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Vasoactive inotropic score and mortality in COVID-19 in pediatric intensive care unit

Vasoactive Inotropic Score e mortalidade em COVID-19 em unidade de terapia intensiva pediátrica

Beatriz Pena Pantoja[I]*, Emmerson Farias[II]

Summary **Purpose:** This study analyzed children with critical illness associated with SARS-CoV-2 infection, focusing on mortality aspects in three pediatric intensive care units (PICU) in Belém, Pará, Brazil. **Methods:** A multicenter prospective study including children from 1 month to 18 years old admitted in three pediatric intensive care units due to acute or late COVID-19 confirmed in the period from April 2020 to July 2022, from three hospitals in the Eastern Amazon, Brazil. The sample was divided into two groups, survivors and non-survivors, and was prospectively followed from the day of hospitalization to its respective outcome. Univariate and multivariate analyses using the Cox regression model and Kaplan-Meier curves for each quartile of the maximum Vasoactive Inotropic Score (VISmax) were used to determine risk factors for unfavorable outcomes. The significance level was defined at <0.05 bilaterally. For mortality prediction, the ROC curve for data was compared to PIM-3, PRISM-IV and PELOD-2 scores. **Results:** Among the sample studied, the male gender, black and brown ethnicity, malnutrition, comorbidities and presence of neurological events are statistically significant risk factors. The VIS, despite a low discriminative capacity, showed a strong association with mortality in patients in the PICU with SARS-CoV-2-related SARS-SR. **Conclusion:** The limitations of the study include the lack of international and national data on the correlation of VIS with SARS- CoV-2, emphasizing the need for more research in this area.

Keywords: COVID-19; mortality; intensive care units, pediatric; pediatrics.

Resumo **Objetivo:** O presente estudo analisou crianças com doença crítica associada à infecção por SARS-CoV-2, focando em fatores que impactam a mortalidade em três unidades de terapia intensiva pediátrica (UTI-P) em Belém, Pará, Brasil. **Método:** um estudo prospectivo multicêntrico incluindo crianças de 1 mês a 18 anos de idade admitidas em unidade de terapia intensiva pediátrica devido COVID-19 aguda ou tardia confirmada no período de abril de 2020 a julho de 2022, de três hospitais na Amazônia Oriental, Brasil. A amostra foi dividida em dois grupos, sobreviventes e não sobreviventes, e foi prospectivamente acompanhada desde o dia da internação hospitalar até seu respectivo desfecho. Análises univariada e multivariada usando o modelo de regressão de Cox e curvas Kaplan-Meier para cada quartil do *Vasoactive Inotropic Score* (VIS) máximo (VISmax) foram usadas na identificação de fatores de risco para desfecho desfavorável. O nível de significância foi definido em <0,05 bilateralmente. Para previsão de mortalidade, a curva ROC para dados foi comparada aos escores PIM-3, PRISM-IV e PELOD-2. **Resultados:** Dentre a amostra estudada, o gênero masculino, etnias preta e parda, desnutrição, comorbidades e a presença de eventos neurológicos configuram como fatores de risco estatisticamente significativos. O VIS, apesar de uma capacidade discriminativa baixa, demonstrou uma forte associação com a mortalidade em pacientes na UTI-P com SRAG relacionada ao SARS-CoV-2. **Conclusão:** As limitações do estudo incluem a escassez de dados internacionais e nacionais sobre a correlação do VIS com o SARS-CoV-2, enfatizando a necessidade de mais pesquisas nessa área.

Descritores: COVID-19; mortalidade; unidades de terapia intensiva pediátrica; pediatria.

[I]Universidade Federal do Pará (UFPA), Programa de Residência Médica em Pediatria, Belém, PA, Brazil.
[II]Fundação Santa Casa de Misericórdia do Pará (FSCMPA), Programa de Residência Médica em Medicina Intensiva Pediátrica, Belém, PA, Brazil.
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Introduction

In children, Coronavirus Disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), clinically presents as asymptomatic or mild forms and represents lower rates of mortality and complications compared to adults[1]. However, some children may manifest severe and potentially fatal forms, especially those under one year of age and those with associated comorbidities[2].

The majority of severe cases and/or complications of COVID-19 occur in children under one year of age, an age group that also required more hospitalizations and admissions to pediatric intensive care units. Regarding the clinical picture of these children, a systematic review describes typical critical features, including high fever, septic shock, recurrent apnea, severe hematuria, hypofibrinogenemia, lymphopenia, and acute kidney injury. The initial clinical manifestation was septic shock, similar to adults[3].

In pediatric intensive care units (PICU), some scores help objectively quantify greater severity and outcomes such as mortality. The Vasoactive Inotropic Score (VIS) is a standardized calculation of vasopressor and inotropic equivalence, using coefficients for each medication to quantify the need for use and amount of vasoactive drugs in critically ill patients. Evidence suggests that VIS can be used as a prognostic factor in various outcomes in PICU, such as its use to reflect postoperative severity of congenital heart disease in children[4].

