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Association of Serum Ferritin Levels with Phoenix Score, Length of Stay and Mortality in Children with Sepsis at Dr. M Djamil Hospital Padang

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ABSTRACT

Sepsis is a systemic response that can lead to organ dysfunction and death in children. Several studies have shown that ferritin can indicate patient prognosis. This study aims to analyze the relationship between serum ferritin levels length of stay, phoenix score, and mortality in children with sepsis at Dr. M. Djamil Padang Hospital.

The research utilized a cross-sectional analysis design conducted in the PICU of M Djamil Hospital Padang from May to November 2024. The subjects of the study were children aged 1 month to 18 years with sepsis who were treated in the PICU. The subject underwent an assessment of age, gender, nutritional status, primary disease diagnosis, ferritin levels, and monitoring of mortality, phoenix score, and length of stay.

The number of research subjects is 40 subjects. The subject characteristics indicated that the majority were under one year old (42,5%), female (57,5%. Approximately 52.7% of subjects were treated for 7 days or less. The median ferritin value in the deceased group was higher (331.6) compared to the survivors, although this difference was not statistically significant (P=0.876). Statistical analysis revealed no correlation between serum ferritin levels and Phoenix score (R=-0.056, p=0.73). Also, no correlation was found between serum ferritin levels and length of stay (R=-0.398, p=0.072).

Serum ferritin levels do not significantly predict phoenix scores, length of stay, or mortality; however, the median serum ferritin level in those who died was higher than in those who survived among children with sepsis.

Keywords: *Sepsis, Serum Ferritin, Phoenix Score, Prognosis.*

INTRODUCTION

Sepsis remains one of the leading causes of childhood mortality worldwide. According to the Global Burden of Diseases, Injuries, and Risk Factor Study (GBD) in 2017, there were 48.9 million sepsis cases globally, with 11 million sepsis-related deaths, accounting for 20% of global mortality. In the United States alone, 1.7 million sepsis cases and 270,000 sepsis-related deaths occur annually. Global estimates indicate 1.2 million pediatric sepsis cases yearly, with 2.9 million cases occurring in children under 5 years. Pediatric sepsis mortality rates range from 4-50%, depending on disease severity and risk factors. In 2017, the United Nations World Health Assembly and World Health Organization (WHO) designated sepsis as a global health priority

requiring improvements in diagnosis, management, prevention, and substantial burden reduction.[1,2,3]

Sepsis is characterized as a complex pathophysiological and biochemical dysregulation resulting from endogenous responses to bacterial, viral, parasitic, or fungal infections. The Sepsis-3 definition, published by the European Society Intensive Care (ESICM) in 2016, describes sepsis as life-threatening organ dysfunction caused by dysregulated host immune response to infection.[1,4,5,] Pediatric sepsis presents with nonspecific clinical symptoms, often leading to delayed diagnosis and treatment, potentially resulting in increased severity and mortality. Early identification and accurate diagnosis are crucial in managing sepsis to minimize morbidity and mortality rates.[4,5]

While biomarkers such as procalcitonin and C-reactive protein (CRP) are commonly used to evaluate bacterial infections causing sepsis, no single biomarker currently offers both high sensitivity and specificity for diagnosis or prognostic assessment. The Pediatric Logistic Organ Dysfunction (PELOD-2) score can measure Multi Organ Dysfunction Syndrome (MODS) severity and serve as a clinical outcome marker in the Pediatric Intensive Care Unit (PICU). In 2016, IDAI established sepsis severity degrees, and in 2024, The International Pediatric Sepsis Definition Task Force introduced The Phoenix Sepsis Criteria.

