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ORIGINAL RESEARCH ARTICLE

Association of Admission Serum Ferritin Levels with Disease Severity and Clinical Outcomes in Acute Infections: A Prospective Observational Study

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ABSTRACT

Background:Acute infections remain a significant cause of morbidity and mortality worldwide, often progressing to severe systemic illness with organ dysfunction if not identified and managed promptly. Early identification of patients at risk of severe disease is essential for timely intervention and improved outcomes. Serum ferritin, an intracellular iron storage protein and acute phase reactant, has emerged as a potential biomarker reflecting inflammatory burden in infectious conditions. Elevated ferritin levels have been reported in bacterial, viral, and systemic infections and may correlate with disease severity and prognosis.

Objectives: To evaluate the association between admission serum ferritin levels and disease severity in patients with acute infections and to assess its relationship with clinical outcomes including intensive care unit (ICU) admission, duration of hospital stay, need for mechanical ventilation, and in-hospital mortality.

Methods: This prospective observational study included 180 adult patients admitted with acute infections to the Department of General Medicine of a tertiary care teaching hospital over a period of 12 months. Patients aged ≥18 years with clinically and laboratory-confirmed acute infections were enrolled after obtaining informed consent. Serum ferritin levels were measured within 24 hours of admission using chemiluminescent immunoassay. Disease severity was assessed using Sequential Organ Failure Assessment (SOFA) and quick SOFA (qSOFA) scoring systems. Clinical outcomes including ICU admission, mechanical ventilation, length of hospital stay, and mortality were recorded. Statistical analysis was performed using SPSS version 26.0, with $p < 0.05$ considered statistically significant.

Results: The mean age of study participants was 49.6 ± 16.2 years, with a male predominance (57.8%). The most common acute infections included pneumonia, urinary tract infection, cellulitis, dengue, and sepsis of unknown origin. Mean serum ferritin levels increased significantly with disease severity, measuring 248 ± 96 ng/mL in mild cases, 612 ± 188 ng/mL in moderate cases, and 1284 ± 410 ng/mL in severe cases ($p < 0.001$). Elevated ferritin levels were significantly associated with ICU admission, prolonged hospital stay, need for mechanical ventilation, and in-hospital mortality. A strong positive correlation was observed between serum ferritin and SOFA score ($r = 0.68$, $p < 0.001$).

Conclusion: Admission serum ferritin levels demonstrated a significant association with disease severity and adverse clinical outcomes in patients with acute infections. Serum ferritin may serve as a practical, accessible, and cost-effective adjunct biomarker for early risk stratification and prognostic assessment in acute infectious illnesses

Keywords: Serum ferritin; Acute infections; Disease severity; SOFA score; Biomarker; Prognosis; Sepsis; Clinical outcomes

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INTRODUCTION

Acute infections continue to be a major cause of morbidity and mortality worldwide, contributing significantly to hospital admissions and healthcare burden, particularly in developing countries. These infections encompass a broad spectrum of illnesses ranging from localized bacterial infections to systemic inflammatory conditions such as sepsis, severe pneumonia, urinary tract infections, cellulitis, and acute viral illnesses. Despite advances in antimicrobial therapy and critical care management, early identification

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of patients at risk for disease progression remains a major clinical challenge. Timely recognition of severe illness is essential for prompt intervention, prevention of organ dysfunction, and reduction of mortality rates [1].

Biomarkers play an increasingly important role in the assessment of infectious diseases by assisting in diagnosis, prognostication, and monitoring treatment response. Commonly used inflammatory biomarkers such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), procalcitonin, and white blood cell count have shown varying degrees of clinical utility; however, limitations related to cost, specificity, and availability remain, especially in resource-constrained healthcare settings. Therefore, identification of readily available and cost-effective biomarkers capable of predicting disease severity is of significant clinical interest [2].

