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Original Research Article

Ferritin–albumin ratio as a prognostic marker in children with sepsis admitted to a tertiary care centre

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ABSTRACT

Pediatric sepsis remains a major cause of morbidity and mortality worldwide, particularly in low- and middle-income countries. Early risk stratification is essential for timely intervention; however, existing clinical scores and biomarkers may be limited by complexity or delayed availability. Serum ferritin, a positive acute-phase reactant, reflects systemic inflammation, while albumin, a negative acute-phase reactant, reflects disease severity and physiological reserve. The ferritin–albumin ratio (FAR) integrates these opposing responses and may serve as a simple prognostic marker in pediatric sepsis. This prospective observational study included 114 children aged 1 month to 12 years admitted with sepsis at a tertiary care hospital. Clinical features, laboratory parameters, and outcomes were recorded. Serum ferritin and albumin levels measured within the first 24 hours of admission were used to calculate the ferritin–albumin ratio. Outcomes assessed included disease severity, pediatric intensive care unit (PICU) admission, requirement of mechanical ventilation, shock, and mortality. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the prognostic performance of FAR. Children with higher FAR values had significantly higher pSOFA scores and were more likely to require PICU admission, mechanical ventilation, and develop shock. Median FAR was significantly higher among non-survivors compared to survivors. FAR demonstrated excellent discrimination for mortality on ROC analysis, with an area under the curve of 1.00 and high sensitivity and specificity at optimal cut-off values. FAR is a simple, inexpensive, and readily available prognostic marker that can reliably aid early risk stratification and outcome prediction in children with sepsis.

Keywords: Pediatric sepsis, Ferritin, Albumin, Ferritin–albumin ratio, Prognosis

INTRODUCTION

Sepsis is a life-threatening condition caused by a dysregulated host response to infection, resulting in widespread inflammation, organ dysfunction, and high mortality.[1] It remains one of the leading causes of morbidity and mortality in children worldwide, particularly in low- and middle-income countries (LMICs), where access to timely diagnosis, advanced supportive care, and intensive monitoring is often limited.[2,3] Globally, pediatric sepsis is estimated to account for over 3 million deaths annually, affecting children across all age groups.[3,4] While neonates and infants are generally more susceptible to severe infection due to immature immune systems, children of all ages remain at risk, reflecting the broad spectrum of vulnerability in pediatric populations. In India, sepsis continues to be a major contributor to pediatric intensive care unit (PICU) admissions and hospital mortality, emphasizing the urgent need for early recognition and targeted intervention.[5]

Timely identification of children at risk of severe sepsis or poor outcomes is critical for initiating appropriate supportive care, timely antimicrobial therapy, and organ support measures. Over the past few decades, several clinical scoring systems have been developed to quantify disease severity and predict outcomes in pediatric sepsis.

Notable examples include the pediatric sequential organ failure assessment (pSOFA) score, pediatric risk of mortality (PRISM) score, and pediatric logistic organ dysfunction (PELOD) score.[6,7] While these tools have demonstrated utility in stratifying disease severity, they require multiple physiological and laboratory measurements, complex calculations, and repeated assessments over time. Such requirements can pose challenges in resource-limited settings or during periods of high patient load, potentially delaying critical decisions regarding escalation of care.

Given these challenges, there is increasing interest in simple, rapid, and reliable biomarkers that can aid early risk stratification. Biomarkers are measurable indicators of biological processes, disease progression, or response to therapy, offering objective insights beyond clinical assessment alone. Among laboratory biomarkers, acute-phase reactants have emerged as important prognostic indicators in sepsis. Ferritin, a cytosolic iron-storage protein, is a well-established positive acute-phase reactant that rises in response to systemic inflammation and immune activation.[8,9] Elevated ferritin levels reflect hyperinflammation, macrophage activation, and cytokine release, phenomena commonly observed in severe infections and sepsis. In adults, hyperferritinemia has been associated with greater disease severity, multiple organ dysfunction, and increased mortality.[10,11] Pediatric studies, though fewer, suggest similar associations, highlighting ferritin's potential as an early indicator of critical illness in children.

