



Journal of Acute Disease

Original Article



jadweb.org

doi: 10.4103/jad.jad_114_25

Association of serum iron profile with in-hospital mortality in adult patients with sepsis: A prospective observational study

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ABSTRACT

Objective: To investigate the association between derangement of the serum iron profile and in-hospital mortality of adult patients diagnosed with sepsis using Sepsis-3 criteria, and to assess its potential role in improving diagnostic and prognostic accuracy.

Methods: This prospective observational study (May 2023–October 2024) was conducted in the emergency and medical ward. Serum iron profile and Sequential Organ Failure Assessment (SOFA) scores were assessed on admission. Clinical outcomes were tracked; associations with serum iron profile were determined using Student's t-test and chi-square test.

Results: One hundred fifty adult Sepsis-3 patients were recruited. 58 Patients (38.7%) died during hospitalization. Mean ferritin for deceased patients was $929.0 \pm 310.0 \mu\text{g/L}$, and was significantly higher than $417.0 \pm 311.0 \mu\text{g/L}$ for survivors ($P < .001$). A serum ferritin value of $700 \mu\text{g/L}$ strongly predicted in-hospital mortality (69.9% mortality above this threshold). The odds ratio was 23.2 (95% CI: 9.2–58.3) for ferritin above $700 \mu\text{g/L}$, indicating likelihood of death 23.2 times higher in patients with serum ferritin above $700 \mu\text{g/L}$. With SOFA, the odds ratio was 3.7, highlighting ferritin as a stronger individual predictor.

Conclusions: Serum ferritin level is an independent predictor of in-hospital mortality in sepsis. Monitoring ferritin levels can enhance early risk stratification, facilitate timely intervention, and improve outcomes.

KEYWORDS: Sepsis; Serum iron; Ferritin; SOFA; Total iron binding capacity; Transferrin saturation

Summary

Question: What is the association between serum iron profile, particularly serum ferritin and in-hospital mortality among adult patients with sepsis?

Findings: Non-survivors had significantly higher mean serum ferritin levels compared with survivors. When compared with SOFA score, serum ferritin demonstrated a higher independent predictive strength (odds ratio 3.7).

Meaning: Serum ferritin serves as an independent predictor of in-hospital mortality in sepsis. Incorporating ferritin assessment into early evaluation may improve risk stratification and support timely clinical decision-making.

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How to cite this article: Naik B, Nath S, Aggarwal A, Sharma R, Kotru M. Association of serum iron profile with in-hospital mortality in adult patients with sepsis: A prospective observational study. J Acute Dis 2026; 15: 9.

Article history: Received 1 August 2025; Revision 12 September 2025; Accepted 29 May 2026; Available online 31 May 2026

1. Introduction

Sepsis remains a major challenge for the medical community due to its complex pathophysiology, high incidence, broad spectrum of aetiology and clinical presentation which results in significant morbidity and mortality. Despite advancements in critical care, early diagnosis and effective treatment remain challenging, contributing to poor patient outcomes and rising healthcare costs worldwide[1]. It can affect people of all ages and occurs across various settings—within the community, in long-term care facilities, and hospitals, regardless of the medical specialty treating the patient[2].

Each year, 19 million individuals are diagnosed with sepsis and one in three patients eventually succumb to it[3]. In 2017, there were an estimated 11.3 million sepsis cases in India, with 2.9 million deaths. These statistics underscore the significance of research in low- and middle-income countries like India to prevent, diagnose, and treat sepsis[4].

Sepsis pathophysiology is multifactorial, and it is characterised by a complex interplay of the immune system, infection, and host response[5]. In sepsis, elevations of many of the common inflammatory markers, including C-reactive protein, procalcitonin, and interleukin-6. Products of iron metabolism have emerged as important marker of inflammation and are being increasingly used to diagnose sepsis as well as monitor the response of the patient to therapy[6]. Iron metabolism is changed during sepsis, with increased iron transport and uptake into cells and decreased iron export. Intracellular iron sequestration restricts the availability of iron to circulating infections, acting as a defense mechanism against the pathogens. Although iron retention has been shown to have beneficial effects, a rise in labile iron may cause oxidative injury and cell death as the illness continues (*e.g.*, proptosis, ferroptosis). Moreover, iron problems are common and associated with the severity of sepsis[7].

The observation that higher levels of iron are linked to more severe outcomes in sepsis patients supports the idea that extra iron might help bacteria grow more effectively, thereby worsening infections. This connection is particularly strong among those already suffering from sepsis, reinforcing the notion that increased iron availability could contribute to more serious bacterial infections[8].

Elevated serum ferritin levels can signal both an increase in iron storage within tissues and inflammation. Ferritin, which is produced by all types of nucleated cells, helps to store iron safely and prevent it from causing damage through reactive oxygen species. It also restricts the availability of iron to bacteria. Macrophages, a type of immune cell, play a key role in this process by either storing iron in ferritin or releasing it through alternative pathways, making them the main contributors to serum

ferritin levels. Therefore, high serum ferritin levels in patients who don't survive might reflect heightened macrophage activity rather than just increased iron storage[9]. Research shows that iron could be used as a diagnostic marker to assess the severity of the disease and predict its prognosis[7].

