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Diagnostic and prognostic utility of prealbumin as a nutritional biomarker in critically ill children: a prospective cross sectional study

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Abstract

Background Paediatric intensive care units (PICU) experience a big challenge with malnutrition. It significantly impacts the development and prognosis of critically ill patients (CIP). CIP are those who require high reliance or serious medical and/or surgical interventions. For their importance, valid and reliable nutritional markers are mandatory to be implemented in the daily practice of our PICU. The aim of this study was to determine the nutritional status of CIP in PICU through measuring prealbumin level and use it as predictor of malnutrition and clinical outcome.

Methods Forty four CIP admitted to the Children's Hospital, Cairo University PICU, throughout six months were the subject of this cross-sectional study. Clinical nutritional status was evaluated using the Z-score, and prealbumin level was measured.

Results 50% of children who were critically sick also had malnutrition, with severe malnutrition accounting for the majority of cases (34.1%). Prealbumin did not significantly correlate with malnutrition, nor the mortality in CIP. However, malnutrition is strongly linked to mortality in critically ill children. To predict malnutrition in CIP, serum prealbumin at cutoff > 163.64 exhibited AUC of 0.556 with sensitivity of 90.91% and a specificity of 31.82%. For prediction of the clinical outcome, serum prealbumin at cutoff ≤ 758.37 had an AUC of 0.535 with a sensitivity of 91.67% and a specificity of 21.87%.

Conclusions Malnutrition significantly increased the risk of death. Prealbumin was neither a significant predictor for malnutrition nor mortality in CIP.

Keywords CIP, Malnutrition, PICU, Pre-albumin, PRISM score

Background

The pediatric intensive care unit (PICU) focuses on treating critically ill patients (CIP) and preventing mortality [1]. The Pediatric Risk of Mortality III (PRISM III) is well accepted scoring system for proper estimation of disease severity and probability of death in PICU, which are important elements in determining the prognosis of CIP. An accurate prognostic assessment allows for more

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appropriate monitoring, proper management, and family counseling especially in resource-limited countries [2].

Malnutrition among children in hospitals is widespread but underreported [3]. The critical disease affects a person's nutritional condition; as a result, their nutritional needs rise, and their intake may not be enough to support growth and development [4, 5].

Clinical results are negatively impacted by poor nutritional status upon admission or worsening during hospitalization, which raises healthcare expenses [6]. Nutritional risk assessment enables prompt nutritional intervention to avert malnutrition's adverse effects [7].

A protein called prealbumin is created in the liver and partially metabolized by the kidneys [8]. During inflammation, cancer, liver cirrhosis, and malnutrition, serum prealbumin, a negative acute-phase reactant, reduces [9, 10].

Prealbumin has one significant benefit over albumin: it has a shorter half-life, which makes it a better indicator of abrupt dietary changes. Additionally, in those with protein-losing enteropathy, intestinal protein losses have little effect on prealbumin levels [11].

The aim of this study was to determine the nutritional status of CIP in PICU through measuring prealbumin level and use it as predictor of malnutrition and clinical outcome.

Methods

Study setting

The Faculty of Medicine of Cairo University conducted this cross-sectional observational study on CIP patients in the PICU over six months at the children's hospital, "Abu El Reesh."

Study population

The study included CIP with ages ranging from one month to twelve years. If a patient died within 24 h of admission, had chromosomal disorders, was small for gestational age (birth weight 2.5 kg), had illness known to decrease pre-albumin level as hepatic disorders or refused to participate in the study, they were excluded from the study.

Procedure

Based on the mentioned inclusion criteria, 44 patients were chosen All patients who underwent testing had a thorough medical history obtained, including their name, age, sex, place of residence, the reason for PICU admission, need for mechanical ventilation (MV), and length of stay (LOS) in the PICU.

Within 24 h of admission, PRISM III scoring was completed for each patient. PRISM III, a paediatric physiology-based index for mortality risk, has been updated from PRISM. It has 17 physiologic variables subdivided into 26 ranges and is population independent. The most abnormal values during the first 24 h of the PICU admission were included with age-based stratification of the included variables [12].