Albumin, in contrast, is a negative acute-phase reactant.[12] Levels decline in response to systemic inflammation due to capillary leak, reduced hepatic synthesis, increased catabolism, and dilutional effects from fluid therapy. Hypoalbuminemia in sepsis has been linked to higher disease severity scores, prolonged hospital stay, and increased mortality among critically ill children.[13,14] However, both ferritin and albumin are influenced by multiple confounding factors. Ferritin may be elevated in liver disease, malignancy, chronic inflammatory disorders, or iron overload, while albumin levels can be affected by malnutrition, chronic illness, and fluid administration. These confounders reduce the reliability of each marker when used independently to predict outcomes in sepsis.

The ferritin–albumin ratio (FAR) offers a promising solution by integrating the opposing physiological responses into a single composite marker. FAR combines the inflammatory burden (represented by ferritin) and physiological reserve (represented by albumin), potentially providing a more stable and reliable prognostic indicator than either parameter alone. By reducing the influence of individual confounding factors, FAR may better reflect overall disease severity and predict adverse outcomes in pediatric sepsis. Adult studies have demonstrated the utility of FAR in predicting mortality and adverse outcomes in sepsis, critical illness, and coronavirus disease 2019 (COVID-19).[15,16] Pediatric data, however, remain limited. Most studies in children have been retrospective, included small cohorts, or focused on specific subpopulations, leaving a significant knowledge gap regarding FAR's generalizability and predictive performance in pediatric sepsis.

In view of this knowledge gap, the present study was undertaken to evaluate the prognostic value of the FAR in children with sepsis.

METHODS

This was a prospective observational study conducted in the Department of Pediatrics at VMMC and Safdarjung Hospital, New Delhi. The study was carried out over a period of 18 months, from January 2024 to June 2025.

Children aged 1 month to 12 years admitted with a diagnosis of sepsis were enrolled. Sepsis was defined according to the International Pediatric Sepsis Consensus Conference 2005 criteria, which include suspected or proven infection associated with age-adjusted systemic inflammatory response syndrome.[1]

A total of 114 children fulfilling the eligibility criteria were included. Exclusion criteria included children with chronic liver disease, chronic kidney disease, known primary or secondary immunodeficiency, malignancy, autoimmune disorders, severe acute malnutrition, prior albumin infusion, prior blood transfusion within 7 days, ongoing immunosuppressive therapy, or incomplete clinical or laboratory data, as these conditions could independently influence ferritin or albumin levels.

After enrollment, detailed demographic data (age, sex) and clinical details, including presenting symptoms, focus of infection, presence of shock, need for pediatric intensive care unit (PICU) admission, and requirement of respiratory support, were recorded. Disease severity was assessed using the pediatric pSOFA score.[6]

Laboratory investigations included routine hematological and biochemical parameters. Serum ferritin and serum albumin levels measured within the first 24 hours of hospital admission were used for analysis, as values obtained later during the course of illness may be influenced by therapeutic interventions such as fluid resuscitation, albumin administration, blood transfusions, antibiotics, and evolving organ dysfunction, potentially confounding their prognostic significance. The FAR was calculated by dividing serum ferritin (ng/ml) by serum albumin (g/dl).

All enrolled children were followed for 28 days from the time of admission or until death or discharge, whichever occurred earlier. Outcomes assessed included 28-day mortality, need for PICU admission, requirement of mechanical ventilation, and development of shock.

Prior to initiation of the study, ethical clearance was obtained from the Institutional Ethics Committee of VMMC and Safdarjung Hospital. Written informed consent was obtained from parents or legal guardians of all participants.

Collected data were entered into a structured proforma and coded in Microsoft Excel. Statistical analysis was performed using appropriate statistical software. Continuous variables were expressed as mean or median as appropriate. Comparisons between groups were made using suitable parametric or non-parametric tests. Logistic regression analysis was performed to identify independent predictors of adverse outcomes. Receiver operating characteristic (ROC) curve analysis was used to evaluate the prognostic performance of the FAR for mortality. A p value of <0.05 was considered statistically significant.[17,18]

RESULTS

A total of 114 children with sepsis were included in the study. The cohort had an equal gender distribution, with 57 (50%) males and 57 (50%) females. The majority of children required PICU admission (79.8%), mechanical ventilation (86.8%), and 65.8% developed shock. Overall mortality was 8.8% (n=10), while 91.2% (n=104) were discharged (Table 1).

