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Septic shock upon admission to pediatric intensive care units: prognostic analysis of mortality in a retrospective cohort

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Abstract

Background: *Septic shock is a common cause of admission to pediatric intensive care units (PICU) and is associated with significant mortality. Our objective was to analyze the association between septic shock diagnosis at PICU admission and mortality during hospitalization.* **Method:** *This retrospective cohort study was conducted in the PICU of Hospital Nacional Edgardo Rebagliati Martins (HNERM) in Lima, Peru, from January 2018 to December 2021. The sample size was determined based on annual mortality rates, and randomization was used to create two groups: patients with and without septic shock. To evaluate mortality risk, we performed a Poisson regression with robust variances and 95% confidence intervals (CI) using both crude and adjusted models.* **Results:** *Of 1,341 patients admitted to the PICU during the study period, 358 were included in the analysis. The study population was 51.9% female, with a median age of 3.7 years. The largest age group was children under 1 year, comprising 29.6% of participants. The septic shock group showed higher rates of mechanical ventilation requirement, longer hospital stays, and increased mortality. The risk of mortality was 2.73 times higher in patients admitted with septic shock compared to those admitted with other diagnoses (relative risks: 2.73; 95% CI: 1.36–5.46).* **Conclusion:** *Patients admitted to the PICU with septic shock demonstrated a 2.73 times higher risk of death compared to those admitted for other reasons.*

Keywords: Septic shock. Pediatric intensive care units. Mortality. Cohort studies. Peru.

Choque séptico al ingreso a una unidad de cuidados intensivos pediátricos: análisis pronóstico de mortalidad en una cohorte retrospectiva

Resumen

Introducción: *El shock séptico es motivo de ingreso a Unidades de Cuidados Intensivos Pediátricos (UCIP) y conlleva una importante mortalidad. Nuestro objetivo fue analizar la asociación entre el diagnóstico de shock séptico al ingreso de una UCIP y la mortalidad durante su estancia.* **Método:** *Estudio de cohortes retrospectivo desarrollado en la UCIP del Hospital Nacional Edgardo Rebagliati Martins (HNERM) de Lima-Perú de enero del 2018 a diciembre del 2021. Se determinó el*

tamaño de muestra con base en tasas de mortalidad anuales y se realizó una aleatorización para conformar dos grupos: uno con shock séptico y otro sin él. Para evaluar el riesgo de muerte se realizó una regresión de Poisson con varianzas robustas y un intervalo de confianza (IC) al 95% con modelos crudos y ajustados. **Resultados:** *De los 1341 pacientes ingresados a la UCIP durante el periodo de estudio se incluyeron 358 pacientes. De ellos, el 51.9 % eran mujeres, la mediana de edad fue de 3.7 años y la mayor cantidad de participantes estuvo en el grupo de menores de 1 año 29.6%. La necesidad de ventilación mecánica, la duración de la estancia hospitalaria y la mortalidad fueron más altas en el grupo de shock séptico. El riesgo de mortalidad fue 1.73 veces más en el grupo que ingresó con shock séptico en comparación al grupo que ingresó con otros diagnósticos (RR: 2.73; IC 95% 1.36 – 5.46).* **Conclusión:** *Los pacientes ingresados a la UCIP por shock séptico presentaron mayor riesgo de morir en comparación con aquellos que ingresaron por otras causas.*

Palabras clave: Choque séptico. Unidades de cuidado intensivo pediátrico. Mortalidad. Estudios de Cohortes. Perú.

Introduction

Septic shock is a significant cause of admission to pediatric intensive care units (PICUs) and is associated with substantial mortality[1-7]. In developing countries, septic shock accounts for up to 20% of ICU admissions, with mortality rates exceeding 30%[2-4]. In contrast, developed countries report approximately 10% of admissions due to septic shock, with mortality rates below 20%[6,8-11]. Despite the disproportionate impact of septic shock on pediatric populations in developing countries, most available research comes from developed nations.

Other common causes of PICU admission have been well documented. Respiratory infections comprise 12% of admissions with approximately 20% mortality, whereas infections at other sites account for an additional 12% with an average mortality of 19%[5]. Trauma cases represent 6% of admissions with 10% mortality[5,8], and post-operative patients constitute up to 40% of admissions with 1% mortality[8]. Overall, PICU mortality rates range from 3% to 25%, with developing countries consistently reporting higher rates than developed nations[1,5,8,12-15].

While it is well established that patients admitted to PICUs with septic shock experience higher mortality rates than those admitted for other conditions, the magnitude of this increased risk remains unclear. Therefore, our primary objective was to quantify the relative mortality risk for patients admitted to PICU with septic shock compared to those admitted with other diagnoses.

