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Original Article

Diagnostic and prognostic utility of c-reactive protein and serum ferritin in children with suspected sepsis: a cross-sectional observational study.

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Abstract

Introduction

Pediatric sepsis requires rapid recognition despite delayed or negative microbiological cultures. C-reactive protein (CRP) and ferritin are accessible inflammatory biomarkers. This study assessed their diagnostic and prognostic associations with culture positivity, septic shock, PRISM III score, and in-hospital mortality.

Materials and Methods

This prospective observational study included 40 children with suspected sepsis. Clinical details and cultures were recorded, and serum CRP and ferritin were measured at admission and 48 hours. Disease severity was assessed using septic shock status and PRISM III score, with survival recorded. Diagnostic utility for culture positivity was evaluated using sensitivity, specificity, predictive values and ROC analysis, with appropriate statistical tests and $p<0.05$ considered significant.

Results

Among 40 children with suspected sepsis, 37.5% were culture-positive. CRP was significantly higher in culture-positive cases at admission (66.93 ± 22.40 vs 51.88 ± 22.68 mg/L; $p=0.048$) and 48 hours (98.26 ± 15.83 vs 58.55 ± 22.74; $p<0.001$), with 48-hour AUC of 0.908. Septic shock was associated with higher CRP (71.23 ± 16.90 mg/L) and ferritin (461.70 ± 262.83 ng/mL). Ferritin was markedly higher among non-survivors (657.20 ± 162.73 vs 218.12 ± 225.54 ng/mL; $p<0.001$). Both CRP ($r=0.507$) and ferritin ($r=0.543$) correlated significantly with PRISM III scores.

Conclusion

CRP, particularly at 48 hours, demonstrated useful diagnostic performance for culture-positive sepsis, while ferritin showed stronger associations with septic shock and mortality. Both biomarkers correlated significantly with PRISM III scores, supporting CRP as a diagnostic marker and ferritin as a useful indicator of severity and prognosis.

Recommendations

Serial CRP measurement can complement clinical and microbiological assessment, while ferritin can assist severity and prognostic stratification. Both should be interpreted with culture findings and PRISM III rather than as standalone tests. Larger prospective studies should validate clinically useful cut-offs.

Keywords: *Pediatric Sepsis, C-Reactive Protein, Serum Ferritin, Septic Shock, Prognosis.*
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Introduction

Sepsis remains a major cause of morbidity and mortality among children and a significant challenge in pediatric emergency and critical care.[1,2] Early recognition is difficult because clinical manifestations are often nonspecific and may overlap with other childhood illnesses.[3] Sepsis is characterized by infection-associated, potentially life-threatening organ dysfunction, while septic shock involves cardiovascular dysfunction and carries substantially increased mortality.[4] Early recognition and timely treatment are therefore essential for improving outcomes.[3,5] Although microbiological cultures are important for identifying causative pathogens and guiding antimicrobial therapy, results are delayed and prior antimicrobial exposure may reduce culture positivity.[6] Consequently, inflammatory biomarkers are increasingly used as adjuncts for diagnosis, risk stratification, and monitoring.[7]

C-reactive protein (CRP) is an acute-phase protein that increases rapidly during inflammation and is widely used in the evaluation and monitoring of pediatric sepsis. However, its elevation is nonspecific and may occur in infectious and noninfectious inflammatory conditions.[7,8] Serum ferritin, traditionally used as a marker of iron stores, is also an acute-phase reactant that increases during systemic inflammation.[7] Elevated ferritin levels in pediatric sepsis have been associated with disease severity, septic shock, multiorgan dysfunction, adverse outcomes, and severity scores such as PRISM III.[9-11]

Despite their availability, the diagnostic and prognostic roles of CRP and ferritin in pediatric sepsis remain incompletely defined. Their associations with disease severity and mortality have been reported, but performance varies across populations and clinical settings.[7,12] Evidence simultaneously evaluating these biomarkers against culture positivity, septic shock, severity scores, and mortality remains limited.[10,12] Therefore, the present study aimed to assess the association of serum CRP and ferritin with culture positivity, septic shock, PRISM III score, and in-hospital mortality, and to determine their diagnostic performance for identifying culture-positive pediatric sepsis.