Ferritin, an acute-phase reactant, reflects both iron metabolism and systemic inflammatory burden. Elevated ferritin levels have been associated with disease severity and adverse outcomes in sepsis, making it a potential prognostic biomarker for mortality prediction[10,11].

In an intensive care unit-based cohort by Lan *et al.*, a significant relationship was noted between elevated serum iron concentrations and increased fatality rates among individuals with sepsis. Stratifying patients by iron quartiles revealed a progressive increase in both 28-day and 90-day mortality ($P=.001$ and $P<.001$, respectively). Cox regression analysis revealed elevated iron as an independent predictor of 90-day mortality. On the other hand, increased transferrin [Hazard ratio (HR): 0.997, $P<.001$] and haemoglobin (HR: 0.936, $P=.001$) were linked to reduced risk, suggesting protective effects. Ferritin levels, however, did not influence outcomes significantly ($P=.39$). Among patients with septic shock, those in the highest iron quartile had a significantly greater risk of death (HR=1.524, $P=.02$). These observations suggest that disruption in iron regulation may negatively influence survival during septic state[12].

In an Indian study by Ghosh S *et al.*, 42 patients with septic shock were enrolled. The median plasma ferritin level at admission in septic shock patients was 581 ng/mL (IQR: 287-1 283 ng/mL). Serum ferritin levels among non-survivors ($n=16$) were 763 ng/mL (IQR, 480-1 820 ng/mL), whereas survivors ($n=26$) had 415 ng/mL (IQR, 262-852 ng/mL), indicating a statistically nonsignificant ($P=.11$) tendency towards higher ferritin levels in non-survivors. Patients with ferritin levels greater than 500 ng/mL (relative risk, 2.48; 95% CI, 0.95-6.43; $P=.06$) and greater than 1 000 ng/mL (relative risk, 1.94; 95% CI, 0.94-4.02; $P=.07$) had a nearly two-fold increase in mortality compared to those with lower levels, though the difference was statistically insignificant. Despite iron deficiency, ferritin rises dramatically in septic shock patients and appears to be correlated with the degree of organ failure and inflammation. Even a lower minimum threshold (500 or 1 000 ng/mL) can indicate a higher mortality rate[13]. Rusu *et al.* found no significant difference in serum ferritin levels between survivors and non-survivors; however, the increase in serum ferritin was larger in non-survivors than in survivors[14].

Brandtner *et al.* prospectively analysed data from sepsis patients admitted to the intensive care unit (ICU) in Austria and measured several markers of iron homeostasis, including serum iron, transferrin, ferritin and hepcidin. During the study period, 61 patients with sepsis were recruited, 47 (77.1%) of whom

had septic shock. They found that alterations in systemic iron homeostasis, specifically high levels of serum iron and low levels of hepcidin, are associated with poor clinical outcomes, including increased mortality and longer ICU stays. The study suggests that monitoring and targeting iron homeostasis may represent a potential therapeutic approach for improving outcomes in sepsis[9].

Despite the growing interest in the role of iron metabolism in sepsis, there are several lacunae in the current body of research. Addressing these gaps is crucial for better understanding and improving the management of sepsis. Therefore, there is a need to research in this path so that prognosis of the outcome can be known. While most studies show a link between elevated ferritin levels and adverse outcomes, clinical applications remain restricted and require more research, particularly to determine the best cut-off value.

2. Methods

2.1. Study design and setting

A prospective observational study was conducted in the emergency and medical ward of Department of Medicine, University College of Medical Sciences and Guru Tegh Bahadur Hospital. It was conducted between May 2023 and October 2024.

2.2. Participants

Patients aged ≥ 18 years who were diagnosed with sepsis according to the Sepsis 3.0 criteria were included in the study. They were chosen through simple random sampling. A total of 150 patients diagnosed using the Sepsis 3.0 criteria were included in the study.

2.3. Exclusion criteria

Patients who were on iron supplementation, immunosuppressive agents prior to the day of admission, who had received blood transfusion in the past four weeks were excluded.

2.4. Sample characteristics

Baseline sociodemographic and clinical data were recorded, including age, sex, and underlying comorbidities such as hypertension, type 2 diabetes mellitus, chronic obstructive pulmonary disease, old coronary artery disease, old cerebrovascular accident, old tuberculosis, chronic liver disease. Information regarding substance use or addiction, concomitant medications

(particularly iron supplements and immunosuppressive agents), and history of blood transfusion was also collected. Patients with chronic kidney disease and those meeting exclusion criteria related to prior iron therapy, immunosuppressant use, or recent transfusion were not enrolled.

2.5. Variables and measurements

A brief history was taken, and a clinical examination was conducted. Age, sex, known comorbidities and their treatment for the same were considered on the day of admission. All the laboratory investigation advised by the treating unit for the diagnosis and treatment of patients were conducted. The iron profile including serum iron, transferrin saturation, serum ferritin, TIBC was measured on the day of admission. The Sequential Organ Failure Assessment (SOFA) scores were assessed at predefined intervals: the baseline SOFA was recorded upon admission (prior to therapeutic interventions) and repeated every 48 hours thereafter until resolution of sepsis or in-hospital mortality. The clinical profile of the patient was monitored throughout the hospital stay and the outcome was recorded. The main outcome variable in our study was in-hospital mortality.

