, which may serve as a potential biomarker for this condition.

Table 3 compares serum ferritin levels between the case group and the normal individual group. The mean serum ferritin level in the case group was 123.39 ng/mL with a standard deviation of 113.83, ranging from 3.70 to 456.00 ng/mL. In contrast, the normal individual group exhibited a significantly lower mean serum ferritin level of 18.45 ng/mL with a standard deviation of 9.68, ranging from 4.00 to 74.00 ng/mL. A p-value of 0.001, which is statistically significant, indicates a substantial

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difference in serum ferritin levels between the two groups, with significantly higher levels observed in the case group.

Discussion

Metabolic syndrome encompasses a cluster of conditions including insulin resistance, hypertension, dyslipidemia, and central obesity. They collectively increase the risk of cardiovascular diseases and type 2 diabetes. Given its significant public health impact, identifying biomarkers that can aid in the early diagnosis and management of metabolic syndrome is crucial. Such early intervention can help prevent complications and improve patient outcomes. Serum ferritin, a blood protein that stores iron, has gained attention as a potential biomarker for metabolic syndrome. Traditionally, ferritin levels indicate the body's iron stores, but elevated levels may also reflect systemic inflammation or metabolic disturbances, both of which are relevant in metabolic syndrome. The role of serum ferritin as a diagnostic biomarker in non-hematological illnesses, including metabolic syndrome, is a growing area of research.

This cross-sectional study included 128 participants, with majority in the age group between 36 and 55 years. Specifically, 31.3% of the participants in both the case and normal individual groups were aged 36-45 years, and another 31.3% were aged 46-55 years. There was no significant difference in age distribution between the groups, ensuring that age did not confound the results. The study conducted by Tran et al in the year 2022 and Ledesma et al in the year 2015 was contrast with the present study that the age was more than 55 years are affected.(11, 12) Gender distribution analysis showed that males comprised 60.9% of the case group and 43.8% of the normal individual group, while females accounted for 39.1% of the case group and 56.3% of the normal individual group. This suggested no significant difference in gender distribution between the groups, confirming that gender was not a confounding factor. This is consistent with study findings conducted by Park et al in the year 2020 , who reported similar age and gender distributions in their study on metabolic syndrome.(13) The case group had a significantly higher mean WHR (0.60) compared to the normal individual group (0.37), suggesting that higher WHR is strongly associated with metabolic syndrome. These findings align with study conducted by Janssen et al in the year 2018, which highlighted abdominal obesity as a significant predictor of metabolic syndrome.(14) Total cholesterol levels were significantly higher in the case group (215.21 mg/dL) compared to the normal individual group (163.20 mg/dL). Similarly, LDL levels were significantly higher in the case group (145.32 mg/dL) compared to the normal individual group (63.28 mg/dL). However, HDL levels were significantly lower in the case group (39.50 mg/dL) compared to the normal individual group (51.12 mg/dL). These findings are consistent with study conducted by Grundy et al in the year 2020, who reported dyslipidemia as a common component of metabolic syndrome, characterized by high total cholesterol, high LDL cholesterol, and low HDL cholesterol.(15) TG levels were significantly higher in the case group, with a mean of 170.98 mg/dL compared to 100.71 mg/dL in the normal individual group.. Elevated TG levels are consistently linked with metabolic syndrome, as supported with a study conducted by Ford et al in the year 2018.(16) Systolic Blood Pressure (SBP) was significantly higher in the case group (139.68 mmHg) compared to the normal individual group (119.53 mmHg). Diastolic Blood Pressure (DBP) was also significantly higher in the case group (88.12 mmHg) compared to the normal individual group (77.34 mmHg). These findings are consistent with study conducted by Alberti et al in the year 2018, who noted hypertension as a critical component of metabolic syndrome.(17) FBS levels were significantly higher in the case group (126.40 mg/dL) compared to the normal individual group (93.71 mg/dL). This aligns with study findings conducted by Meigs et al. in the year 2019 that identified elevated fasting glucose as a hallmark of metabolic syndrome.(18) The primary focus of this study was on serum ferritin levels, which were higher in the case group compared to the normal individual group, indicating a strong association with metabolic syndrome. The mean serum ferritin level was 123.39 ng/mL in the case group and 18.45 ng/mL in the normal individual group. The variability was higher in the case group, with standard deviations of 113.83 ng/mL compared to 9.68 ng/mL in the normal individual group. This finding aligns with study conducted by Jehn et al in the year 2020, which suggested that elevated serum ferritin is linked to metabolic syndrome due to its pro-inflammatory properties.(19) The correlation analysis explored the relationships between serum ferritin and

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various components of metabolic syndrome. Serum ferritin showed weak positive correlations with age (0.149), HDL (0.195), and WHR (0.049), suggesting that higher serum ferritin levels might be associated with increased age, higher HDL levels, and higher WHR, known risk factors for metabolic syndrome. These correlations align with study findings conducted by Gillum et al in the year 2019, who reported a link between higher ferritin levels and central obesity. Weak negative correlations were observed with LDL (-0.204), TG (-0.091), SBP (-0.146), DBP (-0.093), and FBS (-0.067). Although these correlations were weak, they indicate that higher serum ferritin levels might inversely relate to these components, warranting further investigation.(20)

Conclusion

This study demonstrates a significant association between elevated serum ferritin levels and metabolic syndrome, with no confounding effects related to age or gender distribution. Despite demographic similarities between the case and control groups, the case group showed higher levels of abdominal obesity, dyslipidemia, hypertension, and elevated fasting blood sugar—hallmark components of metabolic syndrome. The markedly higher serum ferritin levels observed in the case group highlight its potential as a biomarker for metabolic syndrome, consistent with previous research linking ferritin to inflammatory processes. While the correlations between serum ferritin and individual components of metabolic syndrome were generally weak, these findings suggest that serum ferritin merits further exploration as a diagnostic or prognostic tool for metabolic syndrome.

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Table 1: Association between age distribution and study groups

Age group	Group			
	Patients		Normal individuals	
	Frequency	Percentage	Frequency	Percentage
≤35 years	7	10.9	11	17.2
36 – 45 years	21	32.8	22	34.4
46 – 55 years	20	31.3	24	37.5
56 – 65 years	12	18.8	6	9.4
>65 years	4	6.3	1	1.6

Table 2: Association between mean (SD) of measurable variables and study groups

Variables	Mean ± SD	
	Patients	Normal individual
Age	48.54 ± 10.94	44.34 ± 9.46
WHR	0.60 ± 0.22	0.37 ± 0.07
Total Cholesterol	215.21 ± 33.82	163.20 ± 17.02
LDL	145.32 ± 30.64	63.28 ± 14.01
HDL	39.50 ± 8.94	51.12 ± 8.13
TG	170.98 ± 29.63	100.71 ± 19.94

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SBP	139.68 ± 10.23	119.53 ± 5.75
DBP	88.12 ± 6.13	77.34 ± 4.45
FBS	126.40 ± 16.29	93.71 ± 11.66
Serum Ferritin	123.39 ± 113.83	18.45 ± 9.68

Table 3: Association between mean (SD) serum ferritin and study groups

Variable	**Group**	**Mean ± SD**	**Min**	**Max**	**P value**
Serum Ferritin	**Patients**	123.39 ± 113.83	3.70	456.00	**0.001***
	Normal individuals	18.45 ± 9.68	4.00	74.00	