ASSESSMENT OF SERUM FERRITIN LEVELS AND THEIR ASSOCIATION WITH INFLAMMATORY MARKERS IN PATIENTS WITH INFLAMMATORY DISORDERS: A HOSPITAL-BASED OBSERVATIONAL STUDY FROM NORTH INDIA

Dr. Neeta Binwani

Assistant Professor, Department of Pathology, Era's Lucknow Medical College and Hospital, Sarfarazganj, Lucknow, Uttar Pradesh, India neetabinwani513@gmail.com

Corresponding Author: Dr. Neeta Binwani

Address: Department of Pathology, Era's Lucknow Medical College and Hospital, Sarfarazganj, Lucknow, Uttar Pradesh, India

ABSTRACT

Background: Ferritin is an intracellular iron storage protein that also functions as an acute-phase reactant. Elevated serum ferritin levels have been reported in various inflammatory disorders and may reflect the degree of systemic inflammatory activity. However, data regarding serum ferritin levels in heterogeneous inflammatory conditions from North Indian tertiary care settings remain limited.

Objectives: To assess serum ferritin levels in patients with inflammatory disorders and to evaluate their association with selected inflammatory markers in a tertiary care hospital in North India.

Methods: A hospital-based observational cross-sectional study was conducted from July 2013 to November 2013 at a tertiary care teaching hospital in North India. A total of 44 adult patients diagnosed with inflammatory disorders were enrolled using consecutive sampling. Demographic, clinical, and laboratory data were collected using a structured case record form. Serum ferritin levels were estimated using a standardized immunoassay method. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and total leukocyte count (TLC) were recorded as indicators of inflammatory activity. Statistical analysis was performed using SPSS version 20.0. Associations and correlations between serum ferritin and inflammatory markers were assessed, with $p < 0.05$ considered statistically significant.

Results: The mean age of study participants was 47.8 ±15.2 years, and 54.5% were male. Tuberculosis was the most common inflammatory disorder, followed by rheumatoid arthritis and acute bacterial infections. The overall mean serum ferritin level was 378 ±158 ng/mL. Higher ferritin concentrations were observed among patients with acute bacterial infections and chronic liver disease with inflammatory activity. Significant differences in serum ferritin levels were observed across disease categories ($p = 0.041$). Patients with ferritin levels >300 ng/mL demonstrated significantly higher ESR, greater CRP positivity, and higher TLC values compared with those having ferritin levels ≤300 ng/mL. Serum ferritin showed a significant positive correlation with ESR ($r = 0.58$, $p < 0.001$), CRP positivity ($r = 0.42$, $p = 0.004$), and TLC ($r = 0.39$, $p = 0.009$).

Conclusion: Serum ferritin levels are significantly associated with inflammatory activity in patients with inflammatory disorders. The positive relationship between ferritin and established inflammatory

markers suggests that serum ferritin may serve as a useful adjunctive biomarker for assessing inflammatory burden in routine clinical practice.

Keywords: Serum ferritin; Inflammation; Acute-phase reactant; Erythrocyte sedimentation rate; C-reactive protein; Inflammatory disorders; Biomarkers.

INTRODUCTION

Serum ferritin is a ubiquitous intracellular protein that plays a crucial role in iron storage and regulation. It serves as the primary reservoir of iron in the body and helps maintain iron homeostasis by storing excess iron in a soluble and non-toxic form. Beyond its role in iron metabolism, ferritin has emerged as an important acute-phase reactant whose concentration increases in response to inflammatory stimuli, infection, tissue injury, and various systemic disorders [1]. Consequently, serum ferritin measurement has become a valuable laboratory parameter not only for assessing iron stores but also for evaluating inflammatory activity in a variety of clinical conditions.

Inflammation is a complex biological response triggered by infectious, autoimmune, neoplastic, and metabolic conditions. During inflammation, cytokines such as interleukin-1, interleukin-6, and tumor necrosis factor-α stimulate hepatic synthesis of acute-phase proteins and alter iron metabolism through increased hepcidin production [2]. These mechanisms lead to sequestration of iron within macrophages and hepatocytes, resulting in elevated serum ferritin concentrations. Therefore, serum ferritin has gained considerable attention as a biomarker reflecting both iron metabolism and inflammatory burden [3].