2.6. Laboratory assays

Serum ferritin concentration was determined using an enzyme-linked immunosorbent assay (ELISA) technique. After completion of the incubation and washing cycles, the resultant color intensity was measured at the appropriate wavelength using a micro-ELISA reader, and values were interpreted as per the manufacturer's standard calibration curve.

Serum iron and unsaturated iron-binding capacity (UIBC) were analyzed by the Colorimetric Spectrophotometric method. Total iron-binding capacity (TIBC) was calculated by the conventional formula:

$$\text{TIBC } (\mu\text{g/dL}) = \text{Serum iron } (\mu\text{g/dL}) + \text{UIBC } (\mu\text{g/dL})$$

Transferrin saturation was computed using the conventional formula:

$$\text{Transferrin saturation } (\%) = \frac{\text{Serum iron } (\mu\text{g/dL})}{\text{TIBC } (\mu\text{g/dL})} \times 100$$

All estimations were carried out in the institutional Pathology and Central Research Laboratory, adhering to standard operating procedures and routine internal quality control measures to ensure analytical reliability.

2.7. Ferritin cut-off determination

The optimal threshold of serum ferritin for predicting in-hospital

mortality was derived using a Receiver Operating Characteristic (ROC) curve analysis. The cut-off value was selected at the point on the curve that provided the best balance between sensitivity and specificity, as identified by the maximum Youden Index ($J = \text{sensitivity} + \text{specificity} - 1$).

2.8. Outcome measures

Patients were followed prospectively from the time of hospital admission until discharge or death. The primary outcome variable of the study was in-hospital mortality, defined as any death occurring during the same hospitalization period, irrespective of duration of stay. Patients who were discharged alive were classified as survivors. No post-discharge follow-up was included in the outcome assessment. All clinical parameters and laboratory variables were recorded and monitored throughout the hospital stay until the final outcome was determined.

2.9. Statistical analysis

The data were compiled in a computer-based spreadsheet and analysed using IBM SPSS Statistics for Windows, Version 20.0 (<https://ibm-spss-statistics.software.informer.com/20.0>). Numerical data were shown as mean $\pm$ SD or median with inter-quartile range (IQR) taking in to account the distribution of data, whether the data was normally distributed or not. They are assessed by student t - test

or the Mann-Whitney *U* test. Chi-square test (Fischer's exact test) was used to test the difference in proportions of mortality between the two subgroups.

The ROC curve was applied to determine the prognostic performance of serum ferritin in predicting in-hospital mortality, with the area under the curve (AUC) used as the summary measure. The optimal ferritin cut-off value was derived from the ROC curve parameters. Associations between ferritin levels and mortality were expressed as odds ratios (OR) with corresponding 95% confidence intervals (CI). Univariate analysis was performed to assess the association between clinical and laboratory variables and in-hospital mortality. Multivariate binary logistic regression analysis was performed with in-hospital mortality as the outcome variable. The factors which had a *P* value of 0.20 or less on univariate analysis were selected for entry into the model. Forward likelihood ratio (LR) method for factor entry was used with the probability for stepwise entry into the model set as 0.05. A *P* value < 0.05 was considered statistically significant.

3. Results

A total of 150 patients were initially screened for eligibility. None were excluded during screening, as no patient had received prior iron supplementation, immunosuppressive agents before the day of admission, or blood transfusion in the preceding four weeks.

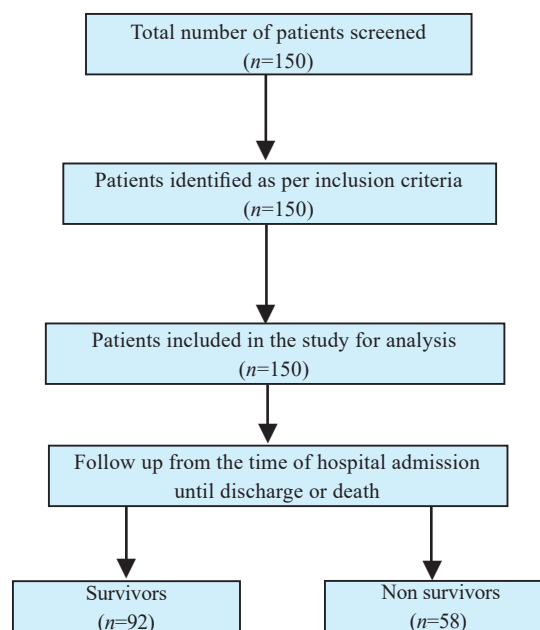


Figure 1. Flowchart of the study.

All 150 patients met the predefined inclusion criteria. There were no refusals to participate and no cases with incomplete data. Consequently, all screened patients were included in the final analysis ($n=150$) and were followed prospectively from the time of hospital admission until discharge or death. The flowchart of the study is shown in Figure 1.

The baseline characteristics including demographic, clinical and laboratory parameters are provided (Table 1).

