

Metabolic hyperferritinaemia (MHF) in Bariatric Surgery Candidates: Prevalence and Cross-Sectional Associations with Liver Function and Metabolic Markers

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Abstract

Background

Metabolic hyperferritinaemia (MHF) is closely linked to obesity and metabolic disorders, yet large-sample quantitative evidence regarding its clinical characteristics and multisystem metabolic correlations in morbidly obese populations remains insufficient. This study aimed to investigate the prevalence of MHF among bariatric surgery candidates and clarify its associations with liver function, glycolipid metabolism, and hematological indicators.

Methods

A cross-sectional case-control study was conducted on 695 patients scheduled for bariatric surgery. Patients were stratified into MHF and normal iron groups based on gender-specific serum ferritin cut-off values. Independent-samples t-test and Wilcoxon rank-sum test were applied to compare 14 core metabolic and clinical indicators, and correlation analysis was performed to assess the association between ferritin levels and key parameters.

Results

The overall MHF prevalence was 18.51%, with a markedly higher rate in males (32.67%) than in females (10.54%) and a significant upward trend with increased BMI. The MHF group exhibited significantly abnormal liver function, glycolipid metabolism, and hematological indices. Serum ferritin showed moderate positive correlations with alanine aminotransferase and γ -glutamyl transferase.

Conclusion

MHF is highly prevalent in patients undergoing bariatric surgery and is closely associated with systematic metabolic and hematological abnormalities. Targeted iron regulation may be a promising strategy to alleviate obesity-related metabolic complications, providing novel clinical insights for high-risk population management.

Key points

1. The prevalence of metabolic hyperferritinemia (MHF) is significantly elevated in patients undergoing bariatric surgery.
2. Patients with MHF are widely associated with multisystem pathophysiological abnormalities, including liver injury, dysglycemia, dyslipidemia, and hematopoietic dysfunction.

3. Routine iron metabolism screening is strongly recommended in obesity management and perioperative assessment for bariatric surgery.

Introduction

Metabolic hyperferritinaemia (MHF) is a prevalent condition characterized by elevated serum ferritin levels (generally > 200 ng/mL in females, > 300 ng/mL in males) occurring in individuals with metabolic dysfunction like obesity, insulin resistance, and metabolic syndrome, whose pathophysiological mechanism involves systemic iron homeostasis imbalance.¹ This disorder not only directly induces liver damage, such as fatty liver disease and hepatic fibrosis, but is also significantly correlated with an increased risk of type 2 diabetes mellitus and cardiovascular diseases, thereby severely impairing patients' quality of life and exacerbating the long-term medical burden.²

Currently, the diagnosis of MHF relies primarily on serum ferritin levels; however, there is no unified diagnostic standard in this field, and targeted interventions remain limited. Moreover, the precise mechanism underlying its association with specific metabolic disorders has not been fully elucidated.³

Metabolic and Bariatric surgery (MBS) has been proven to be one of the most effective treatments for morbid obesity and its related comorbidities.⁴ Since candidates for metabolic and bariatric surgery are patients with morbid obesity, a systematic assessment of the prevalence of MHF and its association with key metabolic indicators is of great value for the early identification of high-risk subgroups and the development of novel therapeutic targets.

As a core biomarker of iron storage in the body, serum ferritin serves as the key exposure factor for defining MHF in this study⁵. Previous studies have indicated that elevated ferritin is associated with hepatic steatosis⁶, insulin resistance⁷, and dyslipidemia⁸; nevertheless, most of these studies were limited by small sample sizes or were conducted in the general population⁹. The comorbid relationship between iron overload and multiple metabolic disorders, as well as its potential specific effects on liver function in individuals with morbid obesity, still requires in-depth quantification through large-sample studies.

The specific objectives of this study include: firstly, to define the case group and control group of MHF based on gender-specific serum ferritin cut-off values in the bariatric surgery population; secondly, to comprehensively compare the differences in liver function, metabolic, and hematological indicators between the two groups; finally, to identify the core metabolic disorder indicators most closely associated with iron overload, in order to clarify its clinical characteristics and potential pathophysiological significance.

Methods

This study adopted a cross-sectional case-control design, based on the preoperative baseline clinical data of patients who underwent bariatric surgery at a single center from 2019 to 2020. The advantage of this method lies in its ability to efficiently utilize the abundant data routinely collected in clinical practice, evaluate the strength of the association between iron overload status and various clinical indicators, thereby providing a solid hypothetical basis for subsequent mechanism exploration or interventional trials.