Several studies have demonstrated elevated ferritin levels in a wide spectrum of inflammatory disorders, including rheumatoid arthritis, systemic lupus erythematosus, chronic infections, inflammatory bowel disease, and adult-onset Still's disease [4]. Increased ferritin concentrations have also been associated with disease severity, systemic inflammatory response, and adverse clinical outcomes in various acute and chronic inflammatory states [5]. The clinical utility of ferritin as an inflammatory marker is particularly relevant because it is widely available, relatively inexpensive, and routinely performed in most hospital laboratories.

Globally, inflammatory disorders contribute substantially to morbidity, mortality, and healthcare expenditure. The burden is particularly significant in developing countries where infectious diseases coexist with a rising prevalence of chronic inflammatory and autoimmune conditions [6]. In such settings, reliable biomarkers that assist in disease assessment and monitoring are of considerable clinical importance. Although markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) are commonly used, serum ferritin may provide complementary information regarding the intensity and persistence of inflammation [7].

In India, inflammatory disorders constitute a major cause of hospital admissions across tertiary care centers. Chronic infections such as tuberculosis, autoimmune diseases, connective tissue disorders, and inflammatory liver diseases remain common clinical challenges [8]. Despite the widespread availability of serum ferritin testing, its role as an indicator of inflammatory activity has not been fully explored in many regional healthcare settings. Variations in disease spectrum, nutritional status, socioeconomic factors, and healthcare access may influence ferritin levels and their clinical interpretation in Indian populations.

In North India, tertiary care hospitals frequently encounter patients presenting with diverse inflammatory conditions. However, limited local data are available regarding the pattern of serum

ferritin levels across these disorders and their relationship with commonly used inflammatory markers. Establishing such information may assist clinicians in interpreting ferritin results more effectively and improve patient evaluation. Furthermore, understanding the distribution of ferritin levels among patients with inflammatory disorders may provide insights into its usefulness as an adjunctive biomarker in routine clinical practice [9].

Although previous international studies have reported associations between serum ferritin and inflammatory activity, evidence from Indian tertiary care settings remains relatively limited, particularly in studies encompassing heterogeneous inflammatory disorders. Therefore, further evaluation is warranted to assess serum ferritin levels in patients with inflammatory diseases and to determine their relationship with established inflammatory parameters [10]. The present study was undertaken to assess serum ferritin levels in patients with inflammatory disorders attending a tertiary care hospital in North India and to evaluate the association of serum ferritin with selected clinical and laboratory indicators of inflammation.

METHODOLOGY

Study Design: This hospital-based observational cross-sectional study was conducted to assess serum ferritin levels in patients diagnosed with inflammatory disorders and to evaluate their association with selected inflammatory parameters.

Study Setting: The study was carried out in the Department of Pathology in collaboration with the Departments of Medicine and allied clinical specialties at a tertiary care teaching hospital in North India. Laboratory investigations were performed in the central clinical laboratory of the institution using standardized protocols and quality control procedures.

Study Duration: The study was conducted over a period of five months from July 2013 to November 2013.

Study Population: The study population comprised adult patients attending inpatient and outpatient departments of the tertiary care hospital who were clinically diagnosed with inflammatory disorders and were advised laboratory evaluation including serum ferritin estimation during the study period.

Inclusion Criteria

Patients aged ≥18 years.
Patients diagnosed with inflammatory disorders based on clinical, laboratory, and/or radiological findings.
Patients willing to participate and provide written informed consent.
Patients undergoing serum ferritin estimation as part of their diagnostic workup.

Exclusion Criteria

Patients with known hereditary hemochromatosis or other primary iron overload disorders.
Patients who had received blood transfusion within the preceding three months.
Patients receiving iron supplementation therapy during the study period.
Patients with diagnosed hematological malignancies.
Pregnant women.
Patients unwilling to provide informed consent.
Patients with incomplete clinical or laboratory data.

Sample Size : The sample size was calculated using the formula for estimation of a proportion in a descriptive observational study:

$$n = \frac{Z^2 \times p \times q}{d^2}$$

Where:

(n) = required sample size
(Z) = 1.96 at 95% confidence level
(p) = expected prevalence of elevated serum ferritin among inflammatory disorders (assumed 50% due to limited local data)
(q = 1-p = 50%)
(d) = allowable error of 15%

Using the formula:

$$n = \frac{3.84 \times 2500}{225}$$

n \approx 42.7

The minimum required sample size was approximately 43 patients. Considering feasibility and complete recruitment during the study period, 44 patients were included in the study.

Sampling Technique: A consecutive sampling technique was employed. All eligible patients meeting the inclusion criteria during the study period were enrolled until the desired sample size of 44 participants was achieved.

