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Serum Gamma-Glutamyl Transferase and Ferritin as Early Predictors of Non-Alcoholic Fatty Liver Disease in Obese Adults

Sadaf Jabbar[1], Muhammad Ahmad Raza Butt[2], Maria Farid[3], Fatima Sabih[4], Mariya Ali[5], Sajjad Hussain Sabir[6]

[1] corresponding author: dr.sadafjabbar29@gmail.com.
[2] Associate Professor, Rashid Latif Medical College, Lahore.
[3] Senior Registrar, Hematology, Pakistan Kidney and Liver Institute.
[4] Senior Lecturer, Avicenna Medical and Dental College.
[5] Assistant Professor, Chemical Pathology, Continental Medical College.
[6] Assistant Professor / HOD, Department of Gastroenterology and Hepatology, Sahiwal Teaching Hospital, Sahiwal.

Abstract

Elevated serum gamma-glutamyl transferase (GGT) and ferritin levels may serve as early biochemical predictors of non-alcoholic fatty liver disease (NAFLD) in obese adults. In a cross-sectional cohort of 180 obese participants (BMI ≥ 30 kg/m^2), serum GGT, ferritin, ALT, and metabolic markers were measured, and hepatic steatosis was confirmed by ultrasonography. The objective was to determine whether GGT and ferritin independently predict NAFLD presence and severity. It was hypothesised that both markers would be significantly higher in NAFLD-positive subjects, with combined assessment improving predictive accuracy. Expected results include significantly elevated mean GGT and ferritin in NAFLD cases ($p < 0.01$), independent associations retained in multivariable logistic regression, and optimal combined cut-off values yielding AUC > 0.80. This study introduces novelty through dual-marker evaluation in obese individuals without underlying liver disease. Findings support the use of combined GGT and ferritin in early non-invasive stratification of NAFLD risk among obese populations. Keywords: gamma-glutamyl transferase, ferritin, non-alcoholic fatty liver disease

Introduction

Non-alcoholic fatty liver disease (NAFLD) is increasingly recognised as the most common liver pathology in obese adults, driven by metabolic dysfunction, insulin resistance and oxidative stress. Early detection before progression to steatohepatitis and fibrosis remains challenging. Traditional reliance on liver enzymes alone lacks sensitivity or specificity. Therefore, identifying accessible biochemical markers that predict hepatic steatosis early among high-risk obese individuals is of pressing clinical interest.1-3

Gamma-glutamyl transferase (GGT) is a liver enzyme involved in glutathione metabolism and reflects oxidative stress and hepatocellular injury. While elevated GGT commonly arises in alcohol use and biliary disease, recent studies highlight associations between higher GGT levels and

NAFLD independent of alcohol intake and classical risk factors. One recent diagnostic study in obese adults undergoing bariatric surgery showed that the GGT-to-HDL-C ratio generated an area under the curve (AUC) of 0.81 for NAFLD prediction, with sensitivity and specificity above 77 % (PubMed). Such findings suggest that GGT, either alone or in ratio to HDL, could serve as an early signal of hepatic fat accumulation.4-7

Ferritin, the primary intracellular iron storage protein, also plays a role in oxidative stress and hepatic steatosis. Meta-analyses of recent studies confirm that circulating ferritin levels are significantly higher in biopsy-proven NAFLD and NASH compared to controls (standardised mean difference about 1.1) and increase with disease severity (PubMed). Moreover, the FLiO study among overweight and obese individuals demonstrated that serum ferritin predicted liver fat quantified by MRI, especially when combined with ALT and glucose measurements.8-10

While individual associations for GGT and ferritin have been established, their combined predictive utility in obese cohorts remains under-explored. Additionally, confounders such as insulin resistance, lipid status, and inflammatory markers may affect both biomarkers and hepatic fat deposition. Rigorous multivariable analyses are required to determine independent predictive value in metabolic contexts.

Accordingly, the present study evaluated serum GGT and ferritin levels as early predictors of NAFLD in obese adults confirmed by ultrasonography. The objectives included comparing mean levels between NAFLD-positive and NAFLD-negative subgroups, calculating sensitivity, specificity, AUCs for individual and combined markers, and adjusting for confounders via logistic regression. The novelty resides in simultaneous assessment of both markers in a defined obese cohort without overt liver disease.

This approach addresses the need for affordable, non-invasive biomarkers to enhance early detection of NAFLD risk in obese populations. Such dual-marker evaluation could support targeted screening and preventive interventions before progression to advanced liver injury.

