Prediction of Poor Outcomes for Septic Children According to Ferritin Levels in a Middle-Income Setting*

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Objectives: To evaluate serum ferritin measured within 48 hours of admission as a prognostic marker and examine the association with unfavorable outcomes in a population of pediatric patients with sepsis and high prevalence of iron deficiency anemia in which this biomarker is routinely measured.

Design: Retrospective cohort study.

Setting: PICU of a tertiary care teaching hospital in a middle-income country in South America.

Patients: All patients 6 months to 18 years old ($n = 350$) admitted with a diagnosis of sepsis, suspected or proven, were eligible for inclusion. Exclusion criteria were length of PICU stay less than 8 hours and inherited or acquired disorder of iron metabolism that could interfere with serum ferritin levels.

Interventions: None.

Measurements and Main Results: Three-hundred twelve patients had their ferritin levels measured within 48 hours, and only 38 did not. The prevalence of iron deficiency anemia (hemoglobin < 11 g/dL and mean corpuscular volume < 80 fl was 40.3%. The median of the highest serum ferritin level within 48 hours was 150.5 ng/mL (interquartile range, 82.25–362 ng/mL), being associated with mortality ($p < 0.001$; Exp(B), 5.170; 95% CI, 2.619–10.205). A 10-fold increase in ferritin level was associated with a five-fold increase in mortality. There was a monotonic increase in mortality with increasing ferritin levels ($p < 0.05$). Regarding the discriminatory power of ferritin for mortality, the area under the receiver operating characteristic curve was 0.787 (95% CI, 0.737–0.83; $p < 0.0001$).

Conclusions: Serum ferritin at lower thresholds predicts mortality in children with sepsis admitted to the ICU in a middle-income country with high prevalence of iron deficiency anemia. (*Pediatr Crit Care Med* 2020; 21:e259–e266)

Key Words: ferritins; hemophagocytic lymphohistiocytosis; mortality; multiple organ dysfunction; pediatric intensive care units; sepsis

Serum ferritin, in addition to representing body iron stores, is an acute-phase protein that increases in the presence of circulating inflammatory cytokines (1, 2). When these mediators are stimulated, iron stored in the form of ferritin tends to increase while iron stored in the reticuloendothelial system tends to decrease (3). Ferritin is believed to be a serum marker of cellular damage and does not appear to produce deleterious effects (2). Garcia et al (4) described for the first time, the association of this biomarker with unfavorable outcomes in children with septic shock in 2007. Since then, interest in ferritin has grown in pediatric intensive care (5–8).

Sepsis is a life-threatening condition that remains a leading cause of death in children worldwide (9, 10). Prognostic markers in sepsis are useful for identifying patients at increased risk of death, selecting which therapies are most appropriate in certain situations and guiding the response to treatment over time (11). The use of ferritin in low- and middle-resource settings is facilitated by its low cost and wide availability in most centers. However, ferritin has never been evaluated as a prognostic marker in a study where it is routinely ordered in a group of patients with a high prevalence of iron deficiency anemia. The

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prevalence of iron deficiency anemia among children in Brazil is believed to be high, reaching up to 58% (12, 13). Studies in high-income countries, where iron deficiency anemia is less prevalent, have shown an association of high ferritin levels with mortality (> 1,000 ng/mL) (5, 6). We believe that in low- and middle-income countries, this association should occur at lower levels.

The purpose of the present study was to evaluate ferritin as a prognostic marker in a relevant sample of pediatric patients with sepsis, in which iron deficiency anemia was highly prevalent, and to examine associations with unfavorable outcomes.

MATERIALS AND METHODS

This retrospective cohort study was conducted in the PICU of a tertiary care teaching hospital (Hospital São Lucas) affiliated with Pontifícia Universidade Católica do Rio Grande do Sul, Brazil, after attaining Institutional Review Board approval, under Ethics Approval Certificate number 04621518.0.0000.5336. Although this is a private hospital, access to care is also provided through the Brazilian Unified Health System, which is a government-funded universal healthcare system that includes the public provision of core physician and hospital services without copayments or patient charges. The hospital has a pediatric emergency department and a PICU with 12 beds for medical and surgical patients 1 month to 18 years old, with a mean of 400 admissions per year. It also has a medical residency program in Pediatrics and Pediatric Intensive Care Medicine, in addition to master's and doctoral programs in Pediatrics.

