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Original Research Article

A STUDY OF CORRELATION BETWEEN SERUM FERRITIN LEVELS AND METABOLIC SYNDROME - A CASE-CONTROL STUDY

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Abstract

Background: Metabolic syndrome, the most commonly encountered and a significant health problem the world is facing has a relationship with various cardiovascular diseases (CVD), diabetes mellitus particularly type 2 and many other adverse health outcomes. Various studies indicate that, globally the metabolic syndrome prevalence is on increase in the past few decades, mirroring the rising trends in obesity and sedentary lifestyles. Ferritin can be elevated to high levels secondary to systemic inflammation and a variety of disorders. Hence, this study was conducted to make out the exact relation between serum ferritin and various components of metabolic syndrome and to assess whether ferritin can be used as a marker of metabolic syndrome. **Materials and Methods:** A hospital -based case-control study was conducted among 100 cases and 100 control population at a tertiary care hospital in Indore, Madhya Pradesh. The study was conducted for a period of 2 years from September 2022 to August 2024. Patients who attended the Endocrine OPD, Medicine OPD and other OPDs and equal number of control population matched for age were included in the study. Detailed history, Physical examination and Investigations were done. Harmonizing criteria was used for the diagnosis of metabolic syndrome. **Result:** Our analysis revealed that cases in comparison with controls had significant high ferritin values suggesting a potential relation between elevated ferritin values and the metabolic syndrome. Mean value of serum ferritin in cases was 98.58 ng/ml and mean value among controls was 53.32 ng/ml. Cases in comparison to controls had significantly high serum ferritin indicating potential relation between serum ferritin and metabolic syndrome. Individuals who have metabolic syndrome have 2.704 times more chance of having raised ferritin values than among those without metabolic syndrome. **Conclusion:** Serum ferritin is an excellent biomarker for identifying metabolic syndrome, with a high level of accuracy in distinguishing between individuals with and without the syndrome. Serum ferritin demonstrated exceptional accuracy in identifying metabolic syndrome with significant odds ratios and correlation with key metabolic parameters.

INTRODUCTION

The multiple factors that increase the risk of developing various cardiovascular abnormalities as well as diabetes mellitus particularly type 2 are included in the entity called as the "Metabolic Syndrome". Also known as "Insulin resistance Syndrome" or "Syndrome X" its individual components are high blood pressure (HBP), impaired fasting glucose values (IFG), elevated triglyceride (TG) values, low level of high-density lipoprotein (HDL) cholesterol values, and visceral adiposity.[1,2]

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Overall, Metabolic syndrome represents a significant global health challenge, and millions of individuals are affected worldwide and it is a major burden on health care systems. Urban regions has greater prevalence of metabolic syndrome as compared to rural areas which is a direct evidence of how urbanization influenced lifestyle factors such as diet patterns, physical exercise, and stress level. However, metabolic syndrome is increasingly being recognized as a health issue in rural India, particularly in regions undergoing rapid socioeconomic transitions.[3-5]

Following healthy diets, regular exercise programs, weight management and other prevention and management programs are crucial for addressing metabolic syndrome in India[11]. Additionally, there is a need for increased awareness, early detection, and comprehensive healthcare interventions to mitigate the impact of metabolic syndrome on public health in India.[5-7]

Ferritin belongs to the category of a positive acute phase reactant. It is also a marker of systemic inflammation. Metabolic Syndrome is characterized by numerous metabolic alterations in the body and systemic inflammation. It is very essential to make out the exact relation between serum ferritin and various components in metabolic syndrome, and these levels of ferritin may serve as a marker of metabolic abnormalities and associated complications.[8-10]

MATERIALS AND METHODS

Study Design: A hospital -based case-control study was conducted at a tertiary care hospital in Indore, Madhya Pradesh. The study was conducted for a period of 2 years from September 2022 to August 2024. Ethical approval for the study was obtained from the Institutes Research Ethics Committee. The objective of the study was to correlate the different parameters of metabolic syndrome with serum ferritin levels and to compare it with controls.

Inclusion critera for cases: All patients with metabolic syndrome newly diagnosed.

Inclusion criteria for controls: Healthy normal males and females, Males and females having metabolically healthy obesity, Males and females not fitting in metabolic syndrome criteria.