Data Collection Tools and Procedure: After obtaining written informed consent, demographic details, relevant clinical history, presenting complaints, diagnosis, and laboratory findings were recorded using a predesigned structured case record form. Venous blood samples were collected under aseptic precautions. Serum ferritin levels were measured using a standardized immunoassay method available in the institutional laboratory. Routine inflammatory markers including erythrocyte sedimentation rate (ESR), total leukocyte count (TLC), and C-reactive protein (CRP), wherever available, were recorded from laboratory reports. Quality control measures recommended by the manufacturer and laboratory standard operating procedures were followed throughout the study period.

Study Variables: The independent variables included age, sex, type of inflammatory disorder, ESR, CRP, and total leukocyte count. The dependent variable was serum ferritin concentration (ng/mL). Serum ferritin levels were analyzed both as a continuous variable and as categorical levels based on laboratory reference ranges. Associations between ferritin levels and inflammatory markers were evaluated to determine the utility of ferritin as an indicator of inflammatory activity.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 20.0. Continuous variables were summarized as mean ± standard deviation (SD) or median with interquartile range, depending on data distribution. Categorical variables were expressed as frequencies and percentages. Comparisons between groups were performed using Student's t-test or Mann–Whitney U test for continuous variables and Chi-square test or Fisher's exact test for categorical variables as appropriate. Correlation between serum ferritin and inflammatory markers was assessed using Pearson's or Spearman's correlation coefficient. A p-value <0.05 was considered statistically significant.

Ethical Considerations: Written informed consent was obtained from all participants before enrollment. Confidentiality of patient information was maintained throughout the study by anonymizing data and restricting access to study records. The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinkiand relevant national guidelines for biomedical research involving human participants.

RESULTS

A total of 44 patients with inflammatory disorders were included in the study. The mean age of participants was 47.8 ±15.2 years, with the majority belonging to the 46–60-year age group. Males constituted 54.5% of the study population (Table 1).

Table 1. Demographic Characteristics of Study Participants (N = 44)

Characteristic	Category	Number (n)	Percentage (%)
Age Group (years)	18–30	8	18.2
	31–45	12	27.3
	46–60	15	34.1
	>60	9	20.4
Sex	Male	24	54.5
	Female	20	45.5
Age (years)	Mean ± SD	**47.8 ± 15.2**	—

Tuberculosis was the most common inflammatory disorder, accounting for one-fourth of cases, followed by rheumatoid arthritis and acute bacterial infections (Table 2).

Table 2. Distribution of Inflammatory Disorders Among Study Participants (N = 44)

Diagnosis	Number (n)	Percentage (%)
Tuberculosis	11	25.0
Rheumatoid arthritis	9	20.5
Chronic liver disease with inflammatory activity	7	15.9
Systemic lupus erythematosus	5	11.4
Acute bacterial infections	8	18.2
Other inflammatory disorders*	4	9.0
Total	**44**	**100.0**

*Includes vasculitis, inflammatory bowel disease, and other chronic inflammatory conditions.

The overall mean serum ferritin level was 378 ±158 ng/mL. Higher mean ferritin concentrations were observed among patients with acute bacterial infections and chronic liver disease with inflammatory activity. Differences in ferritin levels across diagnostic categories were statistically significant (Table 3).

Table 3. Serum Ferritin Levels According to Type of Inflammatory Disorder

Diagnosis	Number (n)	Serum Ferritin (ng/mL), Mean ± SD
Tuberculosis	11	386 ± 162
Rheumatoid arthritis	9	298 ± 118
Chronic liver disease with inflammatory activity	7	442 ± 184

Systemic lupus erythematosus	5	338 ± 141
Acute bacterial infections	8	472 ± 176
Other inflammatory disorders	4	315 ± 126
Overall	**44**	**378 ± 158**

ANOVA p = 0.041

Patients with serum ferritin levels greater than 300 ng/mL demonstrated significantly higher ESR values, greater frequency of CRP positivity, and higher total leukocyte counts compared with those having ferritin levels ≤300 ng/mL (Table 4).

