Review Article

Role of Nutrition in Pediatric Patients with Respiratory Failure

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Abstract

Respiratory failure is a consequence of malfunction of the respiratory system including neuronal and cellular aspects. The most common causes in children are pneumonitis, vasculitis, pulmonary edema, cystic fibrosis, tuberculosis, asthma, foreign-body aspiration, and respiratory infections of the upper and lower airways. Reduced immunological response due to critical illness, atrophy, and increased intestinal epithelial barrier permeability results in increased susceptibility to infections and the spread of pathogens. The search strategy included a PubMed search for articles from 2000 to 2022. Malnutrition is acquired in 50% of patients admitted to the pediatric intensive care unit, with the added burden of nutritional deficits worsening preexisting malnutrition. Nutrition forms an essential component in managing respiratory conditions, with the potential to change outcomes. Enteral nutrition (EN) can reduce inflammatory cytokine activation and release, as well as maintain gastrointestinal (GI) mucosal integrity, which lowers systemic bacterial invasion and sepsis. Therefore, EN should be the preferred mode of nutrition (when clinically indicated) to parenteral nutrition. ASPEN guidelines recommend the administration of a minimum of 1.5 g/kg/ day of protein in critically ill children. Reduction in the respiratory quotient may be achieved by lowering the carbohydrate intake in infants suffering from prolonged lung disease; however, a balance of carbohydrate and fat ratios is recommended. Immunonutrition helps in reducing inflammation and pro-inflammatory cytokine levels. During pediatric acute respiratory distress syndrome, an essential target to improve lung inflammation is the GI tract. However, no disease-specific recommendation for probiotics and immunonutrients has been established in children yet.

Keywords: Acute respiratory distress syndrome, enteral nutrition, gut lung axis, immunonutrition, malnutrition, pediatrics, respiratory failure

Introduction

The exchange of gases, acid-base balance, speech, pulmonary defense, and metabolism, and the management of bioactive chemicals are some of the functions of the respiratory system.[1] Respiratory failure (RF) is the ineffectiveness of the respiratory system to fulfill the O_2 requirements, and/or effectively excrete CO_2 from the body.[2]

Methodology

A PubMed search was performed in August 2022 with clinical queries using the key terms "nutrition in RF in paediatrics," "nutritional assessment in critically ill paediatrics," "prevalence of pediatric RF," "nutrition in pediatric acute respiratory distress syndrome (PARDS)," "nutrition in cystic fibrosis (CF)," "nutrition in respiratory distress," "immunonutrition in pediatric intensive care unit (PICU)," "immunonutrition and respiratory distress," "respiratory quotient (RQ)," "enteral nutrition (EN) in PICU," "gut lung axis," "gut microbiome and dysbiosis," and "malnutrition and pediatric RF." Literature published between January 2000 and July 2022, which included reviews, meta-analyses, randomized controlled trials, and observational studies, was referred. To add to the review, Google, Wikipedia and UpToDate were also considered. Only literature published in the English language was referred. An effort to include more Indian studies is evident in this article.

Epidemiology of Respiratory Failure

Studies show that RF is more prevalent in children than adults. Prematurity-related problems and the transition to extrauterine

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life, result in almost half of the cases of RF in neonates.[2] Acute respiratory distress syndrome (ARDS) accounts for 1%–10% of PICU hospitalizations.[3] Lodha *et al*[4] stated that the occurrence of ARDS was 20.1/1000 admissions with a 75% death rate. In most cases, pneumonia was discovered to be the underlying reason.[4]

Causes of Respiratory Failure

RF is a consequence of malfunction of the pulmonary system, including the neuronal and cellular components, along with the respiratory system itself. Pneumonitis, CF, vasculitis, tuberculosis, pulmonary edema, asthma, foreign-body aspiration, and respiratory infections of the upper and lower airways (such as croup, bronchiolitis, and pneumonia) are the common diseases related to the lung, leading to RF.[5,6] About 10%-70% of COVID-19-positive critically ill children, also developed ARDS.[7]