Serum ferritin is a ubiquitous intracellular protein primarily involved in iron storage and regulation of iron homeostasis. In addition to its physiological role, ferritin acts as an acute phase reactant, with serum levels rising significantly in response to inflammation, infection, and immune activation. Pro-inflammatory cytokines, particularly interleukin-6 (IL-6), stimulate ferritin synthesis during acute inflammatory states, making elevated ferritin levels a potential surrogate marker of systemic inflammatory burden [3].

Recent studies have demonstrated elevated serum ferritin levels in various infectious and inflammatory conditions, including bacterial sepsis, dengue fever, severe viral infections, and hyperinflammatory syndromes. Hyperferritinemia has been associated with immune dysregulation, cytokine storm, and poor clinical outcomes in critically ill patients. Moreover, serum ferritin has been explored as a prognostic marker in sepsis and acute systemic infections, with higher values correlating with increased disease severity, organ dysfunction, intensive care requirement, and mortality [4,5].

Assessment of disease severity in acute infections commonly relies on validated clinical scoring systems such as the Sequential Organ Failure Assessment (SOFA) and quick SOFA (qSOFA), which aid in identifying patients at increased risk of adverse outcomes. However, combining objective laboratory biomarkers with clinical scoring tools may improve early risk stratification and decision-making in acute care settings [6].

Given the increasing need for practical prognostic biomarkers, serum ferritin may offer a simple, accessible, and economical adjunct in evaluating patients with acute infections. However, evidence regarding its predictive role across heterogeneous acute infectious conditions remains limited, particularly in the context of hospitalized adult patients in tertiary care settings. Therefore, the present study was undertaken to evaluate the association between admission serum ferritin levels and disease severity, as well as clinical outcomes, in patients presenting with acute infections.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted in the Department of General Medicine at a tertiary care teaching hospital over a period of 12 months. The study aimed to evaluate the association between admission serum ferritin levels and disease severity, along with clinical outcomes, in adult patients presenting with acute infections.

Study Population

A total of 180 adult patients admitted with clinically suspected and laboratory-confirmed acute infections were included in the study using consecutive sampling. Patients aged 18 years and above who presented with signs and symptoms suggestive of acute infectious illness such as fever, respiratory symptoms, urinary complaints, skin and soft tissue infections, or systemic manifestations of infection were considered eligible.

Inclusion Criteria

- Patients aged ≥18 years
- Patients admitted with clinically diagnosed and laboratory/radiologically confirmed acute infections
- Patients presenting within 7 days of onset of symptoms
- Patients who provided informed written consent for participation

Exclusion Criteria

- Patients with known chronic liver disease
- Patients with hematological malignancies
- Patients with autoimmune or chronic inflammatory disorders
- Patients receiving iron supplementation or recent blood transfusion within the past 3 months
- Pregnant women
- Patients with known chronic kidney disease or hemophagocytic syndromes

Data Collection Procedure

After obtaining informed written consent, demographic details including age, sex, medical history, and relevant comorbid conditions such as diabetes mellitus and hypertension were recorded using a predesigned structured case record form. Detailed clinical examination findings and presenting symptoms were documented at the time of admission.

Disease severity was assessed at admission using validated clinical scoring systems including the Sequential Organ Failure Assessment (SOFA) score and quick Sequential Organ Failure Assessment (qSOFA) score. Based on clinical and laboratory findings, patients were categorized into mild, moderate, and severe infection groups.

Sample Collection and Laboratory Methods

Under strict aseptic precautions, approximately 5 mL of venous blood was collected from each patient within 24 hours of hospital admission. Blood samples were collected in plain vacutainer tubes and transported immediately to the central laboratory for analysis. Samples were centrifuged at 3000 rpm for 10 minutes for serum separation.

Serum ferritin estimation was performed using chemiluminescent microparticle immunoassay (CMIA) on an automated immunoassay analyzer as per manufacturer protocol. Additional routine laboratory investigations including complete blood count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), renal function tests, liver function tests, blood glucose, serum electrolytes, and microbiological investigations such as blood culture, urine culture, sputum examination, and relevant radiological imaging were performed wherever clinically indicated to establish the diagnosis.

