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Original article

Serum Prealbumin: Early Prediction of Malnutrition in Critically Ill Children

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Abstract

Background: Malnutrition in Paediatric Intensive Care Unit (PICU) patients is a major issue that affects both prognosis and PICU outcomes. Timely management and better patient outcomes may be achieved with early identification of malnutrition. **This study aimed to** identify the significance of blood prealbumin in early detection of malnutrition in critically ill children and its relation to hospital stay and respiratory support. **Methods:** Fifty children (both sexes) between the ages of 1 month and 18 years old who had been hospitalized to a tertiary PICU for at least 48 hours were included in prospective cross-sectional research. We used anthropometric measurements such as weight, height, BMI, and mid-upper arm circumference to evaluate nutritional status. Immunoprecipitation analysis was used to assess prealbumin concentrations in serum. **Results**: There was a wide age spread, from infant to teenage. There were 27 male patients (54%) and 23 female patients (46%). Prealbumin levels were considerably lower in malnourished individuals than in well-nourished controls. At a cut-off value of 15.2mg/dl, the prealbumin serum level predict malnutrition with a sensitivity of 69.5 % and a specificity of 85.2% in this research population (AUC: :0.860, p <0.001). **Conclusion:** Malnutrition in critically ill children may be detected by measuring prealbumin levels as undernourishment was linked to low prealbumin levels.

Keywords: Serum Malnutrition; Children in Critical Care; Early Prediction; Prealbumin.

Introduction

According to the American Society for Parenteral and Enteral Nutrition (ASPEN), malnutrition occurs when there is a discrepancy between dietary needs and consumption, leading to energy, protein, or micronutrient deficiencies that may compromise growth, development, and other important outcomes. Malnutrition that develops after a patient is admitted to the hospital is called hospital-acquired malnutrition (HAM) **(1)**. Children who are critically ill often suffer from malnutrition when they are admitted to PICUs **(2).** Although differences in nutritional indices, the presence of chronic disease, age, and the severity of critical illness should be considered, the reported rate of undernutrition upon PICU admission

ranged from 8.1% to 71.7% **(3)**. As a consequence of the illness and inadequate nutrient supply, critically ill children are also at danger of nutritional deterioration **(4).** Current nutritional status indicators in critically ill children include weight, height, body mass index (BMI), and mid-upper arm circumference (MUAC) **(2).**

Medical professionals have traditionally used levels of blood proteins like albumin and prealbumin to evaluate a patient's nutritional condition. Other indicators including C-reactive protein (CRP) and total lymphocyte count (TLC) and inflammatory markers like retinol-binding protein (RBP) and transferrin have also been investigated **(5).** Prealbumin is a protein secreted by the liver and partly broken down by the kidneys; it transports thyroid hormone. Serum prealbumin levels below 10 mg/dl are indicative of malnutrition **(6)**. Prealbumin's use as a nutritional marker, especially during refeeding, has been advocated **(7).** Quadros et al research showed that serum prealbumin was used as a diagnostic tool for estimating the likelihood of weight loss in paediatric hospital patients. They found it to be sensitive in predicting weight loss among hospitalized children, suggesting it may have some benefit in diagnosing and monitoring nutritional status **(8).**

Prealbumin is superior to albumin in monitoring short-term dietary changes because of its shorter half-life (two to three days). Furthermore, intestinal protein losses had no effect on prealbumin levels in individuals with protein-losing enteropathy **(6)**. TLC may also be used as a predictor of whether or not a kid would be malnourished while in the hospital **(9)**. In order to detect possible malnutrition and allow for early nutritional therapy, it is advised to evaluate TLC and prealbumin level in hospitalized children immediately upon arrival. Due to immunological dysfunction and greater susceptibility to infections, malnutrition in critically ill patients, particularly in the PICU, is related with increased morbidity, and longer hospital stays. Improving clinical outcomes and reducing complications after intensive care unit admission by early diagnosis and treatment of paediatric malnutrition **(3).**

The goal of this research was to determine whether or not serum prealbumin may be used as a reliable early indicator of malnutrition in critically ill children. This valuable information should lead to thorough nutritional assessment, early diagnosis of malnutrition, and prompt delivery of nutritional support.