Eligible participants were all patients 6 months to 18 years old admitted to the PICU between July 2013 and January 2017 with a diagnosis of sepsis, suspected or proven, based on the 2005 criteria of Goldstein et al (14), made 24 hours prior or following admission to the PICU. Accordingly, sepsis was defined by the presence of 2 or more criteria for systemic inflammatory response syndrome (body temperature > 38.5°C or < 36°C, tachycardia, tachypnea, leukocytosis, or leukopenia according to age group), one of which had to be abnormal temperature or leukocyte count, in addition to suspected or proven infection. Severe sepsis was defined as sepsis plus cardiovascular organ dysfunction or acute respiratory distress syndrome or two or more other organ dysfunctions. Septic shock was defined as sepsis and cardiovascular organ dysfunction. Exclusion criteria were length of PICU stay less than 8 hours and inherited or acquired disorder of iron metabolism that could interfere with serum ferritin levels. We only included children older than 6 months because after this age serum ferritin is less influenced by maternal stores and the switch from fetal to adult hemoglobin. As a source of data for the diagnosis of sepsis, we reviewed all electronic medical records of patients admitted to PICU during the time of the study, gathering clinical, laboratory, and vital signs information.

Patients who had serum ferritin levels measured within 48 hours of admission to the PICU were considered for analysis. Where patients had more than one measurement, the one with the highest level was included in the analysis. This approach was adopted because ferritin may rise during the first 48 hours after the inflammatory insult. Since the publication of our first study in 2007, we have tried to implement the measurement of this biomarker as a prognostic marker in patients with sepsis as a routine practice in our service (4).

The following data were collected for all patients included in the study: demographic characteristics—age, weight, body mass index *z* score, Pediatric Index of Mortality (PIM) 2 score (15), sex, and medical or surgical admission; laboratory findings—complete blood count, lactate, and serum ferritin; and clinical characteristics—definition of severe sepsis and septic shock, culture identification of etiologic agent, complex chronic condition according to Feudtner et al (16), PICU readmission within 72 hours of discharge, presence of reinfection (defined as a new infection acquired by the patient during hospital stay), presence of a complicated course, need for and duration of invasive or mechanical ventilation (MV), need for and duration of vasoactive drug use, length of PICU stay, length of hospital stay, and death within the current PICU admission. The criteria used to define probable iron deficiency anemia were hemoglobin less than 11 g/dL and mean corpuscular volume less than 80 fl. Serum ferritin was not used as a criterion because septic patients are assumed to be in an inflammatory state and elevated levels do not distinguish those with iron deficiency. Duration of MV and vasoactive drug use was calculated based on ventilator-free days and vasoactive drug-free days, respectively. For both, the following formula was used: (28–duration of MV or duration of vasoactive drug use in days). Patients who died or with duration of MV greater than 28 days were assigned a value of 0 in this calculation. Patients who did not require MV or vasoactive drug use were assigned a value of 28. A complicated course was defined as need for MV, vasoactive drugs or presence of two organ dysfunctions on day 7 of admission (based on the 2005 criteria of Goldstein et al [14]), need for renal replacement therapy at any time during PICU stay or death.

For statistical analysis, categorical variables were expressed as *n* (%), while continuous variables were expressed as mean (SD) or median (interquartile range [IQR]) depending on whether data were parametric or nonparametric, respectively. Categorical variables were analyzed by the chi-square test or Fisher exact test. Student *t* test was used for parametric and the Mann-Whitney *U* test for nonparametric continuous variables. Binary logistic regression was used to assess serum ferritin as a risk factor for mortality. The maximum serum ferritin level measured within 48 hours of admission was log-transformed before analysis. To assess sensitivity and specificity, the area under the receiver operating characteristic (ROC) curve was used. Cumulative survival was estimated using the Kaplan-Meier method. Patients who did not have serum ferritin levels measured within 48 hours of PICU admission were compared to the other patients in terms of demographic characteristics and outcomes. Clinical outcomes and the PIM 2 score were compared between serum ferritin quartiles. Second to this analysis, for borderline *p* values for significance (between 0.05 and 0.1), a second analysis was performed to verify if any quartile differed from the others 3. Data analysis was performed in SPSS, Version 17.0 (IBM SPSS Statistic, Armonk, NY).