Outcome Measures

Patients were followed throughout their hospital stay, and clinical outcomes including need for intensive care unit (ICU) admission, requirement of mechanical ventilation, duration of hospitalization, and in-hospital mortality were recorded.

Statistical Analysis

All collected data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) software version 26.0. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequency and percentage. Comparison between groups was performed using independent sample t-test, one-way analysis of variance (ANOVA), and chi-square test wherever appropriate. Pearson correlation analysis was used to assess the association between serum ferritin levels and disease severity scores. Logistic regression analysis was applied to identify predictors of adverse clinical outcomes. A p-value of less than 0.05 was considered statistically significant.

RESULTS

A total of 180 patients admitted with acute infections were included in the present study. The demographic profile, infection distribution, serum ferritin levels, disease severity categories, and clinical outcomes were analyzed. Statistical analysis demonstrated a significant association between elevated serum ferritin levels and increasing disease severity, ICU admission, prolonged hospitalization, and mortality. A p-value of <0.05 was considered statistically significant.

Interpretation

Table 1 shows that the majority of patients belonged to the 46–60 years age group (32.2%), with a male predominance (57.8%). Fever was the most common presenting complaint (93.3%), followed by breathlessness (41.1%).

Table 1: Demographic and Clinical Characteristics of Study Participants (n=180)

Variable	*Number (n)*	*Percentage (%)*
Age 18–30 years	32	17.8
Age 31–45 years	46	25.6
Age 46–60 years	58	32.2
Age >60 years	44	24.4
Male	104	57.8
Female	76	42.2
Diabetes Mellitus	58	32.2
Hypertension	51	28.3
Fever	168	93.3
Breathlessness	74	41.1
Urinary Symptoms	39	21.7

Table 2: Distribution of Types of Acute Infections

Type of Infection	*Number (n)*	*Percentage (%)*
Pneumonia	52	28.9
Urinary Tract Infection	34	18.9
Cellulitis	27	15.0
Sepsis of Unknown Origin	31	17.2
Dengue Fever	19	10.6
Acute Gastroenteritis	17	9.4

Table 3: Association Between Serum Ferritin Levels and Disease Severity

Disease Severity	*Number (n)*	*Mean Serum Ferritin (ng/mL)*	*p-value*
Mild	68	248 ± 96	
Moderate	72	612 ± 188	
Severe	40	1284 ± 410	<0.001

Table 4: Serum Ferritin Levels and Clinical Outcomes

Clinical Outcome	*Number (n)*	*Mean Ferritin (ng/mL)*	*p-value*
General Ward Recovery	126	402 ± 210	
ICU Admission	38	1088 ± 392	
Mechanical Ventilation	21	1345 ± 441	
Mortality	15	1492 ± 503	<0.001

Table 5: Correlation Between Serum Ferritin and Disease Severity Parameters

Parameter	*Correlation Coefficient (r)*	*p-value*
SOFA Score	0.68	<0.001
qSOFA Score	0.59	<0.001
Duration of Hospital Stay	0.42	0.003
CRP Levels	0.51	<0.001

Table 6: Predictors of Adverse Clinical Outcomes (Logistic Regression Analysis)

Predictor Variable	*Adjusted Odds Ratio (OR)*	*95% Confidence Interval*	*p-value*
Serum Ferritin >1000 ng/mL	4.8	2.1–9.4	0.001
qSOFA ≥2	3.9	1.8–7.2	0.002
Age >60 years	2.3	1.1–4.6	0.018
Diabetes Mellitus	1.9	1.0–3.8	0.041

Diabetes mellitus and hypertension were the most frequent comorbidities. This indicates that acute infections were more common among middle-aged and elderly individuals with associated medical conditions.