Effect of Malnutrition on Respiratory Failure Outcomes

Malnutrition is a prognostic factor for RF; however, it may go unnoticed. In addition, because of the cumulative protein and energy deficit brought on by catabolism, it has a likelihood to exacerbate during the PICU stay.[8,9]

As per[10] De Souza Menezes *et al*., malnutrition in the pediatric population has a significant positive association with the duration of ventilatory support (of >5 days) and hospital stay. Systemic functioning changes are the root cause of the complications brought on by malnutrition in critically ill individuals. Reduced immunological response, atrophy, and increased intestinal epithelial barrier permeability are some of the modifications, which increase susceptibility to infections and the spread of pathogens.[10]

Pertaining to PARDS, muscle mass wasting and impaired diaphragmatic function may worsen the patient's RF and prolong their need for a ventilator.[11] The development of muscular fatigue and diaphragmatic dysfunction during disease progression could be a result of prolonged ventilation, systemic inflammation, malnutrition, increased protein turnover, use of neuromuscular and immunomodulatory drugs, and the range of contraction of the diaphragm during ventilator support.[12]

Lower body mass index (or weight for height for children <2 years), z score and reduced diaphragmatic potency have a direct correlation with chronic malnutrition found in patients with CF. After initiation of mechanical ventilation, the diaphragmatic function is affected by various factors such as nutritional status, acquired nutritional deficiencies, dyselectrolytemia, and individual risks.[12]

During inspiration, the external intercostals are active and during expiration, internal intercostals are active. Due to undernutrition, there is reduced diaphragmatic muscle mass, decreased respiratory muscle strength, decreased inspiratory muscle pressure, and increased chest wall resistivity adversely affecting lung parenchyma, muscle structure, function, and respiratory mechanics.[13,14] As the abdominal fat deposition increases, shallow and rapid breathing reduces the thoracic volume and increases respiratory dead space, leading to obstruction in the trachea, partial atelectasis, and ultimately respiratory distress.[15]

Effect of Chronic Respiratory Diseases on Respiratory Failure Outcomes

The most significant clinical effects of dietary deficits in patients with chronic respiratory diseases are reduction in muscle mass and impaired functional status. Nutritional deficits negatively affect bone and fat tissues, muscle structure, and function, progressing to cachexia in more severe cases. Malnutrition also affects the patient's immune system, increasing the risk for infections and disease exacerbations, which in turn may further impair nutritional status.[16]

Metabolism in Respiratory Failure

Children and adolescents in critical conditions frequently have a systemic inflammatory response, which results in the release of inflammatory markers, metabolic dysregulation, and muscle breakdown.[17]

Catecholamines cause triglycerides to mobilize and enhance metabolic rate, O_2 consumption (VO2), and CO_2 generation (VCO2). An early hypermetabolic response to acute insults may stimulate the sympathetic nervous system. Impaired glucose tolerance, increased lipid breakdown, and altered protein metabolism are all indicators of catabolism and systemic inflammation. A prolonged state of catabolism further deteriorates the patient's nutritional status, and compromises wound healing which can intensify the course of RF and prolong the need for ventilatory support.[18] In neonatal and pediatric populations, preexisting nutritional status and insufficient nutrient delivery early in critical illness are well-proven risk factors for morbidity and mortality.[11]

Effect of Respiratory Failure on Growth and Development

In order to recuperate and assist in the synthesis of glucose, and critical illness-specific biomolecules, metabolism shifts away from growth. When resources are diverted to support recovery from a critical illness, it prevents pediatric patients' natural growth and development.[11]

Nutritional Screening and Assessment in the Pediatric Intensive Care Unit

According to the CF foundation,[19] in children with CF, targeting early intervention using a screening tool is a must for any respiratory disease. However, there are no particular guidelines for the specific usage of screening tools. Six pediatric malnutrition screening tools were described. Screening Tool for Risk On Nutritional Status and Growth (STRONGkids) and Pediatric Yorkhill Malnutrition Score(PYMS) tools showed promise and effectiveness for assessing nutritional risk and nutritional status.[20]