Patients and methods

This is a prospective cross-sectional study that was conducted on 50 children in the pediatric intensive care unit (PICU) of the Pediatric department of Benha University during the period from 1st May to 1st November 2022.

The inclusion criteria were critically ill children between the ages of 1 month and 18 years old who had to stay in a tertiary PICU for at least 48 hours.

The exclusion criteria included children who died within 48 hours after PICU admission, children who were readmitted to

the PICU during the same hospitalization, children with burns, children with liver illness, children with hyperthyroidism, and children who were very overweight or obese at the time of PICU admission.

Patients were divided into 2 groups: Group I: 23 critically ill children with undernutrition (weight lost more than 2% of reference weight during hospitalization or a decrease in body mass index (BMI) Z-score more than 0.25 SD). Group II: 27 critically ill children with normal nutritional status (well nourished).

Ethics statement:

The legal guardians of the cases provided informed written permission. Each participant was given a unique identifier and told why they were participating in the research. The Benha Faculty of Medicine's ethics committee for research involving human beings authorized the study (MS.13-4-2022).

All patients were subjected to the following: A detailed general, demographic, medical, and health history, as well as outcome factors and gastrointestinal issues, were recorded (e.g., diarrhea, vomiting, dysphagia, abdominal pain). Nutritional evaluations were conducted, which included gauging eating capacity and keeping track of what was consumed. Weight, height, body mass index, and mid-upper arm circumference (MUAC) were measured in addition to doing a full clinical assessment.

Children's scales were used for the weigh-in (Filizola BP Baby). We used a paediatric anthropometer to get the dimensions (Caumaq). If a child's height cannot be determined, their knee height was used as a proxy **(10).**

Using the World Health Organization's (WHO) Anthro software, version 3.2.2 (children less than 5 years old) **(11)** or WHO Anthro Plus (children 5-18 years old) **(12**), anthropometric data were collected and transformed into Z-scores to evaluate the patients' nutritional status. Values below -2 Z score were classified as undernourished. MUAC was another indication for screening and identifying malnutrition in babies and children aged 6–59 months, with a MUAC of less than 11.5 cm indicating severe acute malnutrition. A flexible inelastic tape was used to determine MUAC (in centimeters).

A complete blood count (CBC) with differential leucocytic count), C reactive protein (CRP), urea, creatinine, liver enzymes, serum prealbumin, and the CRP/prealbumin ratio calculation are all examples of laboratory tests performed.

Serum Prealbumin: Prealbumin was measured using Human Prealbumin ELISA kit (No.18, Keyuan Road, Daxing Industry Zone, Beijing, China). Prealbumin levels in children range from 15 mg/dL to 45 mg/dL (Kim DH, et al 2021) (12).

The CRP/prealbumin ratio was calculated to assess the patient's prognosis in relation to hospital stay and respiratory support with mechanical ventilation **(13).**

Statistical analysis

Statistical SPSS v26 was used for the analysis (IBM Inc., Armonk, NY, USA). Histograms and the Shapiro-Wilks

normality test were employed to determine if parametric or nonparametric statistical testing was appropriate for the data. The unpaired Student t- test was used to compare the two groups' means and standard deviations (SDs) for the quantitative variables. The Chi-square test or Fisher's exact test was used to determine statistical significance for the qualitative variables provided as frequencies and percentages. To be statistically significant, the P value has to be less than 0.05 with two tails.