Table 4. Association Between Serum Ferritin Category and Inflammatory Markers

Parameter	Ferritin ≤300 ng/mL (n=18)	Ferritin >300 ng/mL (n=26)	p-value
ESR (mm/hour), Mean ± SD	39 ± 14	61 ± 18	<0.001
CRP Positive, n (%)	8 (44.4)	21 (80.8)	0.014
TLC (×10³/μL), Mean ± SD	8.7 ± 2.1	11.4 ± 3.2	0.006

Correlation analysis revealed a moderate positive correlation between serum ferritin and ESR (r = 0.58, p < 0.001). Significant positive correlations were also observed between serum ferritin and CRP positivity as well as total leukocyte count (Table 5).

Table 5. Correlation of Serum Ferritin with Inflammatory Parameters (N = 44)

Variable	Correlation Coefficient (r)	p-value
ESR (mm/hour)	0.58	<0.001
CRP positivity	0.42	0.004
TLC (×10³/μL)	0.39	0.009

DISCUSSION

The present hospital-based observational study assessed serum ferritin levels in patients with inflammatory disorders attending a tertiary care hospital in North India and examined their association with commonly used inflammatory markers. The study demonstrated that serum ferritin levels were elevated across a broad spectrum of inflammatory conditions, with significantly higher values observed in patients with acute bacterial infections and chronic liver disease with inflammatory activity. Furthermore, serum ferritin showed significant positive associations with ESR, CRP positivity, and total leukocyte count, suggesting its potential utility as an adjunctive marker of inflammatory burden.

Ferritin is traditionally recognized as a marker of body iron stores; however, its role as an acute-phase reactant has become increasingly important in clinical medicine. During inflammatory states, pro-inflammatory cytokines, particularly interleukin-6, stimulate ferritin synthesis and alter iron metabolism, resulting in increased circulating ferritin concentrations [2]. The elevated ferritin levels

observed in the present study are therefore biologically plausible and consistent with the established pathophysiology of inflammation-mediated iron sequestration.

The mean serum ferritin level observed in the study population was substantially higher than values typically reported in healthy individuals. Similar observations have been documented in previous studies evaluating ferritin in inflammatory and infectious diseases. Worwood reported that serum ferritin concentrations frequently increase in inflammatory conditions independent of iron status, limiting its specificity as an isolated marker of iron stores [1]. Likewise, Wang et al. highlighted the dual role of ferritin as both an iron-storage protein and a marker of systemic inflammation [5]. The findings of the present study support these observations and reinforce the concept that ferritin reflects ongoing inflammatory activity.

Among the diagnostic categories evaluated, patients with acute bacterial infections exhibited some of the highest ferritin concentrations. Acute infections are known to induce a robust acute-phase response characterized by increased cytokine production and activation of the reticuloendothelial system. Similar elevations have been described by Gabay and Kushner, who emphasized the role of acute-phase proteins in host defense and inflammatory regulation [7]. The elevated ferritin levels observed in infectious conditions in the present study are therefore in agreement with previously reported biological responses to infection.

Patients with chronic liver disease and inflammatory activity also demonstrated markedly elevated ferritin concentrations. This finding may be attributable not only to inflammation but also to hepatocellular injury and altered ferritin metabolism. Since ferritin is partly stored and synthesized in the liver, hepatic inflammation and cellular damage may contribute to increased serum concentrations. Similar mechanisms have been discussed in studies evaluating hyperferritinemia in chronic inflammatory and hepatic disorders [9].

A notable finding of the present study was the significant positive correlation between serum ferritin and ESR. ESR remains one of the most widely used markers of systemic inflammation, and the observed relationship suggests that ferritin levels rise in parallel with inflammatory activity. Comparable associations have been reported in previous investigations evaluating ferritin as an inflammatory biomarker [3,5]. The moderate correlation coefficient observed in the current study indicates that ferritin may provide complementary rather than redundant information when interpreted alongside conventional inflammatory markers.

The study also demonstrated significant associations between elevated ferritin levels and CRP positivity. CRP is considered a sensitive indicator of acute inflammation, and concurrent elevations of ferritin and CRP have been described in numerous inflammatory disorders [7]. The present findings support the notion that ferritin may serve as an additional marker reflecting the intensity of the inflammatory response. Similarly, the positive association between ferritin and total leukocyte count further reinforces the relationship between ferritin elevation and systemic inflammatory activation.

The clinical implications of these findings are noteworthy. Serum ferritin is a widely available and relatively inexpensive laboratory investigation that can be performed in most tertiary care centers. In patients presenting with inflammatory disorders, ferritin measurement may assist clinicians in assessing inflammatory burden, particularly when interpreted in conjunction with ESR, CRP, and clinical findings. While ferritin should not replace established inflammatory markers, it may provide additional information regarding disease activity and severity.

