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Literature Review

Refeeding Syndrome in Malnutrition – Diagnosis and Management

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Abstract:

Background: Refeeding Syndrome (RS) is a one of the potentially life-threatening complications in malnourished children. The diagnosis of RS is often challenging due to its diverse clinical manifestations. A comprehensive understanding of the risk factors, sign, symptoms and the management of RS is important to reduce morbidity and mortality.

Discussion: The management of malnutrition consists of a ten-step process divided into three phases. Adherence to this protocol is important to mitigate the risk of RS. RS is a metabolic complication that occurs when malnourished children rapidly reintroduced to nutrition. This condition is characterized by a shift of electrolytes from the extracellular to the intracellular, leading to hypophosphatemia, hypokalemia, hypomagnesemia, and thiamine deficiency. Children with RS require aggressive electrolyte and vitamin supplementation, followed by a cautious nutritional re-initiation. A gradual approach to nutritional reintroduction and electrolyte supplementation, are a critical preventive measure of RS.

Conclusion: All malnourished children are at risk of RS. Recognizing its risk factors and watchful monitoring are essential for early detection and prevention of RS.

Keywords: malnutrition, refeeding syndrome

Introduction

Malnutrition remains a global challenge as it significantly increases morbidity and mortality.[1] This issue has been elevated to global health concern, included in Sustainable Development Goals (SDGs), specifically target two, with the theme "Zero Hunger," aiming to eradicate undernutrition by 2030 and eliminate stunting and wasting by 2025.[2]

In 2018, 17 million children worldwide experienced malnutrition, with more than three-quarters of these cases occur in low-income countries.[3] In Indonesia, data showed that 3.9% of toddlers suffer from malnutrition, and 13.8% face undernutrition. This condition indices that malnutrition in Indonesia remains a severe health problem.[4] In line with the high prevalence of malnutrition, 45% of child mortality is associated with malnutrition.[5] Study showed that malnutrition has a hazard ratio eight times higher compared to adequate nutrition.[6]

Refeeding syndrome (RS) is one of the complications from malnutrition that increases the risk of mortality. RS is defined by hypophosphatemia, hypokalemia, hypomagnesemia, and/or thiamine (vitamin B1) deficiency.[7] There is still limited data on the prevalence of RS, especially in Indonesia. Due to its wide and varied symptoms, practician often missed electrolyte examination, leading to underdiagnosed RS. Symptoms that may arise includes respiratory system disorders, heart failure, arrhythmia, coma, muscle weakness, and even death. Therefore, prevention, early detection, close monitoring during feeding, and a proper calorie regiment are key to the successful therapy for patients at risk of RS.[8]

This literature review will discuss the extent of the RS problem, risk factors, and outcome in Indonesia. By understanding these factors, it is hoped that the morbidity and mortality rates associated with RS incidents can be reduced.

Malnutrition

Diagnosis of Malnutrition

Malnutrition, a condition characterized by one or more of the following signs: a) weight-for-length/height (WHZ) less than -3 standard deviations (SD); b) clinically visible bilateral pitting edema; c) upper arm circumference (UAC) < 11.5 cm in children aged 6–59 months. Effective and appropriate management of malnutrition is crucial to prevent RS, a condition that significantly increases mortality rates in malnourished children.[3, 9-11]

Management of Malnutrition

The management of malnutrition typically requires approximately six months of treatment. Children with malnutrition need to be hospitalized until the complication subside, pitting edema decreases, and their appetite improved (regardless of nutritional

status based on anthropometry index). Treatment continues through outpatient care until WHZ > -2SD and/or UAC ≥12,5 and bilateral pitting edema completely resolved. Malnutrition management is divided into three phases: stabilization, transition, and rehabilitation. These phases are implemented through ten steps **(Table 1).** Not all malnourished children will undergo these three phases. The stabilization and transition phases are intended for malnourished children requiring inpatient care, while the outpatient malnourished children undergo only the rehabilitation phase.[10, 11]

Stabilization Phase

The goal of stabilization phase is to dealing with the life-threatening emergencies, such as hypoglycemia, hypothermia, and dehydration. The first three steps of the ten actions in malnutrition management are performed during this stabilization phase. This phase usually requires 1-2 days, but may extend to one week depending on the child's clinical condition. During this phase, children are provided with an F-75 formula, is a low protein, low lactose formula containing a mineral mix (potassium, magnesium, and zinc). This formula is administered at 50-75% of the Recommended Dietary Allowance (RDA), equivalent to 80–100 kcal/kg body weight per day. Immediate administration of a 100% RDA during this phase may increase mortality risk. Monitoring parameters in this phase include vital sign, danger signs, edema severity, formula intake, urine output, defecation frequency, stool consistency, and body weight.[10, 11]