Table 1: Baseline demographic characteristics, interventions, and outcomes of children with sepsis.

Variables	Frequency	Percent
Sex		
Male	57	50.0
Female	57	50.0
PICU admission		
Yes	91	79.8
No	23	20.2
Ventilation required		
Yes	99	86.8
No	15	13.2
Type of ventilation		
Invasive	78	68.4
NIV	21	18.4
None	15	13.2
Shock		
Yes	75	65.8
No	39	34.2
Final outcome		
Death	10	8.8
Discharge	104	91.2
Total	114	100.0

pSOFA: Pediatric sequential organ failure assessment; PICU: pediatric intensive care unit

The most common underlying diagnosis was pneumonia (31.6%), followed by liver abscess (12.3%) and empyema (8.8%). Other causes included septic shock, abdominal infections, urinary tract infections, meningitis, and skin and soft tissue infections (Figure 1).

There was no statistically significant difference between male and female children with respect to pSOFA score, total leukocyte count, procalcitonin, serum ferritin, serum albumin, or ferritin–albumin ratio (FAR) (p>0.05 for all), indicating comparable disease severity across genders (Table 2).

Children requiring PICU admission had significantly higher pSOFA scores, total leukocyte counts, serum ferritin levels, and FAR, along with significantly lower serum albumin levels, compared to those not requiring PICU care (p<0.001 for all). Procalcitonin levels did not differ significantly between the two groups (p=0.272) (Table 3).

Children who required mechanical ventilation had significantly higher pSOFA scores, total leukocyte counts, serum ferritin levels, and FAR, with significantly lower serum albumin levels, compared to those who did not require ventilation (p<0.05 for all). Procalcitonin levels were also significantly higher among ventilated children (p=0.014) (Table 3).

Children presenting with shock had markedly higher pSOFA scores, leukocyte counts, serum ferritin levels, and FAR, along with significantly lower serum albumin levels, compared to children without shock (p<0.001 for all). Procalcitonin levels did not show a statistically significant difference between the two groups (p=0.303) (Table 4).

Non-survivors had significantly higher pSOFA scores, total leukocyte counts, serum ferritin levels, and FAR, along with markedly lower serum albumin levels, compared to survivors (p<0.001 for all). Procalcitonin levels did not differ significantly between survivors and non-survivors (p=0.591) (Table 4).

A stepwise increase in disease severity was observed with increasing intensity of respiratory support. Children requiring invasive mechanical ventilation had the highest pSOFA scores, serum ferritin levels, and FAR, followed by those on non-invasive ventilation, while children not requiring respiratory support had the lowest values. One-way ANOVA showed statistically significant differences across groups for pSOFA score, leukocyte count, ferritin, albumin, and FAR (p<0.05). Post-hoc Tukey analysis confirmed significant inter-group differences, particularly between invasive ventilation and no respiratory support groups (Table 5).

FAR showed a strong positive correlation with pSOFA score (r=0.730, p<0.001) and serum ferritin (r=0.961, p 0.001), and a strong negative correlation with serum albumin (r=−0.586, p<0.001). FAR also correlated positively with duration of PICU stay and days of mechanical ventilation, whereas procalcitonin showed weaker and inconsistent correlations with severity

parameters (Table 6). On logistic regression analysis, pSOFA score, total leukocyte count, and procalcitonin emerged as independent predictors of mechanical ventilation requirement. Although FAR showed strong univariate associations with disease severity and outcomes, it did not retain independent significance in the multivariate model (Table 7).

Receiver operating characteristic (ROC) curve analysis demonstrated excellent prognostic performance of FAR for mortality, with an area under the curve (AUC) of 1.00 ($p<0.001$). A FAR cutoff value of 651.06 showed 100% sensitivity and 95.2% specificity, while a cutoff of 918.27 demonstrated 100% sensitivity and 100% specificity for predicting mortality (Table 8 and Figure 2).

