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A Correlation between Nutritional Adequacy and Clinical Outcomes among Children Critically Hospitalized with COVID-19

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ABSTRACT

Introduction: Malnutrition is a prominent cause of mortality and morbidity in hospitalized children. Comorbidity of infection and malnutrition can exacerbate nutritional deficiencies and worsen healing. This study aimed to evaluate nutritional status, dietary intake adequacy, and their correlation with clinical outcomes among children diagnosed with coronavirus disease 2019 (COVID-19).

Methods: This prospective observational study was conducted on 30 children admitted to the pediatric intensive care unit (PICU) ward of Akbar Hospital, Mashhad University of Medical Sciences, Mashhad, Iran, for eight weeks. Age, gender, and nutritional status (weight-for-lengths/heights z-scores, based on the World Health Organization child growth standards) of critically ill children with COVID-19 were recorded and evaluated upon admission. Dietary intake and its adequacy were also calculated during hospitalization. Then, the correlation between mentioned variables with clinical outcomes was examined.

Results: Out of 30 patients, malnutrition was severe in 16.7%, moderate in 16.7%, while nutrition status was normal in 66.7% of patients. There was no significant correlation between z-scores and mortality or length of stay. However, significant differences were found between energy intake adequacy and length of hospitalization (p<0.001), as well as protein intake adequacy and mortality (p=0.008).

Conclusion: The study showed a significant correlation between dietary intake adequacy and clinical outcomes, suggesting the role of optimizing nutrition therapy in ameliorating clinical consequences in critically ill children.

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Introduction

The coronavirus disease 2019 (COVID-19) was declared as a pandemic in March 2020 by the World Health Organization (WHO) (1). This infectious disease mainly affects the respiratory system, causing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (2). Even though children are less affected by COVID-19, a report from the Centers for Disease Control and Prevention (CDC) found that young children had higher hospitalization rates than older children (3). Moreover, COVID-19 has higher mortality among certain groups, including those with poor immunity and underlying comorbidities (4). The lack of definitive treatment for COVID-19 makes it essential that the immune system be robust and efficient (1, 5). Several factors can positively affect the functioning of the immune system such as the person's nutritional status (6). A sufficient dietary intake of macro-and micronutrients is an influential factor in preserving and developing immunity. Thus, protein-energy malnutrition or subclinical deficiencies related to micronutrients can impair the immune system from responding to pathogens appropriately (7-9).

There is a bidirectional correlation between malnutrition and infection (10). On the one hand, malnutrition can increase infection susceptibility (11), which may be caused by an immune system dysfunction (12). On the other hand, infectious diseases worsen the negative energy balance and reduce fat-free mass (FFM) during hospitalization (13) such as decreased appetite,

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increased catabolism, and demand for nutrients (13, 14).
Furthermore, malnutrition is associated with increased mortality, morbidity, and delayed recovery (5, 15). Therefore, assessing the nutritional status of people with COVID-19, especially vulnerable children, seems necessary. This study aimed to evaluate the nutritional quality of children diagnosed with COVID-19 disease admitted to the pediatric intensive care unit (PICU), the adequacy of energy and protein intake by the end of the first week, and the correlation of this adequacy with clinical outcomes.

Materials and Methods

Study Population

This cross-sectional study was conducted from October 2021 to December 2021 at the PICU ward, Akbar Hospital, Mashhad University of Medical Sciences, Mashhad, Iran, on children younger than five diagnosed with COVID-19 and more than 24 hours of hospitalization. The serum was screened for the coronavirus antibody by enzyme-linked immunosorbent assay (ELISA) and confirmed by Western blot or polymerase chain reaction (PCR). The exclusion criteria for the studied group were a history of viral infection, human immunodeficiency virus (HIV), hepatitis B (HBV), hepatitis C (HCV), cardiovascular, thyroid, kidney, liver, and Cushing's diseases, chronic inflammatory diseases such as multiple sclerosis and rheumatoid arthritis.

Outcome Measures and Data Collection

Nutritional status (weight (kg), height (cm), and z-scores) was recorded at the time of admission. The 24-hour dietary recall (24hDR) was calculated as mean energy and protein intake by the end of the first week. Clinical outcomes of hospitalization (mortality and length of PICU stay) were also correlated with z-scores and adequate energy and protein intake (Figure 1).

Measurements

The weight was measured using a digital scale (Balas) to 10 g. Length or height was also assessed using a portable infantometer and stadiometer for children aged <24 and >24 months, respectively. A predictive equation was applied to estimate the stature in cases where standard measurements for length and height were impossible. Z-score was calculated as WHO weight-for-length/height (birth to 5 years) (16).