Materials and methods

Study design

This was a prospective cross-sectional observational study with serial biomarker measurements, conducted over one year from January 2010 to December 2010. Children beyond the neonatal age group presenting with suspected sepsis, severe sepsis, or septic shock were evaluated, and 40 children fulfilling the predefined eligibility criteria were included.

Study setting

The study was conducted at the Indira Gandhi Institute of Child Health (IGICH), South Hospital Complex, Dharmaram College Post, Bengaluru, Karnataka, India. IGICH is a tertiary pediatric referral institute providing comprehensive child-health care. Its principal services include general pediatrics, pediatric and neonatal intensive care, pediatric surgery, orthopedics, endocrinology, dermatology, hematology, otorhinolaryngology, pediatric neurology and neurodevelopmental services, genetics, diagnostic support, emergency care, teaching, and clinical research.

Study population

The study population comprised children beyond the neonatal period with suspected or proven infection and clinical features suggestive of systemic inflammatory response. A detailed clinical history and physical examination were performed for all eligible children. Demographic characteristics, presenting symptoms, vital signs, relevant clinical findings, laboratory investigations, microbiological findings, disease severity, and clinical outcomes were recorded using a structured proforma.

Inclusion criteria

Children beyond the neonatal age group presenting with suspected sepsis, severe sepsis, or septic shock during the study period were considered eligible. Sepsis was defined according to the criteria of the International Pediatric Sepsis Consensus Conference used in the original study. Eligible children had suspected or proven infection associated with features of systemic inflammatory response, including abnormal body temperature (>38.5°C or <36°C), an age-specific abnormal leukocyte count, or >10% immature neutrophils, together with additional clinical features such as tachycardia or tachypnea. Infection was considered proven when supported by a positive microbiological culture and suspected when based on relevant clinical findings, imaging, or laboratory investigations.

Exclusion criteria

Children with chronic inflammatory diseases and conditions known to influence serum ferritin levels independently of sepsis were excluded. These included iron overload states such as hereditary haemochromatosis and transfusional iron overload, porphyria cutanea tarda, ineffective erythropoiesis or sideroblastic anaemia, thalassemia, and hematological malignancies.

Sampling technique

Consecutive children presenting to the study centre during the study period who fulfilled the predefined inclusion and exclusion criteria were considered for participation. After eligibility assessment, 40 children were enrolled in the study. Following microbiological evaluation, participants were categorized into culture-positive and culture-negative groups. The final study population consisted of 15 (37.5%) culture-positive and 25 (62.5%) culture-negative children.

Sample size

The sample size was justified using the single-proportion formula $n = Z^2p(1-p)/d^2$. In the absence of a reliable local estimate, p was taken as 0.50 to provide the maximum variance, with a two-sided 95% confidence level ($Z = 1.96$) and an absolute precision (d) of 0.155. Thus, $n = (1.96^2 \times 0.50 \times 0.50)/(0.155^2) = 39.98$, which was rounded to 40 children. This calculation should be cross-checked against the original study protocol if the original sample-size worksheet is available.

Bias

Potential selection bias was reduced by consecutive enrolment of children meeting predefined eligibility criteria. Information bias was limited by using a structured proforma, uniform clinical definitions, fixed biomarker measurement time points at admission and 48 hours, and predefined outcome categories. Microbiological classification was based on culture results obtained using standard aseptic sampling procedures. Prior antibiotic exposure, a potential source of reduced culture yield, was recorded and compared between culture-positive and culture-negative groups. The same PRISM III framework was used for severity assessment in all participants. Because of the small sample, multivariable adjustment for residual confounding was not performed and this was acknowledged as a limitation.