Table 2: Gender-wise comparison of clinical and laboratory parameters.

Sex	N	Mean	Std. deviation	t-value	P value
Total pSOFA score					
Male	57	9.72	4.81	1.219	0.225
Female	57	8.58	5.17		
Total leukocyte count (/mm^3)					
Male	57	14522.77	4794.92	0.341	0.734
Female	57	14210.56	4983.03		
PCT (ng/ml)					
Male	57	6.59	3.65	0.541	0.590
Female	57	6.96	3.67		
Ferritin (ng/ml)					
Male	57	1083.19	826.39	0.670	0.504
Female	57	977.99	850.26		
Albumin (g/dl)					
Male	57	2.63	0.60	0.443	0.658
Female	57	2.68	0.62		
Ferritin-albumin ratio					
Male	57	472.46	490.55	0.276	0.783
Female	57	445.11	564.96		

Independent t-test applied as appropriate; $p<0.05$ considered statistically significant

Table 3: Comparison of clinical and laboratory parameters according to PICU admission and mechanical ventilation.

Parameters	PICU, yes (n=91), mean±SD	PICU, no (n=23), mean±SD	P value	Ventilation, yes (n=99), mean±SD	Ventilation, no (n=15), mean±SD	P value
Total pSOFA score	11.01±3.73	1.78±0.85	<0.001	10.26±4.40	1.80±0.41	<0.001
Total leukocyte count (/mm³)	15415.92± 4673.61	10215.26± 3150.70	<0.001	15096.70± 4688.90	9548.47± 2990.47	<0.001
PCT (ng/ml)	6.59±3.43	7.53±4.43	0.272	6.45±3.35	8.93±4.82	0.014
Ferritin (ng/ml)	1209.51±845.82	322.70± 99.54	<0.001	1135.77± 848.79	336.42±91.07	<0.001
Albumin (g/dl)	2.48±0.48	3.36±0.59	<0.001	2.55±0.55	3.37±0.52	<0.001
Ferritin–albumin ratio	548.79±554.54	102.71± 43.63	<0.001	512.46± 545.72	104.52±35.70	0.005

Table 4: Comparison of clinical and laboratory parameters based on presence of shock and final outcome.

Parameters	Shock, yes (n=91), mean±SD	Shock, no (n=23), mean±SD	P value	Death (n=10) mean±SD	Discharge (n=104) mean±SD	P value
Total pSOFA score	12.03±3.30	3.62±2.35	<0.001	18.50±1.43	8.25±4.24	<0.001
Total leukocyte count (/mm³)	16269.23± 4567.02	10707.90± 3007.77	<0.001	22600.10± 2268.24	13574.99± 4285.24	<0.001
PCT (ng/ml)	6.52±3.48	7.27±3.95	0.303	6.18±1.89	6.83±3.78	0.591
Ferritin (ng/ml)	1352.62±865.86	411.31± 147.82	<0.001	3190.86±819.45	822.87± 460.53	<0.001

Continued.

Parameters	Shock, yes (n=91), mean±SD	Shock, no (n=23), mean±SD	P value	Death (n=10) mean±SD	Discharge (n=104) mean±SD	P value
Albumin (g/dl)	2.44±0.49	3.06±0.61	<0.001	1.79±0.24	2.74±0.57	<0.001
Ferritin–albumin ratio	622.07±585.41	144.79± 66.17	<0.001	1873.30±777.77	322.78± 196.93	<0.001

Table 5: Disease severity and laboratory parameters according to mode of respiratory support (descriptive statistics, ANOVA and post-hoc Tukey analysis).

