Title: Complex chronic conditions at PICU admission are associated with nutritional status deterioration during PICU stay: PICU-ScREEN multicenter study.

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Background: Critically ill children can experience deterioration of nutritional status (NS) during Pediatric Intensive Care Unit (PICU) stay, which can lead to worse clinical outcomes. Thus, we aimed to describe the prevalence of NS deterioration during PICU stay, and to identify PICU factors on admission that are associated with NS deterioration during PICU stay in critically ill children.

Methods: Multicenter cohort study, performed in 8 Brazilian PICUs, with critically ill children aged 1 month to 18 years with a PICU stay >72 hours. Demographic, clinical, laboratory and nutrition parameters at PICU admission were recorded. Severity risk score was assessed by Pediatric Index of Mortality 2 (PIM 2) and patients were classified into mild (1st tertile), moderate (2nd tertile) and severe (3rd tertile) groups. Anthropometry was assessed at PICU admission, after 7 days, 14 days and/or at PICU discharge if earlier. NS at PICU admission was assessed by weight-for-age (WAz) or height-for-age (HAz) in children <2 years, and body mass index-for-age (BMIz) in children >2 years. NS deterioration was defined as the reduction from admission of 1 z-score in WAz, BMIz or mid-upper arm circumference (MUAC)-for-age; or a 7.5% reduction in weight (kg) or MUAC (cm) during PICU stay (7 days, 14 days and/or PICU discharge). Logistic regression adjusted for PICU site was applied to assess the association of each variable with the outcome, and all the variables with a p-value <0.20 were included at the same time in the multivariate logistic regression model. P-value <0.05 was considered significant.

Results: A total of 269 consecutive eligible patients were included, with a median age of 11.9 months (interquartile range [IQR]: 3.0-45.8), 63.6% were male. Seventy nine percent were admitted for medical reasons and 43.5% of the admissions were for respiratory reasons. The median PIM 2 was 4.2% (IQR: 1.6-9.6), 28.6% of the patients had a severe PIM 2 predicted risk of mortality, 44.9% had complex chronic conditions (CCC) and 27.0% were undernourished (<-2 z-score) at PICU admission. The median PICU length of stay was 11 days (IQR: 7-18), and overall mortality rate was 4.8%. NS deterioration was observed in 27.9% of the cohort, (Table 1). Presence of CCC (Odds ratio [OR]: 1.92; 95%CI: 1.11–3.30; p=0.019) and severe PIM 2 (OR: 1.36; 95%CI: 1.02-1.81; p=0.038) were associated with NS deterioration, after adjustment

for PICU site. However, in the multivariate model adjusted for PICU site, only CCC (OR: 1.80; 95%CI: 1.02–3.18; p=0.044) remained associated with NS deterioration during PICU stay (Table 2).
Conclusions: In our multicenter cohort of Brazilian critically ill children, one in four patients experienced NS deterioration during their PICU stay. Presence of at least one CCC at PICU admission was associated with NS deterioration during PICU stay, independent of the severity of illness. Future studies with a larger sample size could evaluate the predictive value of these parameters in the development of a nutritional screening tool for this population.

Keywords: Pediatric Intensive Care Units. Nutritional Status. Chronic illness. Severity of illness. Hospital-acquired malnutrition.

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Table 1 - Demographic, clinical and nutritional characterization of critically ill children in 8 Brazilian PICUs, between March 2018 and December 2019 (n=269).

Variables	All patients (n = 269)
	N (%) / Median [IQR]
Sex (male)	171 (63.6)
Age (months)	11.9 [3.0 – 45.8]
Admission type	
Medical	215 (79.9)
Surgical	54 (20.1)
Type of diagnosis	
Respiratory	117 (43.5)
Congenital heart disease	18 (6.7)
Sepsis or septic shock	30 (11.1)
Other cardiac disease	21 (7.8)
Miscellaneous / Others [a]	19 (7.1)
Neurology	20 (7.4)
Infectious disease	11 (4.1)
Trauma / Burning	12 (4.5)
Renal / Endocrine	15 (5.6)
Oncology	6 (2.2)
Complex Chronic Conditions	121 (44.9)
PIM 2 (probability of death, %) (n=266)	4.2 [1.6 – 9.6]
Severity risk score (PIM 2) (n=266) [b]	
Mild	87 (32.7)
Moderate	103 (38.7)
Severe	76 (28.6)
Nutritional status (n=267) [c]	
Well-nourished	95 (35.6)
Nutritional risk (<-1 z-score)	82 (30.7)
Undernutrition (<-2 z-score)	72 (27.0)
Overweight / Obesity (>+2 z-score) [d]	18 (6.7)
NT within 48h (n=266)	204 (76.7)
Route of NT (n=257)	
EN	226 (87.9)
PN	30 (11.7)
EN + PN	1 (0.4)
Nutritional status deterioration [e]	75 (27.9)
Nosocomial infection	70 (26.0)
Mechanical ventilation	233 (86.6)
Duration of MV (days) (n=233)	7 [4 – 13]
PICU LOS (days)	11 [7 – 18]
Hospital LOS (days)	21 [12 – 36]
Overall Mortality	13 (4.8)