Results

A total of 50 patients were hospitalized between May 1 and November 1, 2022, and their nutritional status was used to divide them into two groups: those who were undernourished (23 patients) and those who were well nourished (27 patients). In undernourished cases height z-scores varied from -7.67 to 4.75 (mean ± SD: -1.8±3.19), weight z-scores ranged from -3 to -4 (mean ±SD: -1.84 ±0.8)), BMI z-scores varied from -10.94 to 3.47(mean ± SD: -0.77±3.35), Table 1

Undernourished patients tended to be older than their well-nourished counterparts. In contrast, those who were well-nourished had a far greater body mass index than those who were undernourished. Regarding gender, socioeconomic status, body mass index, or MUAC, there was no statistically significant difference between the groups. When comparing the two groups, undernourished people had a lower weight for age z-score and a lower body mass index for age z-score than the well-nourished people did (p 0.001 and p = 0.013, respectively). The z-score for height versus age did not vary significantly across the groups, Table 1.

The most common diagnosis of the study participants was lower respiratory tract infections in 15 (30%) patients, followed by CNS infections in 8 (16%) patients and heart failure in 4 (8%) patients. The least common diseases were diabetic ketoacidosis and gastroenteritis each occurred in only 1 (2%) patient.11 (22%) patients had mixed diseases. Table 2

There was no statistically significant difference in nutritional route and signs of malnutrition between the studied groups, Table 3. Table 4 there was no statistically significant difference between both group regarding of Hb, WBCs, neutrophils, platelets, CRP, AST, ALT, urea, or creatinine except lymphocytes was elevated in well-nourished group (p= 0.002). Table 5 shows that there was a significant decrease in prealbumin in undernourished patients as compared to well-nourished individuals (p = 0.0043), while there was no significant change in the ratio of CRP to prealbumin across the examined group, duration of mechanical ventilation, and hospital stay.

Figure 1 shows a positive correlation (r = 0.436, p = 0.005) between the ratio of C-reactive protein to prealbumin and the duration of hospital stay as well as the amount of time spent on mechanical ventilation.

Prealbumin's potential to foretell malnutrition: With a cutoff value of 15.2mg/dl, the prealbumin can predict

malnutrition with a sensitivity of 69.5% and specificity of 85.2% in this research population (AUC :0.860, p <0.001), Figure 2

Table (1): Baseline characteristics of the participants

Baseline characteristics		Undernourished (n =23)	Well- Nourished (n =27)	P value
Age	Median (IQR)	7 (5.5 - 12.5)	2.6 (0.54 - 9)	**0.015***
(years)	Range	0.58 - 16	0.11 - 15	
Gender	Males	11 (48%)	16 (59%)	0.57
	Females	12 (52%)	11 (41%)	
Economic status	Low	3 (13%)	1 (4%)	0.453
	Mild	9 (39%)	13 (48%)	
	Moderate	11 (48%)	13 (48%)	
	Range	56 - 155	46 - 166	
Weight for age z-score	Mean ± SD	-1.84 ± 0.8	-0.44 ± 1.47	**<0.001***
	Range	-3 - -0.4	-2.2 - 2.6	
Height for age z-score	Mean ± SD	-1.8 ± 3.19	-2.42 ± 3.82	0.545
	Range	-7.67 - 4.75	-13.9 - 4.66	
BMI for age z-score	Mean ± SD	-0.77 ± 3.35	1.51 ± 2.97	**0.013***
	Range	-10.94 - 3.47	-10.14 - 5.29	
MUAC (cm)	Median (IQR)	14 (12.5 - 16.25)	14.5 (13 - 23)	0.274
	Range	8 - 24	11 – 26	

Standard deviation (SD), median (M), interquartile range (IQR), body mass index (BMI), mid-upper arm circumference (MUAC), and *p value 0.05 indicate statistical significance.