Step 1: Prevention and Management of Hypoglycemia

Hypoglycemia in malnourished children is defined as a blood glucose level below 3 mmol/L or <54 mg/dL. In the healthcare facility without access to blood glucose testing, all malnourished children are considered hypoglycemic. The treatment for hypoglycemia involves oral administration of 50 mL of 10% glucose solution.[11]

Step 2: Prevention and Management of Hypothermia

Hypothermia is described as an axilla temperature below 36°C. If this condition is found with hypoglycemia, it may indicate the patient suffering from severe infections. In malnourished children, energy reserves are very limited, so they are unable to produce and maintain body temperature. To prevent hypothermia, children should be kept warm with clothing and blankets covering their entire body.[11]

Step 3: Prevention and Management of Dehydration

Assessing the degree of dehydration in malnourished children can be challenging. All malnourished children experiencing diarrhea and reduced urine output should be considered dehydrated. For malnourished children with mild/moderate dehydration, rehydration can be administered orally or through a nasogastric tube, until oral intake feasible. Rehydration Solution for Malnutrition (ReSoMal), a modified oral rehydration solution with reduced sodium and increased potassium, is recommended.

ReSoMal is made from diluted oral rehydration salts (ORS), sugar, electrolyte/mineral mix solution, and water. The electrolyte solution is given to address imbalance in electrolyte and mineral, including potassium, magnesium, copper, and zinc. For malnourished children with diarrhea, ReSoMal is administered at the following doses for each episode of diarrhea: 50–100 mL per diarrhea for children under 2 years old, or 100–200 mL per diarrhea for children aged 2 years and older.[10, 11]

Transition Phase

The transition phase marks the period when a patient progresses from a stable condition to the point that they qualify for outpatient care. Key characteristics of this phase include resolved complication, absence of hypoglycemia, regained appetite, and reduced of edema. During this phase, the recommended dietary intake is 100-150 kcal/kg body weight per day of F75/F100 or equivalent to 75-90% of RDA.[10, 11]

Rehabilitation Phase

The rehabilitation phase aims to reduce volume of the formula, maintain body weight, and continue breastfeeding. This phase typically lasts for 2-4 weeks and may be implemented in either inpatient or outpatient settings. In this phase, the recommended nutrition is 150-220 kcal/kg body weight per day of F100 and 4-6g/kg body weight per day of protein.[10, 11]

All malnourished children experience vitamin and mineral deficiency. Iron supplementation should only be administered after the child has regained a good appetite and weight gain, usually during the second week of rehabilitation phase. If administered too early, iron supplementation may worsen the infection. Monitoring in this phase includes recording formula intake and weight gain.[10, 11]

Refeeding Syndrome

Definition

Refeeding Syndrome (RS) is a potentially life-threatening condition that can occur in malnourished children caused by the rapid and sudden administration of nutrition. It is characterized by a shift of electrolyte from extracellular to the intracellular space resulting in fluid imbalance and complication such as arrhythmia, dyspnea, seizure, muscle weakness, heart failure and even death. Electrolyte imbalance that typically found in RS are hypophosphatemia, hypokalaemia, hypomagnesemia, and thiamine deficiency.[7, 12]

According to *American Society for Parenteral and Enteral Nutrition* (ASPEN), the diagnostic criteria of RS include a decrease in serum phosphate, potassium, and/or magnesium level by 10-20% for mild cases, 20-30% for moderate cases, and more than 30% or accompanied by organ dysfunction for severe cases. These criteria can

be observed within five days after food re-alimentation or increasing nutritional intake.[7]

Table 1. Ten Steps Management of Malnutrition[10]

No	Steps	Stabilization Phase Day 1-2	Transition Phase Day 3-7	Rehabilitation Phase Week 2-6	Follow Up Phase Week 7-26
1.	Treat/prevent hypoglycemia	→	→		
2.	Treat/prevent hypothermia	→	→		
3.	Treat/prevent dehydration	→	→		
4.	Correct electrolyte imbalance	→	→	→	
5.	Treat/prevent infection	→	→	→	→
6.	Correct micronutrient deficiencies	Without Fe →	→	With Fe →	→
7.	Start cautious feeding	→	↘		
8.	Achieve catch-up growth			→	→
9.	Provide sensory stimulation and emotional support	→	→	→	→
10.	Prepare for follow-up at home		→	→	

Prevalence

There is still limited data on the prevalence of RS. In France, 7.4% of 1,261 malnourished children experienced RS, while in Kenya, 21% of children suffer from RS.[13] Study showed that RS is associated with HIV infection. Children diagnosed with HIV positive have five times increased risk of developing RS compared to those who are HIV negative.[14] There are still few reports on the prevalence of RS in malnutrition with various comorbidities.

