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NUTRITIONAL THERAPY IN CHILDREN WITH SEPSIS AND SEPTIC SHOCK: UNRESOLVED QUESTIONS AND THE NEED FOR AN INDIVIDUALIZED APPROACH

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The aim. *This review provides a meta-analysis of current guidelines on nutrition in critically ill patients, including SCCM–ASPEN (2017), SSC (2012, 2021), ESPNIC (2020), and SSC (2020) pediatric sepsis guidelines. While the ESPNIC (2020) guidance complements the existing ASPEN (2017) guidelines for critical paediatrics, the Children's SSC (2020) did not find sufficient direct evidence to develop strong nutritional recommendations for children with sepsis/septic shock.*

Materials and methods. *Looking for publications on nutritional assessment and nutritional support in children with sepsis have been keywords sepsis in children, nutrition, and critical conditions. Literature searched and analyzed from PubMed, Google Scholar and ScienceDirect databases. Revealed under-a sufficient amount of work on pediatric sepsis (an exception is neonatal sepsis), there are no protocols for assessing nutritional status and its correction in children diagnosed with sepsis/SS.*

Results*. Despite ongoing research in this area, many questions remain unresolved and require systematic study. While some small and large pediatric studies have recommended nutritional therapy, the heterogeneity of children's ICUs in terms of age, pathology, disease severity, comorbidities, and nutritional status precludes a one-size-fits-all approach to nutrition in critically ill children. Therefore, an individualized approach to nutrition is necessary, considering the patient's unique circumstances and the risk/benefit ratio of different nutritional therapies.*

Conclusions. *An extensive literature review did not reveal strong nutritional recommendations for children with sepsis/SS, underscoring the need for future research on the assessment and correction of protein-energy malnutrition in this population. Overall, this review highlights the importance of tailoring nutritional therapy to the individual needs of critically ill children with sepsis/ septic shock to optimize outcomes*

Keywords: *sepsis in children, nutritional support, protein-energy malnutrition, hypercatabolism, hypermetabolism syndrome, enteral nutrition, parenteral nutrition, critical illness*

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1. Introduction

Sepsis is a life-threatening condition caused by dysregulation of the body's response to infection and affects 4.2 million children annually, with 3 million newborns. Neonatal sepsis is one of the leading causes of death due to the increase in antimicrobial-resistant pathogens [1, 2]. The pathogen structure in ICUs of large medical institutions is similar. It includes *Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumonia, Acinetobacter baumannii, Pseudomonas aeruginosa, Enterobacter spp.*, all of which show increasing resistance to antibiotics and formation of pan-resistance [3]. Sepsis is more likely to occur in vulnerable populations such as newborns, hospitalized children, and children with HIV or autoimmune diseases [3, 4].

The pathogenesis of pediatric sepsis is similar to that of adults, and clinicians often use the Pediatric Sequential Organ Failure Assessment (pSOFA) to assess criteria for multiorgan dysfunction in pediatric infections. Although bacteremia is positive in 30–45 % of sepsis cases [5], microbiological monitoring remains crucial in the diagnostic process. In addition, blood markers of systemic inflammation, such as C-reactive protein and procalcitonin, also play a significant role in the diagnosis of sepsis and in determining antibiotic therapy algorithms [6, 7].

Diagnosing and treating sepsis is challenging due to its complex pathogenesis, individual variability in clinical and laboratory manifestations, and immune status. The body's endogenous response to limit infection drives the formation of diverse clinical manifestations of sepsis, and loss of controllability of the response leads to organ dysfunction and protein-energy deficiency, which are the leading causes of death in ICU patients [8].

Nutritional therapy, an essential component of intensive care for sepsis/septic shock, aims to prevent the

multi-inflammatory syndrome and organ-systemic damage, increase immune protection, and reduce mortality.

The aim of the research was to examine the level of excellence in the correction of protein-energy malnutrition in sepsis/septic shock in children based on meta-analyses and guidelines over the past 10 years.