Data collection

A detailed clinical history and physical examination were performed following enrolment. Baseline demographic and clinical information, including age, sex, presenting complaints, vital signs, clinical features of infection, and relevant laboratory investigations, was recorded using a structured proforma. Total leukocyte count, band-cell percentage, CRP, ferritin, microbiological culture findings, septic shock status, PRISM III score, and clinical outcome were documented. Appropriate microbiological specimens were collected before or during treatment as clinically indicated.

Microbiological assessment

Appropriate specimens, including blood and other clinically indicated samples, were obtained for microbiological culture using standard aseptic techniques. Culture results were recorded and used to categorize participants as culture-positive or culture-negative. A positive microbiological culture in a child with clinical features of suspected sepsis was considered evidence of culture-positive sepsis.

Assessment of inflammatory biomarkers

Serum CRP and ferritin levels were measured at two predefined time points: at admission and 48 hours after admission. CRP was assessed as a marker of systemic inflammation and infection, while serum ferritin was evaluated as an inflammatory and disease-severity biomarker. The changes in CRP and ferritin levels between admission and 48 hours were also assessed in relation to culture positivity, septic shock, disease severity, and clinical outcome.

Assessment of conventional inflammatory parameters

Total leukocyte count and band-cell percentage were assessed as conventional inflammatory parameters. These findings were recorded along with the biomarker measurements and other clinical and laboratory variables for comparison between culture-positive and culture-negative children.

Assessment of disease severity

Disease severity was assessed using the presence or absence of septic shock and the Pediatric Risk of Mortality III (PRISM III) score. The PRISM III score was calculated using the relevant clinical and physiological variables obtained during the assessment period. Higher PRISM III scores were considered indicative of greater severity of illness. The relationship between CRP and ferritin levels and PRISM III scores was evaluated using correlation analysis.

Assessment of clinical outcome

The clinical outcome was assessed during the hospital stay and categorized as survival or in-hospital mortality. The association between admission and 48-hour CRP and ferritin levels and mortality was evaluated. Biomarker levels were also compared between survivors and non-survivors to assess their potential prognostic utility.

Outcome assessment

The primary outcome was the association of serum CRP and ferritin levels with culture positivity among children with suspected sepsis. Secondary outcomes included the association of these biomarkers with septic shock, PRISM III score, and in-hospital mortality. The diagnostic performance of CRP and ferritin in identifying culture-positive sepsis was evaluated using receiver operating characteristic (ROC) curve analysis. Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the ROC curve (AUC) were assessed. The diagnostic performance of biomarker measurements at admission and 48 hours was compared.

Statistical analysis

Data were analysed using appropriate statistical software. Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as frequencies and percentages. Comparisons between culture-positive and culture-negative groups were performed using the independent-samples t-test for continuous variables and the chi-square test for categorical variables, as appropriate. Comparisons of biomarker levels according to septic shock and survival status were also performed using appropriate statistical tests. Pearson correlation analysis was used to assess the relationship between CRP and ferritin levels and PRISM III scores. Diagnostic performance was assessed using sensitivity, specificity, PPV, NPV, and ROC curve analysis, with calculation of the AUC. The AUCs for biomarker measurements at admission and 48 hours were compared to assess changes in diagnostic performance over time. A two-sided p-value <0.05 was considered statistically significant.

Ethical considerations

The study protocol was approved by the Institutional Ethics Committee of Indira Gandhi Institute of Child Health, Bengaluru. Written informed consent was

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obtained from the parents or legally authorised representatives before enrolment. Participant confidentiality was maintained, and study data were used exclusively for research purposes.

Results

The available study record documented 40 children who underwent eligibility assessment. All 40 were potentially eligible, confirmed eligible after application of the inclusion and exclusion criteria, and included in the final analysis; no pre-enrolment exclusions were documented. Participant flow is shown in Figure 1. Among the 40 children with suspected sepsis, 15 (37.5%) were culture-positive and 25 (62.5%) were culture-negative, indicating that microbiological confirmation was obtained in approximately one-third of clinically suspected cases.