Mild symptoms of RS often go undetected, and electrolyte imbalance are frequently associated with other underlying medical conditions. Consequently, the true

prevalence of RS remains uncertain. Study in adult patients receiving total parenteral nutrition (TPN) showed that 30 – 43%% of those receiving phosphate supplementation still experienced hypophosphatemia.[7, 15, 16]

Pathophysiology

Pathophysiology of RS remains incompletely understood and has a multifactorial mechanism. During prolonged starvation, the human body adapts to a catabolic state, relying on glycogen and fat stores, and eventually protein, to meet energy demands. Re-alimentation initiate anabolic state, requiring increased energy and nutrient for tissue synthesis and repair. In chronic malnutrition, the body adapts by decreasing metabolic rate and nutrient consumption. Abrupt refeeding, especially with carbohydrate, stimulates insulin secretion leading to increased glucose uptake. This metabolism chain caused electrolyte shifting and fluid imbalance due to potassium, magnesium, and phosphate shift from extracellular to intracellular. Additionally, hormonal and metabolic changes can disrupt acid-base balance, leading to metabolic alkalosis.[7, 14, 17]

Under normal condition, glucose is the primary energy sources, making adequate carbohydrate intake essential. Two to three hours after carbohydrate consumption, glucose is produced and stored as glycogen. Glycogen stores in the body are limited, thus providing a short-term energy source during periods of fasting. Excess caloric intake is typically stored as fat, the body's primary energy reserve. The body conserves protein reserves, utilizing them primarily for structural and functional purposes. Following a short fasting period (approximately 24 hours), hepatic and muscle glycogenolysis occurs to compensate for the glucose deficit. Once glycogen stores are depleted, gluconeogenesis begins. [7, 18, 19]

Amino acid from muscle protein and fatty acid from adipose tissue are utilized in gluconeogenesis to generate glucose as the primary energy source for metabolic reconstruction. Pyruvate and lactate also contribute in gluconeogenesis. During prolonged fasting, protein breakdown increases. To conserve energy, body decreases its basal metabolic rate by 20-25%. In this condition, most organs and tissues rely on fatty acids as their primary energy source.[7, 18, 19]

The brain primarily utilizes glucose as its energy source and can only partially switch to ketones for energy. The body preserves protein and muscle mass by shifting to fat as an energy source. During this period, there is a decrease in proteolysis, an increase in fatty acid mobilization, and ketone body formation. Additionally, there is a decrease in intracellular micronutrient concentrations. While malnourished patients are primarily affected by these metabolic changes, RS can also occur in well-nourished or moderately nourished children after prolonged fasting.[7, 18, 19]

When carbohydrates are reintroduced, either orally, enterally, or parenterally, the body shift back to glucose as its energy source, leading to an increased demand for the production of phosphorylated intermediates of glycolysis, such as adenosine triphosphate (ATP) in red blood cells and 2,3-diphosphoglycerate (DPG), accompanied by the inhibition of fat metabolism. This condition leads to hypophosphatemia. Another mechanism contributing to hypophosphatemia is the depletion of body phosphate stores during starvation and increased cellular uptake of phosphate during the anabolic phase of refeeding.[7, 18, 19]

Phosphate is an essential mineral for metabolism, particularly in the ATP production and 2,3-DPG. Potassium and magnesium also shift to intracellular, caused by the anabolic phase and increased insulin production. Magnesium is a cofactor for NA-K+ ATP-ase pump, therefore uncorrected hypomagnesemia can disrupt potassium balance. Another metabolic disturbance includes fluid imbalance and vitamin deficiencies. Refeeding in malnourished children can lead to extracellular fluid expansion **(Figure 1).** Even though the exact mechanism of fluid imbalance remains uncertain, fluid and natrium retention could be caused by the effect of the hyperinsulinemia or the interplay between the homeostatic mechanisms regulating water, sodium, and carbohydrates.[7, 18, 19]