Table (2): Medical status of the study participants

Diagnosis	Study participants(n=50)
Lower respiratory tract infection	15 (30%)
CNS infection	8 (16%)
Heart failure	4 (8%)
Diabetic ketoacidosis	4 (8%)
Glomerulonephritis and nephrotic	4 (8%)
Upper respiratory tract infection	2 (4%)
Hyperammonemia	1 (2%)
Gastroenteritis	1 (2%)
Mixed	11 (22%)

Table (3): Nutritional status of the studied groups

Participants character		Undernourished (n =23)	Well-Nourished (n =27)	P value
Nutritional route	**Parenteral**	4 (17%)	9 (33%)	0.595
	Nasogastric feeding	7 (30%)	8 (30%)	
	Oral route	4 (17%)	3 (11%)	
	Mixed	8 (35%)	7 (26%)	

Table (4): laboratory investigations of the participants

Laboratory investigations		Undernourished (n =23)	Well Nourished (n =27)	P value
Hb (g/dL)	**Mean ± SD**	11.1 (9.95 - 12.25)	10.6 (9.65 - 11.5)	0.448
	Range	7.2 - 13.7	7.6 - 13.9	
WBC × 10^3 (cells/µL)	**Median (IQR)**	10.7 (7.65 - 18.75)	13.3 (8.75 - 15.9)	0.851
	Range	4.8 - 25.5	5.1 - 52.2	
Lymphocytes × 10^3 (cells/µL)	**Median (IQR)**	2.6 (1.94 - 3.15)	3.4 (2.84 - 4.6)	0.002*
	Range	1.4 - 7.7	2.17 - 10.6	
Neutrophils × 10^3 (cells/µL)	**Median (IQR)**	5.7 (3.55 - 12)	7.8 (4.55 - 11.35)	0.235
	Range	0.95 - 21.6	3.1 - 23.2	
Platelets × 10^3 (cells/µL)	**Median (IQR)**	242 (156 - 310.5)	259 (214.5 - 391)	0.189
	Range	64 – 662	114 – 1348	
CRP (mg/L)	**Median (IQR)**	15.5 (5 - 19.75)	17 (10.5 - 40)	0.164
	Range	2 – 80	3 – 100	
AST (U/L)	**Median (IQR)**	33 (27 - 37)	30 (25 - 35.5)	0.724
	Range	16 – 77	10 – 70	
ALT (U/L)	**Median (IQR)**	34 (30 - 37.5)	32 (28 - 41.5)	0.514
	Range	24 – 85	19 – 112	
Urea (mg/dL)	**Median (IQR)**	13 (12 - 15)	14 (12.5 - 15)	0.466
	Range	11 – 30	11 – 38	
Creatinine(mg/dL)	**Median (IQR)**	0.5 (0.38 - 0.6)	0.43 (0.33 - 0.54)	0.386
	Range	0.24 – 4	0.23 - 2.3	

IQR: Interquartile range, SD: Standard deviation, Hb: Hemoglobin, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C-reactive protein, *Statistically significant as p value <0.05.

Table (5): Nutritional markers and PICU prognosis of the participants

		Undernourished (n =23)	Well- Nourished (n =27)	P value
Lymphocytes × 10^3 (cells/µL)	Median (IQR)	2.6 (1.94 - 3.15)	3.4 (2.84 - 4.6)	0.002*
	Range	1.4 - 7.7	2.17 - 10.6	
CRP to prealbumin ratio	Median (IQR)	0.11 (0.04 - 0.18)	0.1 (0.05 - 0.12)	0.9
	Range	0.01 - 0.46	0.02 - 0.66	
Prealbumin (mg/dL)	Median (IQR)	13.05 (10.13 - 15.56)	17.76 (17.12 - 19.75)	**<0.001***
	Range	4.35 - 30.58	14.15 - 57.44	
Length of stay (days)	Median (IQR)	5 (3 - 11)	3 (2 - 5)	0.008*
	Range	1 - 43	1 - 23	
Duration of MV (days) (n =15)	Median (IQR)	8 (5 - 13.75)	3 (2.5 - 5)	0.029*
	Range	4 - 33	1 - 18	

CRP = C-reactive protein; MV = mechanical ventilation; IQR = interquartile range; SD = standard deviation; *Statistically significant at p 0.05.