All patients met the criteria for bariatric surgery based on the IFSO Surgical Guidelines in 2022: BMI > 32.5 or BMI > 25 with at least two components of metabolic syndrome or comorbidities;¹⁰ The study enrolled only patients scheduled for primary bariatric surgery.

Metabolic hyperferritinaemia (MHF) was defined as in the presence of metabolic dysfunction when ferritin levels are above the upper limit of normal:

Ferritin > 300 ng/mL for males and Ferritin > 200 ng/mL for females, and the Iron normal Group was defined as: Ferritin ≤ 300 ng/mL for males and Ferritin ≤ 200 ng/mL for females.(1)

Independent-samples t-test was used for normally distributed indicators, and Wilcoxon rank-sum test for non-normally distributed indicators. Statistical differences in 14 core metabolic indicators were compared between the MHF group and the normal iron group.

Statistical significance was set at $P < 0.05$, and $P < 0.001$ was considered highly statistically significant.

Ethics Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The present study was approved by the Scientific Research Ethics Committee of the First Affiliated Hospital of Jinan University (Approval No. 2019024).

Results

Baseline Characteristics of Bariatric Surgery Candidates

A total of 695 patients scheduled for bariatric surgery were enrolled in this study, including 251 males and 446 females. The overall prevalence of metabolic hyperferritinaemia (MHF) was 18.51% (129/695), with a prevalence of 32.67% (82/251) in males and 10.54% (47/446) in females, which demonstrated in Fig. 1. The overall mean age of participants was 31.76 ± 9.93 years, and 85% of participants were aged between 18 and 44 years.

Comparison According to Different BMI Categories

The distribution of MHF patients was further analyzed across different BMI groups. As shown in Fig. 2, among the overweight group, only one patient (11.1%) had MHF. In the Obesity I group, 30 out of 223 patients (13.5%) were diagnosed with MHF. In the Obesity II group, 38 out of 201 patients (18.9%) had MHF. In the highest BMI category (BMI > 40), 60 out of 264 patients (22.7%) presented with MHF. We found that as the degree of obesity increases, the prevalence of MHF significantly rises.

The number and proportion of MHF cases in different BMI groups are illustrated in Table 1, Fig. 2 and Fig. 3.

Table 1
Cases of MHF in different BMI categories

BMI Category	Total	Diseased	Prevalence (%)
Overweight(24-27.9)	9	1	11.11
Obesity I(28-34.9)	223	30	13.45
Obesity II(35-39.9)	201	38	18.91
Obesity III(≥ 40)	264	60	22.73

Comparison of Metabolic Parameters Between Groups

Patients were divided into two groups according to the ferritin, and we divided into MHF group and control group and differences in metabolic parameters were compared between the two groups. Comparison of the differences between the two groups revealed significant disparities not only in liver function indicators such as ALT, AST, and γ-GT, but also in lipid metabolism parameters including total cholesterol, triglycerides, HDL-C, and LDL-C. Additionally, differences were observed in markers of glucose metabolism, namely fasting blood glucose, C-peptide, and insulin. Finally, the two groups also showed marked differences in hematological parameters, specifically hemoglobin and platelet count. Detailed data are presented in Table 2.

Table 2
Metabolic Parameters Between MHF and control group

Metabolic Indicator	MHF Group (Mean $\pm$ SD)	Control Group (Mean $\pm$ SD)	Statistical Test	P-value
Liver Function				
ALT (U/L)	32.6 $\pm$ 18.4	68.9 $\pm$ 42.7	Wilcoxon Rank-Sum	< 0.000001
AST (U/L)	28.3 $\pm$ 12.1	49.7 $\pm$ 26.8	Wilcoxon Rank-Sum	< 0.000001
γ -GT (U/L)	35.8 $\pm$ 27.6	92.4 $\pm$ 68.3	Wilcoxon Rank-Sum	< 0.000001
Lipid Metabolism				
Total Cholesterol (mmol/L)	4.52 $\pm$ 0.86	4.87 $\pm$ 0.93	Independent t-test	0.000003
Triglycerides (mmol/L)	1.76 $\pm$ 1.02	2.43 $\pm$ 1.58	Wilcoxon Rank-Sum	< 0.000001
HDL-C (mmol/L)	0.92 $\pm$ 0.21	0.87 $\pm$ 0.23	Independent t-test	0.0042
LDL-C (mmol/L)	2.78 $\pm$ 0.79	2.96 $\pm$ 0.85	Independent t-test	0.0028
Glucose Metabolism				
Fasting Glucose (mmol/L)	5.32 $\pm$ 0.87	5.68 $\pm$ 1.13	Independent t-test	0.000012
Insulin (miU/L)	18.7 $\pm$ 10.3	24.5 $\pm$ 14.6	Wilcoxon Rank-Sum	< 0.000001
C-peptide (ng/mL)	3.26 $\pm$ 1.28	4.12 $\pm$ 1.67	Wilcoxon Rank-Sum	< 0.000001
HbA1c (%)	5.5 $\pm$ 0.5	5.7 $\pm$ 0.6	Independent t-test	0.000008
Hematology				
Hemoglobin (g/L)	145.8 $\pm$ 12.3	153.6 $\pm$ 13.7	Independent t-test	< 0.000001
Platelet Count ($\times 10^9$ /L)	256.3 $\pm$ 58.7	228.5 $\pm$ 54.2	Independent t-test	< 0.000001