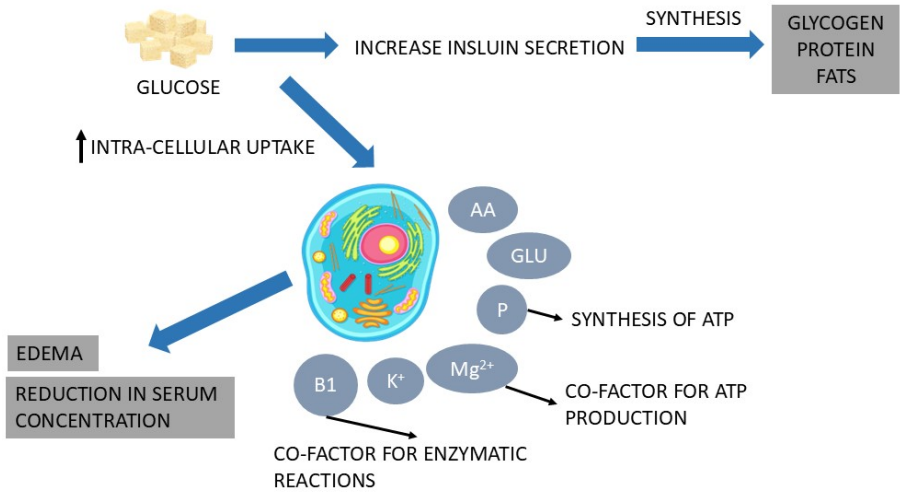

Figure 1. Pathophysiology of fluid and electrolyte imbalance in refeeding syndrome [7]

It is difficult to determine whether thiamine deficiency is caused by RS, or whether the deficiency pre-existed due to starvation. Thiamine, an important cofactor in carbohydrate metabolism, is involved in the conversion of phosphorylated glucose (Glucose-6-phosphate) to pyruvate. Pyruvate dehydrogenase, a thiamine-dependent enzyme, decarboxylates pyruvate to produce acetyl-coenzyme A, which enters the Krebs cycle to generate ATP – the cell's energy source **(Figure 2).** High-dose carbohydrate intake can increase thiamine requirements in malnourished children with low thiamine stores. This can lead to thiamine deficiency and its associated

complications. Therefore, thiamine supplementation is recommended both before and after carbohydrate consumption for patients at risk of refeeding syndrome.[8]