Ferritin, an extensively studied biomarker for sepsis prognosis, is readily available in routine laboratories at relatively low costs, making it particularly suitable for developing countries. Garcia et al. first described the association between ferritin and poor prognosis in children with septic shock. Sarkarm et al. demonstrated good mortality prediction at ferritin levels above 2375 ng/ml, while Gunasekaran et al. showed a correlation between high serum ferritin levels and extended ICU stays.[6,7,8]

This theoretical framework underlies the researcher's analysis of correlations between serum ferritin biomarkers, sepsis scores, length of stay, and their relationship as mortality predictors. Notably, RSUP Dr. M. Djamil has not yet conducted research on the relationship between serum ferritin levels and outcomes in children with sepsis.

MATERIALS & METHODS

A prospective cross-sectional study was conducted to evaluate the correlation between serum ferritin levels with length of stay, Phoenix scores, and mortality in pediatric sepsis patients at Dr. M. Djamil Hospital, Padang, from May 2024 to November 2024. The research was carried out at the Emergency Department, Pediatric Intensive Care Unit, Clinical Pathology Laboratory of Dr. M. Djamil Hospital, and the Biomedical Laboratory of Andalas University Faculty of Medicine. From 48 children with sepsis, 40 subjects met the inclusion criteria and had no exclusion criteria. The study population comprised children aged 1 month to 18 years with clinical sepsis who presented to the Emergency Department and were admitted to the PICU.

The variables were categorized into independent variable (serum ferritin levels) and dependent variables (Phoenix score, length of hospital stay, and mortality). This study was conducted after obtaining informed consent from the children's parents in accordance with the study ethics code established by the Ethics Committee of the Andalas University Faculty of Medicine.

STATISTICAL ANALYSIS

Data were recorded and processed using computerized methods. Univariate analysis was performed to examine sample characteristics (gender, age, nutritional status, underlying diseases, length of stay, and mortality), presented as frequencies and percentages. Bivariate analysis employed Mann-Whitney and Spearman correlation tests to assess relationships between ferritin levels and Phoenix scores, length of stay, and mortality. Statistical significance was set at $p < 0.05$. Data analysis was conducted using SPSS version 26 software. Correlation

strengths were interpreted as very weak (0-0.25), moderate (0.25-0.5), strong (0.5-0.75), or very strong (0.75-0.99).

RESULT

Most subjects were in the age range of less than 1 year (42.5%). There were more female than male subjects with a percentage of 57.5% and 42.5%. Most subjects were well-nourished (40%). Based on the length of stay, subjects who were treated for ≤ 7 days were the largest group, namely 55%. Airway infection was the most common condition experienced by the study subjects (75%).

Table 1. Characteristics of Study Subjects and Median Values of Serum Ferritin Levels

Category	n (%) n: 40	Ferritin (ng/mL) Median
Age		
<1 year	17(42.5)	478,592
1-5 years	8(20)	136,753
>5-10 years	6(15)	331,578
>10-18 years	9(22.5)	225,794
Gender		
Male	17(42.5)	225,794
Female	23(57.5)	250,866
Nutritional Status		
Overweight	1(2.5)	45,912
Well-nourished	16(40)	582,908
Malnourished	10(25)	189,796
Severely Malnourished	13(32.5)	164,092
Length of Stay (days)		
≤7 days	22(55)	417,908
>7 days	18(45)	172,144
Primary Disease Diagnosis		
Respiratory Tract Infection	30(75)	301,861
Digestive Tract Infection	3(7.5)	478,592
Central Nervous System Infection	8(17,5)	164,090
Mortality		
Yes	14(35)	331,562
No	26(65)	244,410

In this study, to determine whether serum ferritin levels were normally distributed, a Shapiro-Wilk test was performed (sample size < 50). The results obtained showed p< 0.05, indicating non-normal distribution, thus using median values. Patients with good nutrition had the highest median ferritin value (582.908 ng/mL). Patients hospitalized for less than or equal to 7 days had higher median ferritin values (417.908 ng/mL) compared to those hospitalized for more than 7 days (172.144 ng/mL). Regarding primary disease diagnosis, patients with gastrointestinal infections showed the highest median ferritin value (478.592 ng/mL) compared to respiratory infections (301.861 ng/mL) and central nervous system infections (164.090 ng/mL). The median ferritin level in the group of patients who died (331.562 ng/mL) was higher compared to the group of patients who survived (244.410 ng/mL).