Parame-ters	Invasive (n=78) mean±SD	NIV (n=21) mean±SD	None (n=15) mean±SD	ANOVA F	ANOVA p	Tuke: Inv versus NIV	Tuke: Inv versus none	Tuke: NIV versus none
Total pSOFA score	11.05±4.58	7.33±1.62	1.80±0.41	38.631	<0.001	<0.001	<0.001	<0.001
Total leukocyte count (/mm³)	16186.74± 4237.58	11047.95± 4092.64	9548.47± 2990.47	25.234	<0.001	<0.001	<0.001	0.523
PCT (ng/ml)	6.13±2.81	7.63±4.78	8.93±4.82	4.685	0.011	0.202	0.016	0.524
Ferritin (ng/ml)	1260.50± 902.49	672.48± 329.22	336.42± 91.07	11.992	<0.001	0.006	<0.001	0.399
Albumin (g/dl)	2.50±0.58	2.70±0.40	3.37±0.52	16.067	<0.001	0.287	<0.001	0.001
Ferritin–albumin ratio	582.37± 592.71	252.82± 130.11	104.52± 35.70	8.029	0.001	0.022	0.003	0.652

Table 6: Correlation of ferritin–albumin ratio with severity and outcome parameters.

Correlations	PICU duration (days)	Ventilation days	Total pSOFA score	Total leukocyte count (/mm³)	PCT (ng/ml)	Ferritin (ng/ml)	Albumin (g/dl)	Ferritin-albumin ratio
Age								
Pearson correlation	-0.213*	-0.160	-0.126	-0.259**	-0.011	-0.140	0.152	-0.094
P value	0.023	0.089	0.180	0.005	0.910	0.137	0.106	0.317
PICU duration (days)								
Pearson correlation	1	0.357**	0.582**	0.328**	-0.141	0.398**	-0.449**	0.306**
P value		<0.001	<0.001	<0.001	0.134	<0.001	<0.001	0.001
Ventilation days								
Pearson correlation	0.357**	1	0.524**	0.454**	-0.190*	0.372**	-0.370**	0.302**
P value	<0.001		<0.001	<0.001	0.043	<0.001	<0.001	0.001
Total pSOFA score								
Pearson correlation	0.582**	0.524**	1	0.776**	-0.129	0.819**	-0.649**	0.730**
P value	<0.001	<0.001		<0.001	0.171	<0.001	<0.001	<0.001
Total leukocyte count (/mm3)								
Pearson correlation	0.328**	0.454**	0.776**	1	-0.074	0.712**	-0.453**	0.611**
P value	<0.001	<0.001	<0.001		0.437	<0.001	<0.001	<0.001
PCT (ng/ml)								
Pearson correlation	-0.141	-0.190*	-0.129	-0.074	1	-0.113	0.045	-0.081
P value	0.134	0.043	0.171	0.437		0.233	0.636	0.394
Ferritin (ng/ml)								

Continued.

Correlations	PICU duration (days)	Ventilation days	Total pSOFA score	Total leukocyte count (/mm^3)	PCT (ng/ml)	Ferritin (ng/ml)	Albumin (g/dl)	Ferritin-albumin ratio
Pearson correlation	0.398**	0.372**	0.819**	0.712**	-0.113	1	-0.532**	0.961**
P value	<0.001	<0.001	<0.001	<0.001	0.233		<0.001	<0.001
Albumin (g/dl)								
Pearson correlation	-0.449**	-0.370**	-0.649**	-0.453**	0.045	-0.532**	1	-0.586**
P value	<0.001	<0.001	<0.001	<0.001	0.636	<0.001		<0.001

Pearson correlation test applied. The correlation values with p value less than 0.05 is having significant relationship between the two variables. Negative correlation values show negative relationship. For e.g. age is negatively correlated with PICU duration and total leukocyte count

Table 7: Multivariate logistic regression analysis for predictors of mechanical ventilation.

Variables	B	S.E.	Wald	P value	Adjusted OR (exp B)	95% CI lower	95% CI upper
Total pSOFA score	-2.077	1.017	4.170	0.041	0.125	0.017	0.920
Total leukocyte count (/mm^3)	-0.001	0.000	4.702	0.030	0.999	0.999	1.000
PCT (ng/ml)	0.864	0.412	4.397	0.036	2.373	1.058	5.322
Ferritin (ng/ml)	0.052	0.039	1.728	0.189	1.053	0.975	1.137
Albumin (g/dl)	-4.448	3.179	1.958	0.162	0.012	0.000	5.939
Ferritin–albumin ratio	-0.145	0.121	1.432	0.231	0.865	0.682	1.097
Constant	19.748	13.237	2.226	0.136	-	-	-

