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ORIGINAL ARTICLE

Nutritional status in children in Intensive Care Unit: a cohort study

Estado nutricional en niños de una Unidad de Cuidados Intensivos: estudio de cohorte

José Tantaleán Da Fieno[a], Rosa León Paredes[b], Patricia Palomo Luck[b,d], Emiliana Rizo Patrón Terrero[c], Carlos Del Águila Villar[a]

[a]Universidad Nacional Federico Villarreal. Lima, Perú.
[b]Instituto Nacional de Salud del Niño. Lima, Perú.
[c]Universidad Peruana Cayetano Heredia. Lima, Perú.
[d]Nutricionista.

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What do we know about the subject matter of this study?

Malnutrition in PICUs is common, and its association with mortality, length of stay, mechanical ventilation, and hospital infections shows conflicting results. Different nutritional outcomes and indicators have been investigated, and there is no consensus on how to classify nutritional status in critically ill children.

What does this study contribute to what is already known?

Using the recommended indicators of W/L and BMI/A, we observed that low weight was associated with a higher frequency of mechanical ventilation use, while excess weight was associated with an increase in ventilator-free days. We did not observe an association between nutritional status and mortality, length of stay, or hospital infections.

Abstract

Studies on the association between nutritional diagnosis and outcomes in critically ill children show mixed results. **Objective**: To evaluate nutritional status and determine its association with outcomes in a Pediatric Intensive Care Unit (PICU). **Patients and Method**: Retrospective cohort study at the National Institute of Child Health, Peru. We assessed nutritional status at admission using weight/height (< 2 years) and BMI for age (≥ 2 years), and determined its association with mortality, PICU length of stay, mechanical ventilation (MV), ventilator-free days, and healthcare-associated infections. We excluded children with diagnoses that affected anthropometry due to non-nutritional causes. We applied bivariate analysis and adjusted Poisson regression. **Results**: In 487 patients, 13.1% were underweight and 23% were overweight. In bivariate analysis, underweight children had less ventilator-free days (21 days vs 25 days; p = 0.0101) and longer ICU stay (8 days vs 5.5 days; p = 0.0153). In the regression analysis, underweight children had a 15% and 21% higher risk of requiring MV compared to children of normal weight and overweight (RR: 0.85; IC: 0.75-0.94 and 0.79;

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Correspondence:
José Tantaleán Da Fieno
jtantalean@unfv.edu.pe

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Gerardo Weisstaub

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IC: 0.69-0.91, respectively; p = 0.001). Overweight children had more ventilator-free days compared to those underweight (RR: 1.11; CI: 1.01-1.21; p = 0.018). Mortality, healthcare-associated infections, or PICU stay were not associated with nutritional diagnosis. **Conclusions:** Underweight was correlated with greater use of MV, while overweight was related to an increase in ventilator-free days. There was no association between nutritional status and mortality, length of stay, or healthcare-associated infections.

Introduction

Undernutrition is the most common form of malnutrition (defined as undernutrition or obesity) in pediatric intensive care units (PICUs), especially in lower-income countries[1]. It is observed in 13-65% of this population[2-10] and, although recent studies in lower-income countries seem to show a decrease in its frequency[11,12], it remains prevalent in Latin America[13]. Malnutrition in critically ill children has been associated with adverse outcomes, including mortality[14].

It is recommended to record weight and length upon admission and during the stay in the PICU, using weight/length in children under 2 years of age[14] and BMI according to age in older children[14,15] as nutritional indicators. However, anthropometric assessment in the PICU is hindered by multiple factors, resulting in fewer PICUs performing systematic assessments of nutritional status that would allow for personalized care[16-18]. On the other hand, 72% of PICUs in Latin America assess nutritional status[19].

The association between undernutrition and mortality, duration of mechanical ventilation (MV), length of stay, or healthcare-associated infections (HAIs) shows heterogeneous results[2,6-8,12,20]. Three systematic reviews/meta-analyses found variable results using different methods of nutritional diagnosis classification[21-23]. On the other hand, overweight and obesity have increased in PICUs[1,2,24] and have been associated with higher[25-27], similar[28], or lower mortality in children with Acute Respiratory Distress Syndrome[29] compared to children of normal weight.