Correlation Analysis of Serum Ferritin

Correlation analysis revealed that serum ferritin exhibited a moderate positive correlation with ALT ($r = 0.57$, $P < 0.05$) and γ -GT ($r = 0.55$, $P < 0.05$), and a weak correlation with AST ($r = 0.437$, $P < 0.05$) and hemoglobin ($r = 0.427$, $P < 0.05$). The correlation heatmap and corresponding correlation coefficients are displayed in Figs. 4 and 5.

Discussion

The innovation of this study lies in being to systematically delineate the comprehensive clinical profile of metabolic hyperferritinaemia (MHF), marked by elevated serum ferritin (SF), in a population of patients with morbid obesity—a group characterized by a high concentration of metabolic disorders—and to quantify its strength of association with multisystem metabolic disturbances. Although previous studies have suggested a link between iron metabolism, obesity, and insulin resistance^{11 12} they have largely focused on the general population or mechanistic explorations in specific organs such as the hypothalamus. Within the core high-risk group of morbid obesity, a large-sample quantitative assessment of the comorbidity relationships between iron overload and liver dysfunction, insulin resistance, dyslipidemia, and hematological alterations, as well as their relative importance, has been lacking.

In this cohort of patients with obesity highly concentrated metabolic disorders who were scheduled to undergo bariatric surgery, we systematically delineated the comprehensive clinical profile of Metabolic hyperferritinaemia (MHF) characterized by elevated serum ferritin (SF) levels, and quantified the strength of its association with multi-system metabolic disturbances.

The prevalence of MHF

In our study, the proportion of MHF was found to be 18.51%, whereas a European study involving more than 6,000 participants reported a prevalence of 13%¹³. The higher prevalence observed in our study may be attributed to differences in study participants. Patients with obesity scheduled for bariatric surgery are more prone to MHF. In addition, Sex distribution may also contribute to the overall prevalence. Our study found that the incidence of MHF in males was more than three times that in females, suggesting that males are more susceptible to metabolic hyperferritinemia. This may be explained by the higher risk of non-alcoholic fatty liver disease, the greater tendency to accumulate visceral adipose tissue, and the higher likelihood of insulin resistance in males. A Brazilian study also demonstrated that males exhibited a higher incidence of metabolic syndrome and liver damage, which accounts for the gender disparity in the prevalence of hyperferritinemia.¹⁴

MHF differed across BMI groups. After stratification by BMI, we observed that the risk of MHF gradually increased with rising BMI, which may be associated with various metabolic disorders and insulin resistance. In our study, the prevalence of MHF in the group with BMI > 40 was 22.5%, which was significantly higher than 11.1% in the overweight group with BMI 24-27.5. This might be caused due to inflammatory conditions prevailing in the presence of increased adipose tissue by Alam's

study.¹⁵ Patients with higher BMI is easily to stay in a chronic inflammatory state with an increased ferritin, secondly the patients with higher BMI also have a higher production of hepcidin, a hormone that traps iron inside cells¹⁶. Finally, Metabolic Dysfunction strongly associated with high BMI, associated steatotic liver disease (MASLD, formerly NAFLD) and insulin resistance—are leading drivers of hyperferritinemia.¹⁴

MHF significantly increase the overall metabolic risk

The present study identified a strong association between iron overload and insulin resistance, hypertriglyceridemia, as well as an adverse lipid profile, indicating that enhanced attention should be paid to the comprehensive risk management of type 2 diabetes mellitus and cardiovascular diseases in patients with obesity complicated with MHF¹⁷. When formulating glucose-lowering and lipid-regulating strategies, clinicians ought to recognize that abnormal iron metabolism may serve as a potential modifiable factor. Despite the cross-sectional design of this study, which precludes the establishment of a causal relationship, these observed associations provide critical hypotheses and clinical evidence for future investigations into whether targeted iron-lowering interventions (e.g., dietary adjustments, iron chelators) can alleviate obesity-related metabolic complications^{18,19}.