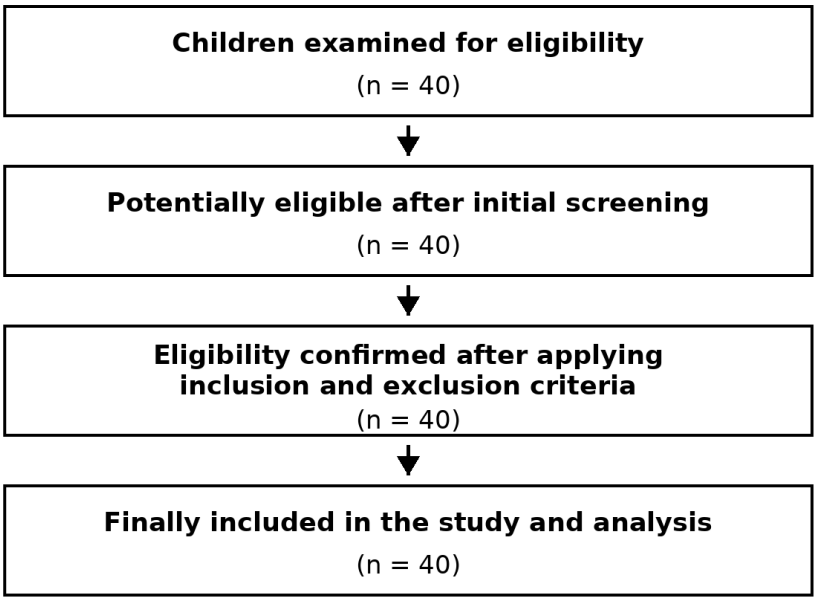

Figure 1. Participant flow through the study

Age, duration of illness, and prior antibiotic exposure were comparable between the groups (all p>0.05). Females constituted 73.3% of culture-positive and 44.0% of culture-negative cases; however, the difference was not statistically significant (p=0.071). Prior antibiotic exposure was common in both culture-positive (73.3%) and culture-negative (68.0%) groups. (Table 1)

Table 1: *Baseline demographic and clinical characteristics of children with suspected sepsis according to culture status (N = 40)*

Characteristic	Culture status		p-value
	Positive (n=15)	Negative (n=25)	
Age, years, mean ± SD	2.04 ± 2.25	2.85 ± 1.97	0.340
Female, n (%)	11 (73.3)	11 (44.0)	0.071
Duration of illness, days, mean ± SD	7.8 ± 3.45	6.6 ± 2.04	0.210
Prior antibiotic exposure, n (%)	11 (73.3)	17 (68.0)	0.721

CRP levels were significantly higher in culture-positive than culture-negative children at admission (66.93 ± 22.40 vs 51.88 ± 22.68 mg/L; p=0.048), with a more pronounced difference at 48 hours (98.26 ± 15.83 vs

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58.55 ± 22.74 mg/L; p<0.001). Ferritin levels were numerically higher among culture-positive children at both admission (379.20 ± 244.89 vs 244.44 ± 251.06 ng/mL; p=0.106) and 48 hours (280.67 ± 289.83 vs 259.28 ± 262.25 ng/mL; p=0.812), but neither difference was statistically significant. (Table 2)

Table 2: *C-reactive protein and serum ferritin levels according to culture status at admission and 48 hours (N = 40)*

Biomarker	Time point	Culture status		p-value
		Positive (n=15)	Negative (n=25)	
CRP (mg/L)	Admission	66.93 ± 22.40	51.88 ± 22.68	0.048
	48 hours	98.26 ± 15.83	58.55 ± 22.74	<0.001
Ferritin (ng/mL)	Admission	379.20 ± 244.89	244.44 ± 251.06	0.106
	48 hours	280.67 ± 289.83	259.28 ± 262.25	0.812