The different nutritional assessment criteria and outcomes evaluated may lead to different results. One study showed longer MV time in undernourished children[7], while others observed the association only when undernutrition was defined by certain nutritional indicators[20] or in severely undernourished children[8]; in children on MV, undernourished children had fewer ventilator-free days[2]. These studies did not identify nutritional diagnosis according to the recommendations of the Guidelines[14], and one study that applied them found no association between undernutrition and MV duration[10].

The objective of this study was to evaluate nutritional status at admission to the PICU using Weight/Length (W/L) and BMI/Age (BMI/A)[14,15], and its association with mortality, length of stay, MV, and HAIs.

Patients and Method

Retrospective cohort study in the PICU of the National Institute of Child Health (PICU-INSN). The PICU-INSN has 15 beds and receives children > 1 month and < 18 years of age with all types of diagnoses, except those who have undergone cardiovascular surgery. Part of the population analyzed was drawn from a previous study[30].

We recorded only the first admissions of patients from April 2018 to April 2020. The information was collected from our database or from the medical records. We excluded children < 1 month of age, < 2 years of age with a history of prematurity, congenital and skeletal malformations, Down syndrome, clinical edema or brain death upon admission, and death or discharge from the PICU during the first 24 hours of admission.

We defined two types of admission diagnosis: postoperative, in cases of postoperative monitoring in scheduled surgeries, and medical, in all other cases. Severity was determined using the PRISM scale[31]. We recorded the use of invasive MV and the duration of MV during the PICU stay; ventilator-free days were calculated by subtracting the duration of MV from 28 days, counted from PICU admission; in cases of reintubation < 48 hours post-extubation, the first and second periods of MV were evaluated as a single episode; in children with > 28 days on MV or who died before 28 days, ventilator-free days were recorded as 0 (zero).

We recorded the length of PICU stay and mortality up to 60 days after PICU admission. We identified three HAIs (urinary tract infection, bloodstream infection, and ventilator-associated pneumonia) in children with a PICU stay of > 48 hours and no evidence of infection at admission, using the criteria of the US Centers for Disease Control and Prevention

(CDC)[32]. Length of stay, ventilator-free days, and HAIs were evaluated exclusively during the stay in the PICU.

We recorded weight and length within the first 48 hours of admission, noting the presence of edema to identify cases to be excluded. Length was measured from head to toe on the patient's bed, two or three times per child, using wooden head and foot supports to minimize body curvature and a flexible, non-stretch metal measuring tape. Questionable data were excluded, and anthropometric measurements were not performed after PICU admission.

We identified nutritional status using the unified z-score for W/L (< 2 years) and BMI/A (≥ 2 years). We defined **underweight** as a W/L or BMI/A z-score of < -2 SD, **normal weight** as ≥ -2 and < +1 SD, and **overweight** as ≥ +1 SD[33,34]. The z-score was identified using WHO Anthro® (< 5 years) and WHO AnthroPlus® (≥ 5 years) software[35,36].

We analyzed the associations between nutritional status and clinical outcomes using the z-score for W/L and BMI/A. The three nutritional categories (underweight, normal weight, and overweight) included all children under 18 years of age. Initially, we applied descriptive statistics for general demographic and clinical results, followed by bivariate analysis. Subsequently, a Poisson regression with robust standard error estimation was performed to analyze length of stay in the PICU, HAIs, use of MV, and mortality, with the underweight group as the reference group. For the outcome of ventilator-free days, a zero-inflated Poisson regression model was used. Regression analyses were first performed in crude form and then adjusted for variables that showed a significant association with the outcomes, such as age, sex, PRISM, sepsis, comorbidity, and postoperative diagnosis.

Missing data were handled using complete-case analysis; cases with missing values in any variable required for the analysis were excluded. No imputation was performed.

The study was approved by the Institutional Ethics Committee with code PI-07/21.

Results

A total of 763 children were admitted, of whom 276 cases were excluded, leaving 487 children for analysis (Supplementary Figure 1, available *online*). Table 1 shows the clinical and demographic characteristics.

The most frequent medical diagnoses were respiratory, neurological, and sepsis. Among the 32 children with HAIs, 18 had ventilator-associated pneumonia, 9 had urinary tract infections, and 8 had bloodstream infections (3 children had 2 infections). Mortality in children < 2 years of age was 12%, and in those ≥2 years of age was 6.7%. The z-score in those who died was significantly lower (-0.7 vs. -0.1; p=0.04), and there was higher mortality in females, in children with comorbidities, and in those with sepsis (p < 0.05).