In the context of COVID-19 and PICU, there is only a few evidence of the correlation of high VIS with severity and mortality outcomes[5], either on national or international studies. Therefore, this study aimed to correlate the VIS score of patients admitted to three pediatric intensive care units in the Eastern Amazon with the outcome of mortality in patients with Severe Acute Respiratory Syndrome due to SARS-CoV-2 and compare its predictive value with mortality scores PRISM-IV, PIM-3, and PELOD-2.

Methods

This is a multicenter prospective study including critically ill children aged 1 month to 18 years, admitted due to laboratory-confirmed acute and late forms of COVID-19 from April 2020 to July 2022, from three hospitals and reference teaching centers in the Eastern Amazon, Brazil. Patients referred from external units were tested upon admission, even if they had a previous positive test.

Those with biologically proven co-infection, immunosuppressed children, as well as patients in the final stage of life under palliative care, were excluded from the sample (Table 1). The study obtained approval from the Research Ethics Committee of Santa Casa de Misericórdia do Pará Foundation (CAAE nº 32150220.2.0000.5171); and other centers were co-participants. All participants or legal guardians provided written informed consent.

The study sample was prospectively followed from the day of hospital admission until discharge or death. The criteria for admission in PICU were the same in all three hospitals, and in cases of readmission in the pediatric intensive care unit, only the first hospitalization was considered. The clinical management

Table 1. Eligibility criteria for admission from the study.

Description	n
Total patients admitted to the PICU with suspected SARS-CoV-2	668
Excluded patients	204
Negative serological or molecular test for SARS-CoV-2	76
Did not meet criteria for PICU admission	38
Immunosuppression	28
End-of-life palliative care	12
Positive microbiological test for other infectious agent	50
Final sample included in the study	**208**

PICU: Pediatric Intensive Care Unit; SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2.

protocol for pediatric patients with COVID-19 and Multisystem Inflammatory Syndrome in Children (MIS-C) was similar in the three centers, based on the recommendations of World Health Organization (WHO) in 2020[6]; however, there was no uniform protocol formulated by the researchers. All parameters were obtained and processed using standard data collection forms, and all involved centers conducted laboratory test analyses at the same institution.

The sample was divided into two groups: survivors and non-survivors. Clinical and epidemiological data, as well as laboratory, imaging, and ventilatory parameters, were obtained on the first day of hospitalization. Critical illnesses, including respiratory failure requiring invasive mechanical ventilation, severe acute respiratory distress syndrome, shock, systemic inflammatory response syndrome, and/or multisystem failure with at least one organ involved. Multiple organ dysfunction syndrome (MODS) was defined by current criteria[7]. Severe COVID-19 was defined by the presence of positive RT-PCR, TR-Ag, or IgG serology and at least one organ dysfunction involved, according to current criteria[6]. MIS-C was defined according to current criteria established by WHO[6]. Echocardiographic findings in patients with signs of shock, unexplained tachycardia, and symptoms suggestive of MIS-C were recorded. Myocardial dysfunction was defined by the presence of global or focal contractility alterations, ventricular dilation, ejection fraction less than 55% measured by the modified Simpson method[8]. Likewise, data such as severity and mortality scores, management, and unfavorable outcomes were also assessed.

Treatment received by patients such as high ventilatory parameters, ventilation time (in days) in those who required Invasive Mechanical Ventilation (IMV), need for inotropic/vasoactive drugs, maximum VIS value, and drug treatment implemented (intravenous methylprednisolone, intravenous human immunoglobulin, and fractionated heparin) were also analyzed. Septic shock due to SARS-CoV-2 infection, severe acute respiratory distress syndrome, and acute kidney injury were diagnosed and managed according to the Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock in Children, Pediatric Acute Lung Injury Consensus Conference (PALICC) definitions, and kidney disease by Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, respectively[9-12]. Pediatric death associated with SARS-CoV-2 was defined as death after admission to the pediatric intensive care unit in a patient with confirmed severe COVID-19 or MIS-C.

Cohort characteristics were summarized using median (interquartile range) for continuous variables and frequencies (%) for categorical variables. We used the χ^2 or Fisher's exact test for comparison between categorical variables, and the Mann-Whitney test for continuous data. Holm-Bonferroni correction for multiple comparisons was applied by adjusting the significance level when patients were compared in two groups (survivors and non- survivors). Survival rate calculations in days and Kaplan-Meier curves were plotted, using quartile categories for continuous variables.

Univariate and multivariate analyses using the Cox regression model were used to determine risk factors for survival. The proportional hazard assumption was tested by plotting the Nelson-Aalen cumulative hazard function and the Schoenfeld residual test. For these analyses, the adopted significance level was set at $p<0.05$ bilaterally. For mortality prediction, we used the ROC curve for data compared to PIM-3, PRISM-IV, and PELOD-2. Univariate and multivariate analysis by Cox regression and Kaplan-Meier curves for each quartile of the maximum VIS (VISmax). Data analysis was performed using SPSS (Statistical Package for the Social Sciences, Chicago, IL) version 27.0.