The anthropometric measurements of each patient were taken, including height and weight. For children under ten, weight for age was the gold standard for interpreting nutritional status. In contrast, BMI was calculated using WHO charts to evaluate nutrition and growth for children over ten [13, 14].

Patients were divided into two comparable groups: group A (well-nourished; $n=22$) and group B (malnourished; $n=22$) according to the Gomez classification. It is one of the earliest systems for classifying protein-energy malnutrition in children, based on percentage of expected weight for age over 90% is normal, 76–90% is mild (first degree) malnutrition, 61–75% is moderate (second degree) malnutrition, and less than 60% is severe (third degree) malnutrition [15]. Group B was further stratified into three levels of malnutrition: mild malnutrition, which ranged from 76 to 90%; moderate; and severe, which fell below 60%.

All patients underwent standard laboratory evaluations, including complete blood count (CBC), blood chemistry, and arterial blood gases. All subjects had their serum prealbumin levels evaluated as a laboratory indicator for malnutrition. The serum from the blood sample was centrifuged at 2000 × g and kept in plastic tubes at -20° C until the assay was run. Following the instructions provided by the manufacturer, a commercial enzyme-linked immunosorbent assay (ELISA) kit was used to test serum prealbumin (Bioassay Technology Laboratory Human prealbumin ELISA Kit, Cat. No E1182Hu, China).

Data management and Statistical analysis

Participants' medical history, clinical evaluation, lab tests, and outcome measurements were among the categories of data that were collected, coded, and evaluated. Quantitative data were given as means ± SD, while qualitative data were presented as frequencies and percentages. The Pearson correlation coefficient was used to examine the correlation between the quantitative variables. Regarding the discrimination performance of pre-albumin for malnutrition and clinical outcome in CIP, receiver operating characteristic (ROC) analysis were conducted. *P*-values less than 0.05 were considered significant. Confidence intervals (95% CI) were calculated when appropriate. Statistical Package for the Social Sciences (SPSS version 20) software was used for analysis.

Sample size estimation

The sample size was calculated based on a previous study, (Reference research article: Tekguc et al. [16] the study aimed to enroll 44 critically ill patients who are admitted to PICU. Sample size calculation was done using Stats Direct statistical software version 2.7.2 for MS Windows, Stata Direct Ltd, Cheshire, UK with confidence interval 10% and confidence level 95%.

Results

After screening 180 admittents to the PICU at Cairo University's Hospital from April 2021 to December 2021, 49 (27.2%) patients were found to satisfy the inclusion and exclusion criteria.The study was conducted on 44 patients only who agreed to participate voluntarily in the study. According to the Gomez classification, the 44 patients were assigned to two groups; group A (well-nourished; $n=22$) and group B (malnourished; $n=22$). Group B was furtherly classified into the three degrees of malnutrition (Table 1).

In the current study, group A had a mean age of 36 months, with 12 (54.5%) males and 10 (45.5%) females (range: 2–132 months). There were 15 (68.2%) females and 7 (31.8%) males in group B, with a mean age of 13 months (range: 2–132 months). Age and sex did not significantly differ between the two groups ($p=0.335$ and 0.128, respectively).

According to the anthropometric evaluation of the enrolled patients, group A's mean weight was 18.8 kg (4–71), and group B's was 7 kg (1.9–54). The weight was significantly different between the two groups ($p=0.007$). The weight percentile between the two groups varied significantly ($p=0.001$) (Table 2). The average heights in groups A and B were 84 cm and 67 cm, respectively. Height did not significantly differ between the two groups ($p=0.204$).

Neurological conditions like cerebral palsy and GBS were the most frequent reasons for admission (32.2%). ARDS (27.2%), cardiac conditions including CHD (18.2%), shock (9.1%), metabolic (6.95), postoperative (4.6%), and renal conditions such ARF (2.3%) were other reasons.