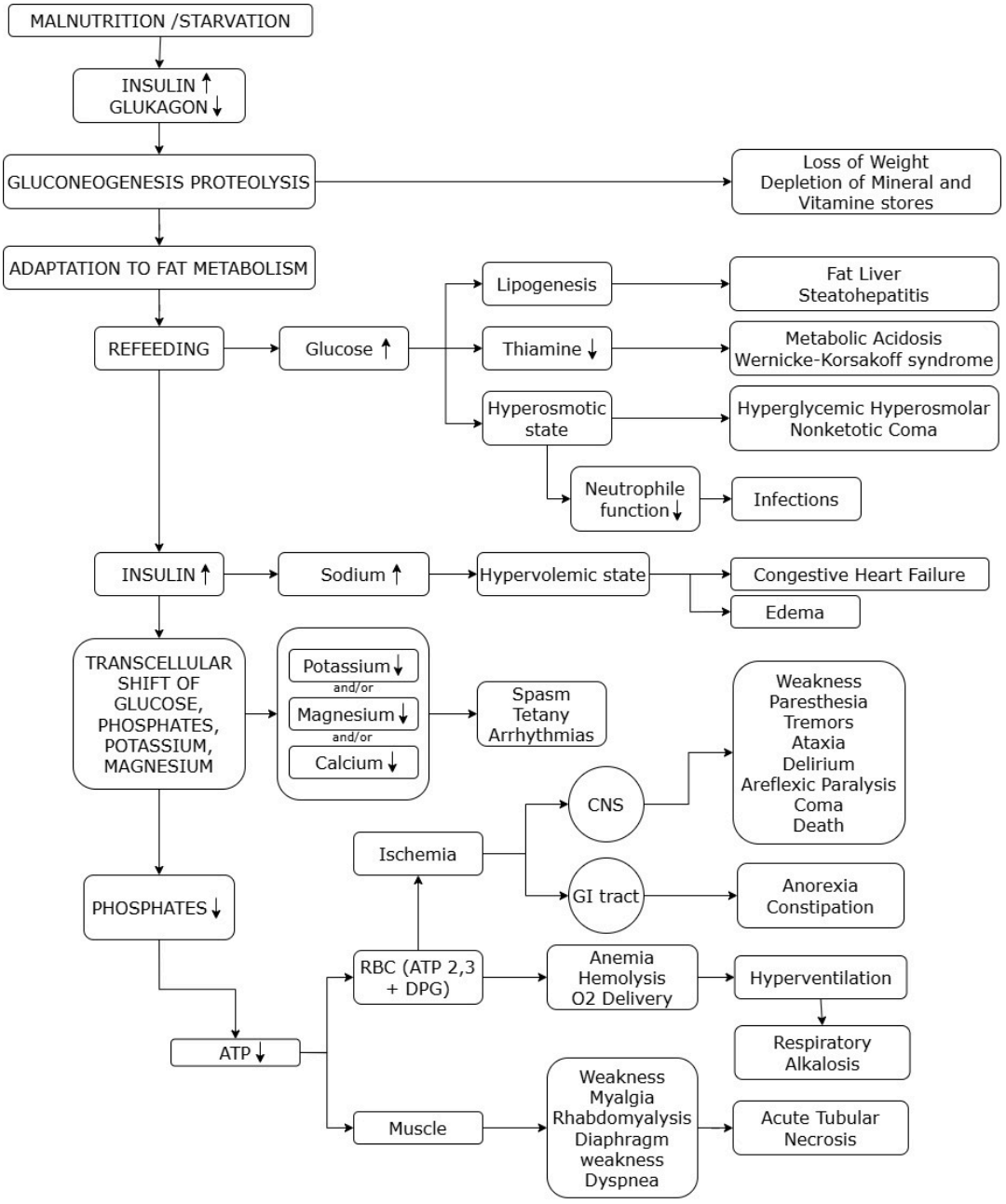

Figure 2. The consequences of major metabolic and biochemical changes in RS.[20]

Risk Factors

Previous nutritional status, history of weight loss, previous caloric intake, comorbidities, previous electrolyte imbalances (such as hypophosphatemia, hypomagnesemia, and hypokalemia) prior to nutritional therapy, muscle loss, and subcutaneous fat loss in malnourished children are risk factors for developing RS.[7]

RS risk factors that need careful attention include: 10% weight loss (or <80% of ideal body mass index) in the past 3 months, weight loss in the past consequent 5 days, low fluid intake for more than 7 days, chronic diseases causing malnutrition, such as cancer, inflammatory bowel disease, anorexia nervosa, marasmus, kwashiorkor, celiac disease, cystic fibrosis, chronic pancreatitis, cyclic vomiting syndrome, cerebral palsy, congenital heart disease, congenital pulmonary disease, post-operative conditions, prolonged fasting, low-energy diets, and hypoalbuminemia.[7] According to American Society for Parenteral and Enteral Nutrition, RS risk in children can be classified into 3 levels: low risk, moderate risk, and high risk **(Table 2).**[21]

Table 2. Criteria for children developing RS [21]

Criteria	Low risk (Minimal 3 of the following criteria)	Moderate risk (Minimal 2 of the following criteria)	High risk (Minimal 1 of the following criteria)
Weight-for-height z-score (1-24 months) or BMI-for-age z-score (2-20 years)	Weight-for-height z-score (1-24 months) or BMI-for-age z-score (2-20 years) between -1 and -1.9	Weight-for-height z-score (1-24 months) or BMI-for-age z-score (2-20 years) between -2 and -2.9	Weight-for-height z-score (1-24 months) or BMI-for-age z-score (2-20 years) ≥-3
Weight loss	Weight gain <75% of expected	Weight gain <50% of expected	Weight gain <25% of expected
Energy intake	Energy or protein intake <75% of needs for 3-5 consecutive days	Energy or protein intake <75% of needs for 5-7 consecutive days	Energy or protein intake <75% of needs for >7 consecutive days
Potassium, phosphate, or magnesium levels before nutritional therapy	Potassium, phosphate, or magnesium levels ≤25% below the lower limit of normal	Potassium, phosphate, or magnesium levels 25-50% below the lower limit of normal	Potassium, phosphate, or magnesium levels >50% below the lower limit of normal
Comorbidities	Mild diseases comorbidities	Moderate diseases comorbidities	Severe diseases comorbidities
Subcutaneous fat loss	Upper arm circumference z-score between -1 and -1.9 or mild subcutaneous fat loss	LILA z-score between -2 and -2.9 or moderate subcutaneous fat loss	LILA z-score >-3 or significant subcutaneous fat loss
Muscle mass loss		Mild loss of muscle mass	Significant loss of muscle mass