The literature search was conducted in the SciELO (Scientific Electronic Library Online), SCIE (Social Care Institute for Excellence), MEDLINE, and EMBASE databases, using the term "Vasoactive inotropic score AND multisystem inflammatory syndrome in children OR covid-19", including full texts freely available in Portuguese and English, published in the last 5 years and relevant to the research theme.

Results

Of the 208 analyzed patients, 117 (56.3%) were male, with a median age of 33 [IQR 9-36] months; of these, 139 (66.8%) were over five years old, 10 (5.8%) were from indigenous populations, 101 (48.6%) were underweight, and 131 (63%) had at least one comorbidity, as shown in Table 2.

Table 2. Clinical, Demographic, Ventilatory, and Laboratory Characteristics in Patients with Critical Disease Associated with SARS-CoV-2, Divided Between Survivors and Non-Survivors in Three Centers in Belém, Pará, Brazil, From April 2020 to July 2022.

Admission Characteristics	Survivors (n=171)	Non-Survivors (n=37)	All Patients (n=208)	p-value*
Clinical-Demographic				
Age in months, median (IQR)	28 (9-91)	51 (8-103)	33 (9-96)	0.410
Gender, n (%), male	97 (56.7)	20 (54.1)	117 (56.3)	0.766
Comorbidity, n (%)	97 (56.7)	34 (91.9)	131 (63)	**<0.001**
Indigenous populations in Brazil	10 (5.8)	0 (0)	10 (4.8)	0.214
Ethnicity: brown, n (%)	67 (39.2)	30 (81.1)	97 (46.6)	**<0.001**
Pediatric comorbidity classification, n (%), neurological and neuromuscular	27 (15.8)	10 (27)	37 (10.5)	0.104
Nutritional status, n (%), malnutrition	68 (39.8)	33 (89.2)	101 (48.6)	**<0.001**
SARS-CoV-2 infection tests confirmed by RT-PCR, n (%)	66 (56.9)	11 (55)	77 (37)	0.930
Dyspnea, n (%)	115 (67.3)	36 (97.3)	151 (72.6)	**<0.001**
Chest CT patterns, n (%), ground-glass opacities	44 (25.7)	17 (45.9)	61 (29.3)	0.017
VIS at admission, median (IQR)	66 (24-86)	161 (116-179)	84 (39-120)	**<0.001**
Invasive mechanical ventilation	63 (36.8)	37 (100)	100 (48.1)	**<0.001**
ARDS, n (%)	39 (22.8)	35 (94.6)	74 (35.6)	**<0.001**
Renal replacement therapy	15 (8.8)	4 (10.8)	19 (9.1)	0.753
KDIGO, n (%), Stage 1/Risk	72 (42.1)	33 (89.2)	105 (50.5)	**<0.001**
Ventilatory Parameters				
PEEP (1) in cmH2O>9, n (%)	14 (8.2)	12 (32.4)	26 (12.5)	**0.0002**
PIP in cmH2O>23, n (%)	9 (5.3)	17 (45.9)	26 (12.5)	**<0.001**
Tidal volume in mL/kg>9.2, n (%)	7 (4.1)	18 (48.6)	25 (12)	**<0.001**
Driving pressure in cmH2O>13, n (%)	7 (4.1)	18 (48.6)	25 (12)	**<0.001**
Laboratory Parameters Respiratory System				
Oxygenation index>10.2, n (%)	12 (7)	13 (35.1)	25 (12)	**<0.001**
PaO2/FiO2 ratio (3)≤161, n (%)	24 (14)	16 (43.2)	40 (19.2)	**<0.001**
Cardiovascular System				
Troponin I (ng/L)>0.43, n (%)	31 (18.1)	21 (56.8)	52 (25)	**<0.001**
Markers of oxygenation and tissue perfusion				
HCO3 (mmol/L)≤17.2, n (%)	35 (20.5)	18 (48.6)	53 (25.5)	**<0.001**

Continue...

Table 2. Continuation.