No significant differences ($p>0.05$) were identified between the two groups for the basic investigations (complete blood count, blood chemistry, and arterial blood gases) and serum prealbumin, according to the findings of laboratory tests.

The PRISM score was computed using the clinical and laboratory data from the first day of hospitalization. For group A, the PRISM scores varied from 8 to 19, with a mean of 11; for group B, they ranged from 4 to 17, with a mean of 12. For the recorded PRISM score, there was no significant difference between the two groups ($p>0.05$). The PRISM III score did, however, significantly positively correlate with the outcome being higher in non-survivors ($p=0.003$) (Table 3).

Prealbumin failed to significantly ($p>0.05$) correlate as a nutritional laboratory biomarker with any of the assessed anthropometric measurements, nutritional state, vital signs, routine laboratory tests, or PRISM score (Table 4).

The mean length of stay (LOS) in the PICU was 11.57 days for group A and 18.68 days for group B. LOS in group B increased significantly ($p=0.027$)

Table 1 Classification of nutritional state of the whole group according to Gomez classification

Malnutrition	Percentage of expected weight for age	Value N (%)
Mild (first degree) malnutrition	76–90%	5 (11.4%)
Moderate (second degree) malnutrition	61–75%	2 (4.5%)
Severe (third degree) malnutrition	less than 60%	15 (34.1%)
No malnutrition (Well-nourished)	over 90%	22 (50%)

Table 2 Significant comparison between well-nourished and malnourished critically ill patients

	Group A $N=22$	Group B $N=22$	*Test*	*P*
Weight (Kg)	18.8 (4.0–71.0)	7.0 (1.9–54.0)	-2.690	0.007
Wt SD	1.65 (0.91–21.18)	-2.73 (-8.67–1.24)	-5.540	0.000
Duration of PICU stay	11.57 ± 4.5	18.68 ± 6.5	0.215	0.027
Need for mechanical ventilation	5 (22.7%)	13 (59%)	0.324	0.004

F Female, *M* Male, *wt* weight, *SD* Standard deviation

Table 3 Comparison between survivors and non-survivors for clinic-laboratory data

		Outcome		Test	*P*
		Survived ***N*** **= 32**	**Non-survivors** ***N*** **= 12**		
Age		42(2–132)	11(2–108)	-1.347	0.178
Sex	**Female**	16(50%)	9(75%)	2.223	0.136
	Male	16(50%)	3(25%)		
Weight		18.0 (1.9–71.0)	7.0(3.0–30.0)	-1.952	0.041*
Height		94(45–165)	69(45–130)	-1.385	0.853
wtSD		1.30 (-8.67–21.18)	-2.135 (-8.30–11.70)	-2.135	0.033*
Grade of malnutrition (Gomez classification)	Mild	5(15.6%)	0(0.0%)	12.788	0.005*
	Moderate	2(6.3%)	0(0.0%)		
	Severe	6(18.8%)	9(75.0%)		
	no	19(59.4%)	3(25.0%)		
Mental status (Glasco Coma Score)	≤ 11	6(18.8%)	8(66.7%)	9.240	0.01*
	11–14	7(21.9%)	1(8.3%)		
	15	19(59.4%)	3(25%)		
Cardiovascular	**HR**	130 (18.4–203)	141.5 (90–168)	-0.963	0.336
	SBP	103 (67–170)	96 (63–136)	-0.502	0.616
	DBP	70 (37–143)	63 (37–96)	-0.924	0.356
PRISM score Median (range)		11(4–19)	15(10–17)	-2.953	0.003*
Pre-albumin U/ml		331.45 (62.1–1721)	304.84 (52.42–1447.9)	-0.356	0.722

Quantitative variables were expressed as Median (range) and compared using Mann–Whitney test, while qualitative variables were expressed as numbers and percentages and compared using Chi-square X2 test

wt weight, *SD* Standard deviation, *SBP* Systolic blood pressure, *DBP* Diastolic blood pressure, *HR* Heart rate, *PRISM* Paediatric Risk of Mortality

* Significant at $p<0.05$

more than in group A (Table 2). Of the 44 patients included in this study, 18 (40.9%) required MV during their time in the PICU, while 26 (59%) did not. 13 (59%) of the cases in group B and five (22.7%) of the cases in group A required MV. The requirement for MV varied significantly ($p=0.004$) across the two groups (Table 2). The relationship between the outcome (mortality) and nutritional status was statistically significant ($p=0.042$).