Furthermore, this study demonstrated statistically significant differences in all 14 core analyzed indices between the MHF group and the control group, highlighting the extensive and systemic effects of abnormal iron metabolism rather than isolated impairments in hepatic or glucolipid metabolism. This characteristic of multisystem involvement suggests the existence of a common iron-dependent upstream pathophysiological pathway, such as chronic inflammation, oxidative stress, or mitochondrial dysfunction²⁰. Specifically, iron overload can induce the excessive generation of reactive oxygen species through the Fenton reaction, which further leads to lipid peroxidation, protein and DNA damage, thereby triggering hepatocellular injury, impairing insulin signal transduction, and disrupting lipoprotein metabolism²¹.

Notably, the elevation amplitude of γ -glutamyl transferase was substantially higher than that of alanine aminotransferase and aspartate aminotransferase, which may imply that iron overload not only damages hepatocytes but also specifically affects the biliary system or exacerbates hepatic metabolic stress.^{22,23} This phenomenon merits in-depth exploration in subsequent studies combined with liver imaging or pathological examinations

In addition, the observed decrease in platelet count and mild elevation in hemoglobin expand the risk spectrum of metabolic iron overload, suggesting its potential impact on the hematopoietic system. The underlying mechanism may be associated with hypersplenism or the complex regulatory effects of iron on bone marrow hematopoiesis, which emphasizes the necessity of conducting comprehensive evaluations in the clinical management of such patients^{24 25}

Limitations

This study has several limitations that need to be addressed. First, the cross-sectional design can only reveal statistical associations between serum ferritin and metabolic parameters, and cannot establish a causal relationship in which iron overload acts as the etiology of metabolic disorders; the two conditions may be mutually causal or driven by shared upstream factors. Second, the study lacked a histopathological gold standard such as liver biopsy and failed to directly quantify the degree of iron deposition in hepatic parenchyma, which limits the depth of mechanistic interpretation at the molecular and cellular levels. Finally, the single-center design may limit the generalizability of the findings to populations of different ethnicities and geographic regions.

Conclusions

Through a systematic analysis of a large cohort of patients undergoing bariatric surgery, this study confirms that the prevalence of metabolic hyperferritinemia is significantly elevated in this population. We further demonstrate that this condition is widely associated with multisystem pathophysiological abnormalities, suggesting that strategies aimed at reducing iron levels hold potential for ameliorating obesity-related metabolic complications.

Declarations

The individual-level raw data contain confidential patient information and cannot be publicly released at present. De-identified summary data are included within the manuscript and supplementary materials. Full raw data can be accessed by the reviewers for peer review purposes only.

Author Contribution

Huajiang Liu and Liqin Zhang collected some data and photos and write some manuscript;Zhiyong Dong and Cunchuan Wang had make the table1,2 and figures1,2,3,4 for the research Songhao Hu started this work and revised the whole manuscript;All authors reviewed the manuscript

Data Availability

The individual-level raw data contain confidential patient information and cannot be publicly released at present. De-identified summary data are included within the manuscript and supplementary materials. Full raw data can be accessed by the reviewers for peer review purposes only.

Conflict of Interest

The authors declare no competing interests.