Exclusion criteria for cases: Anemia (Hb < 13g/dl male, <12g/dl female), subjects who did not give consent to participate in the study, chronic kidney disease, chronic liver disease, steroid therapy, recent blood transfusions, overt thyroid dysfunction, chronic alcoholics, patients on iron supplements/multivitamins, acute infective disorders, taking lipid lowering therapies, patients already on treatment for metabolic syndrome.

Exclusion criteria for controls: Anemia (Hb < 13g/dl male, <12g/dl female), subjects who did not give consent to participate in the study, chronic kidney disease, chronic liver disease, steroid therapy, recent blood transfusions, overt thyroid dysfunction, chronic alcoholics, patients on iron supplements/multivitamins, acute infective disorders, taking lipid lowering therapies, patients diagnosed to be having or already on treatment for metabolic syndrome.

Procedure: A thorough history and physical examination was done in all the patients attending the endocrine OPD, medicine OPD, all other OPDs. FPG, lipid profile was done in patients and metabolic syndrome was diagnosed by harmonizing definition. In those patients with metabolic syndrome fasting serum ferritin was done. Also waist circumference was measured. An equal number of control population was selected based on history, physical examination, investigations, and serum ferritin was done.

The WHO STEPS approach for waist circumference recommends measuring at the midpoint between the last palpable rib and the top of the iliac crest and was used.[8]

Method of data collection: 100 patients with metabolic syndrome newly diagnosed that met the inclusion and exclusion parameters, after taking a written informed consent were selected for study. An equal number of control population was selected. Detail history, physical examination and investigations were conducted.

Criteria for Metabolic Syndrome diagnosis: According to Harmonizing definition, any three of the following out of five should be there for fitting in metabolic syndrome.[3]

Waist circumference: ≥90 cm in men and ≥80 cm in women

Fasting TGs >150 mg/dl or specific medication

HDL cholesterol <50mg/dl and <40 mg/dl for women and men respectively or specific medication.

Blood pressure >130 mmHg systolic or >85mmHg diastolic or specific medication.

Fasting Plasma Glucose levels > 100 mg/dl or specific Medication for diabetes mellitus.

Statistical Analysis: The data was gathered and inputted into Microsoft Excel 2019 sheet (Microsoft® Corp, Redmond, WA), and was analysed using SPSS software version 26 (IBM Corp., Armonk, NY). The same software was employed for table preparation, t-tests were utilized for comparing means of quantitative variables, Chi-square tests for qualitative variables and Pearson's test for correlation between variables. p value of <0.05 had been considered of statistical significance and value of <0.01 had been considered of very high statistical significance.

RESULTS

The study included 100 cases with newly diagnosed metabolic syndrome and 100 controls. Table 1 shows that, for the age variable, there is no statistical significant difference between the "Control" and

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"Cases" based on the independent samples t-test (t = 0.689, p = 0.689).

Among the cases and controls, 50 were males and 50 were females.

Among males the cases group had mean waist circumference of 104.72 cm, with a standard deviation of 10.09 cm. In the control group, the mean waist circumference was notably lower at 84.29 cm with a standard deviation of 4.62. The two groups showed difference in waist circumference that was of statistical significance (p = 0.003).

Among females cases showed mean waist circumference of 102.62 cm, and has a standard deviation value of 7.89 cm. Controls has mean waist circumference of 78.58 cm and has a standard deviation value of 4.05. The mean value for waist circumference was higher in cases and the difference was statistically significant (p = 0.004).

There was statistical significant difference between systolic blood pressure and diastolic blood pressure among cases and control groups with P value < 0.05 as shown in [Table 3].

- LDL (Low-Density Lipoprotein):
- The mean LDL in the cases group is 112.813 mg/dL and has a standard deviation value of 34.66, whereas the mean value for LDL in control group is 75.321 mg/dL and has a standard deviation value of 9.97.
- The F-statistic is 54.91 and p-value <0.001, which indicates that the difference in LDL levels in cases and controls has statistical significance.
- TGs (Triglycerides):
- Mean TGs value in cases is 186.51 mg/dL and has a standard deviation value of 47.71, whereas mean TGs in the control group is 121.34 mg/dL and has a standard deviation value of 13.85.
- The F-statistic is 109.367 and has a p-value <0.001, which indicates that the difference between two groups in TG levels holds statistical significance.
- HDL:
    - For females:
    - In the cases group, the mean HDL level was 42.70 mg/dL, and has a standard deviation value of 2.39 mg/dL, whereas in controls mean HDL level was notably higher at 50.87 mg/dL.
    - Thus, for two groups the difference in HDL levels holds statistical significance (p < 0.001). This implies that females with metabolic syndrome tend to have significantly lower HDL levels compared to their counterparts without metabolic syndrome.