Method

This study was approved by the hospital's Ethics Committee (registration code 1434-GRPR-ESSALUD -2022) and was conducted following the Declaration of Helsinki and Peru's General Health Law regarding health research.

Study design, population, and sample

We conducted a retrospective cohort study using data from patients admitted to the PICU of the National Hospital Edgardo Rebagliati Martins (NHERM) from January 1, 2018, to December 31, 2021. NHERM, located in Lima, Peru's capital, is a national reference center serving approximately 2 million people with over 1,600 beds[16]. The pediatric service comprises approximately 100 hospital beds, whereas the PICU maintained nine beds during the first 3 years of the study period, expanding to 13 beds in the final year.

Following our institution's pediatric classification criteria, the study population included patients aged between 1 month and 13 years, 11 months, and 29 days. We included all PICU admission records regardless of diagnosis and followed patients from PICU admission until hospital discharge. We excluded patients with multiple PICU admissions during the study period, regardless of admission diagnosis.

The sample size was calculated using Epidat version 4.2. For the unexposed group (without septic shock), we assumed a mortality risk of 12.7%, based on the HNERM PICU's annual mortality rate[12]. For the exposed group (with septic shock), we used a mortality risk of 24.8%, derived from a systematic review and meta-analysis of global case fatality rates in severe sepsis and pediatric septic shock[6]. Using an exposed/unexposed ratio of 1:1, 80% power, and 95% confidence level with Yates correction, we calculated a required sample size of 179 patients per group. We created a sampling frame from the digital PICU admission records, which were updated daily. After applying selection criteria, patients were stratified into two groups based on exposure status. Simple random sampling was then performed to achieve the required number of patients in each group.

Variables

The independent variable (exposure) was septic shock diagnosis, defined by suspected or confirmed infection plus a combination of fever or hypothermia, altered capillary refill, reticulated skin, decreased mental status, oliguria, and hypotension, based on international criteria[17]. The primary outcome was all-cause mortality during the PICU stay. Additional variables included sex, age categories, comorbidity presence, prematurity history, and mechanical ventilation use. We also collected numerical data on age, PICU length of stay, and pediatric risk of mortality (PRISM) III scores. The PRISM III score predicts PICU mortality risk by evaluating 17 physiological variables during the first 24 h after admission[18]. When analyzing mortality by comorbidity type, we included only patients with underlying pathologies to avoid bias.

Statistical analysis

Data were collected in Microsoft Excel, with two authors independently verifying each value twice. Statistical analyses were performed using Stata 14.0 (StataCorp, TX, US). We conducted descriptive analyses using frequency measures for qualitative variables and summary measures for quantitative variables. For inferential statistics, we compared quantitative variables between groups using the Mann–Whitney U test, as assumptions of normality and homogeneity of variances were not met. For proportion comparisons, we used χ^2 or Fisher's exact tests depending on expected values.

To evaluate the risk of death during hospitalization in relation to admission cause, we performed a Poisson regression with logarithmic link function and robust variances. We calculated both crude and adjusted models. We included variables that were both accessible and relevant from the authors' perspective, selected from those controlling backdoor pathways identified in the directed acyclic diagram[19]. We estimated relative risks (RR) with corresponding 95% confidence intervals (CI).

Results

Descriptive analysis of the sample

From 1,341 PICU admissions during the study period, we preselected 236 patients admitted with septic shock and 749 with other diagnoses after applying the selection criteria. Following randomization, 179 patients were included in each group (Fig. 1). The total sample comprised 51.96% (n = 186) females, with a median age of 3.7 years. The largest age group was children under 1 year, representing 29.61% (n = 106) of participants. The most prevalent comorbidities were respiratory, cardiological, neuromuscular, oncological, and digestive conditions (Fig. 2). In addition, 15% of patients had a history of prematurity, and 60% (n = 215) presented with at least one comorbidity (Table 1).

Patient characteristics upon PICU admission

The septic shock group showed a significantly higher proportion of children under 1 year compared to those admitted for other reasons (41.33% vs. 17.88%; p < 0.001). This group also demonstrated a slightly higher frequency of at least one comorbidity (60.33% vs. 59.78%; p = 0.021). Patients with septic shock were significantly younger (median age 1.67 vs. 4.67 years; p < 0.001) and had significantly higher PRISM scores (median 13.25 vs. 1.26 points; p < 0.001) (Table 1).