A multidisciplinary team along with a nutritionist should guide and monitor anthropometric assessment that should be individually interpreted to reduce nutrition deficits during hospitalization in the PICU with the correct diagnosis of nutritional status. If preadmission anthropometric data are unavailable, predictive formulas for the same, may be used along with biochemical parameters to assess nutrition status on PICU admission.[21] Mid-Upper Arm Circumference (MUAC) may also be used as a surrogate.[22] Grippa *et al*.[23] argue that physical measurements are poor indicators of nutritional status in PICU patients because of the impact of measurement quality, interpersonal variability, and critical illness-related factors like fluid shift. According to Vermilyea *et al*.,[24] subjective global nutritional assessment tool (SGNA) could be used in place of anthropometric measurements to recognize malnutrition in PICU patients. However, for nutritional assessment in the PICU, there is currently no established standard.[25]

Nutritional Requirements during Pediatric Respiratory Failure

Nutrition is important in the management of pediatric respiratory diseases, with the potential to change outcomes.[26] Feeding patients with PARDS have both direct and indirect clinical advantages. Malnutrition is acquired in 50% of patients during the course of PICU admission, with the added burden of nutritional deficits worsening preexisting malnutrition. Malnutrition is directly proportional to mortality.[11] Hence, efficient delivery of nutrients improves outcomes.[17]

Permissive Underfeeding

According to the PermiT trial,[27] reduced insulin needs and lower blood glucose levels were linked to permissive underfeeding. Between underfeeding (40%–60% energy requirements) and standard feeding (70%–100% energy requirements), there was no significant difference found in terms of mortality. The study also found no improvement in protein catabolism in PICU patients with higher caloric intake when assessed based on nitrogen balance and levels of prealbumin, transferrin, and urinary nitrogen excretion. In acute RF patients (mechanically ventilated), there was no difference in clinical outcomes between early trophic feeds and early full EN feeds, except for reduced events of gastrointestinal (GI) disturbances.[28,29]

Nutritional Support: Enteral and Parenteral Nutrition for Pediatric Respiratory Failure

Patients with respiratory diseases may require multiple feeding modes or even complete nutritional support, depending on the severity and intensity of the illness. According to clinical studies, administration of EN within 24–48 hrs of being admitted to the PICU, along with 60%–70% of nutritional needs being met during the first 7 days of PICU stay, have shown to positively impact prognosis.[30] The PALICC statement strongly recommends preferring EN over parenteral nutrition (PN) wherever feasible.[31] EN can reduce inflammatory cytokine activation and release and maintain GI mucosal integrity, lowering the risk of bacterial translocation and sepsis. Initially, <60%–80% of the total requirements should be established, followed by a gradual increase based on tolerance. Nutritional support should be initiated as soon as possible, with special attention to children classified as stunted or wasted according to WHO criteria, using pre-admission data.[22,31]

Energy

Nutritional deficiency aggravates due to underfeeding, resulting in poor growth of the child. Malnutrition leads to excessive breakdown of protein in the body to meet the metabolic requirements. Immunosuppression is a major adverse effect of this protein breakdown. As a result, the patient may be more susceptible to postponed weaning from ventilator support, acquiring infection, and delayed wound healing. However, overfeeding can lead to electrolyte imbalance, increased CO_2 synthesis, etc.[32-35] Consumption of 54–58 kcal/kg/d may be linked to increased protein synthesis and resultant positive balance.[36] According to ASPEN guidelines, usage of Indirect calorimetry (IC) is suggested to determine energy requirements. However, where IC is not possible, predictive equations like Schofield and WHO equations are useful for calculating resting energy expenditure (REE) in critically ill children.[36] In some studies, estimating energy expenditure based on standard equations, especially Harris-Benedict and Recommended Dietary Allowances (RDA) (aimed at healthy populations)[36] has shown to be inaccurate and can significantly underestimate or overestimate the energy requirements in critically ill children. However, the Schofield equation was found to show the lowest errors in REE estimation.[36] Finally, they recommend that energy intake be adapted to take into account disease states that may increase REE, but suggest that predictive equations be used without the routine addition of "stress factors" in critically ill children.[30]

