EVALUATION OF SERUM FERRITIN LEVEL IN PATIENTS WITH CHOLELITHIASIS – A CROSS SECTIONAL STUDY

Dr Alex Arthur Edwards Dr Saipriya. S. V.

Author 1 : Professor & HOD, Department of General Surgery, Sree Mookambika Institute of Medical Sciences, Kanyakumari, Tamil Nadu, India

Author 2: Junior Resident, Department of General Surgery, Sree Mookambika Institute of Medical Sciences, Kanyakumari, Tamil Nadu, India

Corresponding Author

Dr Saipriya. S. V.

Junior Resident, Department of General Surgery, Sree Mookambika Institute of Medical Sciences, Kanyakumari, Tamil Nadu, India

ABSTRACT

Background: Cholelithiasis is a common hepatobiliary disorder with multifactorial etiology involving metabolic, inflammatory, and oxidative mechanisms. Altered iron metabolism has been implicated in gallstone formation, with serum ferritin serving as a marker of body iron stores and inflammation. However, limited data exist on their combined role in cholelithiasis, necessitating further evaluation to understand their clinical and pathophysiological significance.

Aims: To evaluate serum ferritin levels in patients with cholelithiasis and to analyze their association with disease characteristics.

Materials and Methods: This prospective observational study was conducted over a period of 9 months and included 40 patients diagnosed with cholelithiasis based on clinical and radiological findings. Serum ferritin levels were measured using immunoassay techniques. Demographic data, clinical features, and relevant biochemical parameters were recorded. Statistical analysis was performed to determine the association between ferritin levels and clinical variables, with $p < 0.05$ considered statistically significant.

Results: The mean serum ferritin level was significantly elevated in patients with cholelithiasis, suggesting altered iron metabolism and possible inflammatory activity. A positive correlation was

noted between elevated serum ferritin levels expression, indicating dysregulation of iron homeostasis at both systemic and cellular levels. Patients with higher ferritin levels also demonstrated more pronounced inflammatory changes in histopathological examination. The findings were statistically significant ($p < 0.05$), supporting the role of iron metabolism in gallstone disease pathogenesis.

Conclusion: Alterations in iron metabolism, reflected by elevated serum ferritin may contribute to the pathogenesis of cholelithiasis. This could serve as potential indicators of disease activity and underlying inflammatory processes. Further large-scale studies are required to validate their role and explore therapeutic implications targeting iron regulation in gallstone disease.

Keywords: Cholelithiasis, Gallstones, Inflammation, Iron Metabolism, Serum Ferritin.

INTRODUCTION

Cholelithiasis, or gallstone disease, is one of the most common hepatobiliary disorders encountered in clinical practice, with a rising incidence worldwide due to changes in lifestyle, diet, and metabolic risk factors. It is characterized by the formation of calculi within the gallbladder, primarily composed of cholesterol, pigment, or mixed constituents.[1,2]

The pathogenesis of cholelithiasis is multifactorial, involving supersaturation of bile with cholesterol, impaired gallbladder motility, nucleation of crystals, and chronic inflammation.[3] Established risk factors include female gender, obesity, diabetes mellitus, dyslipidemia, and advancing age. Despite extensive research, the precise molecular mechanisms contributing to gallstone formation remain incompletely understood.[4]

Recent studies have increasingly focused on the role of oxidative stress and inflammation in gallstone pathogenesis. Iron metabolism has emerged as an important contributor to these processes. Iron, an essential trace element, plays a crucial role in various cellular functions, including oxygen transport, enzymatic reactions, and mitochondrial activity.[5] However, excess iron can generate reactive oxygen species through the Fenton reaction, leading to oxidative damage, lipid peroxidation, and tissue injury. This oxidative stress may contribute to alterations in bile composition, mucosal inflammation, and gallbladder dysfunction, thereby promoting gallstone formation.[6]

Serum ferritin, the primary intracellular iron storage protein, is widely used as a biomarker of body iron stores.[7] In addition to reflecting iron status, ferritin also acts as an acute-phase reactant and is elevated in inflammatory conditions.[8] Elevated serum ferritin levels have been associated

with metabolic syndrome, insulin resistance, and chronic inflammatory states, all of which are known risk factors for cholelithiasis.[9,10] However, the exact relationship between serum ferritin levels and gallstone disease remains inadequately explored, particularly in relation to local tissue-level iron regulation.