Clinical course of patients in the PICU

Mechanical ventilation requirement was significantly higher in the septic shock group compared to other admissions (100% vs. 86.59%; p < 0.001). These patients also had longer hospital stays (median 7 vs. 3.99 days; p < 0.001). The overall mortality rate was 21.23% (n = 76), with septic shock patients showing a significantly higher mortality rate of 32.96% (n = 59; p < 0.001) compared to other admissions (Table 2).

Association between PICU admission due to septic shock and mortality

Patients admitted with septic shock demonstrated a 2.73 times higher risk of death compared to those admitted for other causes. This association persisted after adjusting for age, prematurity history, number of comorbidities, PRISM score, mechanical ventilation requirement, and length of hospital stay (RR: 2.73; 95% CI 1.36–5.46; p = 0.005) (Table 3).

Discussion

In this study of pediatric patients admitted to a Peruvian national reference hospital's PICU, we found a statistically significant association between septic
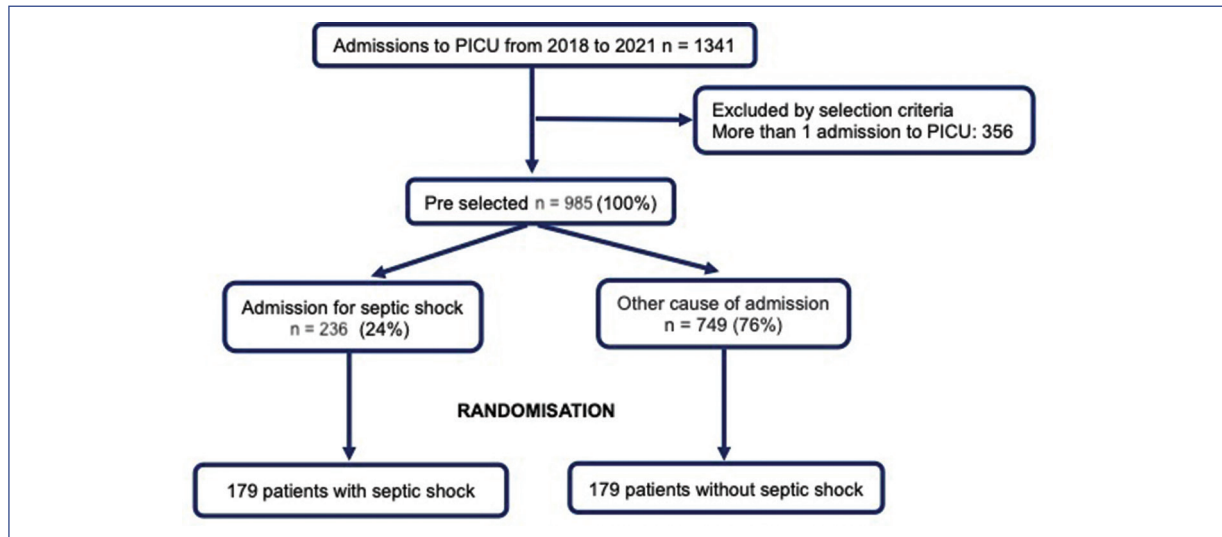
Figure 1. Participant selection flow diagram.
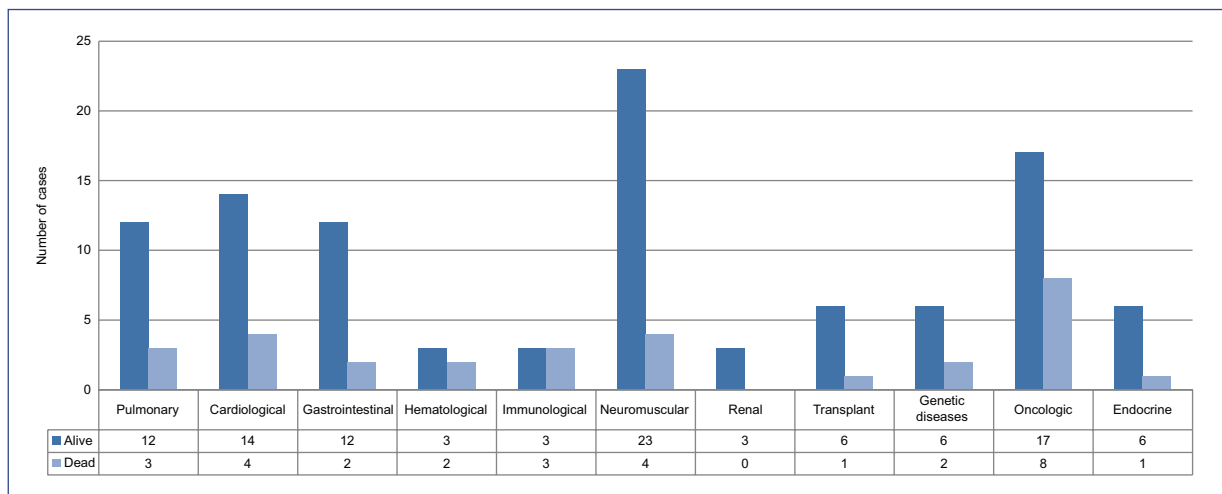
Figure 2. Distribution of prior medical conditions and mortality*.
*Patients who had a single comorbidity were considered, and the mortality evaluated was general.