The Saphiro-Wilk test was used for serum ferritin levels and Phoenix scores with the impression that they were not normally distributed, so the Spearman test was performed to determine the correlation between serum ferritin levels and Phoenix scores. Results can be seen in the following table.

Statistical analysis using Kruskal-Wallis test showed no significant correlation between nutritional status and SDQ scores (p>0.05 for all domains). Similarly, Mann-Whitney U tests revealed no significant associations between age groups (<11 years vs 11-18

years) and SDQ scores (p>0.05), nor between gender and SDQ scores (p>0.05 for all domains).

Table 2. Correlation of Serum Ferritin Levels with Phoenix Score

Variable	R	p-value
Ferritin	-0.056	0.73

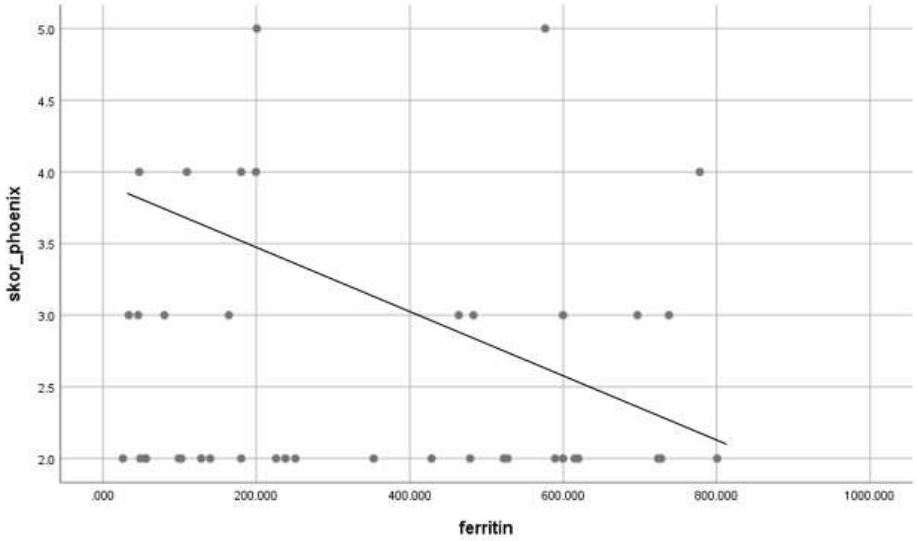

Figure 1. Scatter Plot of Ferritin with Phoenix score

In table 2 and figure 1, there was no statistical correlation between serum ferritin levels and phoenix score (p-value > 0.05).

The correlation of ferritin levels with length of stay can be seen in the following table.

Table 3. Correlation of Ferritin Levels with Length of Stay

Variable	R	p-value
Ferritin	-0.288	0.072

Table 3 and figure 2 show that there is no statistical correlation between serum ferritin levels and length of hospitalization with a p-value of 0.072.