RESULTS

Of 1,407 patients admitted during the study period, 350 patients older than 6 months with sepsis were eligible for inclusion. Of these, 312 had at least one ferritin level measurement within 48 hours of PICU admission. Thirty-eight patients were excluded from the final serum ferritin analysis because they did not have this biomarker measured. **Table 1** shows the comparison of the demographic and clinical characteristics of patients with and without ferritin measured within 48 hours of admission.

Four main reasons led to the nonmeasurement of serum ferritin in the 38 exclusions: 1) 23 (60.6%): it was decided that only C-reactive protein would be measured as an inflammatory biomarker; 2) 13 (34.2%): it was decided not to measure inflammatory biomarkers; 3) 1 (2.6%): laboratory error; and 4) 1 (2.6%): death within 24 hours of admission.

Regarding the population studied, the median serum ferritin level was 150.5 ng/mL (IQR, 82.25–362 ng/mL). As a prognostic marker for death, higher serum ferritin level within 48 hours of admission was associated with mortality ($p < 0.001$; Exp(B), 5.170; 95% CI, 2.619–10.205). A 10-fold increase in ferritin level was associated with a five-fold increase in mortality. There was a monotonic increase in mortality with increasing ferritin levels ($p < 0.05$). Regarding the discriminatory power of ferritin for mortality, the area under the ROC curve was 0.787 (95% CI, 0.737–0.830; $p < 0.0001$; **Supplemental Fig. 1**, Supplemental Digital Content 1, http://links.lww.com/PCC/B225; **legend**, Supplemental Digital Content 4, http://links.lww.com/PCC/B228). **Supplemental Table 1** (Supplemental Digital Content 2, http://links.lww.com/PCC/B226) shows the different serum ferritin levels with their sensitivity and specificity for mortality.

Figure 1 shows the Kaplan-Meier survival curve for serum ferritin, and **Figure 2** consists of a box plot demonstrating in ascending order the ferritin levels quartiles found in the study cohort.

With regard to the clinical outcomes observed, only mortality and vasoactive drug-free days differed between groups when divided according to ferritin quartiles ($p < 0.001$ and $p = 0.015$, respectively). These results are shown in **Table 2**. For the three outcomes (ventilator-free days, need for vasoactive drugs during hospitalization, complicated course on D7 of admission) and PIM 2 score with borderline p values in the analysis of ferritin quartiles, we conducted a secondary analysis comparing the fourth ferritin quartile with the other three quartiles combined. **Supplemental Table 2** (Supplemental Digital Content 3, http://links.lww.com/PCC/B227) shows that these comparisons resulted in significant p values for all three outcomes and PIM 2 score ($p = 0.030$; $p = 0.013$; $p = 0.008$; and $p = 0.013$, respectively). **Table 3** shows clinical characteristics, demographics, and outcomes of survivors and nonsurvivors in the study cohort.

DISCUSSION

We demonstrated a monotonic increase in mortality as serum ferritin levels increased in pediatric patients with sepsis. The median serum ferritin level found in septic patients was lower than that reported in previous studies. In addition, there was an increase in mortality even at ferritin levels less than 500 ng/mL, indicating an interesting use of this test as a prognostic marker even in patients who do not meet the criteria for secondary hemophagocytic syndrome.

Since the late 1980s, serum ferritin has been studied in the intensive care setting (3). It is an acute-phase protein that increases during inflammation when there is the presence of circulating inflammatory cytokines such as interleukin-1 and tumor necrosis factor (1). Because ferritin is an inexpensive biomarker, has a well-established diagnostic application in iron deficiency anemia and is widely available in low- and middle-income countries, its use has aroused interest in low-resource settings. Garcia et al (4) described in 2007 the independent association of serum ferritin with mortality in pediatric patients with sepsis in Brazil. In that pioneering study of 36 patients, the cutoff value of 500 ng/mL was chosen based on adult studies and was probably influenced by the ferritin level that served as a diagnostic criterion in hemophagocytic syndrome. Other studies have focused on investigating ferritin in this syndrome and in other inflammatory phenotypes associated with sepsis, such as macrophage activation syndrome, also using cutoff values as high as 1,980 ng/mL (6, 17). Although Horvat et al (18) have found an association between ferritin levels and mortality using lower cutoff points (373 ng/mL), they evaluated hospitalized children in general and not only those with sepsis. That is, no study involving a large number of pediatric patients with sepsis has adequately evaluated whether there is a difference in mortality in patients with lower serum ferritin levels.