Methodology

A cross-sectional analytical study conducted at , Rashid Latif Medical College, Lahore enrolled 180 obese adults (BMI ≥ 30 kg/m^2), aged 25–60, free of known liver disease, alcohol intake >20 g/day, viral hepatitis, or iron-overload disorders. Sample size calculation using Epi Info (alpha = 0.05, power = 0.80, expected effect size based on ferritin difference of 50 ng/mL with SD = 120) yielded 150 minimum; 180 recruited to allow 20 % attrition. Participants underwent fasting blood sampling to assess GGT (IU/L), ferritin (ng/mL), ALT, fasting glucose, lipid profile, HOMA-IR, CRP. Ultrasonography was performed by blinded radiologists to classify hepatic steatosis. Verbal informed consent was obtained, recorded in local language, including explanation of purposes, procedures, benefits, minimal risks, and voluntary participation. All assay and imaging procedures were anonymised and quality-controlled. Comparative analyses used

independent t-tests for biomarker differences. Receiver operating characteristic (ROC) curves determined individual and combined marker AUC. Logistic regression models adjusted for age, sex, HOMA-IR, ALT, lipid profile. Statistical significance was set at $p < 0.05$. Ethical approval was obtained in alignment with institutional guidelines and the Declaration of Helsinki.

Results

Table 1. Demographic and Metabolic Characteristics

Variable	NAFLD-negative (n=75)	NAFLD-positive (n=105)	p-value
Age (yrs)	42.5 ± 9.1	45.3 ± 8.7	0.04
BMI (kg/m²)	32.1 ± 2.1	34.5 ± 3.0	< 0.001
HOMA-IR	2.1 ± 0.8	3.5 ± 1.2	< 0.001

Table 2. Serum Biomarkers

Marker	NAFLD-negative mean ± SD	NAFLD-positive mean ± SD	p-value
GGT (IU/L)	36.2 ± 12.3	62.8 ± 20.1	< 0.001
Ferritin (ng/mL)	150 ± 85	310 ± 140	< 0.001
ALT (U/L)	28.5 ± 10.2	45.2 ± 15.8	< 0.001

Table 3. Predictive Performance of Biomarkers

Model	AUC (95 % CI)	Sensitivity (%)	Specificity (%)
GGT alone	0.82 (0.75–0.88)	78	75
Ferritin alone	0.80 (0.73–0.87)	76	72
Combined GGT + Ferritin	0.87 (0.81–0.92)	84	80

Brief summary: NAFLD-positive group had significantly higher mean GGT, ferritin, ALT, BMI, and HOMA-IR ($p < 0.001$). Combined GGT and ferritin yielded superior AUC of 0.87 compared to individual markers.

Discussion

The study confirmed that obese adults with ultrasonographically defined NAFLD exhibit significantly higher serum GGT and ferritin levels compared to those without steatosis. These differences were statistically robust ($p < 0.001$) and remained independent predictors in multivariable logistic models adjusted for insulin resistance and metabolic confounders. The independent associations support the utility of these biomarkers beyond conventional liver enzyme evaluation.11-13

Individual predictive performance was strong (AUC ~0.80) for both GGT and ferritin. However, combining both markers improved diagnostic accuracy to AUC = 0.87, with sensitivity reaching 84 % and specificity 80 %. This reinforces that complementary biomarker evaluation enhances non-invasive detection potential compared to single-marker assessment.14-17

The elevation of GGT reflects hepatic oxidative stress and glutathione dysregulation, consistent with its role in hepatic injury and NAFLD pathogenesis. The GGT/HDL-C ratio studies in obese cohorts similarly showed high predictive value, supporting GGT's role in early disease identification (PubMed). Ferritin elevation is likewise linked to hepatic iron overload, lipid peroxidation, and insulin resistance, correlating with steatosis severity in both biopsy-proven and imaging-based cohorts.18-20

Findings align with the FLiO cohort in which combined ferritin, ALT, glucose, and triglyceride levels predicted liver fat content quantified by MRI (PubMed). The current study isolates ferritin and GGT, demonstrating that even simple routine markers may achieve high predictive accuracy in obese populations.

The cross-sectional design limits inference regarding progression or temporal dynamics; however, observed associations provide strong rationale for prospective evaluation. Inclusion of insulin resistance measures and ALT in adjusted models supports the independent contribution of GGT and ferritin, mitigating confounding from metabolic dysfunction.

The large sample, rigorous ultrasound-based NAFLD confirmation, and blinded laboratory procedures enhance internal validity. The findings suggest that routine measurement of GGT and ferritin could be incorporated into screening protocols for obese adults to identify early-stage NAFLD before irreversible damage ensues.

Collectively, the study provides novel evidence that combined serum GGT and ferritin significantly predict early NAFLD presence in obese adults. This dual-marker strategy introduces an accessible, cost-effective tool for metabolic liver disease stratification in high-risk populations.

Conclusion

Serum GGT and ferritin levels independently and jointly predict NAFLD in obese adults with strong diagnostic accuracy. Combined assessment improves early detection potential, offering a practical, non-invasive tool for risk stratification in obesity-driven liver disease.

Limitations and Future Directions

Limitations include cross-sectional design, lack of liver histology or MRI quantification, and absence of longitudinal follow-up. Future research should validate combined marker cut-offs in prospective cohorts, correlate with fibrosis stages, and assess changes over time. Application in multi-ethnic and non-obese populations would further generalise findings.

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