Clinical manifestations

Hypophosphatemia

Phosphate is an intracellular anion essential for metabolic processes involving ATP and 2,3-DPG. Severe hypophosphatemia (serum phosphate <1-1.5 mg/dL) can lead to severe disturbances in neurological, cardiac, respiratory, and hematological systems, increasing the risk of death. Several studies have linked hypophosphatemia to the initiation of nutritional support, either oral, enteral, or parenteral. Severe hypophosphatemia can cause neurological symptoms, such as paraesthesia, weakness, confusion, disorientation, encephalopathy, areflexia, paralysis, seizures, coma, and death.[22]

Hypophosphatemia can lead to decreased ATP and 2,3-DPG levels. This can result in impaired oxygen transport, including reduced oxygen delivery and disturbed glucose metabolism. Decreased 2,3-DPG levels increase hemoglobin's affinity for oxygen, shifting the oxygen dissociation curve to the left. Hypophosphatemia can also significantly decrease erythrocyte glucose-6-phosphate and fructose-6-phosphate levels, while increasing total triose phosphate levels (such as glyceraldehyde-3-phosphate and dihydroxyacetone phosphate). These changes can impair oxygenation and glucose metabolism, contributing to neurological and respiratory disturbances.[23]

Phosphate, an intracellular mineral, plays an important role in all intracellular processes and maintaining cellular membrane integrity. Many enzymes and second messengers are activated through phosphate binding. Phosphate is also essential for energy storage in the form of adenosine triphosphate (ATP). ATP can also influence hemoglobin's affinity for oxygen, regulating oxygen delivery to tissues. Additionally, ATP plays an important role in the kidney's acid-base buffering system.[24-27]

Chronic phosphate depletion occurs in refeeding syndrome. Increased insulin levels will increase cellular phosphate uptake and utilization. These changes result in both intracellular and extracellular phosphate deficits. Under these conditions, even a slight decrease in blood phosphate levels can disrupt cellular processes, that happen in every physiological system.[24-27]

Hypokalemia

Potassium is an important intracellular cation. Approximately 98% of the body's total potassium is intracellular, with the rest found in bones and cartilage. Potassium plays several crucial physiological roles, including regulating electrical activity in cell membranes, cellular metabolism, glycogen synthesis, and protein synthesis. Hypokalemia disrupts the electrical action potential across cell membranes, leading to membrane hyperpolarization and impaired muscle contraction. Mild to moderate hypokalemia (serum potassium concentration between 2.5 and 3.5 mEq/L) can cause nausea, vomiting, constipation, and fatigue. Untreated, severe hypokalemia (serum

potassium concentration <2.5 mEq/L) can result in paralysis, respiratory distress, rhabdomyolysis, muscle necrosis, myocardial contraction abnormalities, and impaired signal conduction.[7, 8]

Severe hypokalemia can lead to electrocardiogram abnormalities, such as ST-segment depression, T-wave flattening, T-wave inversion, or U-wave prominence. Patients with hypokalemia may experience arrhythmias, including atrial tachycardia, bradycardia, atrioventricular block, ventricular premature contractions, ventricular tachycardia, ventricular fibrillation, or sudden cardiac death.[7, 8]

Although blood potassium levels may appear normal in malnourished children, potassium depletion often occurs. With the anabolic shift in refeeding syndrome, insulin secretion increases, driving potassium into cells. This can lead to severe hypokalemia, disrupting cellular membrane electrochemistry, and potentially causing arrhythmias and cardiac arrest.[7, 8]

Hypomagnesemia

Magnesium is the second most common intracellular cation, primarily found in bones, muscles, and soft tissues. Approximately 1% of the body's magnesium is extracellular. Magnesium serves as an important cofactor for numerous enzymes involved in various biochemical reactions, including oxidative phosphorylation and ATP-dependent reactions.[21]

Hypomagnesemia (serum magnesium concentration <1.5 mg/dL) is frequently observed in critically ill patients and is associated with increased morbidity and mortality. Signs and symptoms of hypomagnesemia can be similar to those with hypokalemia or hypophosphatemia. Patients with mild to moderate hypomagnesemia may experience weakness, muscle twitching, tremors, altered mental status, anorexia, nausea, vomiting, and diarrhea. Severe hypomagnesemia (serum magnesium concentration <1.0 mg/dL) can manifest as electrocardiogram abnormalities, such as prolonged PR interval, widened QRS complex, prolonged QT interval, ST-segment depression, peaked T-waves, or T-wave flattening. Additionally, severe hypomagnesemia can lead to arrhythmias (atrial fibrillation, torsade de pointes, ventricular arrhythmias, ventricular tachycardia), tetany, seizures, coma, or even death.[21]