3.1. Baseline demographic, clinical and laboratory parameters of the study population

The mean age of our study population was 51.7 ± 17.7 years. The minimum age of participants was 18 years and the maximum age was 94 years. The age distribution of our study population. 31.3% ($n=47$) patients were between age of 18-40 years. The largest group of patients in our study fell between age group of 41-60 years. Age group between 41-60 years constituted 36.7% ($n=55$). Patients above age of 60 years constituted 32% ($n=48$). In our study males constituted 59% ($n=88$) of the study population and females constituted 41% ($n=62$) of study population. Hypertension was the most common known comorbidity in our study participants at 60.7% ($n=91$) followed by Type 2 diabetes mellitus at 58% ($n=87$). The mean SOFA score of our study population at the time of admission (day 0) was 6.9 ± 3.3 and at the time of outcome discharge/death was 5.8 ± 5.1 . In our study the mean serum iron was $70.1 \pm 48.2 \mu\text{g/dL}$. The mean total iron binding capacity was $214.9 \pm 101.8 \mu\text{g/dL}$. The mean of transferrin saturation was $35.5 \pm 22.3\%$. The mean of serum ferritin was $615.2 \pm 398.1 \mu\text{g/L}$.

3.2. Baseline comparison between survivors and non-survivors

In our study death occurred in 38.7% ($n=58$) of the study population and discharged constituted 61.3% ($n=92$) of study population. Table 2 presents the baseline demographic, clinical, and laboratory characteristics of survivors and non-survivors. Both groups were comparable with respect to age, gender distribution, mean SOFA scores with no statistically significant differences observed. Among the clinical variables, urine output was significantly lower in non-survivors ($P=.01$), whereas parameters such as GCS, temperature, blood pressure, pulse rate, and oxygen saturation did not differ significantly ($P>.05$).

The comorbidity profile was also similar between groups. Regarding laboratory indices, a significant reduction in platelet count was noted among non-survivors ($P=.008$), while other parameters including hemoglobin, total leukocyte count, bilirubin, creatinine, blood urea, serum glutamic-oxaloacetic transaminase

Table 1. Baseline demographic, clinical, and laboratory characteristics of patients with sepsis.

Characteristics	$n=150$
Age, years, Median (range)	
18-40	47 (31.3)
41-60	55 (36.7)
>60	48 (32.0)
Sex	
Male	88 (59.0)
Female	62 (41.0)
Temperature, °C	37.2 ± 0.8
Systolic BP, mmHg	108.0 ± 26.6
Diastolic BP, mmHg	63.0 ± 15.7
MAP, mmHg	77.0 ± 18.8
Pulse rate, /minutes	94.0 ± 23.0
SpO ₂ , % room air	83.0 ± 11.4
Urine output, mL/day	842.0 ± 569.7
Hemoglobin, g/dL	10.0 ± 1.5
TLC, cells/mm ³	$14\ 045.0 \pm 4\ 110.0$
Platelet count, $\times 10^3/\text{mm}^3$	183.0 ± 85.9
Total bilirubin, mg/dL	1.8 ± 2.5
SGOT, IU/L	129.0 ± 107.8
SGPT, IU/L	89.0 ± 75.0
Blood urea, mg/dL	60.0 ± 27.1
Serum creatinine, mg/dL	1.9 ± 1.0
Serum iron, $\mu\text{g/dL}$	70.1 ± 48.2
Total iron binding capacity, $\mu\text{g/dL}$	214.9 ± 101.8
Transferrin saturation, %	35.5 ± 22.3
Serum ferritin, $\mu\text{g/L}$	615.2 ± 398.1

Numbers are expressed as n (%), and mean $\pm$ SD. Parameters were recorded at admission, and relevant biochemical values reflect initial investigations. BP: Blood pressure, GCS: Glasgow Coma Scale, IQR: Interquartile range, MAP: Mean arterial pressure, SD: Standard deviation, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, SOFA: Sequential Organ Failure Assessment, SpO₂: Peripheral capillary oxygen saturation, TLC: Total leukocyte count.

(SGOT), and serum glutamic pyruvic transaminase (SGPT) showed no meaningful difference ($P>.05$). Overall, these findings indicate that the two groups were largely comparable at baseline, with only minor variations in select clinical and hematologic variables.

On univariate analysis, most demographic and comorbidity variables were not significantly associated with in-hospital mortality. However, non-survivors had significantly lower urine output ($P=.01$) and platelet counts ($P=.008$). Detailed findings are presented in Table 2.

3.3. Comparison between survivors and non-survivors

3.3.1. Serum ferritin

The distribution pattern of serum ferritin values was examined visually using histograms and descriptive statistics, which indicated an approximately normal distribution. Therefore, a parametric t -test was applied to compare ferritin levels between survivors and non-survivors. The mean ferritin concentration was significantly higher among non-survivors ($929.0 \pm 310.0 \mu\text{g/L}$) compared with survivors

($417.0 \pm 311.0 \mu\text{g/L}$; $P < .001$). The observed difference reflected a large effect size, indicating a substantial separation between the two groups. No logarithmic transformation was required, as the data were symmetrically distributed.

3.3.2. Other iron parameters

The distributions of serum iron, transferrin saturation, and total iron-binding capacity (TIBC) were non-normal; therefore, data are expressed as medians with interquartile ranges (IQR). The median transferrin saturation was 34.9% (IQR 17.25%–54.0%), and the median serum iron level was $68 \mu\text{g/dL}$ (IQR 40–96 $\mu\text{g/dL}$), both slightly higher among non-survivors, though the differences were not statistically significant on Mann–Whitney U testing ($P > .05$). The median TIBC was $186 \mu\text{g/dL}$ (IQR 128–274 $\mu\text{g/dL}$), lower in non-survivors, but again not significant ($P = .40$). Overall, no significant differences were found in other iron metabolism parameters between survivors and non-survivors.