BMIZ: body mass index-for-age z-score; EN: enteral nutrition; IQR: Interquartile range; PIM 2: Pediatric Index of Mortality 2; MV: mechanical ventilation; NT: nutrition therapy; PICU: Pediatric Intensive Care Unit; PN: parenteral nutrition; LOS: length of stay; WAz: weight-for-age z-score.

[a] Hypovolemic shock, congenital, gastrointestinal, genetic, immunological, metabolic, orthopedic and rheumatological disease; [b] Assessed by PIM 2: mild (1st tertile), moderate (2nd tertile) and severe (3rd tertile); [c] WAz or HAz when <2 years, and BMIz when >2 years of age; [d] WAz when <2 years, and BMIz when >2 years of age; [e] Reduction of 7.5% on weight or MUAC OR reduction of 1 z-score of WAz, BMIz or MUACz during PICU stay.

Table 2 – Logistic regression and multivariate logistic regression model of factors associated with nutritional status deterioration during PICU stay [a] in critically ill children in 8 Brazilian PICUs, between March 2018 and December 2019.

Variables at PICU admission	Nutritional Status deterioration during PICU stay (n = 75) [a]			
	Logistic regression		Multivariate logistic regression model [++]	
	OR (95% CI)[+]	p-value	OR (95% CI)[+]	p-value
DEMOGRAPHIC AND CLINICAL				
Sex (female)	0.69 (0.39–1.23)	0.208		
Age (<24 months)	1.64 (0.92–2.93)	0.093	1.80 (0.95–3.41)	0.071
Admission type (medical)	1.16 (0.57–2.37)	0.687		
Type of diagnosis		0.472		
Other diseases	1.00			
Infection-related	0.59 (0.28–1.26)			
Respiratory	0.72 (0.36–1.46)			
Surgical	0.65 (0.28–1.48)			
CCC	1.92 (1.11–3.30)	**0.019**	1.84 (1.04–3.26)	**0.037**
Severity risk score (PIM2) [b]				
Mild / Moderate	1.00		1.00	
Severe	1.36 (1.02–1.81)	**0.038**	1.27 (0.94–1.72)	0.125
Fluid overload (> 10%) [c]	0.90 (0.49–1.65)	0.730		
BIOCHEMICAL				
Leukocytes (x10 $^{-3}$)	1.03 (0.99–1.07)	0.067	1.03 (0.99–1.07)	0.109
Hypoalbuminemia (<3.0 g/dL)	1.26 (0.64–2.48)	0.502		
CRP (>100 mg/dL)	1.07 (0.53–2.17)	0.854		
CRP/Albumin ratio (mg/dL:g/dL)				
1st + 2nd tertile	1.00			
3rd tertile	0.95 (0.68–1.34)	0.786		
NUTRITIONAL STATUS				
Nutritional risk (<-1 z-score) [d]	1.40 (0.80–2.44)	0.234		
Undernutrition (<-2 z-score) [d]	1.60 (0.92–2.79)	0.097	1.29 (0.71–2.35)	0.400
Overweight / Obesity (>+2 z-score) [e]	1.61 (0.59–4.34)	0.350		
NUTRITION THERAPY				
NT prior to PICU (yes)	1.10 (0.58–2.06)	0.770		
Early NT (48 hours)	0.64 (0.34–1.17)	0.147	0.71 (0.37–1.36)	0.303

BMIz: body mass index-for-age z-score; CCC: Chronic Complex Condition; CI: Confidence Interval; CRP: C-reactive protein; HAz: height-for-age z-score; LOS: length of stay; MUACz: mid-upper arm circumference-for-age z-score; NT: Nutritional Therapy; OR: Odds Ratio; PICU: Pediatric Intensive Care Unit; PIM 2: Pediatric Index of Mortality 2; WAz: weight-for-age z-score.

[a] Reduction of 7.5% on weight or MUAC OR reduction of 1 z-score of WAz, BMIz or MUACz during PICU stay;

[b] Assessed by PIM 2: mild (1st tertile), moderate (2nd tertile) and severe (3rd tertile); [c] of the first 72 hours of PICU stay;

[d] WAz or HAz when <2 years, and BMIz when >2 years of age; [e] WAz when <2 years, and BMIz when >2 years of age.

[+]Adjusted for PICU site; [++] Variables with p-value <0.20 in the previous analysis were included in the multivariate analysis.