2. Materials and methods

To gather information on the evaluation of nutritional status and nutritional support in children with sepsis, a literature search was conducted using the keywords "sepsis in children," "nutrition," and "critical conditions." PubMed, Google Scholar, and ScienceDirect databases were searched and analyzed. However, only a limited number of studies were found on pediatric sepsis (excluding neonatal sepsis), and there were no established protocols for evaluating and correcting the nutritional status of children diagnosed with sepsis/septic shock. Therefore, the 2020 SSC pediatric guidelines for sepsis/septic shock were reviewed, and a review of articles on clinical trials of nutritional therapy in critically ill children and 2012, 2021 SSC guidelines, the 2017 SCCM-ASPEN guidelines, and the 2020 ESPNIC guidelines was also conducted. Despite extensive literature searches since 2009, the 2017 SCCM-ASPEN guidelines acknowledge the lack of high-level evidence regarding nutritional support in pediatric ICU settings.

3. Results

The issue of nutritional correction for the hypermetabolism-hypercatabolism syndrome in critically ill children has been well documented in multiple studies [9, 10]. The pathogenesis of systemic inflammatory response (SIR) in sepsis involves both humoral and cellular reactions, pro-inflammatory and anti-inflammatory mechanisms, and widespread damage to the microcirculation system resulting in endothelial dysfunction and destruction [11]. The hormonal changes in sepsis to gather information on the evaluation of nutritional status and nutritional support in children with sepsis, a literature search was conducted using the keywords "sepsis in children," "nutrition," and "critical conditions." PubMed, Google Scholar, and ScienceDirect databases were searched and analyzed. However, only a limited number of studies were found on pediatric sepsis (excluding neonatal sepsis), and there were no established protocols for evaluating and correcting the nutritional status of children diagnosed with sepsis/septic shock. The 2020 SSC pediatric guidelines for sepsis/septic shock were reviewed, and a review of articles on clinical trials of nutritional therapy in critically ill children and 2012, 2021 SSC guidelines, the 2017 SCCM-ASPEN guidelines, and the 2020 ESPNIC guidelines was also conducted. Despite extensive literature searches since 2009, the 2017 SCCM-ASPEN guidelines acknowledge the lack of high-level evidence regarding nutritional support in pediatric ICU settings.

Mainly result from an increase in cyclic adenosine monophosphate levels in lymphoid cells, leading to stress-induced immune dysfunction [11]. The main feature of metabolic disorders in sepsis is a combination of increased body requirements for different substrates and decreased tissue tolerance. This combination is now recognized as the hypermetabolism-hypercatabolism syndrome. The hypermetabolism syndrome plays a critical role in developing sepsis-induced organ dysfunction as it represents the body's overall metabolic response to the systemic inflammatory response and the release of large amounts of biologically active substances. The hypermetabolism-hypercatabolism syndrome is characterized by a more than two-fold increase in the metabolic rate compared to the baseline metabolism, leading to increased oxygen demand, elevated CO_2 production, negative nitrogen balance (Table 1 for a comparison between simple fasting and hypermetabolism).

Table 1

Main characteristics of simple fasting and hypermetabolism [10]

No.	Characteristic	Simple fasting	Hypermetabolism
1	Cardiac output	–	++
2	Total peripheral vascular resistance	Without changes	–
3	O2 consumption	–	++
4	Energy needs	–	+++
5	Activity of mediators	Without changes	++
6	Response to regulatory incentives	++++	+
7	Respiratory coefficient	0,75	0,85
8	Primary substrate	Lipids	Lipids, carbohydrates and proteins
9	Proteolysis	+	+++
10	Protein oxidation	+	+++
11	Synthesis of acute phase proteins in the liver	+	+++
12	Ureogenesis	+	+++
13	Glycogenolysis	+	+++
14	Gluconeogenesis	+	+++
15	Lipolysis	++	+++
16	Ketonemia	++++	+
17	The rate of development of nutritional deficiencies	+	++++

Note: (–) – decrease; (+) – increase

The progression of the hypermetabolism syndrome results in protein-energy insufficiency, significant protein catabolism, and a sharp decrease in the child's body weight. The breakdown of proteins affects skeletal muscles and respiratory muscles, causing respiratory failure due to decreased strength and mass. Uncontrolled systemic stress exacerbates sepsis-induced organ dysfunction and leads to cardiovascular failure, acute respiratory distress syndrome, hepatic-renal damage, and gastrointestinal disorders. The functions of the gastrointestinal tract, which has high metabolic and immune activity, are among the first to be affected due to protein-energy deficiency, as 50–80 % of its nutrition is provided by intracavitary substrates necessary for cell growth and regeneration. Recent studies have shown that the main factor in the pathogenesis of multiple organ dysfunction syndrome in critical conditions is the syndrome of intestinal insufficiency (IIS) [8]. Inhibition of gastrointestinal motility and digestive disorders, combined with morphocirculatory changes in the intestinal wall, resulting in bacterial translocation into the systemic circulation [10, 11]. Bacterial translocation itself is an important contributor to sepsis-induced organ dysfunction. Overall, SCI exacerbates the formation and maintenance of the hypermetabolism-hypercatabolism syndrome, while the intestine, as a highly active organ, requires an adequate nutrient supply to maintain its functions [12, 13].