On univariate analysis, elevated serum ferritin levels were significantly associated with in-hospital mortality ($P < .001$). A ferritin level $\geq 700 \mu\text{g/L}$ and its combination with a SOFA score ≥ 8 were also significantly associated with mortality ($P < .001$). Detailed results are presented in Table 2.

3.4. Multivariate logistic regression analysis for predictors of in-hospital mortality

Multivariate binary logistic regression analysis was performed to identify independent predictors of in-hospital mortality. Serum ferritin demonstrated a strong independent association with mortality, with markedly increased odds (adjusted odds ratio [aOR] = 33.203; 95% CI: 11.85–93.01; $P < .001$). Conversely, higher urine output was independently associated with a reduction in mortality risk, with each 100 mL/day increment conferring a protective effect (aOR = 0.915; 95% CI: 0.84–0.98; $P = .026$). Similarly, platelet count exhibited a protective association, with each increase of 10,000/mm³ significantly lowering the odds of mortality (aOR = 0.932; 95% CI: 0.88–0.98; $P = .009$). These findings indicate that hyperferritinemia is a strong adverse prognostic marker, whereas preserved urine output and higher platelet counts are associated with improved survival, independent of disease severity and other clinical parameters. Other variables, including SOFA score, chronic liver disease, SGOT, and serum creatinine, were not retained in the final model after adjustment. Detail findings given in Table 3.

3.5. Association of serum ferritin cut off level with in-hospital mortality

The ROC analysis demonstrated that serum ferritin had an AUC

of 0.884 (95% CI: 0.82–0.94; $P < .001$) for predicting in-hospital mortality, is illustrated in Figure 2. The threshold of 700 $\mu\text{g/L}$ was derived from the ROC curve using the Youden index (maximum [sensitivity+specificity–1])=0.65, corresponding to 88% sensitivity and 77% specificity. This threshold represents the point of maximum diagnostic discrimination.

The SOFA score (day 0) showed lower predictive accuracy (AUC=0.599; $P = .04$). Other iron parameters, including serum iron, TIBC, and transferrin saturation, exhibited poor discriminative ability and were not statistically significant predictors of mortality. Therefore, serum ferritin emerged as the strongest predictor of in-hospital mortality among the variables studied. The comparative diagnostic performance of serum ferritin and the SOFA score (day 0) is illustrated in the ROC curve (Figure 3).

We found that the serum ferritin cut off value of 700 $\mu\text{g/L}$ had strong predictive power for in-hospital mortality. Taking 700 $\mu\text{g/L}$ as cut-off, we divided the study population in high and low serum ferritin groups are provided in the table 2. The low serum ferritin subgroup death occurred in 9.1% ($n=7$) cases whereas in the high ferritin group death occurred in 69.9% ($n=51$) cases which was statistically significant ($P < .001$). The odds ratio between these groups was 23.2 with 95% CI (9.2–58.3).

4. Discussion

The focus of our study was to explore the association between serum iron profile and in-hospital mortality of patients diagnosed with sepsis. Death occurred 38.7% ($n=58$) of the study population. We found a significant association between serum ferritin levels at the time of hospitalization and in-hospital mortality. Demographic parameters like age, and gender had no significant association with in-hospital mortality. Although hypertension followed by diabetes mellitus were the most common comorbid condition in our cohort. We did not find any statistically significant difference in comorbidity profile of survivors and non-survivors. Similarly clinical parameters like oxygen saturation, pulse and mean arterial pressure had no statistically significant bearing on patient. We did however conclude that low urine output was associated with adverse outcome. We observed that there was a significant difference in platelet count between survivors and non-survivors ($P = .008$). Other laboratory values, including as haemoglobin, total leucocyte count (TLC), bilirubin, creatinine, blood urea, serum glutamic-oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT), did not differ significantly between the outcome groups ($P > .05$). Our findings corroborated the findings of similar studies which have used clinical and laboratory parameters to predict outcome in sepsis patients[15,16].

The study findings substantiate our hypothesis that products

Table 2. Comparison of various parameters in patients with sepsis based on outcome.