At the predefined threshold of >40 mg/L, CRP demonstrated a sensitivity of 86.7% and a negative predictive value of 86.7% for identifying culture-positive cases, with a specificity and positive predictive value of 52.0% each (p=0.035). Ferritin >200 ng/mL showed lower sensitivity (53.3%), specificity (56.0%), positive predictive value (42.0%), and negative predictive value (66.0%), with no statistically significant association (p=0.576). Overall, CRP demonstrated better threshold-based performance than ferritin for identifying culture-positive cases. (Table 3)

Table 3: *Diagnostic performance of admission C-reactive protein and serum ferritin at predefined thresholds for identifying culture-positive cases among children with suspected sepsis (N = 40)*

Biomarker	Threshold	Sensitivity	Specificity	PPV	NPV	p-value
CRP	>40 mg/L	86.7%	52.0%	52.0%	86.7%	0.035
Ferritin	>200 ng/mL	53.3%	56.0%	42.0%	66.0%	0.576

CRP showed modest discrimination for culture positivity at admission (AUC=0.683; p=0.047), which improved markedly at 48 hours (AUC=0.908; p<0.001). The increase in AUC by 0.225 was statistically significant (p=0.036). Ferritin demonstrated limited discriminatory ability at both admission (AUC=0.620; p=0.201) and 48 hours (AUC=0.576; p=0.425), with no significant difference between time points (AUC difference=0.044; p=0.148). (Table 4)

Table 4: *Receiver operating characteristic analysis of C-reactive protein and serum ferritin for identifying culture-positive cases at admission and 48 hours (N = 40)*

Biomarker	Admission		48-hour		Difference in AUC	
	AUC	p-value	AUC	p-value	AUC	p-value
CRP	0.683	0.047	0.908	<0.001	0.225	0.036
Ferritin	0.620	0.201	0.576	0.425	0.044	0.148

Children with septic shock had significantly higher CRP levels than those without septic shock (71.23 ± 16.90 vs 47.39 ± 22.73 mg/L; p=0.001). Ferritin levels were also significantly higher in the septic shock group (461.70 ± 262.83 vs 171.73 ± 210.33 ng/mL; p=0.004). Among non-survivors, CRP levels were higher but not

statistically significant (p=0.063), whereas ferritin was markedly elevated compared with survivors (657.20 ± 162.73 vs 218.12 ± 225.54 ng/mL; p<0.001). (Table 5)

Table 5: *Association of C-reactive protein and serum ferritin levels with septic shock and in-hospital mortality among children with suspected sepsis (N = 40)*

Clinical outcome	CRP (mg/L)	p-value	Ferritin (ng/mL)	p-value
Septic shock status				
Septic shock (n=17)	71.23 ± 16.90	0.001	461.70 ± 262.83	0.004
Without septic shock (n=23)	47.39 ± 22.73		171.73 ± 210.33	
In-hospital outcome				
Non-survivors (n=7)	72.60 ± 6.13	0.063	657.20 ± 162.73	<0.001
Survivors (n=33)	54.45 ± 24.68		218.12 ± 225.54	

Both biomarkers showed significant positive correlations with illness severity as assessed by PRISM III score. CRP demonstrated a moderate positive correlation with PRISM III (r=0.507; p<0.001), while ferritin showed a slightly stronger moderate correlation (r=0.543; p<0.001). These findings indicate that higher admission CRP and ferritin levels were associated with greater disease severity among children with suspected sepsis. (Table 6)

Table 6: *Correlation of C-reactive protein and serum ferritin levels with PRISM III score among children with suspected sepsis (N = 40)*

Biomarker	Correlation coefficient (r)	p-value
CRP (mg/L)	0.507	<0.001
Ferritin (ng/mL)	0.543	<0.001

Discussion

Pediatric sepsis can progress rapidly to septic shock and death, while microbiological culture may be delayed or yield negative results, particularly after prior antibiotic exposure. Hence, readily available biomarkers such as CRP and ferritin may aid early diagnosis, severity assessment, and prognostication. This prospective

observational study was conducted at Indira Gandhi Institute of Child Health from January to December 2010 and included 40 children beyond the neonatal age with suspected sepsis, severe sepsis, or septic shock; 15 were culture-positive and 25 culture-negative. Clinical characteristics and cultures were recorded. CRP and ferritin were measured at admission and 48 hours.