Dietary Intake

The energy and protein intake were assessed by 24hDR. The hospital dieticians performed food analysis based on the menu, hospital food analysis, and enteral and parenteral formulas. The adequate energy and protein intake based on age, weight, and gender were calculated based on nutrition guidelines (17). The energy and protein adequacy definition was the achievement of at least two-thirds of the individually determined goals regarding energy and protein requirements (18).

Statistical Analysis

The data were analyzed by the statistical package for social sciences (SPSS) software version 20. The obtained results were expressed as mean and standard deviations for quantitative data, and the qualitative data were expressed as frequency and percentage. A *p*-value <0.05 was considered to indicate statistical significance. The correlation between nutritional indices and clinical outcomes was measured by Spearman's test.

Table 1. Frequency distribution of malnutrition among children hospitalized with Covid-19

	Normal	Moderate malnutrition	Severe malnutrition
Nutritional status upon PICU admission [a]	20 (66.7)[b]	5 (16.7)	5 (16.7)

a Z-score (WHO weight-for-length, height) for birth to 5 years; Z > -2: natural status, -3 < Z < -2: moderate Malnutrition, Z < -3: severe malnutrition), [b] Data expressed in terms of frequency (percentage)

Results

A total of 30 hospitalized children with COVID-19 were evaluated in PICU (68.6% female, 31.4% male), whose mean age, weight, and height were 43 ± 49 (months), 13 ± 9 (kg), and 89 ± 28 (cm), respectively.
Based on the Z-score classification (Table 1), 16.7% of subjects had severe malnutrition, 16.7% had moderate malnutrition, and 66.7% were normal. In addition, the adequacy of energy and protein intake among hospitalized children was 73% and 90%, respectively, at the end of the first week.
The correlation analysis between nutritional status and intake adequacy with clinical outcomes among children hospitalized with

COVID-19 showed no significant differences between Z-scores (at the beginning of hospitalization) and length of stay and between Z-scores and mortality ($p > 0.05$). However, there were significant differences between energy intake adequacy and size of hospitalization ($p<0.001$), as well as protein intake adequacy and mortality ($p=0.008$) (Figure 1).