Parameters	Outcome		P
	Discharged (n= 92)	Death (n= 58)	
Age, years			.56 ^b
18-40	29 (31.5)	18 (31.0)	
41-60	31 (33.7)	24 (41.4)	
>60	32 (34.8)	16 (27.6)	
Sex			.74 ^b
Male	53 (57.6)	35 (60.3)	
Female	39 (42.4)	23 (39.7)	
Known comorbid condition present			
Hypertension	55 (59.8)	36 (62.1)	.78 ^b
Diabetes mellitus	55 (59.8)	32 (55.2)	.57 ^b
Chronic obstructive pulmonary disease	31 (33.7)	23 (39.7)	.45 ^b
Chronic liver disease	4 (4.3)	8 (13.8)	.06 ^c
Cerebrovascular accident	22 (23.9)	14 (24.1)	.97 ^b
Old tuberculosis	16 (17.4)	10 (17.2)	.98 ^b
Coronary artery disease	34 (37.0)	17 (29.3)	.33 ^b
Clinical profile			.54 ^d
Glasgow Coma Scale, mean±SD	13.0±2.8	12.0±2.6	
Temperature, °C	37.8±0.9	37.2±0.8	.25 ^d
Systolic BP, mmHg	108.0±26.2	107.0±27.7	.79 ^d
Diastolic BP, mmHg	63.0±15.2	63.0±16.7	.77 ^d
MAP, mmHg	78.0±18.3	77.0±19.8	.90 ^d
Pulse rate, /minutes	93.0±23.8	95.0±21.4	.48 ^d
SpO ₂ , % room air	84.0±10.7	83.0±12.3	.64 ^a
Urine output, mL/day	898.0±546.8	753.0±598.1	.01 ^d
Laboratory profile			
Hemoglobin, g/dL	10.0±1.4	10.0±1.6	.74 ^d
TLC, cells/mm ³	13 836.0±4026.2	14 376.0±4253.7	.40 ^d
Platelet count, ×10 ³ /mm ³	197.0±84.1	163.0±85.3	.008 ^d
Total bilirubin, mg/dL	1.6±2.3	2.2±2.8	.32 ^d
SGOT, IU/L	117.0±100.1	149.0±117.2	.10 ^d
SGPT, IU/L	83.0±69.4	98.0±82.9	.12 ^d
Blood urea, mg/dL	59.0±25.9	62.0±28.8	.63 ^d
Serum creatinine, mg/dL	1.9±1.1	2.0±0.9	.17 ^d
Serum iron, μ g/dL	66.3±45.3	76.1±52.2	.23 ^d
Total iron binding capacity, μ g/dL	219.0±100.8	208.0±103.8	.40 ^d
Transferrin saturation, %	32.8±20.7	39.7±24.1	.08 ^d
Serum ferritin, ng/mL	417.0±311.0	929.0±310.0	<.001 ^a
Serum ferritin			<.001 ^b
High (≥700 μ g/L)	22 (30.1)	51 (69.9)	
Low (<700 μ g/L)	70 (90.9)	7 (9.1)	
SOFA ≥8 and High (≥700 μ g/L)	12 (37.1)	22 (62.9)	<.001
Rest all other combination	79 (68.7)	36 (31.3)	<.001

Numbers are expressed as n (%), unless otherwise specified.

***Significant at $P<.05$, ^a: *t*-test, ^b: *Chi-Squared* Test, ^c: Fisher's Exact Test, ^d: Wilcoxon-Mann-Whitney *U* Test

Significant differences were observed in several indicators between survivors and non-survivors. Increased SOFA scores (admission and discharge), elevated ferritin (≥700 μ g/L), higher serum iron, and SOFA–ferritin combinations showed strong associations with death (all $P<.05$). Lower transferrin saturation also correlated with poor prognosis. Values are shown as mean ± standard deviation or proportions. BP: Blood Pressure, GCS: Glasgow Coma Scale, IQR: Interquartile range, MAP: Mean Arterial Pressure, SD: Standard deviation, SGOT: Serum glutamic-oxaloacetic transaminase, SGPT: Serum glutamic pyruvic transaminase, SOFA: Sequential Organ Failure Assessment, SpO₂: Peripheral capillary oxygen saturation, TLC: Total leucocyte count.

Table 3. Multivariate logistic regression analysis of factors associated with in-hospital mortality.

	Adjusted odds ratio	95% CI for the adjusted odds ratio		P
		Lower	Upper	
Ferritin	33.203	11.85	93.01	<.001
Urine output (for every 100 mL increase/day)	.915	.84	.98	.026
Platelet count (for every 10000 increase per mm ³ of blood)	.932	.88	.98	.009

Model adjusted for other factors: SOFA score, Chronic liver disease, SGOT, Serum Creatinine

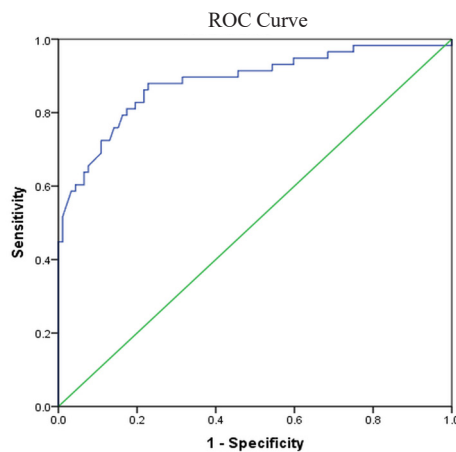


Figure 2. The graph illustrates ROC plots assessing the prognostic performance of serum ferritin ($\mu\text{g/L}$) in forecasting in-hospital death among septic individuals. The blue curve corresponds to ferritin. The green diagonal denotes the line of no discrimination. Blue line: Serum ferritin; Green line: Reference line.