The importance of early and adequate nutritional therapy for patients with hypermetabolism-hypercatabolism syndrome cannot be overstated. This is a crucial component in treating sepsis, as it aims to correct increased energy consumption and ensure optimal nutrient supply for the body [14]. The primary objective of nutritional therapy is to prevent the progression of the multi-inflammatory syndrome and organ dysfunction, boost immune protection, and reduce mortality in these patients.

However, providing natural nutrition to children in intensive care units can present several challenges, such as difficulty in feeding, high nutrient requirements, nutrient intolerance or poor digestibility, among others. Early initiation of enteral nutrition (EN) in septic patients helps to maintain the intestinal microbiota, has a trophic effect on the gastrointestinal tract, and enhances its barrier function. Despite the vast information available on protein-energy deficiency in sepsis/septic shock patients, there is a lack of methods for early diagnosis and correction of hypermetabolism syndrome. The diagnostic criteria for sepsis in children are similar [15] but not identical to those for adults and are based on the decisions of the International Consensus Conference on Pediatric Sepsis [8].

According to the Surviving Sepsis Campaign (2012) recommendations, in all cases where patients with sepsis cannot receive adequate natural nutrition, proper nutritional support is mandatory and can be provided via oral, enteral, or parenteral routes [16]. The main recommendations of the SSC (2012) for nutritional therapy in sepsis/septic shock include prioritizing oral or EN when feasible within the first 48 hours of diagnosis (2C), starting with low-dose feeding and gradually increasing the volume if tolerated (2B), using intravenous glucose in conjunction with EN in the first week of diagnosis instead of total parenteral nutrition or mixed parenteral-enteral nutrition (PEN) (2B), and using clinical nutrition without immunomodulatory supplements when possible. However, the updated guidelines of the Surviving Sepsis Campaign (2021) did not introduce significant changes in nutritional support for sepsis, indicating a lack of randomized clinical trials in this field, even for adult patients [16].

One recommendation with a low level of certainty suggests starting EN within 72 hours after admission to the ICU for adult patients with sepsis/SS in the absence of contraindications [16]. Early initiation of EN in septic patients has been shown to prevent bacterial translocation, mitigate the inflammatory response, and potentially decrease insulin resistance [17, 18]. However, only one low-quality randomized clinical trial (44 ICUs, n=2410) has been conducted to analyze the effect of early EN in septic patients receiving invasive mechanical ventilation with shock [19]. Despite the lack of significant effect, the SSC (2021) recommended early EN for sepsis/septic shock patients due to the lack of apparent harm. The SSC (2021) guideline only dedicates one page to nutritional support for sepsis in adults, with a low level of evidence.

The European Society for Clinical Nutrition and Metabolism (ESPEN) recommendations for nutritional support in sepsis only have two provisions: if patients with sepsis have difficulty with a natural diet in the first three days, they should receive parenteral nutrition (PN) for 24–48 hours if EN is contraindicated, and if EN is insufficient, parenteral nutrition should be prescribed after two days. The main limitations of early parenteral nutrition include the non-physiological method and the risk of various complications, such as infections, thromboembolic events, metabolic disorders, and technical issues.

The literature search revealed that the majority of the studies focus on nutritional therapy in critically ill children with conditions such as shock, acute respiratory distress syndrome, injuries, burns, and those on mechanical ventilation. The SCCM-ASPEN Joint Guidelines (2017) [20] provide recommendations for nutritional support in critically ill children based on an analysis of 2000 clinical trials and cohort studies. The main recommendations are as follows:

A minimum protein intake of 1.5 g/kg/day is recommended. This is to prevent a cumulative negative protein balance, as shown in previous studies [21, 22].

Early enteral nutrition (EN) is recommended within 24-48 hours of admission for critically ill children in the ICU. This is due to the indirect evidence showing lower mortality rates in children who received early EN compared to those who did not [23, 24].