Our finding of low ferritin levels (median, 150.5 ng/mL; IQR, 82.25–362 ng/mL) for this population with sepsis was not surprising. Ghosh et al (19) have already pointed to the need for new cutoff points for hyperferritinemic sepsis in settings with high prevalence of iron deficiency anemia, supporting the need for larger studies in settings where this biomarker is collected as part of routine clinical care. However, we believe that this confirmation is not our major finding, but rather the evidence of a linear increase in mortality as serum ferritin increases at levels traditionally considered low. Carcillo et al (6) themselves have not demonstrated this linearity. This progressive and relevant increase in mortality at low serum ferritin levels points toward two important aspects. First, ferritin may have or play some negative role even at low serum concentrations, and second, we urgently need to redefine our cutoff points for hyperferritinemic sepsis and its inflammatory phenotypes, including secondary hemophagocytic syndrome, at least in settings with high prevalence of iron deficiency anemia. We chose not to define a cutoff point because it is our understanding that no fixed value can determine this negative effect, but rather a progressive increase as ferritin levels increase.

We were unable to demonstrate a worsening of all clinical outcomes, except for mortality and vasoactive drug-free days, with increasing serum ferritin levels in our cohort. Length of PICU and hospital stay, need for vasoactive drugs and MV, number of organ dysfunctions, presence of a complicated

TABLE 1. Clinical and Demographic Characteristics of Patients With and Without Serum Ferritin Measured Within 48 Hours of Admission to the PICU

Characteristic	With Ferritin Measured (*n* = 312)	Without Ferritin Measured (*n* = 38)	*p*
Age, mo, median (IQR)	24.5 (11.6–67.4)	30.3 (12.7–67.8)	0.988
Weight, g, median (IQR)	12,000 (8,532–19,000)	12,150 (78,875–18,000)	0.640
Body mass index *z* score, median (IQR)	−0.11 (−1.32 to 1.10)	−0.23 (−1.19 to 1.19)	0.864
Male, *n* (%)	171 (54.8)	25 (65.8)	0.198
Age < 24 mo, *n* (%)	155 (49.7)	16 (42.1)	0.378
Medical patient, *n* (%)	274 (87.8)	36 (94.7)	0.206
Severe sepsis and septic shock as defined by Goldstein et al (14), *n* (%)	37 (11.9) 134 (42.9)	3 (7.9) 12 (31.6)	0.200
Etiologic agent identified, *n* (%)	168 (53.8)	24 (63.2)	0.276
Presence of complex chronic condition, *n* (%)	131 (42.0)	27 (71.1)	0.001[a]
Reinfection, *n* (%)	18 (5.8)	8 (21.1)	0.001[a]
Readmission within 72 hr, *n* (%)	8 (2.6)	3 (7.9)	0.106
Anemia hemoglobin < 11 g/dL, *n* (%)	218[b] (70.3)	21[c] (56.8)	0.092
Probable iron deficiency anemia (anemia hemoglobin < 11 g/dL and mean corpuscular volume < 80 fl), *n* (%)	125[b] (40.3)	11[c] (29.7)	0.212
Need for MV, *n* (%)	187 (59.9%)	25 (65.8)	0.486
Duration of MV, d, median (IQR)	7 (4–11)	7.5 (3.5–12.0)	0.763
Need for vasoactive drugs, *n* (%)	154 (49.4)	12 (31.6)	0.038[a]
Duration of vasoactive drug use, d, median (IQR)	4 (2–8)	6.5 (3–13.7)	0.224
Presence of a complicated course, *n* (%)	128 (41.0)	17 (44.7)	0.661
Pediatric Index of Mortality 2, median (IQR)	0.021 (0.010–0.074)	0.054 (0.007–0.149)	0.157
Length of PICU stay, d, median (IQR)	7 (3–13)	8 (3.75–14.25)	0.670
Length of hospital stay, d, median (IQR)	15 (9–24.7)	14 (9.7–30)	0.771
Death, *n* (%)	27 (8.7)	7 (18.4)	0.055

IQR = interquartile range, MV = mechanical ventilation.

[a]Pearson χ^2 test.

[b]Two patients in this group had no complete blood count collected.