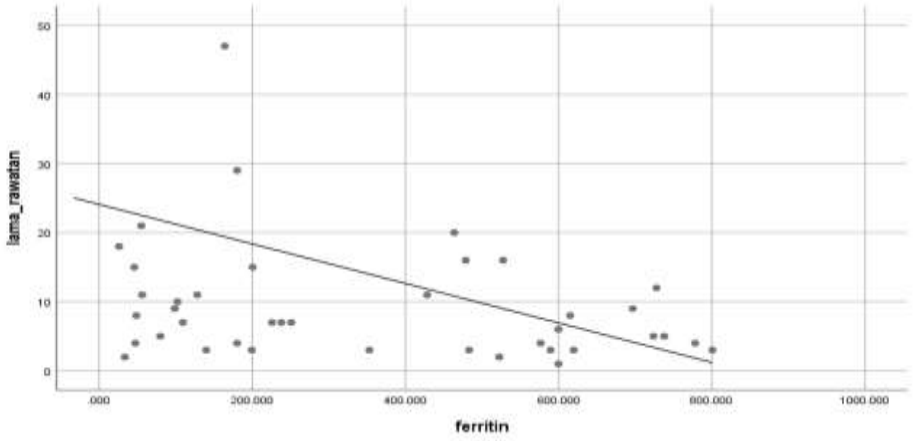

Figure 2. Scatter Plot of Ferritin with length of stay

The Shapiro-Wilk test was used for serum ferritin levels with mortality, showing a non-normal distribution, therefore the Mann-Whitney test was performed to determine the relationship between serum ferritin levels and mortality.

Table 4. Relationship between Serum Ferritin Levels and Mortality

Variable	Mortality		p-value
	Yes	No	
Ferritin(ng/mL) Median (Min-Max)	331,562 (33,65-778,07)	244,410 (26,09-800,67)	0.876

In table 4, the median serum ferritin level of deceased patients (331.562 ng/mL) was higher than that of living patients (244.410 ng/mL). The test results showed a p>0.05 value, which means that the difference in serum ferritin levels between the deceased and living patient groups was not statistically significant.

The graph in figure 3 explains how well ferritin values can be used to predict child mortality. The Receiver Operating Characteristic (ROC) value obtained is 0.515, indicating that the ability of serum ferritin levels to predict mortality in the population studied is not good enough. This value is almost equivalent to random guessing (50%), so ferritin cannot be used as an accurate predictor to predict mortality in this study.

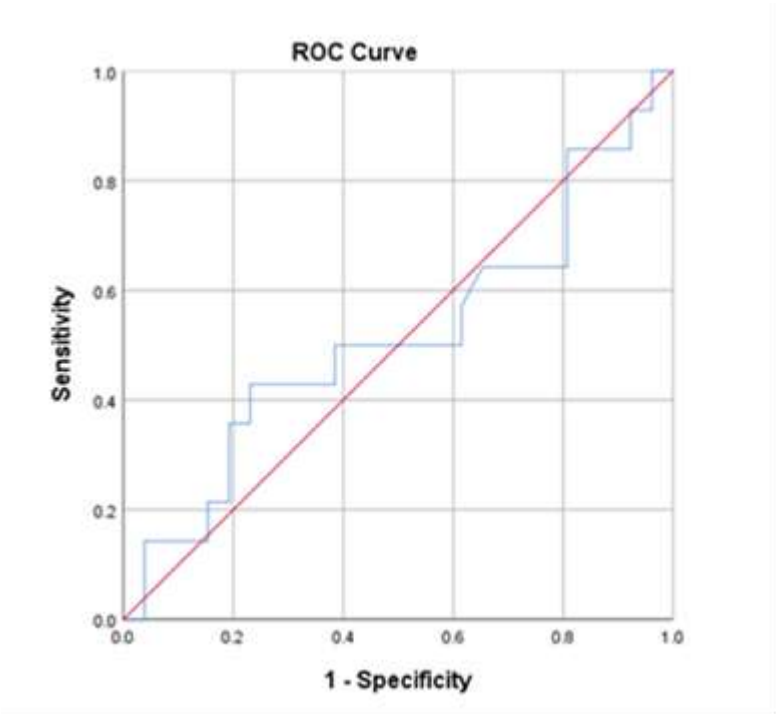

Figure 3. ROC Curve of Serum Ferritin Levels with Mortality

DISCUSSION

The majority of subjects were infants under 1 year old, consistent with findings by Fleischmann-Struzek et al., who identified neonates and infants as the highest-risk group for sepsis due to immature immune systems.[9] This vulnerability is exacerbated by comorbidities such as congenital abnormalities, prematurity, or malnutrition.[10,11] For instance, Angus et al. reported no significant sex-based differences in sepsis risk among prepubertal children, aligning with this study's female-male ratio.[12] However, Ghuman et al. observed higher post-pubertal male