EN is recommended to be delivered through a nasogastric tube, and for children with a high risk of aspiration or who are unable to tolerate gastric nutrition, the post-pyloric or small bowel site is recommended.

The start of parenteral nutrition in children should be delayed until they are well-assimilating EN, as there is not enough research in this area.

Immune nutrition is not recommended for critically ill children, as there are conflicting studies on its effectiveness.

An observational study [21] of 76 ventilated children with a mean age of 21 months found that a protein

intake of ≥1.5 g/kg/day and an energy intake of ≥58 kcal/kg/day were required for nitrogen and energy balance. Similar studies [22, 23] also showed that the target levels of protein and calories were between 1.5–1.9 g/kg/day and 58-69 kcal/kg/day, respectively. A large international multicenter study (59 ICUs, 15 countries) examined the relationship between protein intake and 60-day mortality in critically ill children (n=1245, mean age 1.7 years) requiring mechanical ventilation (≥48 h) and found that higher protein intake was associated with lower 60-day mortality (P < 0.001) [22]. A recent study by Wong J.J. et al. (n=107, mean age: 5.2 years) also showed that early initiation of adequate protein nutrition was associated with improved clinical outcomes in children with acute respiratory distress syndrome (Table 2). The study concluded that protein supplementation may be more important than the total calorie content for optimal results.

Table 2

Outcomes of patients with ARDS based on adequate caloric intake [23]

Clinical outcome	Not enough calories n=81	Enough calories n=26
Mortality in the ICU	49 (60.5 %)	9 (34.6 %)
Multiple organ dysfunction	58 (72.5)	14 (53.8)
ECMO	6 (7.4)	1 (3.8)

A multicenter retrospective review (n=5015, mean age 2.4 (0.5–9.8) years) conducted in 12 pediatric centres found that early enteral nutrition (EN) was associated with lower mortality in critically ill children compared to those who did not receive EN. The duration of mechanical ventilation and the age of the children did not differ between groups [24, 25].

The authors recommend initiating EN within the first 24-48 hours and gradually increasing its volume to provide at least two-thirds of the daily energy requirement by the end of the first week of treatment in the ICU, with a minimum protein intake of 1.5 g/(kg day) (evidence category C). In many other studies [26, 27] benefits of early EN as a physiological pathway delivery of the population, the safety of motor-evacuation curative, immune and barrier function of the gastrointestinal tract in children are in critical condition [28, 29].

There is conflicting evidence in the literature regarding the benefits of immune nutrition. G. Briassoulis conducted three studies [29–31] on a small number of critically ill children with different conditions found no significant differences in energy and protein intake, mortality, and duration of mechanical ventilation between groups receiving immune nutrition formula and those receiving standard infant formula. Another randomized controlled trial (RCT) [32] evaluated the efficacy of immune nutrition (zinc, selenium, glutamine, and metoclopramide) in 293 critically ill children and found no significant differences in hospital complications and duration of mechanical ventilation compared to the control group who received whey protein. However, the trial reported a significant reduction in nosocomial infections/sepsis in immunocompromised children.

Two RCTs [33, 34] evaluated the effect of two different lipid emulsions in critically ill patients with CHD undergoing cardiopulmonary bypass surgery. The results showed that the use of Lipoplus (50 % medium chain triglycerides, 40 % long chain triglycerides, 10 % fish oil) was associated with lower procalcitonin levels, a lower ratio of ω-6 to ω-3, higher concentrations of ω-3, and higher levels of EPA phospholipids. The concentration of TNF-α was also lower in the Lipoplus group. A review of the literature on the use of glutamine in parenteral nutrition in critically ill children [35] cites meta-analyses that highlight the effectiveness of parenteral nutrition with additional glutamine in patients.

The authors of several studies have highlighted the benefits of immune nutrition, including improvement in the immune status, increased intestinal barrier function, improved cellular metabolism, and reduced organ system damage. These studies have shown that early recovery of protein metabolism and improved clinical outcomes can be achieved with immune nutrition [36, 37]. Moreover, the use of glutamine in PN regimens for critically ill children has been shown to be safe and without serious complications over the last decade [38]. Another study evaluating the effectiveness of immune nutrition in critically ill children also demonstrated its positive aspects, including a decrease in the duration of mechanical ventilation by an average of 3 days and faster normalization of protein levels in children treated with glutamine + PP, compared to those who did not receive it [39].