[c]One patient in this group had no complete blood count collected.

course did not differ between ferritin quartiles. Because ferritin is an acute-phase protein that increases during inflammation, it would be expected that patients with higher ferritin levels would have more organ dysfunctions and longer duration of MV or vasoactive drug use (18). In a secondary analysis, after grouping the first three ferritin quartiles and comparing this new group to the fourth ferritin quartile, we found differences in three additional clinical outcomes besides PIM 2. This result demonstrates that differences between some clinical outcomes may appear only with higher values of elevated serum ferritin,

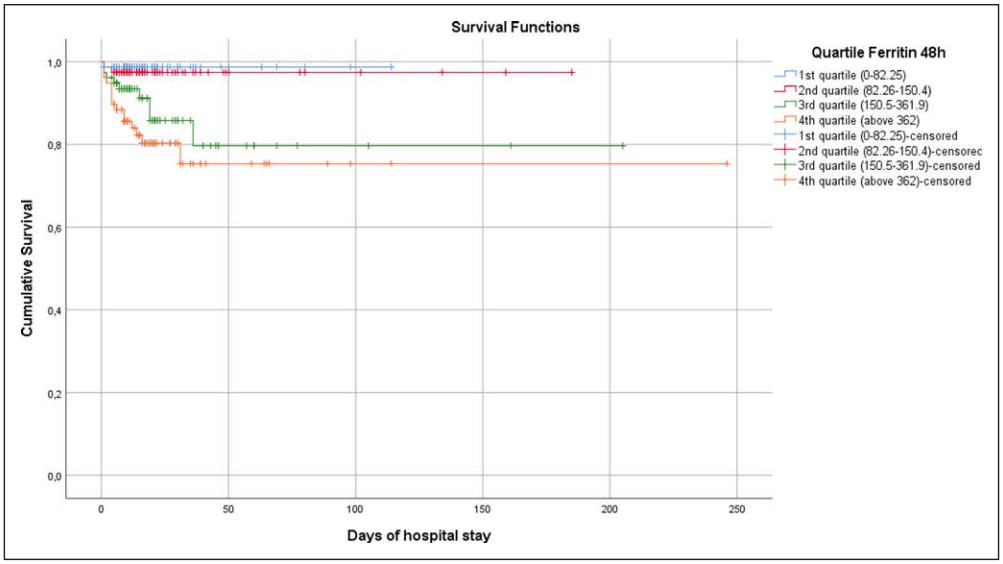

Figure 1. Kaplan-Meier survival curve. A marked increase in mortality was observed in the third and fourth quartiles. Censoring represents the time of hospital discharge.

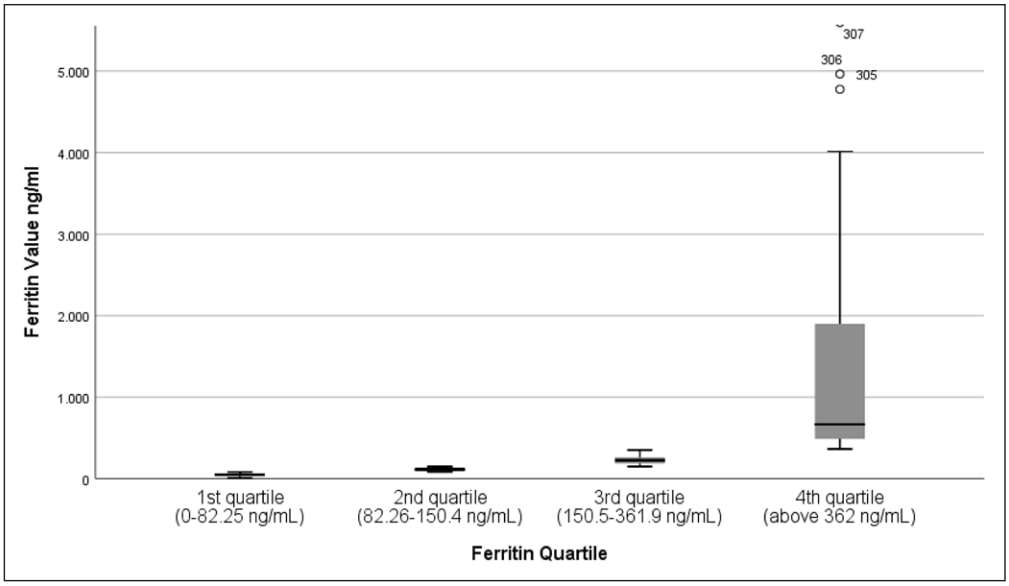

Figure 2. *Box plot* showing in ascending order the ferritin levels quartiles found in the study cohort.

shown here in the last quartile. In a small cohort study published in 2017, we found an association of higher ferritin levels with ventilator-free days, maximum vasoactive drug score, and PIM 2 score (7). These findings confirm that patients with higher ferritin levels are in more severe condition at admission and have less favorable outcomes during PICU stay.