We found 158 children < 2 years old (32.4%) and 329 ≥ 2 years old (67.5%). The frequency of underweight and overweight children was 13.1% and 23%, respectively. Among those < 2 years old, 18.3% were underweight and 19% were overweight, while among those ≥ 2 years old, the figures were 10.6% and 24.9%, respectively. Table 2 shows the frequencies of nutritional status in both age groups.

In the **bivariate analysis**, we found lower mortality as the z-score increased; nutritional status did not significantly affect the frequency of infections or MV use, but children with low weight had fewer ventilator-free days and longer hospital stays (Table 3).

We observed multiple interactions between variables that affected the outcomes, which were considered for the regression analysis. We did not observe an association between the combined presence of nutritional status indicators and clinical outcomes (data not shown).

Regression analysis

Mortality

Regression analysis showed no association between nutritional status and mortality. When analyzing the z-score as a continuous variable, we observed that an increase was associated with a decreased risk of death (RR 0.85; CI 0.73–0.99) in the crude model, but this significance was lost in the adjusted model (data not shown). (Supplementary Table 1, available *online*).

Use of MV and ventilator-free days

Higher z-scores were associated with a lower risk of MV use (data not shown). Low-weight children had a 15% and 21% higher risk of requiring MV compared with normal-weight and overweight children, respectively (Table 4). When postoperative patients were excluded, the risk of requiring MV in underweight children increased to 22% compared to normal weight children (RR 0.78; 95% CI: 0.67-0.92) and to 34% compared to overweight children (RR 0.66; 95% CI: 0.51-0.84) (data not shown).

The adjusted analysis showed no association between low weight and ventilator-free days compared to normal-weight children, but overweight ~~and obese~~ children had a higher number of ventilator-free days compared to low-weight children (Table 5).

Table 1. Clinical and demographic characteristics of participants

Characteristics	n = 487
Age in months, median (IQR)	64 (11-132)
Male sex, n (%)	289 (59.3)
Diagnosis, n (%)	
Post Operative	215 (44.2)
Medical	272 (55.9)
Respiratory diagnosis, n (%)	102 (20.9)
Sepsis, n (%)	46 (9.5)
PRISM, average (SD)	
Comorbidity, n (%)	111 (22.8)
Mortality, n (%)	41 (8.4)
PICU Length of stay in days, median (IQR)	6 (3-13)
Use of IMV, n (%)	376 (78)
VFD, median (n=376) (IQR)	24.9 (14-27)
HAI (n=462), n (%)	32 (6.9)
Nutritional diagnosis, n (%)	
Underweight	64 (13.1)
Normal weight	311 (63.9)
Overweight	112 (23)

PRISM: Pediatric Risk of Mortality Score; IMV: invasive mechanical ventilation; VFD: ventilator free days; HAI: Healthcare-Associated Infection.

Healthcare-associated infections

There was no association between nutritional status and infections (Supplementary Table 2, available *online*).

Pediatric Intensive Care Unit Stay

We analyzed only survivors; no association was observed between nutritional status and length of stay (Supplementary Table 3, available *online*).

Discussion

In this study, 13% of admissions were underweight, and 23% were overweight. Underweight children had a higher frequency of MV use, and overweight children had a higher number of ventilator-free days. We found no association with mortality, HAIs, or length of stay in the PICU.

The low frequency of malnutrition in our PICU (13%), also observed in Brazil[11,12], seems to reflect an epidemiological transition. In contrast, a recent meta-analysis found 37.2% undernutrition[1]; this study included H/A and W/A as indicators, which tend to yield higher frequencies of undernutrition[20]. The increase in excess weight in PICUs is well known[2,3,24],

Table 2. Nutritional diagnosis in children < 2 and ≥ 2 years old: comparison by anthropometric indicators*

Indicator	Category	< 2 years (n: 158) n (%)	≥ 2 years (n: 329) n (%)	Total (n: 487) n (%)
Height/age	Short stature	49 (31.0)	63 (19.1)	112 (23.0)
BMI or W/L	Underweight	29 (18.3)	35 (10.6)	64 (13.1)
	Normal weight	99 (62.7)	212 (64.4)	311 (63.9)
	Overweight	30 (19.0)	82 (24.9)	112 (23.0)

*W/L indicator was applied in < 2 years and BMI in ≥ 2 years. BMI: Body Mass Index for age; W/L: Weight for Length.