Regarding the results of our study, Mann–Whitney tests showed that non-survivor's weight and weight SD significantly decreased compared to survivors (U = -1.952, $p=0.041$ and U = -2.135, $p=0.033$, respectively). However, there were no appreciable distinctions between survivors and non-survivors regarding demographic traits, height measurements, or vital signs ($p>0.05$). The serum prealbumin level of survivors and non-survivors did not differ significantly according to the Mann–Whitney test (U = -0.356, $p=0.722$). However, research showed that non-survivors had a significantly higher PRISM score than survivors (U = -2.953, $p=0.003$). Grade of malnutrition and mortality had statistically significant positive correlations (2 = 12.78, $p=0.005$) (Table 3).

The receiver operating characteristic (ROC) curve of serum prealbumin was plotted to assess the diagnostic precision of serum prealbumin for malnutrition in CIP. The results indicated that serum prealbumin performed poorly as a screening test for malnutrition in CIP, with an AUC of 0.556 (95% CI:0.398 to 0.705), a sensitivity of 90.91% (95% CI:70.8–98.9%), and specificity of 31.82% (95% CI:13.9–54.9%) in separating malnourished from well-malnourished CIP (Fig. 1).

Regarding the prediction accuracy of the serum prealbumin for the clinical outcome, the ROC curve showed that the serum prealbumin has a sensitivity of 91.67% and a specificity of 21.8% in discriminating survivors from non-survivors with a best cutoff-point of ≤ 758.37 U/ml. The area under the curve (AUC) was 0.535 (Fig. 2).

Discussion

Malnutrition was 50% prevalent among CIP in the current investigation. Teshager et al. [17], who discovered that malnutrition was prevalent in CIP at a rate of 48%,

Table 4 Correlations between serum Pre-albumin level and certain studied parameters in the whole group

	Pre-albumin	
	r	P
PRISM score	-0.027	0.863
Age/m	0.280	0.066
Weigh/kg	0.229	0.135
Height/cm	0.223	0.146
Wt/SD	-0.053	0.732
SBP mm/gH	-0.048	0.758
DBP mm/gH	-0.099	0.523
Temp/C°	0.007	0.965
HR/min	-0.001	0.996
PH	-0.072	0.645
PaCO2 mm/Hg	-0.105	0.497
HCO3 mEq/L	0.048	0.757
GLU mg/dl	0.162	0.292
K mEq/L	0.105	0.498
BUN mg/dl	0.073	0.639
Cr mg/dl	-0.055	0.725
WBCs x 10^3	0.072	0.642
PLT/mm^3	0.028	0.859
PT/seconds	0.025	0.871

r = Correlation Coefficient

backed this conclusion. We compared the weights of the two groups because they would impact the results. Compared to group A, they were significantly lower in group B ($p=0.007$ & 0.001, respectively). The results reported by Bagrie et al. are consistent with these findings [18]. Additionally, it was discovered that children with malnutrition had considerably lower weight than CIP with adequate nutrition (p-value = 0.0001). No statistically significant difference in serum prealbumin between the two groups in the current investigation ($p>0.05$). This is consistent with what Gürlek et al. reported [19]. In malnourished children, the prealbumin level was below the normal range but not significantly. Reduced weight in CIP and higher mortality were statistically significantly correlated in our study ($p=0.004$). The results published by Numa et al. are consistent with these findings [20]. The latter discovered that death was independently linked with lower weight centile and had a p-value of 0.001. There was no correlation between blood prealbumin level and mortality among CIP in the current investigation ($p>0.05$). As far as we know, no study has examined the connection between serum prealbumin and CIP mortality. Wang et al. [21] study was the only one to look at the link between prealbumin levels and mortality; however, it only looked at kidney injury. The latter discovered that, in cases of acute renal injury, the prealbumin level was a significant predictor ($p=0.03$) of 90-day death.