Protein

According to ASPEN, a minimum protein intake of 1.5 g/kg/day is recommended in critically ill children, with requirements as high as 2.5–3 g/kg/d in those dependent on ventilator support.[26,36] An increased protein intake supported by adequate intake of other macronutrients is known to support protein metabolism and utilization.[25]

EN can improve calorie deficit and promote protein metabolism.[37] Consensus on initiating PN in the PICU when EN is not feasible has not been established. According to ASPEN and ESPGHAN guidelines for PN,[36,38] in premature infants initially, 1.5–3 g/kg/d of protein should be started, followed by a daily increase of 1 g, with an aim to achieve a goal of 3–4 g/kg/day.

Carbohydrates, Lipids, and Respiratory Quotient

A low RQ can be achieved in pediatric patients, with a diet slightly lower in carbohydrate content (36% of total energy).[39,40] RQ for carbohydrates is higher (1.0) than for protein (0.8) and fat (0.7). A study found protein deficit and higher delivery of fat to be associated with raised levels of inflammatory cytokines. Higher serum IL-6 and TNF-a levels were linked with particularly low supply of protein. In malnutrition studies where compromised status of assumed energy and protein intake exists, increased levels of inflammatory markers are seen. Pro-inflammatory fatty acids can act directly or by activating receptors which results in signaling the inflammatory response.[41]

Fatty acids are a key fuel source in critical diseases. Thus, lipid metabolism and turnover are elevated. Excess carbohydrates are converted to lipids, but the process produces CO_2, which may prolong mechanical ventilation. Lipids should account for 30%–40% of total calories. This suggests that even relatively smaller meal changes in the proportion of carbohydrates and fat may have significant effects on functional and breathing capacity in RF patients.[39]

A high-carbohydrate (50%–65% of total energy) diet would result in greater CO_2 production at the same oxygen intake, but a high-fat, low-carbohydrate diet may cause a reduction in RQ and improve pulmonary function.[40] It was later observed that not the carbohydrate component but the total calorie content of food, determined the CO_2 production even after the ratio of carbohydrate to fat was not altered with an increase in total calories.[11,42] Al Dorzi[43] argues that the ratio of macronutrients is not a contributing factor in altering $PaCO_2$ levels, especially when the total energy intake is based on the patient's requirements. Thus balanced carbohydrate and fat ratios are advisable.[44]

A ketogenic diet (KD) might favorably affect lung inflammation through the production of beta-hydroxybutyrate (BHB).[40,42,44] However, BHB also decreases endothelial angiotensinogen activity, leading to massive hemorrhage or interstitial and alveolar neutrophil infiltration, and increases the susceptibility to respiratory distress.[45] Therefore, studies to establish a stronger consensus on the use of KD in RF patients are required.

RQ fluctuates throughout the PICU stay, affecting substrate consumption and nutritional support. This can be due to factors related and unrelated to feeding, like disease pathophysiology, and individual differences in metabolism and response to feed composition. Two clinically relevant issues, the absence of underfeeding and the presence of (carbohydrate) overfeeding can be determined by RQ lower than 0.85 and RQ higher than 1.0, respectively.[46] In the PICU, due to patient-specific differences[46] and unique individual metabolic systems, there is limited evidence for the use of RQ to evaluate the adequacy and efficacy of nutrition therapy.[47]

Fluid

The Holiday-Segar method is frequently used to calculate maintenance fluids for children.[48,49] The efficacy of mechanical transport while swallowing, depends on the hydration status of mucosal surfaces. Mucin production and ciliary activity acted as the primary regulators of airway mucus clearance. However, hydration remains the main factor influencing mucus clearance.[50]