While previous studies have independently assessed the role of iron or inflammation in cholelithiasis, there is limited literature examining the combined interplay between these parameters. Understanding this relationship may provide deeper insights into the pathophysiology of gallstone disease. By correlating serum ferritin levels the study aims to bridge the gap between systemic and cellular aspects of iron regulation in cholelithiasis. This may help identify potential biomarkers for disease activity and open avenues for targeted therapeutic strategies focusing on modulation of iron homeostasis.

AIMS AND OBJECTIVES

- To evaluate serum ferritin levels in patients with cholelithiasis and to analyze their association with disease characteristics.

MATERIALS AND METHODS

The present prospective observational study was conducted over a period of 9 months from January 2025 to September 2025 at department of General Surgery, Sree Mookambika Institute of Medical Sciences. A total of 40 patients diagnosed with cholelithiasis based on clinical features and ultrasonographic confirmation were included in the study.

Inclusion Criteria

- Patients aged ≥18 years diagnosed with cholelithiasis
- Patients undergoing elective cholecystectomy
- Patients willing to provide informed consent
- Both male and female patients

Exclusion Criteria

- Patients with chronic liver disease or cirrhosis
- Patients with known hematological disorders affecting iron metabolism
- Patients with malignancy or chronic inflammatory diseases
- Patients on iron supplementation or recent blood transfusion
- Pregnant women

Written informed consent was obtained from all participants prior to enrolment. A detailed clinical evaluation was performed for each patient, including demographic data, symptomatology, duration of illness, and relevant medical history. Baseline laboratory investigations such as

complete blood count, liver function tests, fasting blood sugar, and other routine biochemical parameters were recorded.

Venous blood samples were collected preoperatively under aseptic conditions for estimation of serum ferritin levels, which were measured using a standardized chemiluminescent immunoassay method. (Adult men: 20–500 ng/mL and Adult women: 20–200 ng/mL)

All patients subsequently underwent elective cholecystectomy under standard surgical and anesthetic protocols. Intraoperatively, gallbladder specimens were carefully collected and preserved in formalin for histopathological examination. Tissue sections were processed and stained using routine hematoxylin and eosin techniques to assess inflammatory and structural changes. The histopathological findings were correlated with serum ferritin levels to evaluate the relationship between systemic iron status and local cellular iron regulation.

All data were entered into a structured proforma and analyzed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. The association between serum ferritin levels, and clinical variables was assessed using suitable statistical tests such as the chi-square test and independent t-test. Correlation analysis was performed where applicable, and a p value of less than 0.05 was considered statistically significant.

OBSERVATION AND RESULTS

Majority of patients (12; 30.0%) were in the 41–50 years age group, followed by 51–60 years (25.0%), indicating higher prevalence in middle-aged individuals. (Table 1)

Age (Years)	**Number (n)**	**Percentage (%)**
18–30	5	12.5
31–40	8	20.0
41–50	12	30.0
51–60	10	25.0
>60	5	12.5
Total	**40**	**100**

Table 1: Age Distribution

Females constituted the majority (65.0%), reflecting known epidemiological trends of higher gallstone prevalence in females. (Table 2)

Gender	**Number (n)**	**Percentage (%)**
Male	14	35.0
Female	26	65.0
Total	**40**	**100**

Table 2: Gender Distribution

Elevated serum ferritin levels were observed in 28 (70.0%) patients, suggesting altered iron metabolism in cholelithiasis. (Table 3)

Serum Ferritin (ng/mL)	**Number (n)**	**Percentage (%)**
Normal	12	30.0
Elevated	28	70.0
Total	**40**	**100**

Table 4: Serum Ferritin Levels

Serum ferritin levels increased with severity of inflammation (p = 0.02), indicating its role as an inflammatory marker in gallbladder pathology and supporting its role in disease progression. (Table 6)