Admission Characteristics	Survivors (n=171)	Non-Survivors (n=37)	All Patients (n=208)	p-value*
Hematologic and Coagulation System				
Lymphocytes/mm³≤1,130, n (%)	34 (19.9)	18 (48.6)	52 (25)	**<0.001**
Platelets/mm³≤111,000, n (%)	33 (19.3)	20 (54.1)	53 (25.5)	**<0.001**
PT in seconds>17.2, n (%)	28 (16.4)	24 (64.9)	52 (25)	**<0.001**
Acute inflammatory markers				
ESR>18 seconds	17 (9.9)	29 (78.4)	46 (22.1)	**<0.001**
Urinary System				
Urea (mg/dL), median (IQR)	23 (15-43)	22 (16-38)	23 (15-40)	0.679
Creatinine (mg/dL), median (IQR)	0.4 (0.2-0.6)	0.4 (0.3-0.6)	0.4 (02-0.6)	0.620
Hepatic System				
AST (IU/L), median (IQR)	43 (29-58)	41 (28-68)	43 (29-62)	0.945
ALT (IU/L), median (IQR)	34 (19-42)	34 (21-52)	34 (19-43)	0.509
Albumin (g/dL)≤2.3, n (%)	44 (25.7)	10 (27)	54 (26)	0.862
Treatment				
Methylprednisolone pulse therapy	6 (3.5)	17 (45.9)	23 (11.1)	**<0.001**
Human IVIG therapy	48 (28.1)	22 (59.5)	70 (33.7)	**<0.001**
Clinical Outcomes				
PICU length of stay, in days, median (IQR)	6 (3.5)	17 (45.9)	23 (11.1)	**<0.001**
Hospitalization length, in days, median (IQR)	48 (28.1)	22 (59.5)	70 (33.7)	**<0.001**
Mechanical ventilation time, in days, median (IQR)	6 (4-11)	6 (4-13)	5 (3-10)	0.107
Successful ventilatory weaning on the first attempt, n (%)	3 (1-9)	0 (0-1)	20 (0-24)	**<0.001**
Ventilator-associated pneumonia, n (%)	17 (9.9)	10 (27)	27 (13)	**0.008**
Mortality and Severity Scores				
PELOD-2, median (IQR)	6 (3-12)	11 (4-20)	7 (3.5-14)	**0.014**
PIM-3, median (IQR)	1.2 (0.3-5)	12 (2.2-23)	1.9 (0.3-10)	**<0.001**

VIS: Vasoactive Inotropic Score; ARDS: Acute Respiratory Distress Syndrome; PEEP: Positive End-Expiratory Pressure; PIP: Peak Inspiratory Pressure; PaO2/FiO2: ratio of the partial pressure of oxygen in arterial blood (PaO2) to the inspired oxygen fraction (FiO2) ; PT: Prothrombin Time; ESR: Erythrocyte sedimentation rate; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; IVIG: Intravenous immunoglobulin; PICU: Pediatric Intensive Unit Care; PELOD-2: Paediatric Logistic Organ Dysfunction 2 ; PIM-3: Paediatric Index of Mortality 3.

Ventilatory parameters such as elevated driving pressure and severe hypoxemia, as well as laboratory findings of lymphopenia and elevated Erythrocyte Sedimentation Rate (ESR) at admission, were more frequent in non-survivor patients when compared to the survivor group, as illustrated in Table 2.

Neurological and neuromuscular diseases were more frequent [10 (27%)] in non- survivor patients. Thirty-seven (17.8%) patients died during the follow-up with a mean time of 7 days (IQR=4-13; range 2-40).

The average age of non-survivor patients was 51 months, and 34 (91.9%) had at least one comorbidity. After a median follow-up of 277 days (IQR=72-370; range 2-759), there were 37 deaths (17.8%); at the end of the study period, 2 (0.96%) remained in the PICU, and 169 (81.2%) were discharged (Table 2).

In the univariate analysis (Figure 1), the effect of all independent variables was significant in explaining the risk of death from COVID-19. The highest risk ratio for this association occurred in patients with severe acute respiratory distress syndrome (ARDS) at admission (HR=42.26, p<0.001) and VIS>84 (HR=31.24, p<0.001).