Our study significantly correlated increased PRISM scores and death among CIP patients ($p=0.003$). This

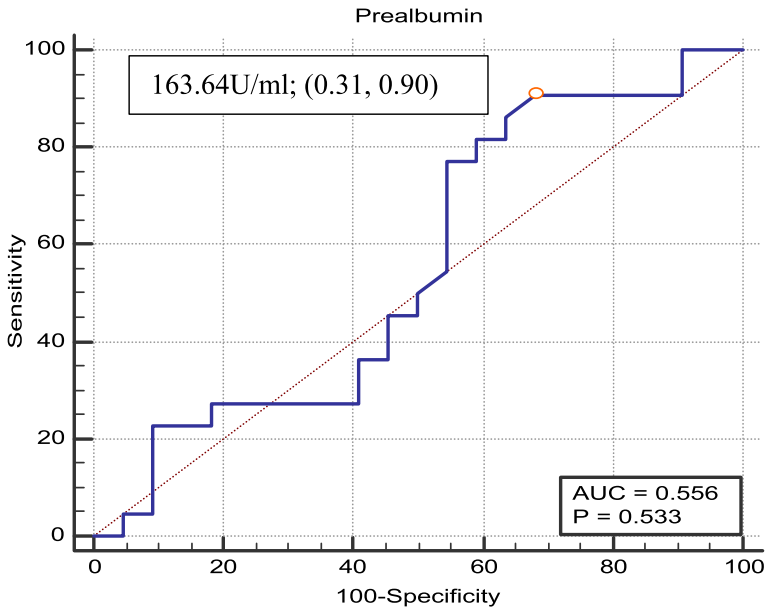

Fig. 1 The Receiver operating characteristic (ROC) curve analysis of serum pre-albumin level as a diagnostic marker for malnutrition

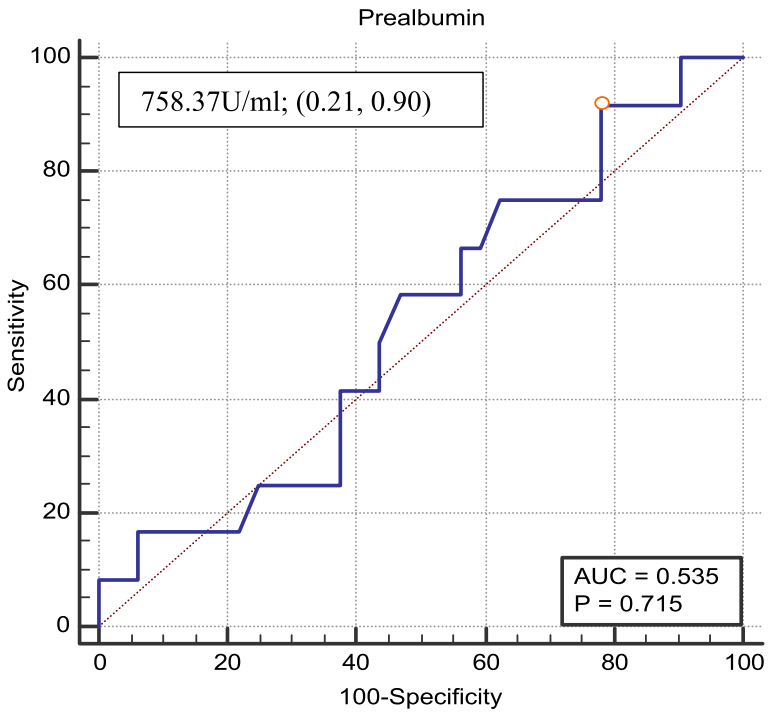

Fig. 2 The Receiver operating characteristic (ROC) curve analysis of serum Pre-albumin level as a diagnostic marker for clinical outcome

conclusion is consistent with what Khajeh et al. [22], Gonçalves et al. [23], and Kaur et al. [24] reported. According to their findings, mortality was noticeably higher (p 0.001) among kids with high PRISM scores than those with low PRISM scores.