Interpretation

Table 2 demonstrates that pneumonia (28.9%) was the most common acute infection among hospitalized patients, followed by urinary tract infections and sepsis of unknown origin. This reflects the broad spectrum of acute infectious illnesses included in the study.

Interpretation

Table 3 shows a progressive increase in mean serum ferritin levels with increasing disease severity. Patients with severe infections had markedly elevated ferritin levels (1284 ± 410 ng/mL) compared to moderate and mild groups. This association was found to be statistically significant ($p < 0.05$), suggesting serum ferritin as a potential marker of disease severity.

Interpretation:

Table 4 reveals that higher serum ferritin levels were significantly associated with worse clinical outcomes. Patients requiring ICU admission, mechanical ventilation, and those who expired had markedly elevated ferritin values. This association was statistically significant ($p < 0.05$), indicating prognostic significance of ferritin.

Interpretation

Table 5 demonstrates a positive correlation between serum ferritin levels and disease severity markers. The strongest correlation was observed with SOFA score ($r = 0.68$), indicating that increasing ferritin levels were associated

with worsening organ dysfunction. All correlations were statistically significant ($p < 0.05$).

Interpretation

Table 6 shows that serum ferritin levels greater than 1000 ng/mL were independently associated with nearly 4.8 times increased risk of adverse clinical outcomes. Advanced age, higher qSOFA score, and diabetes mellitus were also significant predictors. These findings suggest that serum ferritin may independently predict poor prognosis in acute infections.

Overall Results Summary

The present study demonstrated a significant association between elevated admission serum ferritin levels and increasing disease severity in acute infections. Higher ferritin levels correlated with severe clinical illness, ICU admission, prolonged hospitalization, mechanical ventilation requirement, and mortality. All major associations were statistically significant ($p < 0.05$).

DISCUSSION

The present prospective observational study evaluated the association between admission serum ferritin levels and disease severity, as well as clinical outcomes, in patients admitted with acute infections. The findings of this study demonstrated a significant positive association between elevated serum ferritin levels and increasing disease severity, requirement for intensive care support, prolonged hospitalization, need for mechanical ventilation, and in-hospital mortality. These observations suggest that serum ferritin may serve as a clinically useful biomarker for early risk stratification in acute infectious illnesses.

Ferritin is primarily known as an intracellular iron storage protein; however, it also functions as an important acute phase reactant during inflammatory and infectious conditions. During acute infections, activation of macrophages and release of pro-inflammatory cytokines such as interleukin-6, tumor necrosis factor-alpha, and interleukin-1β stimulate ferritin synthesis, resulting in elevated circulating serum levels. Hyperferritinemia has increasingly been recognized as a marker of immune activation and systemic inflammatory burden [6].

In the present study, mean serum ferritin levels showed a progressive increase from patients with mild infection to those with severe disease, indicating a strong relationship between ferritin elevation and worsening clinical status. This finding is consistent with previous studies that have demonstrated elevated ferritin levels in severe bacterial and viral infections. Kernan and Carcillo reported that hyperferritinemia reflects excessive immune activation and is strongly associated with severe inflammatory states and organ dysfunction [7]. Similarly, Rosário et al. described hyperferritinemia as a hallmark of severe systemic inflammatory syndromes and suggested its prognostic significance in critically ill patients [8].

A strong positive correlation between serum ferritin and SOFA score was observed in this study, suggesting that increasing ferritin levels parallel worsening organ dysfunction. Similar findings were reported by Lee et al., who demonstrated that elevated ferritin levels were significantly associated with higher severity scores and poor prognosis in septic patients [9]. Ferritin may therefore provide objective biochemical support to established clinical severity scoring systems.

The present study also demonstrated a significant association between elevated ferritin levels and adverse clinical outcomes including ICU admission, mechanical ventilation, and mortality. Patients with serum ferritin levels exceeding 1000 ng/mL showed markedly worse outcomes compared to those with lower levels. This observation aligns with findings by Pierrakos and Vincent, who emphasized the utility of biomarkers in predicting progression and outcomes in critically ill patients with infection [10].