Table 3. Bivariate analysis of outcomes according to nutritional status

Outcome	Underweight (< -2 DE)	Normal weight (≥ -2 y < +1 DE)	Overweight (≥ +1 DE)	p
Mortality, n (%)	8 (12.5)	28 (9.0)	5 (4.5)	0.15
HAI, n (%)	6 (9.5)	21 (7.1)	5 (4.8)	0.48
Use of mechanical ventilation, n (%)	56 (87.5)	238 (77.3)	82 (74.6)	0.12
VFD, median (IQR)	21 (3-25.5)	25 (13.5-27)	26 (20-27)	0.0101
PICU stay, median (IQR)	8 (4-24)	5.5 (3-12)	5.5 (3-10.5)	0.0153

HAI: Healthcare-Associated Infection; VFD: ventilator free days, analysis in patients with PICU stay > 48 hours; IQR: Interquartile range.

Table 4. Multivariate analysis of mechanical ventilation use

Characteristic	Crude analysis RR (IC 95%)	p	Adjusted analysis† RR (IC 95%)	p
Age (months)			0,99 (0,99 - 1,0)	0,566
Sex (male)			0,90 (0,82 - 0,99)	0,027
Nutritional diagnosis				
Underweight	Referencia		Referencia	
Normal weight	0,88 (0,79 - 0,99)	0,028	0,85 (0,75 - 0,94)	0,001
Overweight	0,85 (0,74 - 0,98)	0,028	0,79 (0,69 - 0,91)	0,001
Postoperative			1,39 (1,25 - 1,54)	< 0,001
Sepsis			0,84 (0,67 - 1,04)	0,139
PRISM			1,03 (1,02 - 1,04)	< 0,001

†Adjusted for age, sex, PRISM score, Postoperative, sepsis and comorbidity. PRISM: Pediatric Risk of Mortality Score.

Table 5. Multivariate analysis of ventilator free days

Characteristic	Crude analysis RR (IC 95%)	p	Adjusted analysis† RR (IC 95%)	p
Age (months)			1.00 (0.99 - 1.00)	0.715
Sex (male)			0.99 (0.94 - 1.04)	0.809
Nutritional diagnosis				
Underweight	Referencia		Referencia	
Normal weight	1.14 (1.06 - 1.22)	< 0.001	1.04 (0.96 - 1.13)	0.29
Overweight	1.18 (1.09 - 1.22)	< 0.001	1.11 (1.01 - 1.21)	0.018
Postoperative			1.07 (0.97 - 1.16)	0.159
Neurologic diagnosis			0.85 (0.76 - 0.95)	0.007
Respiratory diagnosis			0.79 (0.71 - 0.88)	< 0.001
PRISM			0.99 (0.98 - 0.99)	< 0.001

Zero-Inflated Poisson Regression Model. †Adjusted for age, sex, PRISM score, Postoperative, sepsis and comorbidity. PRISM: Pediatric Risk of Mortality Score.

but in our case, it was surprising that it exceeded low weight. In Latin America, using the same nutritional criteria, low weight was found in 17.8% and obesity in 10.5%[13]. Likely, the higher frequency of excess weight in our case (23%) is because we considered overweight and obesity for the analysis.

The different results in the association between undernutrition or excess weight and outcomes[2,7,8,10,12,21-23,25-29] make it necessary to further study these relationships. The lack of consensus on nutritional diagnosis in PICUs[18], the evaluation of different outcomes, and different definitions of variables hinder the comparison of results.

Mortality

Although our study found no association between low weight and mortality, previous evidence is heterogeneous. Some studies reported a higher risk of death in undernourished children[2,12], while others found no differences compared to normal-weight children[7,8,10]. Similarly, systematic reviews/meta-analyses have shown inconsistent results. Two meta-analyses did not agree on the magnitude or direction of the association[21,22], also pointing to heterogeneity in the criteria used to classify nutritional status[21-23]. Another study observed higher mortality with low weight, but the adjustment for covariates, unlike in our case, did not include disease severity[37], and a recent meta-analysis found higher mortality in low weight[38]. The lower z-score we found in deceased patients suggests a relationship between low weight and mortality, which was not confirmed in the regression analysis.