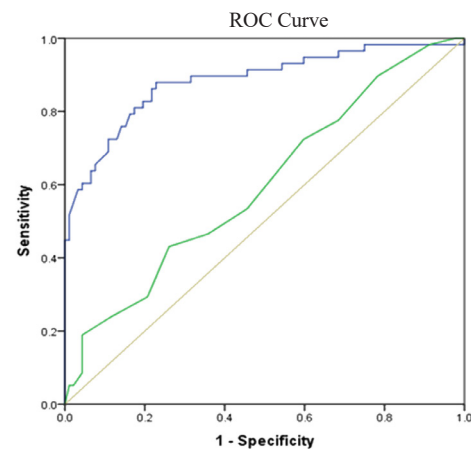


Figure 3. Predictive comparison of SOFA score and serum ferritin levels for mortality in sepsis. The graph illustrates ROC plots assessing the prognostic performance of serum ferritin ($\mu\text{g/L}$) and SOFA score on day 0 in forecasting in-hospital death among septic individuals. The blue curve corresponds to ferritin, and the green represents SOFA score. The diagonal denotes the line of no discrimination. Ferritin demonstrated superior predictive accuracy over SOFA. Blue line: Serum ferritin; Green line: SOFA; Yellow line: Reference line.

of iron metabolism can serve as markers of poor prognosis in sepsis patients. Among the various parameters of iron metabolism including serum ferritin, total serum iron, transferrin saturation and TIBC, serum ferritin had best association with in-hospital mortality of sepsis patients ($P < .001$). In a similar study by Fang *et al.* Serum ferritin levels were notably higher in non-survivor patients with median value of 892 ng/mL (IQR: 352 to 2881) for non-survivors[17]. These findings highlight the potential of serum ferritin as a key marker in predicting in-hospital mortality in sepsis patients due to its role in inflammation and homeostasis[9,11,18,19].

Fang *et al.* also reported that serum ferritin demonstrated moderate predictive power for in-hospital mortality, with an area under the curve (AUC) of 0.651. The optimal cut-off value for ferritin was determined to be 591.5 ng/mL, and levels above this threshold acted as an independent predictor of increased mortality risk, raising the likelihood of in-hospital death by 119%[17]. In our study we found that the serum ferritin cut off value of 700 $\mu\text{g/L}$ had a strong predictive power for in-hospital mortality in sepsis patients. Taking 700 $\mu\text{g/L}$ as cut-off we divided the study population in high and low serum ferritin groups. In the low serum ferritin subgroup death occurred in 9.1% ($n=7$) cases whereas in the high ferritin group death occurred in 69.9% ($n=51$) cases which is statistically significant ($P < .001$). Patients with serum ferritin levels ≥ 700 $\mu\text{g/L}$ had a markedly increased risk of succumbing to sepsis, with an odds ratio of 23.2 (95% CI: 9.2–58.3) indicating that patients with high ferritin ≥ 700 $\mu\text{g/L}$, the chance of death is 23.2 times more

as compared to those with serum ferritin level < 700 $\mu\text{g/L}$. Other serum iron profile components (serum iron, TIBC, and transferrin saturation) exhibited low discriminatory power and were not statistically significant predictors of mortality ($P > .05$). Although contrasting findings were present in recent study by Rusu *et al.* in which no significant difference in serum ferritin levels of survivors and non-survivor was found, albeit, the increase in serum ferritin was larger in non-survivors as compared to survivors[14]. Ample evidence exists that serum ferritin levels can be used as a simple point of care test to predict mortality in sepsis patients[9,14,17,20,21].

We also found that, although SOFA score is an established tool for predicting mortality in patients with sepsis. In our study it had moderate predictive value with an AUROC of 0.599. The SOFA score's sensitivity and specificity for predicting in-hospital mortality were 43% and 74% respectively. Nevertheless, as suggested by current literature the mean SOFA score of non-survivors was higher in comparison to survivors[15,22].

In our study, serum ferritin, urine output, and platelet count emerged as independent predictors of in-hospital mortality, emphasizing the roles of hyperinflammation, renal dysfunction, and coagulopathy in adverse outcomes and supporting their utility in risk stratification.

The biggest strength of our study is inclusion of well-defined subset of sepsis patients and their extensive profiling. Our findings reinforce that accumulating evidence regarding association of serum iron profile with in-hospital mortality in patients with sepsis.

With the evidence provided by our study serum iron profile can be used as a point of care test in patients of sepsis especially in resource limited settings by identifying patients prone to adverse outcomes.

However, limitation in research are difficult to avoid. The single-centre design and small sample size may limit the generalisability of our results. Furthermore, we did not assess the effectiveness of specific therapeutic measures and impact of underlying aetiology that could have altered iron metabolism and patient outcomes.

Longitudinal studies that track iron and ferritin levels in septic patients over time could provide vital insights into role of iron metabolism in evolution and advancement of sepsis its recovery, or the development of consequences such as organ failure. Longitudinal studies with larger sample size may provide a better cut-off value of iron profile parameters for predicting in hospital mortality.

In conclusion, serum ferritin is a powerful and independent predictor of in-hospital death in sepsis patients. When assessed alongside the SOFA score, ferritin measurement enhanced the accuracy of mortality prediction compared to the SOFA score alone. These findings suggest that incorporating serum ferritin testing into the routine evaluation of septic patients may assist clinicians in identifying high-risk cases earlier and guiding timely, targeted therapeutic interventions. However, as this study was conducted in a single centre with a moderately sized cohort, the results should be regarded as preliminary evidence, and further large-scale, multicentre studies are warranted to validate these observations.

Conflict of interest statement

The authors report no conflict of interest.

Ethical statement

The study was approved by the Institutional Ethical Committee for Human Research of University College of Medical Sciences and GTB Hospital, University of Delhi (Approval number: IECHR-2023-59-54). All participants provided informed consent and participated voluntarily.

Funding

This study received no extramural funding.

Data availability statement

The data supporting the findings of this study are available from the corresponding authors upon request.