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Figures

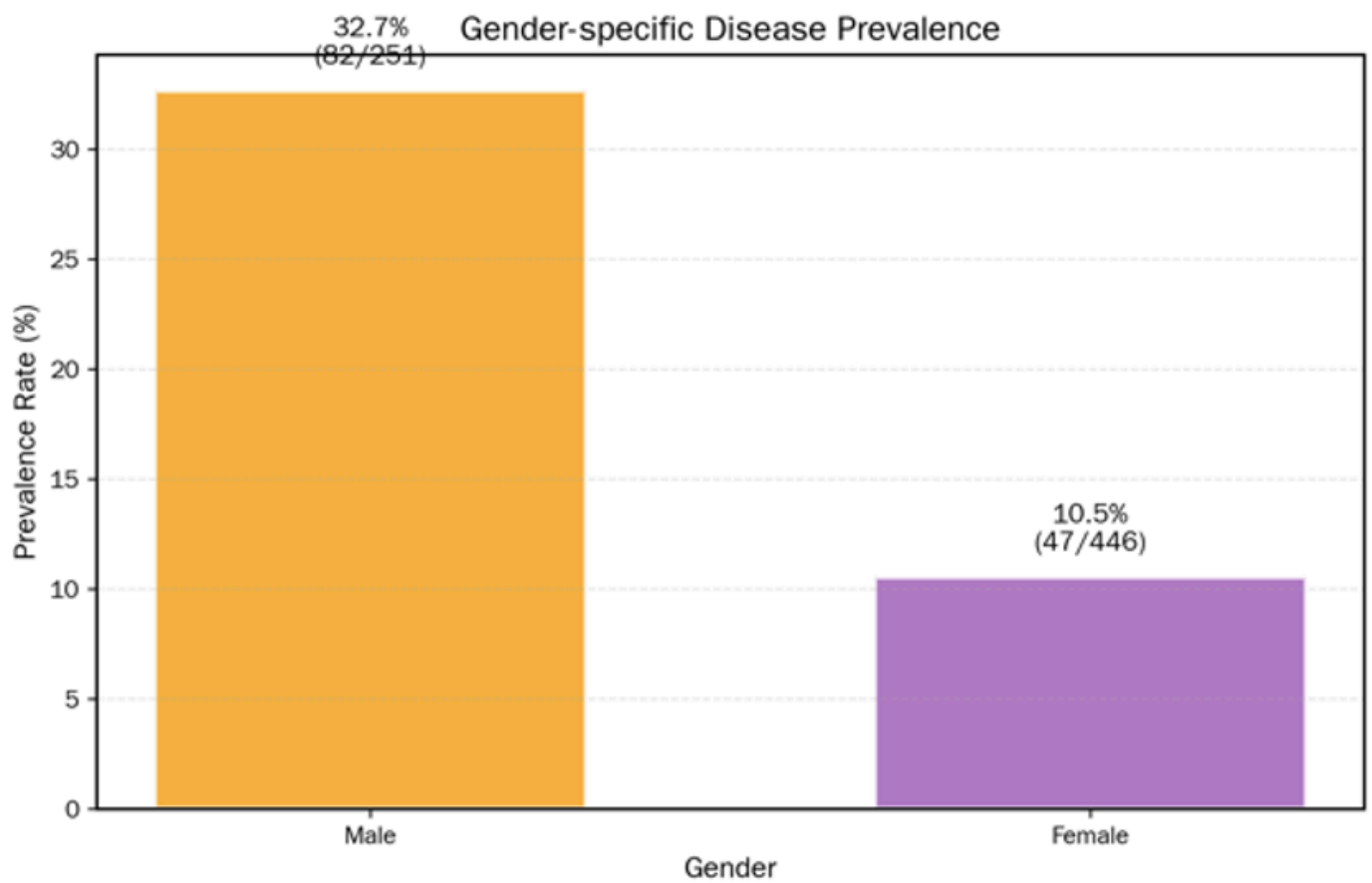


Figure 1

Prevalence of MHF between Gender