The relationship between excess weight and mortality is less well known. Lower mortality was found in obese children with lung injury, consistent with the "obesity paradox"[29], but a meta-analysis found higher mortality in obese children[27], and two studies observed a U-shaped association between weight and mortality (higher at both ends of the percentiles)[25,26]; while another meta-analysis showed no association with excess weight[38]. Greater energy reserves or attenuation of the inflammatory response likely explain this protective effect described in some studies[29,39]. We observed a progressive decrease in the risk of death when comparing underweight children with those of normal weight, a decrease that continued to decline in overweight children (Supplementary Table 1, available *online*), but the interpretation of this pattern remains a matter of debate.

Mechanical ventilation and ventilator-free days

Low-weight children had greater use of MV, consistent with findings in two meta-analyses[22,38].

Ventilator-free days represent ventilation time and mortality in the first 28 days of MV. Of the five studies that evaluated nutritional diagnosis and MV, four observed an association between low weight and longer MV time or fewer ventilator-free days[2,7,8,20].

Undernutrition represents depletion of metabolic reserves and loss of muscle mass, which, together with limited nutritional intake due to a critical condition, impair respiratory function[22]. Critical condition, *per se,* can affect muscle and respiratory muscle function due to hypercatabolism, causing deterioration of the diaphragm and muscle mass, increasing MV time[40,41]. In children with PICU-acquired myopathy, the duration of MV is increased[42]. These muscle disorders can prolong the duration of MV[22,38] or decrease the number of ventilator-free days, as in our case (Table 5).

Obese individuals do not have longer MV time[27], but overweight children were less likely to require MV and had more ventilator-free days (Tables 4 and 5). The intensification of these associations with increasing z-scores suggests a protective effect of excess weight.

Healthcare-associated infections

The association with nutritional diagnosis shows contradictory results[2,10]. The relationship between undernutrition and infection is historical, due to deterioration in immune system function, but few studies found undernutrition to be a risk factor for infection[43,44]. Meta-analyses/systematic reviews in critically ill children[21-23,27] did not include infections in their outcomes, and the most recent one found no association with nutritional status[38], consistent with our results. (Supplementary Table 2, available *online*). The only study that found a higher risk of infection in low weight and obesity analyzed 1,622 children, a figure three times higher than ours[2].

Pediatric Intensive Care Unit Stay

Its association with nutritional status is uncertain. In undernourished children, two meta-analyses/systematic reviews found longer stays in undernourished children[22,38], and two observed heterogeneous results or no association[21,23]. Other studies found shorter stays in overweight children[10]. We found no association with nutritional diagnosis (Supplementary Table 3, available *online*).

Due to the heterogeneity in nutritional diagnosis methods[21-23,27], it is recommended to standardize the criteria, even in non-critical children[14,15,45]. The 2017 Guidelines recommended using W/L and BMI/A, without indicating cut-off points[14], but few subsequent studies applied them[10,13]. We believe that these recommendations provide an opportunity for standardization.

The long-term consequences of malnutrition in PICUs are less well known. Undernutrition at an early age leads to impaired neurodevelopment, decreased IQ, poor school performance, and behavioral problems that persist into adulthood[46]. A systematic review found lower scores in intelligence, psychomotor development, and memory after critical illness[47]. In critically ill adults, muscle function and quality of life are reported to be impaired for years, and children hospitalized in the PICU have difficulties with physical activities for up to 4 years afterward[48]. The simultaneous occurrence of malnutrition and critical illness can act synergistically, compromising the child's health in the short and long term. Studies with prolonged follow-up are needed to determine residual morbidity.

Our study has several limitations. The retrospective design may hinder the reliable recording of variables; however, the data were collected prospectively and subsequently used for analysis, which may limit this problem. The study was conducted in a single center, hindering the extrapolation of the findings to centers with populations and characteristics different from those of our institution. There is also a risk of error in anthropometric measurements, especially in children with more serious conditions; we reduced this risk by having the measurements made by the authors or the nutritionist on duty. Finally, it is known that nutritional status deteriorates during the stay in the PICU, and periodic evaluations are recommended[15,49], but we do not perform them routinely in the PICU-INSN.

Conclusions

Undernutrition in the PICU remains common, but excess weight has increased. Low weight was associated with greater use of MV, while excess weight was associated with more ventilator-free days. We observed no association between nutritional status and mortality, length of stay, or HAIs. The different associations between nutritional status and outcomes highlight the need to standardize nutritional diagnostic criteria and develop prospective multicenter studies.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: This study was approved by the respective Research Ethics Committee, which, according to the study's characteristics, has accepted the non-use of Informed Consent.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

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