The ESPNIC 2020 Nutrition Guideline for Critically Ill Children and Newborns acknowledges the limited evidence in this area, with a lack of large RCTs and a low level of evidence in the published literature [40]. The main ESPNIC recommendations include:

Early enteral nutrition (EN) should start within 24 hours after admission to the ICU if no contraindications exist.

Early EN is recommended for term infants and children who are stable with medical hemodynamic support.

Energy intake during the acute phase of critical illness should not exceed resting energy expenditure, and energy debt, rehabilitation, physical activity, and growth should be considered when calculating energy intake after the acute phase.

Recommended protein intake during the acute phase is 1.5 g/kg/day with EN.

To prevent hypoglycemia, sufficient intravenous glucose administration is necessary, and excessive glucose should be avoided.

Immune nutrition is not recommended for newborns and children in critical condition due to insufficient evidence.

Refusal of PN for up to one week is recommended for newborns and term children, with the provision of micronutrients, regardless of nutritional status.

Lipid emulsions with or without fish oil are recommended as the first choice for parenteral nutrition [34].

The International recommendations for the treatment of sepsis and sepsis-related organ dysfunction in children as part of the Surviving Sepsis Campaign (2020) revealed only a few main recommendations for nutrition in children, which overlap with the ESPNIC recommendations [40, 41]:

There is no recommendation for early hypocaloric/trophic EN followed by a slow transition to complete EN compared with early complete EN in septic children with sepsis or sepsis-induced organ dysfunction in the absence of contraindications to EN.

Early EN within 48 hours of admission for sepsis or sepsis-induced organ dysfunction is preferred, in the absence of contraindications to EN, followed by a gradual increase to target levels.

After adequate hemodynamic resuscitation, EN may be indicated in children with sepsis if there is no further need for increased vasoactive drug doses.

Refraining from parenteral nutrition for the first 7 days of ICU stay is recommended for children with sepsis or sepsis-induced organ dysfunction.

Abandoning the use of specialized lipid emulsions is recommended for children with sepsis or sepsis-induced organ dysfunction due to insufficient evidence.

The use of selenium, glutamine, arginine, and zinc in children with severe sepsis or sepsis-induced multiple organ failure is not recommended.

The rationale behind this recommendation is based on a randomized controlled trial conducted by Briassoulis et al. [30], which involved 30 children with severe sepsis. The study compared the use of an immuno-nutrition formula (which contained GLN, L-arginine, antioxidants, ω-3 fatty acids, fibre, vitamin E, β-carotene, zinc, copper, and selenium) against the use of standard infant formula. No significant differences were observed between the two groups in terms of survival rates (80 % vs 87 %) or duration of mechanical ventilation (10.4±2.2 days vs 11.4±2.5 days). Another study [32] compared two groups of 283 patients, one receiving a mixture of whey protein and the other receiving a mixture of zinc, selenium, glutamine, and metoclopramide intravenously. The authors found no significant differences between the groups in terms of hospital complications and sepsis at 100 days ($p = 0.81$), length of stay in the PICU ($p = 0.16$), or 28-day mortality (8/139 [5.8 %] versus 15/145 [10.3 %]).

However, these recommendations should be interpreted with caution as they have a low to very low level of evidence. The SSC Guidelines for Childhood Sepsis (2020) extensively reviewed the literature. However, they did not find sufficient evidence to develop strong nutritional recommendations for children with sepsis or severe sepsis."

4. Discussion

This review has compiled data from various sources, including meta-analyses on nutrition in critically ill patients, SCCM–ASPEN Guidelines (2017), SSC Guidelines (2012, 2021), ESPNIC (2020), and SSC Childhood Sepsis (2020). Despite the extensive literature search since 2009, many issues in critical medicine remain unresolved, including the optimal nutritional therapy for critically ill children. The SCCM-ASPEN (2017) guidelines acknowledge the lack of high-level evidence regarding the experience of nutritional therapy in pediatric ICU settings. The correlation between optimal protein intake and clinical outcomes is an area of great interest [21, 24]. The choice of the optimal route of nutrition (EN and/or PN) and the timing of substrate delivery remain ongoing research topics in critical paediatrics [19].

EN remains the preferred method of nutritional support in critically ill children, similar to adult patients [25]. The maintenance of normal EN has been proven to contribute to the maintenance of the immunity of the whole organism [41, 42]. Recently, the optimization of EN by additional delayed administration of PN in children has been emphasized. However, the role and timing of initiation of additional PN to compensate for EN deficiency is unknown and should be individualized on a case-by-case basis [43, 44].