Overall, the cases group consistently demonstrates higher mean values for SBP, DBP, LDL, TGs, and lower mean HDL than the controls, indicating significant difference of lipid panel between two groups except for HDL levels in male cases and control group.

The mean FPG in the cases group is 142.02 mg/dL and has a standard deviation value of 34.73, whereas mean FPG in the controls is 88.146 mg/dL and has a standard deviation value of 9.88. The F-statistic is 121.902 with p-value that is <0.001, which indicates that the difference in FPG values in two groups holds statistical significance.

Mean value for serum ferritin among Cases is 98.58 ng/ml with a standard deviation of 12.48 whereas mean values in controls is 53.3276 ng/ml, with a standard deviation of 15.38. The F-statistic is 6.414 and has a p-value 0.012, which indicates that the difference between the two groups has statistical significance.

Overall, the analysis reveals that cases in comparison with controls have significant high ferritin values. It suggests a potential relation between elevated ferritin values and the metabolic syndrome.

Further analysis of the parameter serum ferritin was done to explore the underlying factors contributing to this difference in serum ferritin levels and its potential implications for metabolic syndrome.

A positive relationship exists between ferritin values and waist circumference in the male controls. The correlation coefficient is 0.362. The correlation has statistical significance at the 0.023 level for male controls, and not significant for cases of both males and females and female controls.

In both cases and controls, there is no consistent pattern observed in relation of ferritin values and blood pressure values across cases as well as controls. No statistical significance suggests that serum ferritin may not be strongly associated with variations in blood pressure levels among the studied population.

Overall ferritin values have positive relation to LDL and TGs levels among cases, indicating that high ferritin values are related to high level of these lipid markers among individuals with metabolic syndrome. Among controls, there is a negative correlation between ferritin values as well as TGs, which suggests that ferritin values are related to low triglyceride levels among individuals without metabolic syndrome. The finding above suggests main role ferritin plays in lipid metabolism, particularly in relation to LDL and TGs levels.

For both cases and controls, the correlation has statistical significance at 0.01 levels and has a P value of <0.001. Positive relation among cases suggests that high ferritin values have association with high FPG values among individuals with the metabolic syndrome. Conversely, the negative correlation among controls suggests, higher ferritin values have association with lower FPG levels among individuals without the metabolic syndrome.

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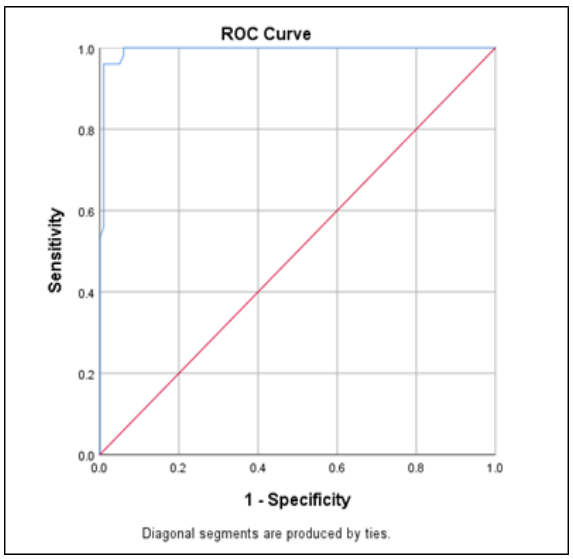

[Table 13] represents the AUC value for serum ferritin, which is 0.994. The cutoff value for serum ferritin to identify individuals with metabolic syndrome is determined to be >82.8 ng/dL. This means that individuals with serum ferritin levels greater than 82.8 ng/dL are considered positive for metabolic syndrome. The high AUC value of 0.994 and the determined cutoff value of >82.8 ng/dL suggest that serum ferritin is an excellent biomarker for identifying metabolic syndrome, with a high level of accuracy in distinguishing between individuals with and without the syndrome.