Model performance - overall classification accuracy: 99.1%, sensitivity (ventilation yes): 99.0%, specificity (ventilation no): 100.0%. Requirement of mechanical ventilation was independently associated with pSOFA score, total leukocyte count, and procalcitonin levels

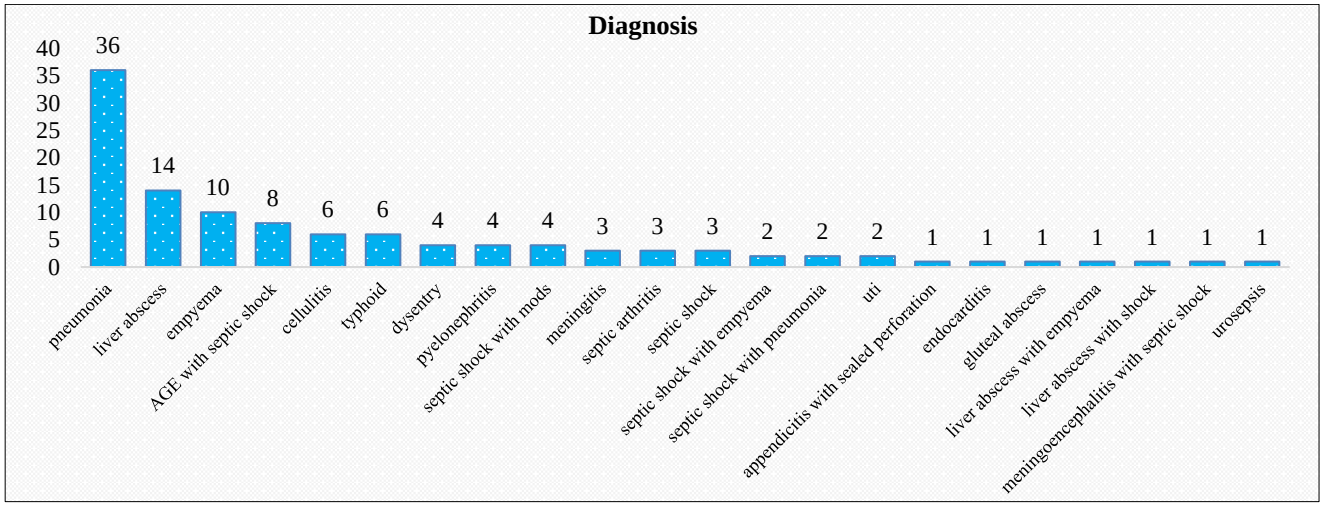

Figure 1: Distribution of underlying diagnoses among children with sepsis.

Table 8: ROC curve analysis of ferritin–albumin ratio for prediction of mortality.

Parameters	Value	
Test variable	Ferritin–albumin ratio	
Area under the curve (AUC)	1.000	
Standard error[a]	0.000	
Asymptotic significance (p value)[b]	0.000	
95% confidence interval	1.000 – 1.000	
Cut-off value (≥)	Sensitivity	Specificity
651.0675	1.000	0.952

Continued.

Parameters	Value	
710.3070	1.000	0.962
757.3945	1.000	0.971
772.5685	1.000	0.981
824.1275	1.000	0.990
918.2700	1.000	1.000

a: Under the nonparametric assumption, b: null hypothesis: true area=0.5. The cut-off value of FAR with 100% sensitivity and 95% specificity is 651.06, however, the cutoff value with 100% sensitivity and specificity is 918.27

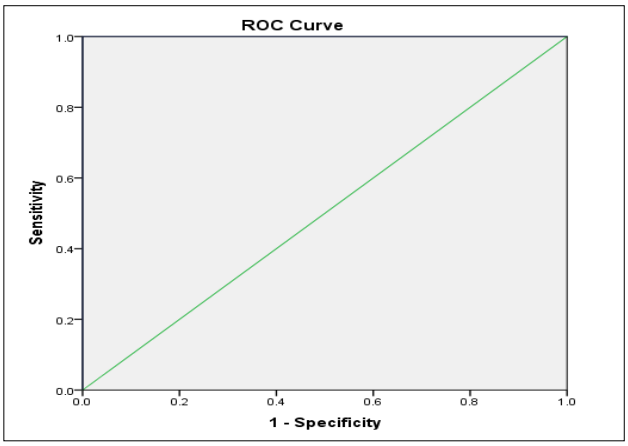

Figure 2: Receiver operating characteristic (ROC) curve of ferritin–albumin ratio for predicting mortality.