mortality, potentially linked to testosterone's immunosuppressive effects.[13] Nutritional status significantly influenced outcomes. While 97.7% of subjects were well-nourished, malnutrition (including obesity) impaired immune responses, as demonstrated by Rainingsih et al.[14] who found that 90% of sepsis-related deaths occurred in malnourished children. This aligns with the role of malnutrition in secondary immunodeficiency and gut barrier dysfunction.[15,16] Respiratory infections, particularly pneumonia, were the primary sepsis source, corroborating Weiss et al., who identified pneumonia as the most common etiology due to pathogen inhalation/aspiration.

Well-nourished subjects had higher median ferritin levels than obese/undernourished subjects, contrasting with Cheung et al. who linked obesity to elevated ferritin via macrophage activation. Ferritin elevation in sepsis correlated with proinflammatory cytokines (e.g., IL-6, TNF-α), reflecting its role as an acute-phase reactant.[17,18] Subjects hospitalized ≤7 days had higher ferritin (482,960 ng/mL vs. 128,147 ng/mL), likely due to rapid mortality in severe cases, as noted by Rainingsih et al.[14] Non-survivors exhibited significantly higher ferritin (331,562 ng/mL vs. 231,874 ng/mL), consistent with Sucianto et al. who reported 75% mortality in patients with ferritin >1,000 ng/mL.[19] Sharma et al. further validated ferritin >1,000 ng/mL as a mortality predictor (sensitivity: 58.9%, specificity: 75.3%).[20]

A weak negative correlation ($p > 0.05$) was observed between ferritin and Phoenix scores, conflicting with studies where ferritin strongly predicted poor outcomes. Shaikh et al. linked levels >300 ng/mL to worse outcomes. This discrepancy suggests confounding factors (e.g., comorbidities, treatment timing) require further exploration.[21]

A moderate negative correlation ($R = -0.288$, $p > 0.05$) indicated higher ferritin levels associated with shorter stays, contradicting studies linking hyperferritinemia to prolonged hospitalization.[22] Garcia et al. noted 23% vs. 58% mortality for ferritin <200 µg/L and >500 µg/L, respectively, while Bennett et al. highlighted escalating mortality risks with ferritin ≥1,000–3,000 µg/L. Age, organ failure, and nutritional status may confound this relationship.[23]

Non-survivors had higher ferritin levels, though statistically insignificant. A ROC curve (AUC = 0.515) indicated poor predictive accuracy, conflicting with Qian et al. who emphasized dynamic ferritin monitoring. Tonial et al. associated 10-fold ferritin elevation with mortality, underscoring the need for serial measurements.[24]

CONCLUSION

The study revealed that the majority of subjects were infants under 1 year old, predominantly female, with good nutritional status, and a median hospital stay of ≤7 days. Respiratory tract infections were the most common sepsis source. The highest serum ferritin levels were observed in well-nourished subjects, those with respiratory infections, and those hospitalized for ≤7 days. However, serum ferritin levels showed no significant correlation with Phoenix scores or length of hospitalization. Although non-survivors exhibited higher median serum ferritin levels compared to survivors, no statistically significant association was found between ferritin and mortality in pediatric sepsis. To enhance clinical management, routine monitoring of serum ferritin levels in pediatric sepsis patients is recommended to evaluate its potential impact on hospitalization outcomes. Future studies should incorporate additional variables, such as comorbidities, treatment protocols, and inflammatory markers, to better understand the complex relationships between serum ferritin, Phoenix scores, length of stay, and mortality. This approach could refine prognostic models and inform targeted interventions for high-risk populations.

Declaration by Authors

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Conflict of Interest: The authors declare no conflict of interest.

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