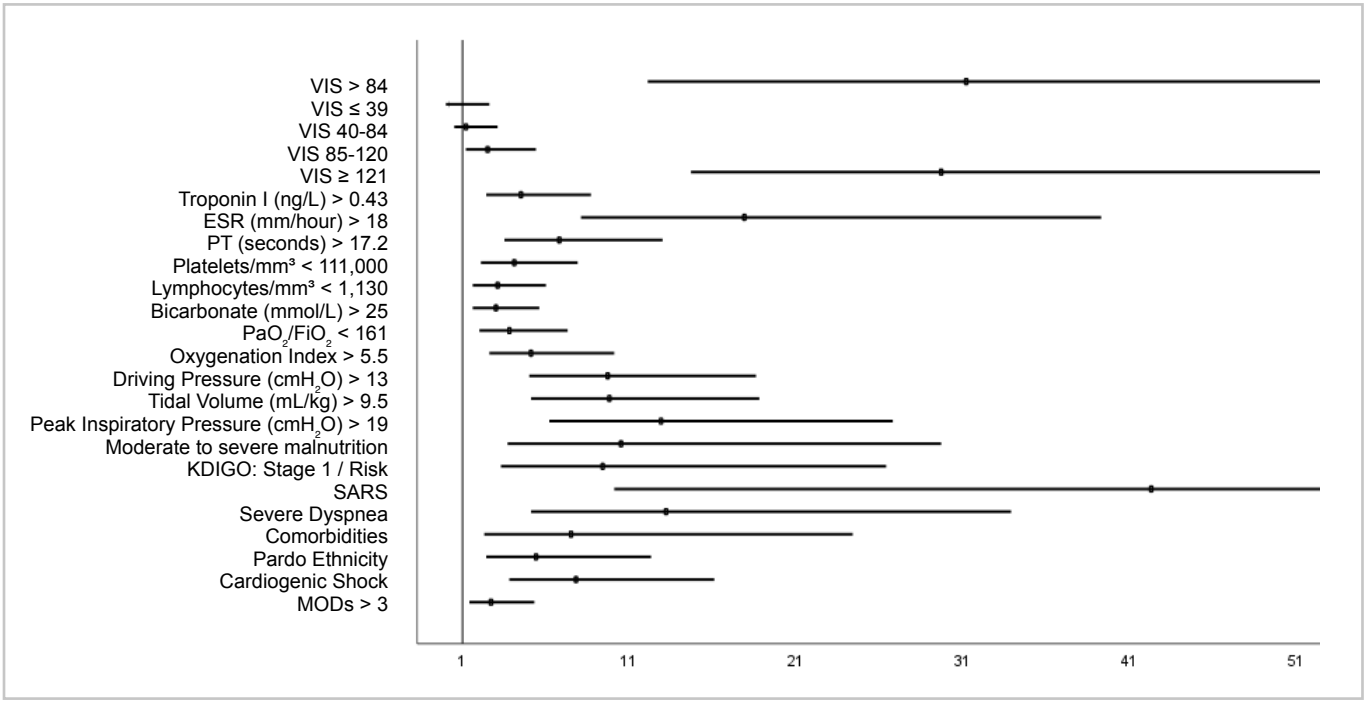

Figure 1. Univariate Cox Proportional Hazards Regression Analysis for Factors Associated with Mortality in the Pediatric Intensive Care Unit (ICU) due to SARS-CoV-2 Infection in Children in Three Centers in Eastern Amazon from April 2020 to July 2022, Belém, Pará, Brazil.

After multivariate analysis (Figure 2), independent risk factors associated with mortality included malnutrition (HR=6.64, 95%CI 1.41–31.16, p=0.016), VIS>84 (HR=4.76, 95%CI 1.0–24.48, p=0.05), ARDS (HR=8.63, 95%CI 1.36–54.93, p=0.022), and ESR>18 (HR=3.95, 95%CI 1.11–14.1, p=0.035). The highest risk ratio for this association was found in patients with ARDS at admission (HR=42.26, p<0.001) and VIS>84 (HR=31.24, p<0.001).

In the analysis of severity and mortality scores, VIS showed higher sensitivity and specificity compared to PELOD-2, PIM-3, and PRISM-IV as a predictive tool for unfavorable outcomes in children with severe critical illness due to SARS-CoV-2 (Figure 3).

Discussion

From the obtained data, the patient profile in this study shows a male prevalence, consistent with studies by other authors who highlight this frequency as an effect of biological differences between genders in terms of infection sensitivity, adaptive immune response, immune regulation, and tissue repair[5].