shock admission and mortality during PICU stay. This association persisted after adjusting for other variables. Our findings contrast with those of Ahmed et al., who found no statistical association between sepsis and mortality in Ethiopian neonates[20]. This discrepancy may be attributed to differences in study populations, clinical practices, health-care conditions, or statistical power. Our results are particularly relevant as our literature review revealed no previous studies comparing mortality rates between patients admitted to PICU with septic shock versus other diagnoses.

Among patients admitted with septic shock, 60% presented with one or more comorbidities, slightly higher than the 43%[3] and 50%[2,4] reported in other studies. This difference might be explained by our study's exclusive focus on septic shock patients, whereas other studies included sepsis and severe sepsis cases. Current understanding suggests that patients with comorbidities have an increased likelihood of progressing from sepsis to shock, organ dysfunction, and mortality[21]. We concur with De Souza et al.'s findings of an association between multiple comorbidities and

Table 1. General characteristics of the patients at the time of admission to the PICU

Variable	Total, n (%)	With septic shock, n (%) (n = 179)	Without septic shock, n (%) (n = 179)	p
Sex				
Female	186 (51.96)	94 (52.51)	92 (51.40)	0.832[a]
Male	172 (48.04)	85 (47.49)	87 (48.60)	
Age				
p50 [IQR]	3.70 [9.42-0.75]	1.67 (7.75-0.42)	4.76 (10.5-1.58)	< 0.001[b]
Age group (years)				
< 1	106 (29.61)	74 (41.34)	32 (17.88)	< 0.001[a]
1-< 5	98 (27.37)	39 (21.79)	59 (32.96)	
5-< 10	75 (20.95)	38 (21.23)	37 (20.67)	
10 to more	79 (22.07)	28 (15.64)	51 (28.49)	
History of prematurity (wks. of gestation)				
No	304 (84.92)	155 (86.59)	149 (83.24)	0.306[c]
PTNB < 28	8 (2.23)	2 (1.12)	6 (3.35)	
PTNB 28-< 32	25 (6.98)	14 (7.82)	11 (6.15)	
PTNB 32-< 37	21 (5.87)	8 (4.47)	13 (7.26)	
Number of comorbidities				
None	143 (39.94)	71 (39.66)	72 (40.22)	0.021[a]
1	135 (37.71)	58 (32.40)	77 (43.02)	
2 or more	80 (22.35)	50 (27.93)	30 (16.76)	
PRISM, score				
p50 [IQR]	3.89 (21.3-0.95)	13.25 (46.6-3.8)	1.26 (3.94-0.52)	< 0.001[b]

PICU: pediatric intensive care unit, n: sample, %: percent, p50: median, IQR: interquartile range, wks: weeks, PTNB: preterm newborns, PRISM: pediatric risk of mortality score
a. p value obtained with χ^2 test
b. p value obtained with Mann–Whitney U-Test
p value obtained with Fisher's exact test

Table 2. Clinical course of patients in PICU

Variable	Total	With septic shock, n (%) (n = 179)	Without septic shock, n (%) (n = 179)	p
Mechanical ventilation				
No	24 (6.70)	0 (0.0)	24 (13.41)	< 0.001[a]
Yes	334 (93.30)	179 (100.00)	155 (86.59)	
Length of hospital stay (days)				
p50 [IQR]	5.37	7 (15-4)	3.99 (7.37-1.94)	< 0.001[b]
Discharge condition				
Alive	282 (78.77)	120 (67.04)	162 (90.50)	< 0.001[a]
Dead	76 (21.23)	59 (32.96)	17 (9.50)	

PICU: pediatric intensive care unit, n: sample, %: percent, p50: median, IQR: interquartile range
[a]p value obtained with χ^2 test
[b]p value obtained with Mann–Whitney U-Test

mortality in children with sepsis[3]. However, this analysis was exploratory, as our sample size calculation was not specifically designed to evaluate this relationship.