Inflammation	**Mean Ferritin (ng/mL)**
Mild	145.2 ± 28.6
Moderate	198.5 ± 35.4
Severe	265.3 ± 42.1
p value	**0.02***

Table 4: Serum Ferritin vs Histopathological Inflammation

DISCUSSION

The present study included 40 patients with cholelithiasis, with a predominance of females (26; 65.0%) compared to males (14; 35.0%), reflecting the higher susceptibility of females to

gallstone disease. The majority of patients were middle-aged, particularly 41–50 years (12; 30.0%) and 51–60 years (10; 25.0%), suggesting that cholelithiasis is more common in this age range. This distribution highlights the influence of metabolic and hormonal factors, which become more prominent with advancing age.

A key finding of this study was the high prevalence of elevated serum ferritin levels, observed in 28 (70.0%) patients, while only 12 (30.0%) had normal levels. This suggests that altered iron metabolism is common in patients with cholelithiasis and may be associated with underlying inflammatory processes. Ferritin, as both an iron storage protein and an acute-phase reactant, reflects not only increased iron stores but also ongoing inflammation within the gallbladder.

The progressive increase in ferritin levels with the severity of histopathological inflammation ($p = 0.02$) indicates that iron dysregulation may contribute to gallbladder inflammation through oxidative stress and tissue injury. These findings suggest that dysregulated iron metabolism may play a role in the pathogenesis of cholelithiasis.

Consistent with these observations, Wagh MR et al.[11] reported a mean age of 43.12 years in cases and 41.05 years in controls, with 64% females in the case group. They observed that 65.7% of patients with gallstones had subnormal serum iron levels (<40 µg/dL), predominantly females, and the mean serum iron difference between cases and controls was statistically significant ($p \leq 0.05$). No significant difference in serum cholesterol levels was found ($p > 0.7$). The study concluded that low serum iron is associated with a higher risk of cholelithiasis, whereas serum ferritin levels may be influenced by other inflammatory conditions.

Dube BA et al.[12] similarly reported that low serum iron and ferritin are risk factors for cholelithiasis, and that increased bile cholesterol further raises the probability of gallstone formation. Arora BK et al.[13] observed that gallstones were more prevalent in females (ratio 5.4:1). In males, low serum iron was not strongly associated with cholelithiasis, whereas low ferritin levels were observed in 64.5% of cases versus 16.66% of controls, suggesting ferritin may be a relevant marker in males. In females, low serum iron was seen in 23.07% of cases versus 23% in controls, while low ferritin was noted in 35.5% of cases versus 15.38% of controls, indicating that low body iron stores may contribute to gallstone risk in females.

Naik S et al.[14] reported that serum ferritin was normal or raised in 68.1% of patients with iron deficiency, emphasizing that ferritin alone is insensitive for diagnosing iron deficiency. They suggested that preoperative assessment of iron status in patients undergoing cholecystectomy

could help identify subclinical iron deficiency and potentially reduce the risk of gallstone disease at a population level. Punnoose SK et al.[15] found that low ferritin values were present in 13.6% of cases and none of the controls (P = 0.05), consistent across both sexes, supporting the association of iron deficiency with gallstone formation.

The findings suggest that dysregulated iron metabolism plays a role in the pathogenesis of cholelithiasis, particularly in females with low serum iron levels. Elevated serum ferritin may reflect concurrent inflammation rather than directly predicting gallstone risk. These results highlight the importance of assessing iron status preoperatively in patients planned for cholecystectomy, not only to identify those at risk of gallstone disease but also to address potential anemia in the population.

CONCLUSION

Elevated serum ferritin levels were commonly observed in patients with cholelithiasis, indicating significant alterations in both systemic and cellular iron metabolism. A strong association between these parameters and histopathological inflammation suggests that iron-induced oxidative stress may play a contributory role in gallstone formation and disease progression. These findings emphasize the importance of evaluating iron homeostasis in cholelithiasis and suggest that targeting iron-related pathways may offer new insights for risk assessment and therapeutic strategies.

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Nil.

CONFLICTS OF INTEREST

There are no conflicts of interest

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