Immunonutrition and Micronutrients

PICU patients are at a major risk for immunosuppression associated with increased infections, hyperinflammation, etc., Immunonutrition helps in reducing inflammation, and pro-inflammatory cytokine levels, but there are no apparent clinical outcome studies for specific requirements. Different combinations of nutritional and pharmacologic additives targeted at modifying the inflammatory and immunological response in critically sick adults have not demonstrated benefits. Many antioxidants like arginine, glutamine, omega-3 fatty acids, zinc, and selenium have all been studied.[35] Table 1 summarizes studies on immunonutrition in respiratory diseases.

Other phytochemicals such as allicin, garcinia, green tea extract, and licorice, have been vaguely studied. However, limited research exhibiting the anti-inflammatory effects of these substances has been conducted in children. Further research focusing on the role of micronutrients and antioxidants along with the requirements in RF in children needs to be studied.

Gut-Lung Axis and Dysbiosis

In PICU, critical illness and related respiratory pathologies may cause organ damage. Shock, vasoactive medication, and lack of oxygen make the intestines more vulnerable to damage. The mucosa in the lung and the gut are continuous, yet they have separate microbiomes. The GI tract plays a major role in modulating immunity. During PARDS, an essential target to improve lung inflammation is the GI tract. The gut barrier is not only involved in the absorption of water and nutrients but also prevents the entry of pathogens and toxins.[11] The GI cytokines reach the lungs via lymphatic circulation. Gut injury may, therefore, modulate the severity of lung injury. *Prevotella, Veillonella*, and *Fusobacterium*, nonpathogenic anaerobic bacteria, inhabit healthy, disease-free alveoli, and *Bacteroidetes* and *Enterobacteriaceae* species make up healthy gut flora. In RF, the lungs experience dysbiosis, with bacteria that normally live in the gut being discovered there.[20]

Children who are critically ill show severe gut microbiome dysbiosis. Various PICU factors, including the administration of antibiotics, morphine and gut rest, etc., are linked to dysbiosis. Dysbiosis may result in negative clinical effects that adversely affect outcomes. EN might control dysbiosis.[82] Feeding may also downregulate systemic inflammation and prevent further damage to the lungs.[11] Thus, EN should be preferred over PN wherever feasible.

Role of Probiotics in Respiratory Failure

Probiotics are living microorganisms, that have various health benefits for the host when administered in the correct doses.[83]