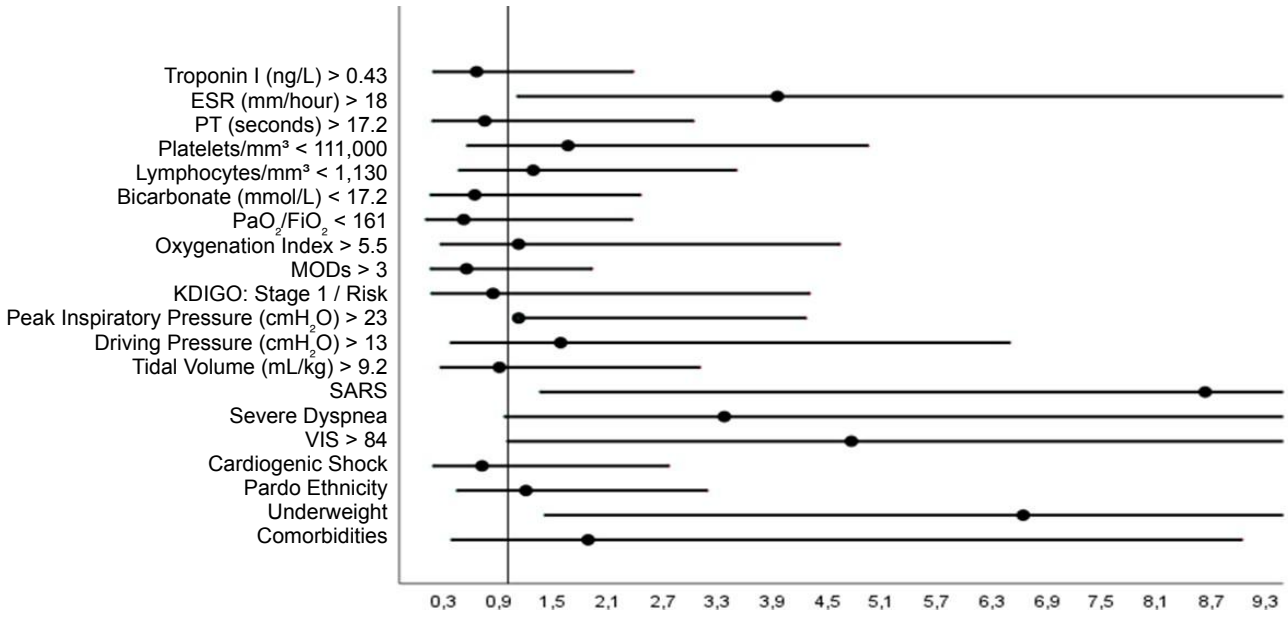

Figure 2. Univariate Analysis of Cox Proportional Hazards Regression for Factors Associated with Mortality in the ICU due to SARS-CoV-2 Infection in Children in Three Centers in Eastern Amazon from April 2020 to July 2022, Belém, Pará, Brazil.

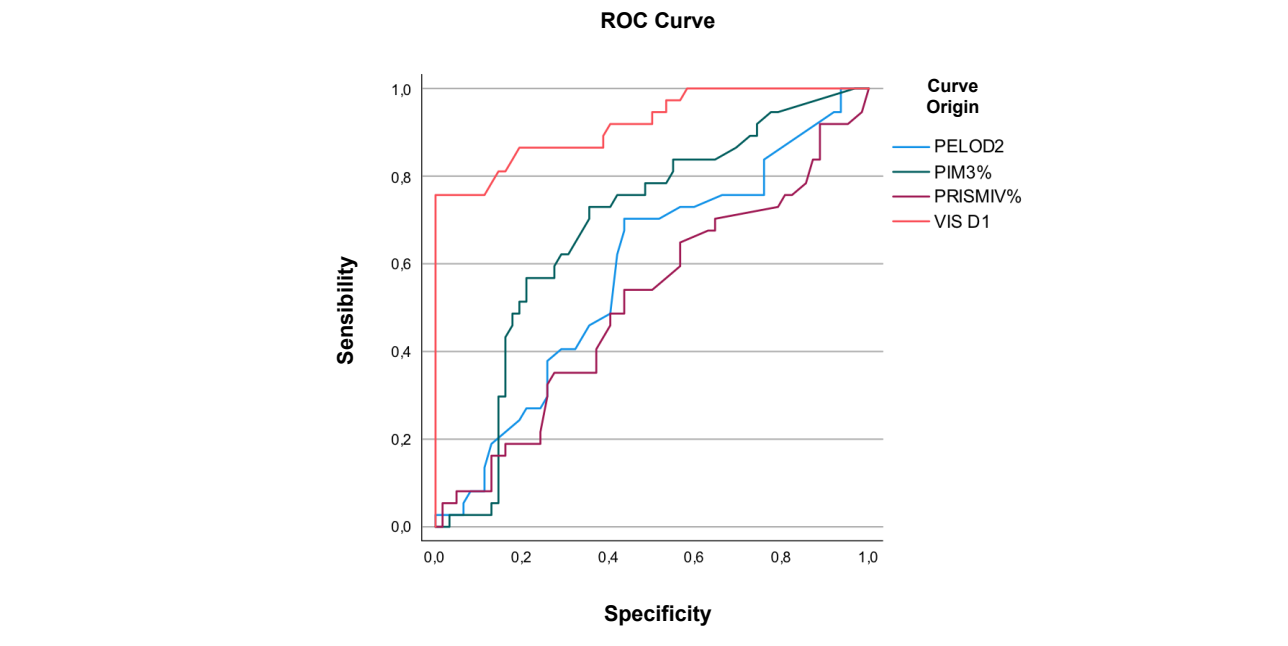

Figure 3. Sensitivity and Specificity Profile of Different Pediatric Severity and Severity Scores and Unfavorable Outcomes in Children Admitted in PICU due to Critical Disease caused by SARS-CoV-2 in Three Centers in Eastern Amazon from April 2020 to July 2022, Belém, Pará, Brazil.

According to the survey, 46.6% of patients with critical illness associated with SARS- CoV-2 self-declared as brown, corresponding to 81% of the non-survivor group. Oliveira et al. demonstrate that data on black and brown patients are associated with worse outcomes in univariate analyses[3]. Although not remaining significantly associated with death after multivariate analysis, these values may be related to the fact that the brown ethnicity represents the majority of the overall sample.

It is worth noting that within the results, it was observed that 4.8% of the individuals studied are part of the country's indigenous population, with all patients in the survivor category. A multicenter case-control study highlighted that children from racial minority backgrounds had a disproportionate risk of developing severe conditions, as low- and middle-income countries have high-quality primary care, thus enabling rapid and adequate diagnoses and less unfavorable prognoses[13].