Severity was assessed using septic shock status and PRISM III score, with mortality recorded.

Culture positivity in the present study was 37.5% (15/40), while 62.5% were culture-negative. This finding indicates that clinical suspicion of pediatric sepsis frequently persists despite the absence of microbiological confirmation, emphasizing the limited sensitivity of

culture as a sole diagnostic standard and the practical need for adjunctive inflammatory markers. Comparable rates were reported by Thapar V et al.13 (2024) (32.5%), Tantray JA et al.14 (2025) (33.7%; 64/190), and Vani KKV et al.15 (2022) (41.0%; 41/100), although only 25.0% in the latter were specifically blood-culture positive. Tonial CT et al.16 (2021) reported a higher confirmed etiological agent rate of 54.1% (159/294). Thus, the generally modest microbiological yield supports the use of complementary biomarkers, particularly when prior antimicrobial exposure can reduce culture positivity.

In the present study, culture-positive and culture-negative children were comparable in age (2.04 ± 2.25 vs. 2.85 ± 1.97 years; p=0.340), duration of illness (7.8 ± 3.45 vs. 6.6 ± 2.04 days; p=0.210), and prior antibiotic exposure (73.3% vs. 68.0%; p=0.721); the higher proportion of females among culture-positive cases was not statistically significant (73.3% vs. 44.0%; p=0.071). The similarity of these baseline characteristics reduces the likelihood that the observed biomarker differences were simply explained by major demographic or illness-duration imbalance between groups. At the same time, the high frequency of previous antibiotic exposure in both groups provides a plausible explanation for the substantial culture-negative fraction. Tantray JA et al.14 (2025) reported 55.8% males and 44.2% females, predominantly aged 1–5 years, while Thapar V et al.13 (2024) reported a mean age of 7.75 ± 5.1 years and male predominance (57.5%). Conversely, Tonial CT et al.16 (2021) observed a nearly equal sex distribution, while Vani KKV et al.15 (2022) reported significantly longer illness duration in children with septic shock than those without shock (12.17 vs. 7.57 days; p=0.03).

CRP was significantly higher in culture-positive than culture-negative children at admission (66.93 ± 22.40 vs. 51.88 ± 22.68 mg/L; p=0.048) and 48 hours (98.26 ± 15.83 vs. 58.55 ± 22.74 mg/L; p<0.001). The widening separation at 48 hours suggests that serial CRP reflects persistence or progression of infection-associated systemic inflammation better than a single baseline value. In contrast, ferritin was only numerically higher in culture-positive cases at admission (379.20 ± 244.89 vs. 244.44 ± 251.06 ng/mL; p=0.106) and at 48 hours (280.67 ± 289.83 vs. 259.28 ± 262.25 ng/mL; p=0.812), indicating that ferritin is less closely linked to microbiological confirmation and is likely influenced more by the intensity of systemic inflammation. Tantray JA et al.14 (2025) also reported a significant association between CRP and culture positivity (p<0.05), while Vani KKV et al.15 (2022) found higher CRP at admission and 48 hours. Conversely, Vani KKV et al.15 reported significant ferritin differences at both time points, illustrating variability in ferritin performance across populations.