DISCUSSION

This prospective observational study demonstrates that the FAR is a strong prognostic marker in children with sepsis. Higher FAR values were significantly associated with increased disease severity, higher pSOFA scores, need for PICU admission, mechanical ventilation, development of shock, and mortality. FAR also showed excellent discriminatory ability for predicting mortality on ROC analysis, supporting its potential role in early risk stratification.

Ferritin is a positive acute-phase reactant reflecting systemic inflammation, immune activation, and macrophage dysfunction in sepsis. In the present study, serum ferritin levels were significantly higher in children with greater disease severity, those requiring PICU admission and mechanical ventilation, and in non-survivors. These findings are consistent with previous pediatric studies that have demonstrated an association between hyperferritinemia and poor outcomes in sepsis and severe inflammatory states. Elevated ferritin has also been linked to immune dysregulation and cytokine storm, further supporting its role as a severity marker in sepsis.[8,10,11]

Albumin is a negative acute-phase reactant, and hypoalbuminemia in sepsis reflects inflammation-induced capillary leak, reduced hepatic synthesis, increased catabolism, and redistribution into the interstitial compartment. In this study, lower serum albumin levels were observed in children with shock, higher disease severity, and mortality. Similar associations between hypoalbuminemia and adverse outcomes have been reported in critically ill pediatric and adult populations. These findings support the role of serum albumin as a marker of physiological reserve and disease severity.[12-14]

While ferritin and albumin individually provide prognostic information, their interpretation in isolation may be influenced by multiple confounding factors. The ferritin–albumin ratio integrates the opposing acute-phase responses of rising ferritin and falling albumin, thereby providing a composite measure of inflammatory burden and physiological reserve. In the present study, FAR showed stronger and more consistent associations with disease severity and outcomes than either marker alone. Similar findings have been reported in adult sepsis and COVID-19 studies, where higher FAR values were associated with increased severity and mortality. This suggests that FAR may offer superior prognostic performance compared to single biomarkers.[15,16,19]

The progressive increase in FAR with increasing intensity of respiratory support and its significantly higher values among non-survivors highlight its role as a marker of escalating disease severity. FAR also showed a strong correlation with pSOFA score, reinforcing its relationship with organ dysfunction. These findings suggest that FAR reflects the cumulative impact of inflammation and organ failure more comprehensively than individual laboratory parameters.

In contrast to FAR, procalcitonin showed inconsistent associations with severity and outcomes in this study. While procalcitonin levels were higher in some subgroups, they did not consistently correlate with shock or mortality. This observation is in line with previous reports suggesting that procalcitonin may be more useful for diagnosing bacterial infection than for prognostication.[20,21] Composite markers such as FAR may therefore offer greater prognostic utility in pediatric sepsis.

FAR is derived from routinely available laboratory tests and can be calculated without additional cost. When measured within the first 24 hours of admission, FAR may help identify high-risk children early, allowing timely escalation of care and closer monitoring. FAR may serve as a useful adjunct to established severity scores such as pSOFA, particularly in resource-limited settings where access to advanced biomarkers is restricted.[22,23]

The strengths of this study include its prospective design, early biomarker assessment, and comprehensive evaluation of clinically relevant outcomes in a pediatric population. Limitations include the single-center design, relatively small number of deaths, and absence of serial FAR measurements. Future multicentric studies with larger sample sizes are required to validate these findings, establish standardized cut-off values, and assess the utility of serial FAR monitoring.

CONCLUSION

In summary, the ferritin–albumin ratio integrates inflammatory burden and physiological reserve and appears to be a reliable prognostic marker in pediatric sepsis, with potential utility in early risk stratification and clinical decision-making.

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