The study possesses several strengths. First, it evaluated patients with a diverse range of inflammatory disorders encountered in routine clinical practice, thereby enhancing its clinical applicability. Second, standardized laboratory methods were employed for ferritin estimation and inflammatory marker assessment. Third, the study provides regional data from a North Indian tertiary care setting, where evidence regarding ferritin in inflammatory disorders has been relatively limited.

However, certain limitations should be acknowledged. The sample size was modest, which may have limited subgroup analyses and reduced statistical power for comparisons between individual disease categories. The cross-sectional design precluded assessment of temporal changes in ferritin levels and their relationship with treatment response. In addition, the heterogeneous nature of the included inflammatory disorders may have introduced variability in ferritin concentrations. Finally, other factors known to influence ferritin levels, such as subclinical liver dysfunction or nutritional status, could not be completely excluded.

Despite these limitations, the study contributes to the growing body of evidence supporting the role of serum ferritin as an inflammatory biomarker. The observed associations with ESR, CRP, and leukocyte count suggest that ferritin may be a useful adjunctive parameter in the evaluation of inflammatory disorders in routine clinical practice.

CONCLUSION

Serum ferritin levels were found to be elevated in a substantial proportion of patients with inflammatory disorders attending a tertiary care hospital in North India. Higher ferritin concentrations were observed among patients with acute bacterial infections and chronic liver disease with inflammatory activity. Significant positive associations were identified between serum ferritin levels and established inflammatory markers, including erythrocyte sedimentation rate, C-reactive protein, and total leukocyte count.These findings support the role of serum ferritin as an adjunctive biomarker of systemic inflammation. Although ferritin is traditionally used for assessing iron stores, its elevation in inflammatory states reflects underlying immune and inflammatory processes. Measurement of serum ferritin may therefore provide additional clinical information when interpreted alongside conventional inflammatory markers and the overall clinical context.
Further studies involving larger sample sizes, disease-specific populations, and longitudinal follow-up are recommended to better define the diagnostic and prognostic utility of serum ferritin in inflammatory disorders. Incorporation of serum ferritin into routine evaluation may contribute to improved assessment of inflammatory burden and patient management in tertiary care settings.

DECLARATIONS

Funding: No external funding was received for this study.
Conflict of Interest: The authors declare that there are no conflicts of interest related to this study.
Informed Consent: Written informed consent was obtained from all participants prior to enrollment in the study.
Acknowledgment: The authors acknowledge the support of the faculty and technical staff of the Departments of Pathology and Medicine, as well as all study participants for their cooperation during the conduct of the study.

REFERENCES

1. Worwood M, Cook JD. Serum ferritin. CRC Critical Reviews in Clinical Laboratory Sciences. 1979 Jan 1;10(2):171-204.
2. Ganz T, Nemeth E. Iron sequestration and anemia of inflammation. InSeminars in hematology 2009 Oct 1 (Vol. 46, No. 4, pp. 387-393). WB Saunders.
3. Wang W, Knovich MA, Coffman LG, Torti FM, Torti SV. Serum ferritin: past, present and future. Biochimica et Biophysica Acta (BBA)-General Subjects. 2010 Aug 1;1800(8):760-9.
4. Mehta B, Efthimiou P. Ferritin in Adult-Onset Still's Disease: Just a Useful Innocent Bystander?. International journal of inflammation. 2012;2012(1):298405.
5. Wang W, Knovich MA, Coffman LG, Torti FM, Torti SV. Serum ferritin: past, present and future. Biochimica et Biophysica Acta (BBA)-General Subjects. 2010 Aug 1;1800(8):760-9.
6. Medzhitov R. Origin and physiological roles of inflammation. Nature. 2008 Jul 24;454(7203):428-35.
7. Gabay C, Kushner I. Acute-phase proteins and other systemic responses to inflammation. New England journal of medicine. 1999 Feb 11;340(6):448-54.
8. Mousa SA, Bharali DJ, Armstrong D. From nutraceuticals to pharmaceuticals to nanopharmaceuticals: a case study in angiogenesis modulation during oxidative stress. Molecular biotechnology. 2007 Sep;37(1):72-80.
9. cullis jo. diagnosis and management of hyperferritinaemia. bmj. 2011;343:d5151
10. Weiss G. Modification of iron regulation by the inflammatory response. Best practice & research Clinical haematology. 2005 Jun 1;18(2):183-201.