Untreated hypomagnesemia can lead to hypokalemia and hypocalcemia. Hypomagnesemia-induced hypokalemia results from disturbances in Na+/K+-ATPase activity. Hypomagnesemia-induced hypocalcemia is caused by impaired parathyroid hormone secretion or activity.[21]

Thiamine Deficiency

Thiamine, or vitamin B1, is an important cofactor in carbohydrate metabolism. As a water-soluble vitamin, thiamine is easily depleted during weight loss and malnutrition. Glucose administration following a starvation period suppresses gluconeogenesis through insulin secretion. Excessive glucose administration can lead to hyperglycemia, osmotic diuresis, dehydration, metabolic acidosis, and ketoacidosis. Additionally, excessive glucose can stimulate lipogenesis (due to insulin stimulation), resulting in fatty liver, increased carbon dioxide production, hypercapnia, and respiratory failure.[28]

With increased carbohydrate consumption, thiamine demand also increases as it is an important cofactor in glycolysis. Thiamine deficiency can lead to Wernicke encephalopathy (characterized by ocular abnormalities, ataxia, confusion, hypothermia, and coma) or Korsakoff syndrome (characterized by retrograde and anterograde amnesia, and confabulation). In anaerob metabolism, pyruvate is converted to lactate. Excessive lactate production can cause lactic acidosis, potentially leading to death. This has been reported in patients receiving parenteral nutrition without thiamine supplementation.[28]

While deficiencies in various vitamins can occur due to inadequate intake, thiamine deficiency is particularly important in refeeding syndrome complications, as it is an important coenzyme in carbohydrate metabolism.[28]

The summary of clinical manifestations of electrolyte imbalance in RS patients is depicted in **Figure 3**.[7]

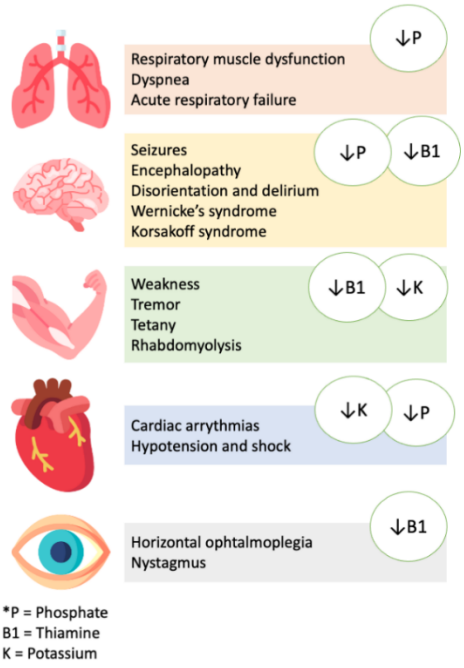

Figure 3. Summary of clinical manifestations of electrolyte imbalance in RS patients.[7]

Prevention

Preventing RS is our primary objective when starting nutritional support for malnourished children. Several steps can be taken to avoid RS and reduce its associated morbidity and mortality. Identifying patients at high risk for RS is very important before starting nutritional support, and overfeeding must be avoided.[28] The recommendation on RS prevention and management in children by ASPEN is summarized in **Table 3.**

When initiating nutritional support for patients at high risk for refeeding syndrome (RS), the primary rule is "start low, go slow." Nutritional support should be initiated carefully, starting at approximately 25-50% of recommended dietary allowance (RDA) targets on the first day and gradually increasing to the target intake by the third to fifth day. Hypophosphatemia, hypokalemia, and hypomagnesemia should be corrected before initiating nutritional support. Electrolyte supplementation (in patients with normal kidney function) is recommended before and during nutritional support. Increased caloric intake can lower serum phosphate concentrations, therefore phosphate supplementation of 10-15 mmol per 1000 kcal is recommended to maintain normal serum phosphate levels (in patients with normal kidney function). Patients with malnutrition, critical illness, trauma, or burns often experience phosphate depletion (despite normal serum phosphate levels), and their phosphate requirements are typically higher.[28]