Individuals with metabolic syndrome are approximately 2.704 times more likely to have elevated serum ferritin levels compared to those without the syndrome.

Table 1: Age distribution.

Parameters	Group	N	Mean	Std. Deviation	Sig.	t
AGE	Control	100	42.59	7.08262	0.144	0.689
	Cases	100	41.83	8.46509		

Table 2: represents descriptive statistics and the results of one way-ANOVA comparing waist circumference between Control and Cases.

Parameters	Group	N	Mean	Std. Deviation	F	Sig.
Waist Circumference (in cm) (Males)	Controls	50	84.29	4.62	9.491	0.003
	Cases	50	104.72	10.09		
Waist Circumference (in cm) (Females)	Controls	50	78.58	4.05	8.346	0.004
	Cases	50	102.62	7.89		

Table 3: represents descriptive statistics and the results of one-way ANOVA comparing the Blood pressure of Control and Cases.

Parameters	group	N	Mean	Std. Deviation	F	Sig.
SBP	Control	100	118.18	7.15	12.791	<0.001
	Cases	100	145.28	10.41		
DBP	Control	100	75.42	5.24	31.687	<0.001
	Cases	100	91.62	8.62		

Table 4: represents descriptive statistics and the results of one-way ANOVA comparing the lipid profile of Control and Cases.

Parameters	group	N	Mean	Std. Deviation	F	Sig.
LDL	Control	100	75.32	9.97	54.91	<0.001
	Cases	100	112.81	34.66		
TGs	Control	100	121.34	13.85	109.36	<0.001
	Cases	100	186.51	47.71		
HDL (Males)	Control	50	40.56	2.43	2.68	0.105
	Cases	50	45.51	2.73		
HDL (Females)	Cases	50	42.70	2.39	18.88	<0.001
	Controls	50	50.87	1.065		

Table 5: represents descriptive statistics and the results of one-way ANOVA comparing glucose profile between control and cases.

Parameters	Group	N	Mean	Std. Deviation	F	Sig.
FPG	Control	100	88.14	9.88	121.902	<0.001
	Cases	100	142.02	34.73		

Table 6: provides descriptive statistics and the results of one-way ANOVA that compared ferritin values in cases and controls

Parameter	Group	N	Mean	Std. Deviation	F	Sig.
Serum Ferritin	Control	100	53.32	15.38	6.414	0.012
	Cases	100	98.58	12.48		

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Table 7: Correlation of Serum Ferritin with Anthropometric measurements

Parameters	Correlations	Serum Ferritin	
		Cases	Controls
Waist C (Males)	Pearson Correlation	-0.056	.362*
	Sig. (2-tailed)	0.694	0.023
	N	50	50
Waist C (Females)	Pearson Correlation	-0.167	0.047
	Sig. (2-tailed)	0.25	0.772
	N	50	50
** Correlation has significance at 0.01 levels(2-tailed).			
* Correlation has significance at 0.05 levels(2-tailed).			

Table 8: Correlation of Serum Ferritin (Y-axis) with Blood pressure

Parameters	Correlations	Serum Ferritin	
		Cases	Controls
SBP	Pearsons Correlation	0.079	-0.043
	Sig. (2-tailed)	0.437	0.674
	N	100	100
DBP	Pearsons Correlation	0.174	0.159
	Sig. (2-tailed)	0.084	0.115
	N	100	100
** Correlation has significance at 0.01 levels (2-tailed).			
* Correlation has significance at 0.05 levels (2-tailed).			

Table 9: Correlation of Serum Ferritin with Lipid panel

Parameters	Correlations	Serum Ferritin	
		Cases	Controls
LDL	Pearsons Correlation	.493**	-0.152
	Sig. (2-tailed)	<0.001	0.13
	N	100	100
TGs	Pearsons Correlation	.597**	-0.706**
	Sig. (2-tailed)	<0.001	<0.001
	N	100	100
HDL (Males)	Pearsons Correlation	-0.055	-0.009
	Sig. (2-tailed)	0.7	0.955
	N	50	50
HDL (Females)	Pearsons Correlation	0.044	-0.028
	Sig. (2-tailed)	0.765	0.864
	N	50	50
** Correlation has significance at 0.01 levels (2-tailed).			
* Correlation has significance at 0.05 levels (2-tailed).			