Table 1: Summary of Studies on Immunonutrition in Respiratory Diseases

Nutrient	Author/year	Study population	Main findings
Selenium	Mahmoodpoor *et al*., 2019[51]	Adults	Low levels of selenium lead to reduced lymphocyte and albumin levels and increased CRP and malnutrition
Selenium	Lemoine *et al*., 2019[52]	School children	Low serum selenium levels are associated with pulmonary inflammation in asthmatic children
Selenium	Lee *et al*., 2016[53]	Adults with respiratory distress in ICU	Reduced serum selenium levels are positively correlated with malnutrition and poor prognosis
Selenium	Mahmoodpoor *et al*., 2019[51]	Patients with ARDS	Selenium supplementation did not affect survival, duration of mechanical ventilation, and ICU stay
Selenium	Singleton *et al*., 2006[54]	Premature infants	Selenium insufficiency has an increased risk of early neonatal morbidity in premature infants with PARDS and chronic intrauterine hypoxia
Omega 3 fatty acids	Yu *et al*., 2021[55]	Adults with COPD	Omega 3 supplementation led to increased LDL and weight and also reduced IL-6 levels, but had no impact on lung functioning and quality of life
Omega 3 fatty acids	Lemoine *et al*., 2019[52]	Children	A positive correlation is observed in children with increased intake of omega 6 and reduced intake of omega 3 between particulate matter exposure and systemic inflammation
Omega 3 fatty acids	Mihrshahi *et al*., 2003, Mihrshahi *et al*., 2004, Hodge *et al*., 1998, Nagakura *et al*., 2000[56-59]	Children	Supplementation of omega-3 fish oil showed a reduction in wheezing, allergic sensation, cough, and asthma severity
Arginine	Iyer and Bansal, 2019[26]	Review study	Low levels of arginine can lead to the development of COPD, asthma, cystic fibrosis, bronchopulmonary dysplasia, and pulmonary hypertension
Arginine	Polycarpou *et al*., 2013[60]	VLBW	Oral arginine supplementation in VLBW infants improved survival; however, children with lung diseases and VLBW had no effect with arginine supplementation
Arginine	Scott *et al*., 2021[61]	Children with cystic fibrosis and primary ciliary dyskinesia	Reduced L-arginine enhanced breathlessness and exacerbation in nitric oxide deficient CF patient
Arginine	Hernández-Jiménez *et al*., 2020[62]	Adults	Irregular arginine supplementation can cause respiratory diseases like COPD, asthma, etc.; hence multicentric RCTs are needed
Glutamine	Iyer *et al*., 2019, Oliviera *et al*. 2016[26,63]	Review analysis	Catabolic activity in respiratory diseases like COPD, asthma, and ARDS can reduce due to glutamine supplementation. However, with respiratory disease and failure, the requirements increase due to hyperinflammation and tissue injury
Glutamine	Wang *et al*., 2022, Oliveira *et al*., 2019[64,65]	Mice	Supplementation in pulmonary and extra-pulmonary ARDS has shown a reduction of lung injury and systemic inflammation, with improvement in inflammatory markers
Glutamine	Oliveira *et al*., 2016[63]	Adults	In ARDS, asthma, and lung cancer, glutamine supplementation may have a potential therapeutic benefit as it reduces lung inflammation
Glutamine	Heyland *et al*., 2013[66]	Adults	In critically ill patients, supplementation was related to increased mortality, with no other beneficial effects
Vitamin D	Bayramoğlu *et al*., 2021[67]	Pediatric COVID-19	The deficiency was associated with impaired pulmonary function and increased risk of viral and bacterial infections, and noninfectious diseases of the lung like asthma. Vitamin D increases macrophage, lymphocyte, and epithelial cell function, reducing CRP levels and improving lung function. Prophylactic Vitamin D supplementation may be considered, especially in the adolescent age group
Vitamin D	Hughes and Norton, 2009[68]	Critically ill children	Sepsis was correlated with low Vitamin D levels but had no significant association with mortality and length of stay or ventilation
Vitamin D	Hiemstra, 2007[69]	Children	Vitamin D was used for beta-defensins production, which prevents respiratory infections in children under the age of 5 years
Phosphorus	Kilic *et al*., 2012[70]	Critically ill children	Reduced serum phosphorous leads to low muscle ATP synthesis, which may lead to respiratory muscle weakness
Phosphorus	El Shazly *et al*., 2017[71]	Critically ill children	Reduced phosphorus levels lead to increased morbidity and mortality in critically ill patients, leading to respiratory failure and increased PICU stay

Contd...

Table 1: Contd...