In the multivariate analysis, malnutrition stood out as an independent risk factor associated with mortality, similar to what was described by Kazi et al.[14], and in contrast to data that highlight overweight and obesity as risk factors for severe forms of Covid-19[1,13,15]. It is known that malnourished children have impairments in the mechanisms of cellular immune response, making them more prone to invasive infectious processes[16]. Such alterations in metabolic and physiological responses, coupled with difficulty in access to health services and the low socioeconomic development of the Northern Region, may justify these findings[3].

Among the important clinical issues, the presence of comorbidities stands out, as 37% of patients admitted during the study period had them, whether of neurological or neuromuscular origin. Despite the lack of data in the pediatric population regarding the impact of comorbidities on child mortality, studies show that the presence of pre-existing medical conditions is associated with a higher rate of admission in PICU[3].

The data collected by this study point to severe hypoxemia as one of the factors affecting the majority of non-surviving patients. The study by Kazi et al.[14] indicates that patients with hypoxia had higher rates of admission in PICU, presenting disorders that may be correlated with this condition.

Current analyses have identified some common laboratory findings in hospitalized patients, highlighting leukopenia, leukocytosis, and lymphopenia, as well as elevated inflammatory markers such as C-Reative Protein (CPR) and ESR[1,5,13-15]. Zhang et al. associated elevated D-dimer as a predictor of mortality in adult patients with critical illness due to SARS-CoV-2[17]. These data corroborate with this study, whose results demonstrated that patients who had laboratory tests with lymphopenia and elevated ESR at hospital admission had a higher rate of non-survival.

It is important to emphasize that in univariate analysis, the highest risk rate associated with mortality refers to patients with severe ARDS at hospital admission. Thus, it is emphasized that the availability for timely medical care is of utmost importance in patients with ARDS[13].

In our study, 96 (46.2%) of the children needed inotropic support, with a median VIS of 84 (IQR=39-120), much higher than that reported by Acevedo et al.[13] and Chang et al.[18], (IQR=10-35) and 7 (IQR=5-9), respectively. More studies are needed to assess possible tendencies for severe cardiac dysfunctions associated with Covid-19 in our population.

Sik et al.[5] correlate the median VIS of 105 with mortality (IQR=55-144; $p<0.001$); Kazi et al.[14] associates a high VIS with the unfavorable outcomes group (prolonged stay in the PICU and/or death), ($p=0.007$). These data were obtained from samples in Turkey and India, respectively[5,14]. Until the present date, only one Brazilian study correlating mortality factors in children affected by severe SARS-CoV-2-associated disease was found, and there was part of the sample of this study[19].

Conclusion

The risk factors demonstrated in the study, as seen in both univariate and multivariate analyses, included male gender, black and brown individuals, malnutrition, and the presence of comorbidities, with or without

associated neurological events. Additionally, the development of inflammatory multisystemic syndrome and severe acute respiratory syndrome (SARS) proved to be significant factors in assessing mortality.

Through the obtained data and the conducted analysis, it was possible to identify that the Vasoactive Inotropic Score (VIS), despite presenting low discriminative capacity for predicting mortality in patients with SARS-CoV-2-related severe acute respiratory distress syndrome (SARS) admitted or interned in the Pediatric Intensive Care Unit (PICU), showed a strong association with mortality in this group of patients, correlating with the presented clinical severity and certain risk factors.

Despite one of the most notable results of the study being the recognition of VIS as a predictor of COVID-19 mortality, one of the most important limitations of the study relates to the lack of both national and international studies addressing the relationship between the VIS score and SARS-CoV-2-caused disease. This underscores the pioneering nature of the research, reinforcing the need for more studies addressing this correlation.