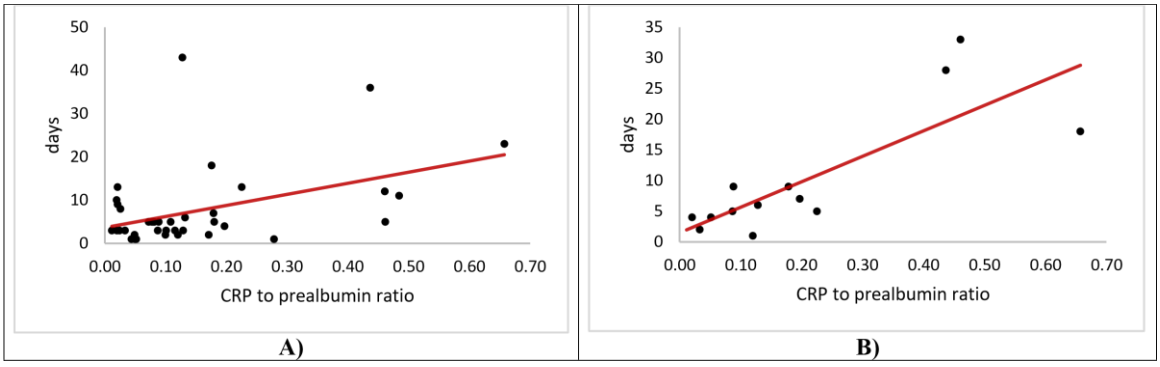

Fig. (1): Shows a strong positive correlation between C-reactive protein to prealbumin ratio and both length of hospital stays(A) and duration of mechanical ventilation (B) in the study population.

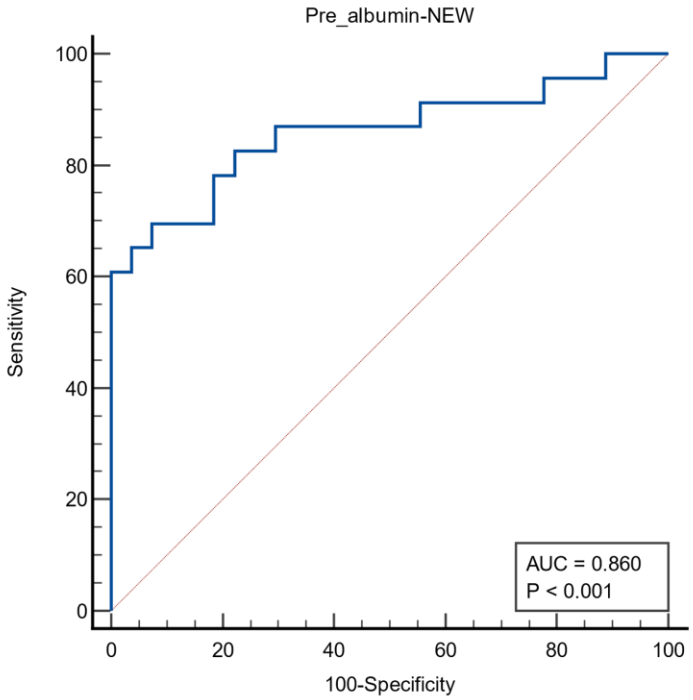

Fig. (2): ROC curve analysis for prealbumin in undernutrition prediction in critically ill children.

Discussion

Malnutrition is a major problem that has both medical and societal repercussions since it increases the risk of illness and the expense of treating it. In long-term care institutions, its frequency might be as high as 85**%. (6).** Age was significantly higher in undernourished compared to well-nourished patients. There was no significant difference in gender, economic status, height, and MUAC between the studied groups. In contrast, BMI was significantly higher in well-nourished patients compared to undernourished patients.