At a CRP threshold >40 mg/L, sensitivity and NPV were both 86.7%, whereas specificity and PPV were 52.0% each (p=0.035). This pattern means that admission CRP at this threshold is more useful as a sensitive adjunct for identifying children unlikely to have culture-positive disease when the value is low than as a confirmatory test when the value is high. The marked improvement in CRP AUC from 0.683 at admission to 0.908 at 48 hours (AUC difference 0.225; p=0.036) further indicates that serial CRP measurement provides substantially better discrimination than a single admission value. Ferritin >200 ng/mL showed poor threshold performance and non-significant AUCs, limiting its role as a diagnostic discriminator for culture positivity in this cohort. Vani KKV et al.15 (2022) reported CRP sensitivity, specificity, PPV, and NPV of 82.9%, 45.8%, 51.5%, and 79.4%, respectively, while Tantray JA et al.14 (2025), at CRP ≥10 mg/L, reported 87.5%, 42.9%, 43.8%, and 86.7%. Differences in serial AUC trends between the present study and Vani KKV et al.15 suggest that timing, disease spectrum, treatment, and local microbiology can influence biomarker performance.

Septic shock was associated with significantly higher CRP (71.23 ± 16.90 vs. 47.39 ± 22.73 mg/L; p=0.001) and ferritin (461.70 ± 262.83 vs. 171.73 ± 210.33 ng/mL; p=0.004). These findings indicate that both biomarkers rise with greater clinical severity, but the mortality analysis differentiates their prognostic roles: ferritin was markedly higher among non-survivors (657.20 ± 162.73 vs. 218.12 ± 225.54 ng/mL; p<0.001), whereas the CRP difference did not reach statistical significance (p=0.063). The stronger mortality signal for ferritin suggests that pronounced hyperferritinemia reflects severe immune activation, tissue injury, and physiological derangement rather than infection alone. Vani KKV et al.15 (2022) reported similar elevations in CRP and ferritin among children with septic shock. Thapar V et al.13 (2024) also showed increasing ferritin from uncomplicated sepsis to septic shock and MODS. Ghanate DD et al.17 (2023), Tonial CT et al.16 (2021), and Thapar V et al.13 (2024) similarly supported ferritin as a stronger mortality marker, with Tonial CT et al.16 reporting ferritin AUC 0.785 versus CRP AUC 0.648.

Both biomarkers correlated significantly with PRISM III scores, with a moderate positive correlation for CRP (r=0.507; p<0.001) and a slightly stronger correlation for ferritin (r=0.543; p<0.001). This demonstrates that increasing biomarker concentrations parallel worsening physiological instability captured by an established

pediatric severity score, supporting their use for risk stratification rather than isolated interpretation. The slightly stronger correlation for ferritin is consistent with its association with septic shock and mortality in this cohort. Ghanate DD et al.17 (2023) similarly demonstrated a significant correlation between ferritin and PRISM III (r=0.364; p=0.002). Thapar V et al.13 (2024) found a strong correlation between admission CRP and ferritin (r=0.734; p<0.001), with both significantly associated with sepsis severity. Tonial CT et al.16 (2021) reported significantly higher PIM2 scores among non-survivors, while combining PIM2 with ferritin, CRP, and lactate yielded excellent prognostic discrimination (AUC=0.945).

The differing behavior of CRP and ferritin is clinically relevant and supports complementary rather than interchangeable roles. CRP demonstrated stronger diagnostic discrimination for culture-positive sepsis, particularly at 48 hours, which is consistent with its rapid acute-phase response to ongoing inflammatory stimulation. Ferritin showed weaker association with culture positivity but stronger relationships with septic shock, mortality, and PRISM III scores, indicating that it more closely reflects the magnitude of systemic immune activation and tissue injury. Taken together, serial CRP is better positioned as an adjunct to microbiological diagnosis, whereas ferritin contributes more to severity assessment and prognostic stratification. Neither marker should be interpreted independently of clinical findings, cultures, treatment exposure, and validated severity scores.