Children under 1 year of age constituted the largest group with septic shock (41%). Similarly, Schlapbach et al., analyzing data from Australia and New Zealand, found that children under 1 year represented 30% of cases[9]. Jaramillo-Bustamante et al. from Colombia reported that 56% of patients with sepsis, severe sepsis, or septic shock were under 2 years old[4]. These findings consistently indicate that young children, particularly those under 1 year, are most vulnerable to septic shock. However, in our study, age group was not associated with mortality risk in either crude or adjusted analyses.

Table 3. Association between septic shock admission to the PICU and mortality: Crude and adjusted model

Variable	Crude Model			Adjusted Model[a]		
	RR	95% CI	p	RR	95% CI	p value
Diagnosis						
Not Septic shock	Ref.			Ref.		
Septic shock	3.47	2.11-5.72	< 0.001	2.73	1.36-5.46	0.005
Age						
Years	1.00	0.96-1.05	0.830	1.04	0.99-1.09	0.119
History of prematurity weeks						
No	Ref.			Ref.		
PTNB < 28	0.58	0.09-3.71	0.569	1.37	0.29-6.54	0.694
PTNB 28-< 32	1.50	0.81-2.76	0.196	0.86	0.45-1.64	0.653
PTNB 32-< 37	0.45	0.12-1.70	0.236	0.41	0.11-1.55	0.191
Number of comorbidities						
None	Ref.			Ref.		
1	1.14	0.71-1.82	0.590	1.42	0.88-2.27	0.148
2 or more	1.32	0.80-2.21	0.281	1.83	1.08-3.09	0.024
PRISM						
Score	1.02	1.02-1.03	< 0.001	1.02	1.01-1.03	< 0.01
Requirement of mechanical ventilation						
No	Ref.			Ref.		
Yes	1.75	0.59-5.14	0.310	1.23	0.17-9.06	0.840
Length of hospital stay						
Days	0.96	0.92-0.99	0.046	0.97	0.94-0.99	0.041

PICU: pediatric intensive care unit, RR: relative risk, CI: confidence interval, Ref.: reference value
preterm newborns (PTNB), PRISM: pediatric risk of mortality score
[a]Model adjusted by age, prematurity, number of comorbidities, PRISM score, requirement of mechanical ventilation, and length of hospital stay.

The mortality risk in the PICU was significantly higher for patients admitted with septic shock compared to those admitted with other diagnoses, as evidenced by the higher mortality rates in the septic shock group. Multiple publications have reported similar findings regarding calculated mortality percentages and observed mortality rates favoring the septic shock group[3,6,22]. In addition, patients with septic shock demonstrated longer PICU stays compared to those admitted for other diagnoses, consistent with findings from several other studies[2,3,6]. These observations suggest that PICU patients admitted with septic shock present with greater severity and have a higher risk of prolonged unit stays compared to patients admitted with other diagnoses.

In the context of Sustainable Development Goals (SDGs)[23], our findings align directly with SDG 3 (Health and Wellbeing), providing vital information that could inform strategies to improve pediatric health outcomes and reduce mortality. In addition, by conducting this study in a South American population and considering population-specific characteristics and health-care access limitations, our research addresses SDG 10 (Reduce Inequalities) by quantifying clinical outcomes in pediatric PICU patients. From a clinical perspective, our study makes a valuable contribution to the scientific literature. The incorporation of our findings into future systematic reviews[24] will enable a more comprehensive evaluation of the incidence and magnitude of death risk associated with pediatric septic shock. This information will support health managers, political representatives, and stakeholders in better managing and planning for this disease burden[25].

We acknowledge several limitations in our study that may affect the interpretation of our results. The single-hospital sample source represents a selection bias that limits generalizability to other populations. However, as our institution is a national reference hospital adhering to national standards, some extrapolation may be possible within similar contexts. We also acknowledge an information bias due to omitting potentially influential factors on mortality, such as nutritional status and time to medical care, which were not evaluated or included in the adjusted analysis. Nevertheless, our adjustment

for confounding variables helps mitigate this bias and supports the study's internal validity.

Our study has notable strengths. The randomization of patients between groups enhances sample representation, while the 4-year study period allows for the observation of long-term trends. These strengths, combined with our rigorous methodology, reinforce the reliability of our findings.

Conclusion

Patients admitted to PICU with septic shock demonstrated a significantly higher mortality risk compared to those admitted for other causes. This association persisted after adjusting for age, prematurity history, number of comorbidities, PRISM score, mechanical ventilation requirement, and length of hospital stay. We recommend conducting multicenter studies to investigate the generalizability of these findings across different populations.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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