Table 10 shows correlation of Ferritin values with Glucose profile

Parameter	Correlations	Serum Ferritin	
		Cases	Controls
FPG	Pearsons Correlation	.340**	-0.510**
	Sig. (2-tailed)	0.001	<0.001
	N	100	100
** Correlation has significance at 0.01 levels (2-tailed).			
* Correlation has significance at 0.05 levels (2-tailed).			

Table 11: Area under Curve -Serum Ferritin

Area Under the Curve - Serum Ferritin	
Area	0.994
Cut off	Sr Ferritin >82.8 (Values greater than this are positive for Metabolic syndrome)

Table 12: Novel Risk factors of Metabolic syndrome

Parameters	Present		Absent		p value	Odds ratio (95% CI)
	Cases	Controls	Cases	Controls		
FERRITIN >82.8 ng/dL	49	3	51	97	<0.001	2.704 (1.988-3.719)

DISCUSSION

We tried to establish the relation between ferritin levels and metabolic syndrome parameters via this research. Various risk factors and metabolic syndrome parameters has strong relationship. We compared the control population with those having newly diagnosed metabolic syndrome. In this section, we interpret and analyse the findings obtained from our study, focusing on their implications for understanding the pathophysiology of metabolic syndrome. Our study revealed several significant findings regarding various clinical and laboratory parameters in patients with metabolic syndrome. We

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performed variance analysis using independent t-test and one-way ANOVA for comparison of anthropometric measures, clinical and laboratory profile of cases with controls.

The mean ferritin levels for our study in cases was 98.58 ng/ml and had a standard deviation of 12.48. The mean ferritin levels in controls were 53.32 ng/ml, and had a standard deviation of 15.38. This finding suggests a potential relation among elevated ferritin values and metabolic syndrome.

There was no significant association between ferritin values and waist circumference in both male and female cases and female controls. In both cases and controls, there is no consistent pattern observed in the relation among ferritin values and blood pressure across cases and controls. The lack of statistical significance suggests that serum ferritin may not be strongly associated with variations in blood pressure levels among the studied population. Overall ferritin values had positive correlation with LDL as well as TGs levels among cases, indicating that elevated ferritin values were associated with high values of various lipid markers among individuals with metabolic syndrome. Among controls, there had been a negative correlation between ferritin values and TGs, which suggests that ferritin values were associated with lower triglyceride levels among individuals without the metabolic syndrome. This indicates that serum ferritin may have role in lipid metabolism especially concerning LDL and TG levels. Overall, the above findings suggest among individuals with the metabolic syndrome ferritin levels were positively correlated with glycaemic parameters (FPG), and among individuals without metabolic syndrome they were negatively correlated with glycaemic parameters. This indicates a novel correlation between serum ferritin and glucose metabolism.

The cutoff value for serum ferritin to identify individuals with metabolic syndrome was determined to be >82.8 ng/dL. This meant that individuals with serum ferritin levels greater than 82.8 ng/dL were considered positive for metabolic syndrome. The high AUC value of 0.994 and the determined cutoff value of >82.8 ng/dL suggest that serum ferritin had been an excellent biomarker for identifying metabolic syndrome, with a level of accuracy that is high enough to distinguish among individuals with and without the syndrome. Individuals with metabolic syndrome have approximately 2.704 times more chances to have elevated serum ferritin levels than to those without metabolic syndrome

CONCLUSION

Serum ferritin demonstrated exceptional accuracy in identifying metabolic syndrome, suggesting its potential as a reliable biomarker for syndrome identification. Serum ferritin, LDL and triglycerides also showed associations, suggesting a potential role in lipid metabolism. Serum ferritin also had significant positive correlation with fasting plasma glucose among cases. However, serum ferritin did not correlate significantly with blood pressure or HDL levels (in both males and females) in either cases or controls. The findings in our study offer valuable insights for clinical practice, potentially enhancing the early identification and management of metabolic syndrome and its associated cardiovascular risks.

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