Our results showed that group B had a considerably ($p=0.027$) longer LOS than group A when the LOS between the two groups was examined. This is consistent with Shahin et al. [25] findings from 2022, which showed that seriously unwell malnourished children had a considerably (p 0.001) higher LOS. The results of the present investigation demonstrated a substantial increase ($p=0.004$) in the requirement for mechanical ventilation (MV) in group B compared to group A; what Nangalu et al. [26] reported backs up this conclusion. With a p-value of 0.0063, they discovered that CIP with severe malnutrition had a much higher demand for MV. This discovery has an explanation, according to Mota et al. [27]. According to the latter study, starvation causes the respiratory muscles' ability to function to diminish to the point where respiratory failure and artificial ventilation are required.

In the present investigation, fatality rates were determined to be 27.3%, compared to 51.4% in the study by Teka et al. [28]. Variations in sample sizes could explain the disparity between the two studies. Teka et al. [28] analyzed 243 instances; we looked at 44.

Our results support our prediction that CIP would be underweight because the Z score of well-fed and underfed kids differed significantly. The prealbumin level did not differ appreciably at the same time. Except for the PRISM score, our second hypothesis that malnourished CIP would have increased LOS, MV need, and death is accepted.

Conclusion

50% of children who were critically sick also had malnutrition, with severe malnutrition accounting for the majority of cases (34.1%), followed by mild malnutrition (11.4%) and moderate malnutrition (4.5%). Low weight, and low weight percentiles were all indicators of malnutrition. Of the critically ill children included, mortality made up 27.3%. Malnutrition is strongly linked to mortality in seriously unwell children. Prealbumin was not a reliable indicator of malnutrition nor the clinical outcome in children with life-threatening illnesses.

The primary drawback of our work is the need for indirect calorimetry, the gold-standard method for determining basal metabolic rate. Additionally, the included patients' nutritional patterns and age distribution varied widely. It is advised to conduct additional longitudinal studies with sizable sample sizes to quantify the prealbumin role in severe disease in more detail. A crucial factor influencing the outcome of critically ill children is their nutritional plan, which should be continuously examined.

Abbreviations

ARDS	Adult Respiratory Distress Syndrome
ARF	Acute Renal Failure
AUC	Area Under Curve
BMI	Body Mass Index
CBC	Complete Blood Count
CHD	Congenital Heart Disease
CIP	Critically Ill Patients
ELISA	Enzyme-Linked Immunosorbent Assay
GBS	Guillain Barre Syndrome
LOS	Length Of Stay
MV	Mechanical Ventilation
PICU	Paediatric intensive care unit
PRISM III	Pediatric Risk of Mortality III
ROC	Receiver Operating Characteristic
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
WHO	World Health Organization

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Authors' contributions
MAA drafted the work and revised it, being the major contributor in writing the manuscript. IKA made substantial contribution to the concept and design of the work and interpretation of data. OYA contributed to data interpretation. RAA contributed to data acquisition. MSG contribute to write and review the manuscript. AOM contribute to write and review the manuscript. SAM contribute to write and review the manuscript. All authors read and approved the final manuscript. Each agreed both to be personally accountable for the author's own contributions and ensured that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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Availability of data and materials
All data are available upon request.

Declarations

Ethics approval and consent to participate
This study was approved by the Institutional Ethical Review Board, Faculty of Medicine, Cairo University, Approval number: MS 50-2020.

Consent for publication
Not applicable (no individual details, images or videos).

Competing interests
The authors declare that they have no competing interests.

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