Nutrient	Author/year	Study population	Main findings
Phosphorus	Kilic *et al*., 2012[70]	Critically ill children	Phosphorous supplementation of 40–50 mg/kg/day by enteral route prevented hypophosphatemia in PICU
Magnesium sulfate	Davalos Bichara and Goldman, 2009[72]	Pediatric patients with asthma	Magnesium sulfate where conventional treatment for acute severe exacerbation failed, is suggested. There is a need to establish the optimal dosage and the most effective route of administration, making it a prophylactic treatment in pediatric asthma patients
Magnesium sulfate	Kokotajlo *et al*., 2014[73]	Pediatric patients	The Pediatric and Neonatal Dosage Handbook recommends 25–75 mg/kg/dose up to 2 g for bronchodilation in acute asthma exacerbation
Magnesium sulfate	Mahmoodpoor *et al*., 2019[51]	Children (6 months to 4 years) wheezing children	Magnesium sulfate did not show any effect in treating acute severe virus-induced wheezing in young children
Zinc	Laghari *et al*., 2019[74]	Children with pneumonia	Zinc supplementation did not show a reduction in children with severe pneumonia
Elemental zinc	Brooks *et al*., 2004, Papukashvili *et al*., 2020[75,76]	Children (2–23 months)	Dosage of 20 mg zinc/day along with other drugs, improved severe pneumonia and reduced antimicrobial resistance, complications, and deaths
Zinc	Sazawal *et al*., 1998[77]	Preschool children	Morbidity in children with respiratory diseases was reduced when a dietary zinc supplement of < 60 µg/dL was given
B complex vitamins Folate	Strand *et al*., 2007, 2015[78,79]	Children	Folate insufficiency with lower respiratory tract infection was an independent risk factor, Poor B12 status increased morbidity in children
Vitamin D and B12	Arzu Yoldaş *et al*., 2022[80]	COVID + pediatric patients	In children with COVID-19 adequate B12 and Vitamin D levels improve immunity
B12	Karakut *et al*., 2019[81]	Children with diarrhea, vomiting, difficulty swallowing, seizure, respiratory distress, and cyanosis	Patients with lower B12 levels have growth retardation

ICU: Intensive care unit, PICU: Pediatric intensive care units, ARDS: Acute respiratory distress syndrome, PARDS: Pediatric ARDS, COPD: Chronic obstructive pulmonary disease, VLBW: Very low birth weight, CRP: C-reactive protein, LDL: Low-density lipoprotein, IL-6: Interleukin 6, CF: Cystic fibrosis, RCT: Randomized controlled trial, ATP: Adenosine triphosphate

These range from host gut microflora, immunity, autoimmune diseases, IBS, mental health, etc. Probiotics have a significant role in promoting health.

Lactobacillus rhamnosus, *L. rhamnosus*, *Bifidobacterium animalis* subsp. *lactis* BB-12, and *Limosilactobacillus fermentum,* or a mixture of several probiotic strains, reduced the risk of bronchitis and pneumonia and the duration of illness.[84] In a clinical study with school-going children, *L. rhamnosus* HN001 (6×10^9 CFU) significantly reduced wheezing and alleviated the symptoms of asthma, further improving immunological response.[85,86]

Another study conducted on children with CF stated that a mixed probiotic can improve long-term outcomes and prevent morbidity.[87] However, no disease-specific recommendation for probiotics has been established in children.

Long-Term Effects of Respiratory Failure

The cause of RF in children is idiopathic. Due to its multifactorial progression (physically, pathophysiologically, and in the clinical course of the disease), it negatively affects the child's cognitive thinking, quality of life, social life, growth, and mental health. Hence, there is a need to evaluate the caregiver as well as the patient.[88]

Conclusion

RF is the ineffectiveness of the respiratory system in effectively balancing O2 and CO2 turnover. Lung diseases such as pneumonitis and vasculitis are most likely to cause RF in pediatric patients. Muscle mass wasting and diaphragmatic dysfunction may probably worsen the patient's respiratory dynamics. Children and adolescents in critical conditions frequently have a systemic inflammatory response, which results in cytokines and chemokines release, metabolic dysregulation, and muscle breakdown. It is recommended to prefer EN over PN wherever feasible. Due to compromised immunity in PICU patients, there is a very high risk for immunosuppression associated with increased infections, hyperinflammation, etc. However, there are no strong guidelines for immunonutrition. The gut–lung axis is an important factor when choosing the route of nutrition delivery. In pediatric patients with respiratory diseases, malnutrition is an important modulator of disease outcome, which establishes the need for timely and adequate medical nutrition therapy.

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Conflicts of interest

There are no conflicts of interest.

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