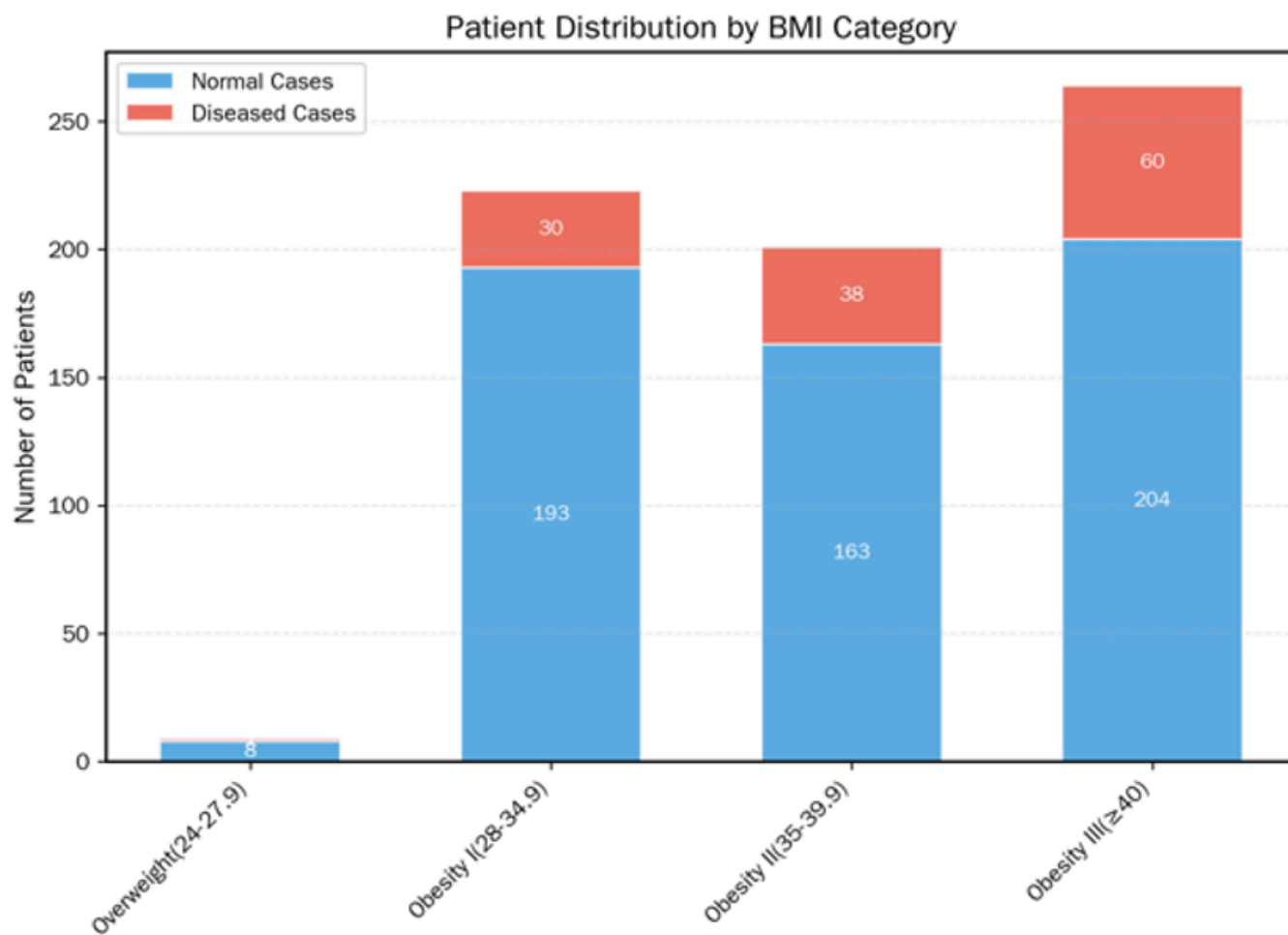


Figure 2

Prevalence of MHF by different BMI Catrgories

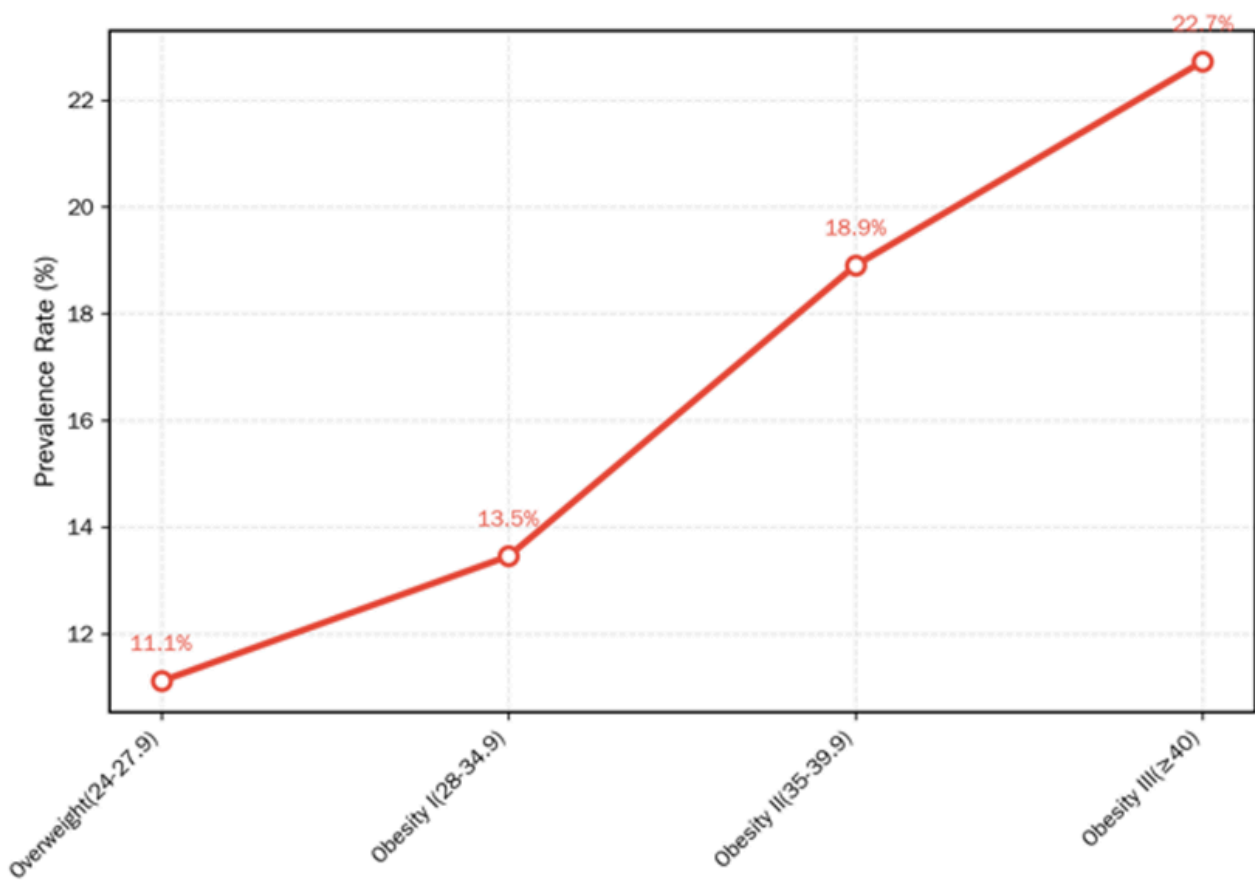


Figure 3