To address the lack of high-quality evidence, the ESPNIC (2020) guidance has complemented most of the existing ASPEN (2017) guidelines for critical paediatrics based on new evidence. However, the heterogeneity of the pediatric ICU in terms of age, pathology, type of disease, the severity of the condition, presence of comorbidities and complications, and nutritional status means that a one-size-fits-all nutrition strategy is unlikely to be appropriate for all critically ill patients. Instead, researchers now recommend an individualized approach to nutritional therapy, based on the initial nutritional status and severity of the patient, with a mandatory risk-benefit ratio of different nutritional methods [45, 46].

The literature on immune nutrition has sparked a lot of discussion and contradictory conclusions due to the limited data sample and an inadequate number of studies. As a result, current guidelines do not recommend immune nutrition for critically ill patients. However, recent research has demonstrated the safety of the pharmaconutrient glutamine in parenteral nutrition (PN) regimens in critically ill children [36, 39]. Ongoing research in this area continues to expand our knowledge and understanding.

Based on an analysis of the literature on nutrition in critical care, several key provisions can be formulated for nutritional support in children with sepsis/SS:

Timely initiation of nutrition. Early initiation of enteral nutrition (EN) within 24–48 hours of admission to the ICU for seriously ill children is a priority, provided there are no contraindications. A stepwise approach to increasing EN should be employed, with at least two-thirds of daily energy requirements reached by the end of the first week of treatment and a recommended minimum protein intake of 1.5 g/(kg per day) [22, 24]. Although there are no targeted randomized controlled trials (RCTs) on nutrition in children with sepsis/SS, indirect data on nutritional therapy in critically ill children [22, 23] with a sufficient sample of material confirms that early EN groups have an increased survival rate. Early initiation of EN promotes wound healing after surgery, reduces the

risk of hospital complications, reduces the length of stay on mechanical ventilation, and, in general, reduces overall mortality.

Hypocaloric/trophic EN should be initiated and gradually increased to target levels in children with sepsis/SS in the absence of contraindications to EN [46, 45]. This approach helps prevent atrophy of the intestinal mucosa, reduces the risk of bacterial translocation, and reduces the risk of organ dysfunction.

Children with SS on vasoactive drugs may benefit from EN as long as there is no need to increase their dose in the future. The results of several studies in children with shock receiving vasoactive drugs have shown that EN is feasible without increasing side effects and complications [43, 44].

Parenteral nutrition (PN) is recommended from days 2-3 of a child's stay in the ICU when EN is inadequate or contraindicated. The role and timing of starting PN in children with sepsis/SS are not well-established, and the need for delayed PN 7 days after admission to the ICU is unclear. Further targeted research is needed [15, 16].

Mixed parenteral-enteral nutrition may be indicated in cases of pronounced hypermetabolism-hypercatabolism [16, 20]. More research is needed to support this approach.

In the case of gastrointestinal tract dysfunction, when EN is contraindicated, total parenteral nutrition (TPN) is recommended. Immune nutrition, such as glutamine at a dosage of 1.5-2.0 ml/kg/day, can also be considered [35].

Lipid emulsions, with or without fish oil, may be recommended as the first-line treatment for PN [34, 40].

An individualized approach to prescribing nutritional therapy for children with sepsis/SS is recommended [20, 40, 41, 45].

The limitation of our study. There were no study restrictions.

Prospects for further research. We plan to conduct further research in this direction in children of different age groups, including newborns.

5. Conclusion

Despite recent reviews of nutrition in critically ill patients based on guidelines from SCCM–ASPEN (2017), SSC (2012, 2021), ESPNIC (2020), and SSC on pediatric sepsis (2020), many questions still remain unresolved, highlighting the need for further systematic study. Most dietary recommendations in these guidelines are based on consensus or low-level evidence, indicating a lack of an evidence base for nutritional therapy in children with sepsis/SS. Future research is needed in this area to address these gaps.

Given the highly heterogeneous nature of the pediatric ICU population in terms of disease severity, nutritional status, age, comorbidities, and other criteria, an individualized approach to nutritional therapy is necessary to improve clinical outcomes.

Conflict of interest

The authors declare that there is no conflict of interest concerning this paper, as well as the published research results, including the financial aspects of conducting the research, obtaining and using its results, as well as any non-financial personal relationships.

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Data availability

Manuscript has no associated data.

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