Authors' contributions

BN conducted the literature review, patient/clinical work, data collection, analysis, and statistical evaluation; drafted the manuscript, revised it critically, and served as the guarantor of the study. SN conceived the study idea, developed the scientific framework, supported literature review, and critically revised the manuscript. AA contributed to study conceptualization and intellectual input and reviewed and revised the manuscript. RS supervised the study design, performed statistical analysis, and contributed to manuscript revision and final approval. MK participated in the clinical and experimental execution of the study. All authors approved the final manuscript for submission..

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Edited by Liu JJ

References

- [1] Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The third international consensus definitions for sepsis and septic shock (Sepsis-3). *JAMA* 2016; **315**(8): 801-810.
- [2] Lever A, Mackenzie I. Sepsis: Definition, epidemiology, and diagnosis. *BMJ* 2007; **335**(7625): 879-883.
- [3] Prescott HC, Angus DC. Enhancing recovery from sepsis: A review. *JAMA* 2018; **319**(1): 62-75.
- [4] Jeganathan N. Burden of sepsis in India. *Chest* 2022; **161**(6): 1438-1439.
- [5] Gotts JE, Matthay MA. Sepsis: Pathophysiology and clinical management. *BMJ* 2016; **353**: i1585.
- [6] Kibe S, Adams K, Barlow G. Diagnostic and prognostic biomarkers of sepsis in critical care. *J Antimicrob Chemother* 2011; **66**(suppl 2): ii33-40.
- [7] Liu Q, Wu J, Zhang X, Wu X, Zhao Y, Ren J. Iron homeostasis and disorders revisited in the sepsis. *Free Radic Biol Med* 2021; **165**: 1-13.

- [8]Tacke F, Nuraldeen R, Koch A, Strathmann K, Hutschenreuter G, Trautwein C, et al. Iron parameters determine the prognosis of critically ill patients. *Crit Care Med* 2016; **44**(6): 1049–1058.
- [9]Brandtner A, Tymoszuk P, Nairz M, Lehner GF, Fritsche G, Vales A, et al. Linkage of alterations in systemic iron homeostasis to patients' outcome in sepsis: A prospective study. *J Intensive Care* 2020; **8**(1): 66.
- [10]Lachmann G, Knaak C, Vorderwülbecke G, Rosée P La, Balzer F, Schenk T, et al. Hyperferritinemia in critically ill patients. *Intensive Care Med* 2020; **46**(4): 739-748.
- [11]Sang L, Teng W, Zhao M, Ding P, Xu X, Wang Y, et al. Association between serum ferritin and outcomes in critically ill patients: Aretrospective analysis of a large intensive care unit database. *Chin Med J* 2022; **135**(21): 2634-2636.
- [12]Lan P, Pan K han, Wang S jia, Shi Q cheng, Yu Y xian, Fu Y, et al. High serum iron level is associated with increased mortality in patients with sepsis. *Sci Rep* 2018; **8**(1): 11072.
- [13]Ghosh S, Baranwal AK, Bhatia P, Nallasamy K. Suspecting hyperferritinemic sepsis in iron-deficient population: Do we need a lower plasma ferritin threshold? *Pediatr Crit Care Med* 2018; **19**(7): e367–373.
- [14]Rusu D, Blaj M, Ristescu I, Patrascanu E, Gavril L, Siriopol I, et al. Outcome predictive value of serum ferritin in ICU patients with long ICU stay. *Medicina (Kaunas)* 2021; **57**(1): 1.
- [15]Paary TTS, Kalaiselvan MS, Renuka MK, Arunkumar AS. Clinical profile and outcome of patients with severe sepsis treated in an intensive care unit in India. *Ceylon Med J* 2016; **61**(4): 181.
- [16]Ye L, Feng M, Lin Q, Li F, Lyu J. Analysis of pathogenic factors on the death rate of sepsis patients. *PLoS One* 2023; **18**(12): e0287254.
- [17]Fang YP, Zhang HJ, Guo Z, Ren CH, Zhang YF, Liu Q, et al. Effect of serum ferritin on the prognosis of patients with sepsis: Data from the MIMIC-IV database. *Emerg Med Int* 2022; 2022: 2104755.
- [18]Jiang Y, Jiang FQ, Kong F, An MM, Jin BB, Cao D, et al. Inflammatory anemia associated parameters are related to 28 day mortality in patients with sepsis admitted to the ICU: A preliminary observational study. *Ann Intensive Care* 2019; **9**(1): 67.
- [19]Moreira AC, Mesquita G, Gomes MS. Ferritin: An inflammatory player keeping iron at the core of pathogen-host interactions. *Microorganisms* 2020; **8**(4): 589.
- [20]He L, Guo C, Su Y, Ding N. The relationship between serum ferritin level and clinical outcomes in sepsis based on a large public database. *Sci Rep* 2023; **13**(1): 8677.
- [21]Bairwa M, Jatteppanavar B, Kant R, Singh M, Choudhury A. Impact of iron profile and vitamin D levels on clinical outcomes in patients with sepsis and septic shock: A cross-sectional analysis at a tertiary care center. *Indian J Crit Care M* 2024; **28**(6): 569-574.
- [22]Li W, Wang M, Zhu B, Zhu Y, Xi X. Prediction of median survival time in sepsis patients by the SOFA score combined with different predictors. *Burns Trauma* 2020; **8**: tkz006.