That also applies to potassium and magnesium. After initiating and titrating nutritional support, electrolyte supplementation should be adjusted based on serum electrolyte concentrations and therapeutic response. As RS patients are at risk of impaired cardiac reserve and fluid overload, sodium and fluid intake should be minimized during the initial days of nutritional support (recommended sodium intake is ≤20 mEq/day with total fluid intake ≤1000 mL/day).[7, 28]

Thiamine requirements are increased in patients with cachexia. Thiamine supplementation at a dose of 50-100 mg/day intravenously or 100 mg orally for 5-7 days is recommended to prevent refeeding syndrome (RS). Patients should be closely monitored for signs and symptoms of RS, including vital signs (heart rate, blood pressure, respiratory rate, mental status, and neurological signs). These signs should be monitored for several days until target nutritional goals are achieved. Pulse oximetry can also be used. Electrocardiograms should be performed, especially for patients with hypokalemia. Additionally, patients should be monitored for neuromuscular signs and symptoms through physical examination. Fluid balance, edema, fluid overload, and weight measurements should also be closely calculated and monitored.[7, 28]

Table 3. ASPEN's recommendation on RS prevention and management in children.[21]

Aspect of Care	Recommendations
Initiation of Nutrition	• Start nutrition at a maximum target of 40-50%, but typically start glucose infusion at around 4-6 mg/kg/min and increase by 1-2 mg/kg/min daily, adjusting the glucose level to a maximum of 14-18 mg/kg/min (including enteral and parenteral glucose). • Calories from intravenous dextrose solutions and medications infused in dextrose should be considered within the above limits and/or started cautiously in patients with moderate to high risk. If the patient has received intravenous dextrose for several days and/or medications in dextrose and has not shown symptoms with stable electrolytes, calories from nutrition can be reintroduced at higher amounts than recommended above.
Fluid Restriction	No recommendation
Sodium Restriction	No recommendation
Protein Restriction	No recommendation
Electrolytes	• Check serum potassium, magnesium, and phosphate levels before initiating nutrition. • Monitor every 12 hours for the first 3 days in high-risk patients. Monitoring may be more frequent based on clinical presentation. • Replace electrolytes based on established standards of care. • No recommendation can be given on whether prophylactic electrolyte doses should be given if pre-feeding levels are normal. • If electrolytes are difficult to correct or decrease suddenly when starting nutrition, reduce calories/gram of dextrose by 50% and increase dextrose/calories by about 33% of the target every 1-2 days based on clinical presentation. Recommendations may change based on practitioner assessment and clinical presentation, and discontinuation of nutritional support may be considered when electrolyte levels are very low or decrease suddenly, posing a life-threatening risk.
Thiamine and Multivitamins	• Thiamine 2 mg/kg with a maximum limit of 100-200 mg/day before starting feeding or before starting intravenous fluids containing dextrose in high-risk patients. • Continue thiamine supplementation for 5-7 days or longer in patients with severe starvation, chronic alcoholism, or high

	risk of thiamine deficiency and/or signs of thiamine deficiency. Routine thiamine level checks may not be valuable. • Intravenous multivitamins are added to parenteral nutrition daily, unless contraindicated, as long as parenteral nutrition continues. For patients receiving oral/enteral nutrition, add oral/enteral multivitamins, complete once a day for 10 days or more based on clinical status and therapy mode. After the patient reaches adult weight, refer to adult multivitamin recommendations.
Monitoring and Long-Term Care	• Check vital signs every 4 hours for the first 24 hours after initiation in at-risk patients. • Cardiorespiratory monitoring is recommended for unstable patients or those with severe deficiencies, based on established standards of care. • Daily weight with intake and output monitoring. Estimate energy needs if necessary for patients receiving oral food. Evaluate short-term and long-term nutritional care goals daily for the first few days until the patient is considered stable (e.g., not requiring electrolyte supplementation for 2 days) and then based on institutional standards of care.

Conclusion

Refeeding syndrome is a life-threatening condition that can occur in malnourished children after the initiation of nutritional support. It is characterized by hypophosphatemia, hypomagnesemia, hypokalemia, and/or thiamine deficiency that develop after rapid re-alimentation within the initial 3-5 days of nutritional management. Children with signs and symptoms of refeeding syndrome require aggressive electrolyte and vitamin supplementation, supportive management (such as electrolyte correction and management of subsequent clinical manifestations), and the re-initiation of nutritional support with close monitoring

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Conflict of Interest

None declared.

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