References

1. Adeyinka A, Bailey K, Pierre L, Kondamudi N. COVID 19 infection: Pediatric perspectives. John Wiley and Sons; 2021. v. 2.
2. Nunes MDR, Pacheco ST de A, Costa CIA, da Silva JA, Xavier W da S, Victória JZ. Diagnostic tests and clinical characteristics of covid-19 in children: An integrative review. Texto Contexto Enferm. 2020;29:e20200156. https://doi.org/10.1590/1980-265X-TCE-2020-0156
3. Oliveira VS, Oliveira LG, Bastos GS, Dias LA, Pinto RM, Souza CSB. Fatores determinantes de evolução grave e crítica da COVID-19 em crianças: revisão sistemática e metanálise. Resid Pediatr. 2020;10(2):1-8. https://doi.org/10.25060/residpediatr-2020.v10n2-405
4. Gaies MG, Gurney JG, Yen AH, Napoli ML, Gajarski RJ, Ohye RG, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. Pediatr Crit Care Med. 2010;11(2):234-8. https://doi.org/10.1097/PCC.0b013e3181b806fc
5. Sik G, Inamlık A, Akçay N, Kesici S, Aygun F, Kendırlı T, et al. Mortality risk factors among critically ill children with MIS-C in PICUs: a multicenter study. Pediatr Res. 2023;94(2):730-7. https://doi.org/10.1038/s41390-023-02518-0
6. World Health Organization (WHO). Multisystem inflammatory syndrome in children and adolescents with COVID-19 [Internet]. Geneva: WHO; 2020 [cited 2025 Mar 12]. Available from: https://www.who.int/news-room/commentaries/detail/ multisystem-inklammatory-syndrome-in-children-and-adolescents-with-covid-19
7. Ramírez M. Multiple organ dysfunction syndrome. Curr Probl Pediatr Adolesc Health Care. 2013;43(10):273-7. https://doi.org/10.1016/j.cppeds.2013.10.003
8. Mercier JC, DiSessa TG, Jarmakani JM, Nakanishi T, Hiraishi S, Isabel-Jones J, et al. Two- dimensional echocardiographic assessment of left ventricular volumes and ejection fraction in children. Circulation. 1982;65(5):962-9. https://doi.org/10.1161/01.CIR.65.5.962
9. Feldstein LR, Tenforde MW, Friedman KG, Newhams M, Rose EB, Dapul H, et al. Characteristics and outcomes of US children and adolescents with multisystem inflammatory syndrome in children (MIS-C) compared with severe acute COVID-19. JAMA. 2021;325(11):1074-87. https://doi.org/10.1001/jama.2021.2091
10. Weiss SL, Peters MJ, Alhazzani W, Agus MSD, Flori HR, Inwald DP, et al. Surviving sepsis campaign international guidelines for the management of septic shock and sepsis- associated organ dysfunction in children. Pediatr Crit Care Med. 2020;21(2):e52-106. https://doi.org/10.1097/pcc.0000000000002198
11. Emeriaud G, López-Fernández YM, Iyer NP, Bembea MM, Agulnik A, Barbaro RP, et al. Executive summary of the second international guidelines for the diagnosis and management of pediatric acute respiratory distress syndrome (PALICC-2). Pediatr Crit Care Med. 2023;24(2):143-68. https://doi.org/10.1097/pcc.0000000000003147
12. Summary of Recommendation Statements. Kidney Int Suppl (2011). 2011;2(1):8-12. https://doi.org/10.1038/kisup.2012.7
13. Acevedo L, Piñeres-Olave BE, Niño-Serna LF, Vega LM, Gomez IJA, Chacón S, et al. Mortality and clinical characteristics of multisystem inflammatory syndrome in children (MIS-C) associated with covid-19 in critically ill patients: an observational multicenter study (MISCO study). BMC Pediatr. 2021;21(1):516. https://doi.org/10.1186/s12887-021-02974-9

14. Kazi MA, Roychowdhury S, Ghosh S, Mahapatra MK, Bhakta S, Konar MC, et al. Characteristics and predictors of outcomes of critically Ill children with SARS-CoV-2 infection - the PICU experience. J Pediatr (Rio J). 2022;98(5):504-12. https://doi.org/10.1016/j.jped.2021.12.006

15. Salman H, Aslan N, Akçam M, Arslan M, Akkuzu E, Yllmaz Keskin E, et al. COVID-19-associated multisystem inflammatory syndrome in children: Experiences of three centres in Turkey. Mod Rheumatol. 2022;32(2):460-6. https://doi.org/10.1093/mr/roab042

16. Dipasquale V, Cucinotta U, Romano C. Acute malnutrition in children: pathophysiology, clinical effects and treatment. Nutrients. 2020;12(8):2413. https://doi.org/10.3390/nu12082413

17. Zhang L, Yan X, Fan Q, Liu H, Liu X, Liu Z, et al. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost. 2020;18(6):1324-9. https://doi.org/10.1111/jth.14859

18. Chang JC, Matsubara D, Morgan RW, Diorio C, Nadaraj S, Teachey DT, et al. Skewed cytokine responses rather than the magnitude of the cytokine storm may drive cardiac dysfunction in multisystem inflammatory syndrome in children. J Am Heart Assoc. 2021;10(16):e021428. https://doi.org/10.1161/jaha.121.021428

19. de Farias ECF, Pavão Junior MJC, de Sales SCD, do Nascimento LMPP, Pavão DCA, Pinheiro APS, et al. Factors associated to mortality in children with critical COVID-19 and multisystem inflammatory syndrome in a resource-poor setting. Sci Rep. 2024;14(1):5539. https://doi.org/10.1038/s41598-024-55065-x

Corresponding author

Beatriz Pena Pantoja
Universidade Federal do Pará, Hospital Universitário Bettina Ferro de Souza, Pediatric Residency Program
Perimetral Avenue, Km 01, Guamá University Campus, Health Sector, s/n, Guamá
Zip Code 66075-110, Belém, PA, Brazil
Email: beatrizpantojabkp@gmail.com

Authors' information

BPP is a resident physician in the Pediatric Residency Program at the Universidade Federal do Pará. ECFF is the supervisor of the Pediatric Intensive Care Medicine Residency Program at the Fundação Santa Casa de Misericórdia do Pará.

Authors' contributions

BPP, ECFF: conceptualization; data curation; formal analysis; writing – first draft; writing – editing and review.

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