The current study agreed with a previous one (14) which studied 226 children aged 7 months to 16 years (140 (61.9%) male) admitted to the medical or surgical wards or out-patient clinics during a period of 9 weeks in the winter of 1994–5. It was observed that MUAC measurements were obtained in 221 children, and results were correlated with indices of weight and height. They ranged from 12.5 cm to 21.5 cm **(14).**

Nutritional factors in the first four days of a PICU stay were shown to be significant predictors of both 60-day survival and timely release. Children having body mass index (BMI)-to-age z scores less than minus two at the time of PICU admission. Only 33 (18%) were considered to be undernourished (2 z score), whereas 133 (70%) were considered to be well-nourished **(2).**

In the current study the most common diagnosis of the study participants was lower respiratory tract infection in 15

(30%) patients, followed by CNS infections in 8 (16%) patients and heart failure in 4 (8%) patients. It was predicted that the prevalence and potential risk factors for nutritional deterioration in hospitalized children: inadequate energy intake, increased energy expenditure, impaired intestinal absorption, or loss of nutrients due to illness and were analyzed in connection with the study groups' medical conditions. Patients between the ages of 1 month and 18 years old at tertiary care institutions participated in multicenter prospective research. Cancer (32%), chronic heart disease (15%), and epilepsy (10%) where the most common chronic conditions patients were already living with (10 %) **(1).**

In the current research there was statistically significant difference between the two study groups regarding hospital stay (p=0.008) and time spent on mechanical ventilation (p=0.0029). Undernourished patients had longer hospital stays and more time spent on MV than their well-nourished counterparts. Nutritional intake and indicators of malnutrition did not vary noticeably across the groups. Malnutrition was also shown to have a significant association with the length of time that children required mechanical breathing in a prospective cohort analysis of Brazilian PICU admissions **(15)**. Malnutrition was linked to an elevated risk of acquired infections and duration of stay in a cohort of children admitted to an Indian PICU **(16).**

Prealbumin is preferable to albumin as a measure of acute changes in nutritional condition because of its shorter half-life (two to three days). Protein losses in the intestine did not affect prealbumin levels in individuals with protein-losing enteropathy. Participants at high risk of malnutrition showed significantly lower body mass index (p 0.001), prealbumin (p 0.001), and total protein (p 0.05) than those at low risk **(6).**

There was a significant positive correlation between CRP to prealbumin ratio and length of stay (r =0.436 and p =0.005) and duration on mechanical ventilation (r =0.803 and p <0.001).

The prealbumin level (AUC:0.860, p <0.001), with a cut-off value of 15.2 mg/dl, was a significant predictor of malnutrition in the research participants, with a sensitivity of 69.5% and specificity of 85.2%.

This finding supports the use of prealbumin as sensitive (69.5% sensitivity) screening tool for malnutrition, according to the research **(17).** Additionally, serum prealbumin was shown to have a high association with the nutritional status in a study of 45 consecutive ICU patients with head injuries. Prealbumin was discovered to be the most sensitive blood marker for both the early diagnosis of malnutrition and the evaluation of the adequacy of nutritional treatment for malnourished individuals **(18).**

Conclusion

This study showed that prealbumin levels were significantly lower in undernourished patients than in well-nourished patients, demonstrating the usefulness of prealbumin as a sensitive biomarker for malnutrition diagnosis in this population. These results highlighted the necessity of receiving timely nutritional treatments as well as the possible detrimental effects of malnutrition on patient outcomes.

Limitations

The study did not assess long-term follow-up and outcomes beyond the pediatric intensive care unit (PICU) stay.

Recommendations

Future research should involve larger sample sizes and include multiple healthcare centers to improve the generalizability of the findings. In addition to evaluating PICU outcomes, future studies should assess long-term morbidity, mortality, and quality of life in undernourished critically ill children.

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