Prevalence of MHF changed by different BMI Categories

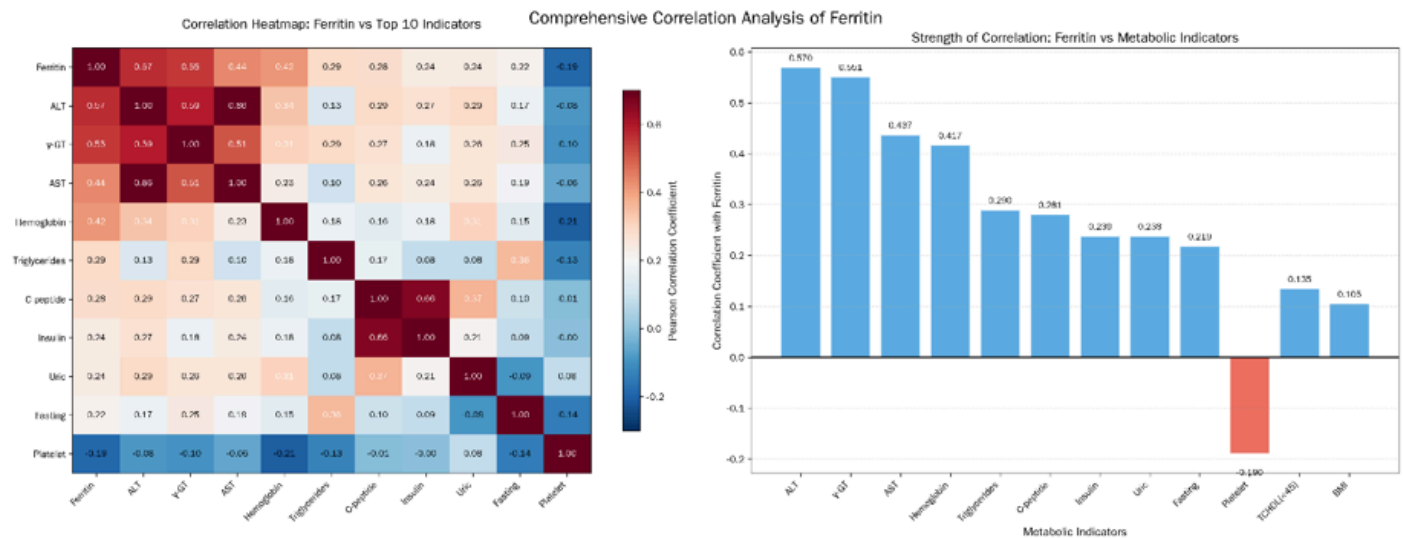


Figure 4

Correlation heatmap and strength of Correlation figure.