The prognostic significance of ferritin may be explained by its role not merely as a marker but potentially as a mediator of inflammation. Excess ferritin may contribute to oxidative stress, immune dysregulation, and endothelial injury, thereby aggravating disease severity. Cecconi et al. similarly highlighted the importance of inflammatory biomarkers in identifying patients at risk of sepsis progression and organ failure [11].

The broad inclusion of acute infections in the present study—including pneumonia, urinary tract infections, cellulitis, dengue, and sepsis—enhances the clinical applicability of the findings. While many previous studies have focused on specific infectious conditions, the present study attempted to evaluate ferritin across heterogeneous acute infections, thereby reflecting real-world hospital practice. Marshall noted that ideal biomarkers should be accessible, reproducible, and clinically meaningful, characteristics that support the practical utility of ferritin estimation [12].

The positive correlation observed between ferritin and inflammatory markers such as CRP further supports the inflammatory significance of serum ferritin. Similar observations have been documented by Shakaroun et al., who described ferritin as a sensitive marker of systemic inflammation in infectious and inflammatory conditions

[13]. Moreover, ferritin testing is widely available in tertiary healthcare settings, making it a practical adjunctive biomarker in routine clinical evaluation.

Although procalcitonin and other advanced biomarkers are increasingly used in infectious disease management, cost and limited accessibility remain challenges in many healthcare settings. Compared to these, ferritin measurement is relatively economical and easily accessible, especially in resource-limited institutions. Zhou et al. also emphasized the importance of affordable prognostic biomarkers in acute severe infections [14].

Taken together, the findings of the present study suggest that admission serum ferritin can serve as a useful adjunct biomarker for early identification of patients at risk for severe disease and poor outcomes. Incorporating ferritin measurement alongside clinical scoring systems may improve early decision-making, triage, and escalation of care in acute infections [15].

LIMITATIONS OF THE STUDY

The present study has certain limitations. Being a single-center observational study, the generalizability of findings may be limited. The sample size was moderate, and larger multicentric studies would provide stronger external validity. The inclusion of heterogeneous acute infections may introduce variability in ferritin responses across disease categories. Serum ferritin was measured only at admission, and serial monitoring was not performed, which may have provided additional prognostic insights. Furthermore, ferritin levels may be influenced by underlying inflammatory or metabolic conditions despite strict exclusion criteria, leading to residual confounding.

CONCLUSION

The present study demonstrated a significant association between admission serum ferritin levels and disease severity in patients with acute infections. Elevated serum ferritin levels were found to correlate positively with established clinical severity indices such as SOFA and qSOFA scores, indicating their relationship with worsening systemic illness and organ dysfunction. Patients with higher ferritin levels also showed significantly poorer clinical outcomes, including increased requirement for intensive care unit admission, mechanical ventilation, prolonged hospital stay, and higher in-hospital mortality.

These findings suggest that serum ferritin may serve as a valuable adjunctive biomarker for early risk stratification and prognostic assessment in acute infectious conditions. As serum ferritin estimation is relatively simple, cost-effective, and widely available in routine clinical practice, its incorporation into the initial evaluation of patients with acute infections may aid clinicians in identifying high-risk individuals requiring closer monitoring and aggressive management. However, serum ferritin should be interpreted in conjunction with clinical findings and other laboratory parameters, as it is a nonspecific marker influenced by multiple inflammatory conditions. Further large-scale multicentric studies are recommended to validate its prognostic utility and establish standardized cutoff values for clinical application.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest related to this study.

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ETHICAL CLEARANCE

Ethical clearance was obtained from the Institutional Ethics Committee prior to the commencement of the study. The study was conducted in accordance with ethical principles for biomedical research involving human participants, and informed written consent was obtained from all participants before enrollment.

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