Generalizability

The findings of the present study should be interpreted in the context of its prospective single-centre design and relatively small sample size of 40 children. The study population consisted of children beyond the neonatal age presenting with suspected sepsis, severe sepsis, or septic shock at a tertiary pediatric centre, and therefore the findings may not be directly generalizable to neonates, children with less severe infection, or populations managed in different healthcare settings. Differences in antimicrobial exposure, local microbiological patterns, referral practices, and disease severity may also influence culture positivity and biomarker concentrations. Nevertheless, the observed association of serial CRP with culture positivity and the association of ferritin with septic shock, mortality, and PRISM III scores provide clinically relevant evidence supporting the complementary use of these biomarkers in pediatric sepsis assessment. Larger multicentre studies involving diverse pediatric populations are required to determine standardized biomarker thresholds and validate their diagnostic and prognostic utility.

Conclusion

The present study demonstrates that CRP and serum ferritin may provide complementary information in the evaluation of pediatric sepsis. CRP, particularly when measured at 48 hours, demonstrated useful diagnostic performance for identifying culture-positive sepsis, with an AUC of 0.908, and showed significantly higher levels among culture-positive children. In contrast, ferritin demonstrated limited diagnostic utility for culture positivity but was significantly associated with septic shock and in-hospital mortality. Both CRP and ferritin showed significant positive correlations with PRISM III scores, supporting their role as markers of disease severity. Thus, CRP appears to have greater utility as an adjunctive diagnostic marker for culture-positive sepsis, whereas ferritin may be more useful for identifying severe disease and predicting adverse outcomes. Their interpretation alongside clinical assessment, microbiological findings, and established severity scores may improve the overall assessment of children with suspected sepsis.

Limitations

The study had several limitations. First, the sample size was relatively small, with only 40 children and 15 culture-positive cases, which limited statistical power and resulted in relatively wide variability in biomarker concentrations. The number of non-survivors was also limited, reducing the precision of mortality-related estimates. Second, the study was conducted at a single tertiary care centre, which may limit the generalizability of the findings to other pediatric populations and healthcare settings. Third, prior antibiotic exposure was common in both groups and may have reduced the microbiological yield, potentially affecting the relationship between biomarkers and culture positivity. Although the study evaluated important clinical variables, potential confounding factors were not assessed through multivariable regression analysis. In addition, the study did not evaluate other potentially relevant biomarkers or combine CRP and ferritin with lactate or severity scores in a predictive model. Finally, the study was conducted over a defined historical period, and changes in antimicrobial practices, microbiological epidemiology, and sepsis management over time may limit direct applicability to contemporary pediatric practice.

Recommendations

Serial CRP measurement, particularly at 48 hours, may be considered as an adjunctive investigation in children with suspected sepsis when microbiological confirmation is unavailable or delayed. Serum ferritin may be considered as an additional marker of disease severity and prognosis, particularly in children with suspected septic shock or a high risk of adverse outcomes. Neither biomarker should be used as a standalone diagnostic test, and results should be interpreted together with clinical findings, microbiological investigations, and validated severity scores such as PRISM III. Future prospective multicentre studies with larger sample sizes should evaluate standardized age-specific and clinically relevant cut-off values, assess the incremental value of combining CRP and ferritin with established severity scores and other

biomarkers, and develop validated prediction models for culture positivity, septic shock, and mortality.

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Abbreviations:

CRP, C-reactive protein; AUC, area under the curve; CI, confidence interval; D&C, dilatation and curettage; HPE, histopathological examination; NPV, negative predictive value; PPV, positive predictive value; PRISM III, Pediatric Risk of Mortality III; ROC, receiver operating characteristic; SD, standard deviation; SIS, saline infusion sonohysterography; TVS, transvaginal sonography; USG, ultrasonography.

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The study received no funding.

Conflict of interest

The authors declare no conflict of interest.

Author contributions

All authors contributed to the conception and design of the study, review of the literature, interpretation of results, preparation and revision of the manuscript. Statistical analysis and interpretation of the data were performed by the designated authors.

Data availability

Data Available

Authors Biography

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