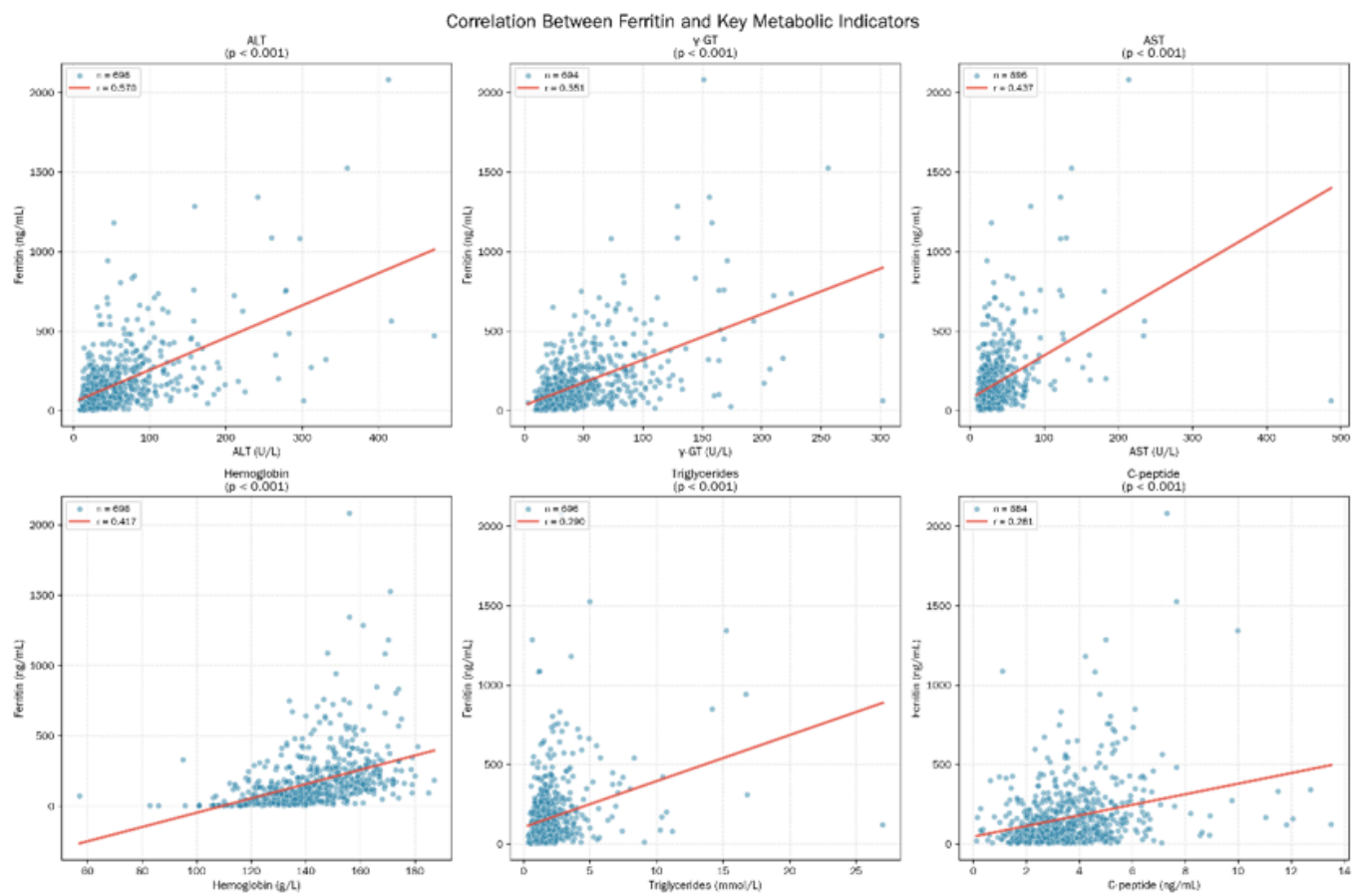


Figure 5

Correlation between Ferritin and key metabolic indications

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [rawdataofMHF.xlsx](#)