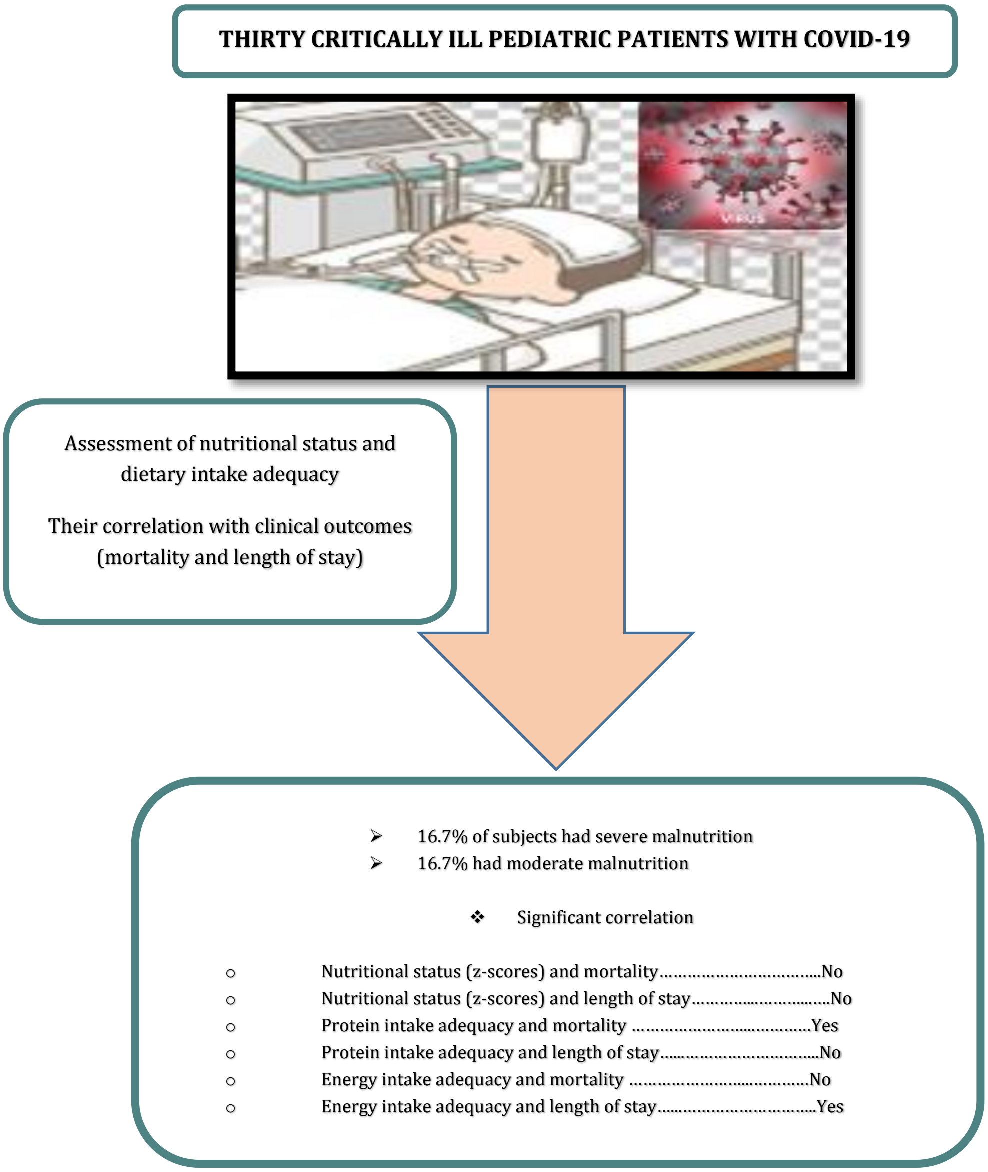

Figure 1. Graphical flowchart of study steps and results

Discussion

The present study examined the nutritional status and dietary intake adequacy among children diagnosed with COVID-19 disease who were admitted to PICU. In addition, the correlation between nutritional quality and dietary intake adequacy was assessed with clinical outcomes.

The results indicated that malnutrition prevalence was relatively high among hospitalized children at admission, consistent with various studies that reported malnutrition among hospitalized children (19-21). This prevalence of malnutrition can disrupt the treatment and recovery process, which should be considered when effective prophylactic and remedial treatment is unavailable in the present pandemic of COVID-19 (5). Thus, a balanced energy and protein intake can help manage viral infections, considering the bi-directional correlation between malnutrition and infection (9, 22).

The proportion of critically ill children receiving adequate energy and protein supplements in the PICU by the end of the first week was 73% and 90%, respectively. Furthermore, the findings did not demonstrate any significant correlation between Z-scores with the length of stay and mortality. Kyle et al. showed the adequacy of energy (75%) and protein (40%) intake in the first eight days of the PICU stay (23). In another study, cumulative energy and protein deficits were related to decreases in anthropometric parameters (24). Studies have shown that many critically ill children are not receiving enough protein and energy. Some of the reasons mentioned for the under-delivery of energy or protein might be the severity of the illness (23), fluid restriction (25), and the gap between energy and protein delivery and requirements (26). A practical solution can be following the nutrition support guidelines (26) or feeding protocols related to PICU (27) to improve the nutritional patterns of critically ill children.

The results did not determine significant differences between Z-scores (at the beginning of hospitalization) and length of stay, as well as Z-scores and mortality. The nutritional status at admission (using Z-scores) and clinical outcomes (as 30-d mortality, length of intensive care unit (ICU) stay, and mechanical ventilation) were examined in a prospective cohort study (28). Menezes et al. demonstrated an independent correlation between malnutrition and the size of mechanical ventilation. However, there was no correlation between malnutrition with mortality (28). In addition, Grippa et al. considered malnutrition with the Z-scores variable among 72 children hospitalized in PICU and showed that malnutrition was associated with the mechanical ventilation duration among critically ill children (29). In addition, mid-upper arm circumference (MUAC) has been shown to predict mortality in hospitalized children better than Z-scores. (30). Although the variables considered for clinical outcomes are different, assessing nutritional status on admission to the PICU is critical. Therefore, targeted nutritional rehabilitation can decrease malnutrition and later hospitalization clinical outcomes.

This study showed a significant correlation between energy intake adequacy and hospitalization length, as well as protein intake adequacy and mortality. In a prospective cohort study of mechanically ventilated children, adequate protein intake as enteral was significantly associated with mortality (19). This study did not independently examine the effect of energy on outcomes compared to energy intake (19). Moreover, Hulst et al. showed a negative association between cumulative deficits (energy and protein), ICU stay length, and mechanical ventilation days (24). Therefore, ongoing assessments of protein and energy intake are essential in PICU to avoid the under-delivery of energy or protein and the clinical outcomes. On the other hand, PICU staff training in nutritional therapy can effectively improve nutritional support among critically ill children. Moreover, nutritional adequacy during acute stress such as COVID-19 can help to reduce impaired growth and complications during children's illness.

This study was one of the few ones on nutritional adequacy regarding critically ill children with COVID-19. To our knowledge, only one study has been conducted, similar to ours (31). However, this study was limited to the PICU of one hospital and may not be generalized to other PICUs.

Conclusion

Based on the results, there was a correlation between dietary intake adequacy and clinical outcomes. This correlation was observed between energy intake adequacy and hospitalization length, as well as protein intake adequacy and mortality. However, more studies are required to confirm the role of nutritional interventions, especially the adequacy of energy and protein intake, among critically ill children.

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