The major practical implication of our study is the confirmation of ferritin as a good prognostic marker in pediatric patients with sepsis. To this end, we used a large population in which this biomarker is routinely measured. Serum ferritin is an inexpensive test available in most low- and middle-income countries and widely used for other purposes. Furthermore, unlike other markers that are elevated only in bacterial diseases, it can also be used as a prognostic marker in viral sepsis (20). We believe that ferritin may be incorporated in the near future into prognostic scores for mortality or even be used more frequently for this purpose.

When interpreting the results of the present analysis, it is important to keep in mind the high prevalence of iron deficiency anemia in our cohort when compared to those of similar studies in high-income countries. We found a prevalence of probable iron deficiency anemia (40.3%) consistent with the Brazilian population. The low ferritin level found here supports previous findings in countries where iron deficiency anemia is prevalent (19). Conversely, Horvat et al (18) found an association between low ferritin levels and mortality in all-cause admission at a U.S. quaternary care hospital. The prevalence of iron deficiency anemia in high-income countries tends to be low; however, such variable was not evaluated in that study. This article shows that, regardless of the prevalence of iron deficiency anemia, we need to review our criteria for hyperferritinemic sepsis.

Our study has some limitations that need to be addressed. First, we studied ferritin in patients older than 6 months. As explained earlier, we believe that after this age, ferritin levels would be less influenced by maternal stores. Second, we assessed ferritin alone; no other biomarkers were assessed. Third, 10.8% of patients admitted for sepsis who were older than 6 months did not have ferritin measured within 48 hours of admission. Presence of complex chronic conditions, reinfection rates and need for vasoactive drugs were different in this group, although mortality was similar. Perhaps the fact that these are chronic patients who developed sepsis during hospitalization has aroused less interest in measuring serum ferritin. Fourth, we did not perform a separate analysis of patients with suspected hemophagocytic syndrome. The reason for this was the difficulty in confirming the diagnosis by biopsy or CD25 measurement in our service. Fifth, we studied ferritin within 48 hours of admission, because the objective was to evaluate it as a useful prognostic marker upon patient arrival in the

TABLE 2. Comparison of Clinical Outcomes, Presence of Anemia, Complex Chronic Conditions, and Pediatric Index of Mortality 2 Scores Between Serum Ferritin Quartiles

Outcome	1st Quartile (0–82.25 ng/mL)	2nd Quartile (82.26–150.4 ng/mL)	3rd Quartile (150.5–361.9 ng/mL)	4th Quartile (above 362 ng/mL)	*p*
Death rate (%)	1.3	2.6	11.5	19.2	< 0.001[a]
Length of hospital stay, d, median (IQR)	13.5 (10–22.5)	15 (8.75–24.5)	15.5 (8–28.2)	17 (9–29)	0.934
Length of PICU stay, d, median (IQR)	7 (4–12.2)	7 (2–12)	7 (2–12.5)	10 (3.75–15)	0.246
Need for mechanical ventilation during hospitalization (%)	66.7	56.4	55.1	61.5	0.439
Ventilator-free days, median (IQR)	23.5 (19–27.2)	25 (19–28)	25 (17–28)	21 (14.7–28)	0.074
Need for vasoactive drugs during hospitalization (%)	47.4	42.33	46.2	61.5	0.085
Vasoactive drug-free days, median (IQR)	28 (23–28)	28 (24.75–28)	28 (22–28)	24.50 (17–28)	0.015[b]
More than two organ dysfunctions on D7 of admission (%)	14.1	9	17.9	16.7	0.394
Complicated course on D7 of admission (%)	38.5	34.6	37.2	53.8	0.063
Hemoglobin < 11 g/dL upon arrival in the PICU (%)[c]	69.2	66.2	70.5	75.3	0.663
Probable iron deficiency anemia (hemoglobin < 11 g/dL and mean corpuscular volume < 80 fl) upon arrival in the PICU (%)[c]	51.3	40.3	37.2	32.5	0.103
Presence of complex chronic condition (%)	38.5	46.2	42.3	41.0	0.804
Pediatric Index of Mortality 2, median (IQR)	0.027 (0.012–0.066)	0.018 (0.008–0.061)	0.014 (0.006–0.090)	0.029 (0.014–0.139)	0.051
Lactate upon arrival in the PICU, median (IQR)	1.2 (0.8–1.8)	1.2 (0.9–2.3)	1.1 (0.8–1.9)	1.2 (0.9–1.8)	0.628

D7 = day 7 of admission to the PICU, IQR = interquartile range.

[a]Pearson χ^2 test.

[b]Mann-Whitney *U* test.

[c]One patient in this group had no complete blood count collected.

TABLE 3. Clinical Characteristics, Demographics, and Outcomes of Survivors and Nonsurvivors in the cohort

Variable	Survivors (*n* = 285)	Nonsurvivors (*n* = 27)	*p*
Age, mo, median (IQR)	22.9 (11.3–64.6)	53.3 (18.6–126.3)	0.008[a]
Weight, g, median (IQR)	11,600 (8,500–18,500)	16,000 (11,500–24,500)	0.030[a]
Body mass index *z* score, median (IQR)	−0.09 (−1.26 to 1.11)	−0.89 (−2.26 to 0.83)	0.221
Male, *n* (%)	157 (55.1)	14 (51.9)	0.747
Serum ferritin level, ng/mL, median (IQR)	138 (80.5–287)	586 (226–1,093)	0.001[a]
Age < 24 mo, *n* (%)	146 (51.2)	9 (33.3)	0.075
Medical patient, *n* (%)	248 (87)	26 (96.3)	0.223
Severe sepsis and septic shock as defined by Goldstein et al (14), *n* (%)	33 (22.6) 113 (77.4)	4 (16) 21 (84)	0.603
Presence of complex chronic condition, *n* (%)	112 (39.3)	19 (70.4)	0.002[b]
Readmission within 72 hr, *n* (%)	8 (2.8)	0 (0)	1
Anemia hemoglobin < 11 g/dL, *n* (%)	201 (71)[c]	17 (63)	0.381
Probable iron deficiency anemia (anemia hemoglobin < 11 g/dL and mean corpuscular volume < 80 fl), *n* (%)	119 (42)[c]	6 (22.2)	0.045[b]
Reinfection, *n* (%)	14 (4.9)	4 (14.8)	0.059[d]
Need for MV, *n* (%)	160 (56.1)	27 (100)	< 0.001[d]
Duration of MV, d, median (IQR)	7 (4–11)	4 (2–10)	0.074
Ventilator-free days, median (IQR)	24 (20–28)	–	–
Need for vasoactive drugs, *n* (%)	130 (45.6)	24 (88.9)	< 0.001[d]
Vasoactive drug-free days, median (IQR)	28 (24–28)	–	–
Presence of a complicated course, *n* (%)	101 (35.4)	27 (100)	< 0.001[d]
Etiologic agent identified, *n* (%)	149 (52.3)	19 (70.4)	0.072
Pediatric Index of Mortality 2, median (IQR)	0.020 (0.009–0.064)	0.278 (0.028–0.450)	0.001[a]
Duration of vasoactive drug use, d, median (IQR)	5 (2–8)	3.5 (1–9)	0.524
Length of PICU stay, d, median (IQR)	8 (3–13)	4 (2–14)	0.103
Length of hospital stay, d, median (IQR)	16 (10–27)	4 (1–14)	0.001[a]
Lactate upon arrival in the PICU, median (IQR)	1.1 (0.8–1.8)	2 (1.4–4.7)	0.001[a]

IQR = interquartile range, MV = mechanical ventilation.

[a]Mann-Whitney *U* test.

[b]Pearson χ^2 test.

[c]Two patients in this group had no complete blood count collected.

[d]Fisher exact test.

Ventilator-free days and vasoactive drug-free days could not be analyzed because all patients who died were given a value of 0 in this variable.

PICU. Its behavior during PICU stay and outcomes are further aspects to be studied in the future (2). Other biomarkers, such as C-reactive protein and procalcitonin, have proved useful as markers of poor outcome in patients with sepsis (21–23). Finally, we defined iron deficiency anemia based on complete blood count testing without checking other iron deficiency markers.

CONCLUSIONS

Serum ferritin was shown to be a useful biomarker as a predictor of mortality. In children older than 6 months admitted to the ICU with sepsis, serum ferritin at lower thresholds predicts mortality in a middle-income country with high prevalence of iron deficiency anemia.

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