

Nutrition in Pediatric Kidney Disease

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Abstract

Nutrition has a major impact on the health of children with chronic kidney disease (CKD). Special diets and additional replacement therapies may be chosen according to the specific renal disease. Persistent low-grade inflammation, which contributes to CKD-associated cardiovascular and all-cause mortality, protein-energy wasting, oxidative stress, acidosis, chronic and recurrent infections, and altered metabolism of adipose tissue may result from dietary deficits and are important targets for nutritive intervention. Therefore, many guidelines have been developed regarding nutrient intake adequation to assist pediatricians treating these children. Acute kidney injury (AKI) has multifactorial etiology and complicated clinical course that may ultimately necessitate renal replacement. AKI presents unique treatment challenges because of associated metabolic derangements, difficulties in nutrient requirement estimation, the negative effects of renal replacement therapy, and the complex effects on nutrient balances. Maintenance of protein balance in such conditions requires adequate energy and protein intake, especially during acute illnesses. Malnutrition in pediatric AKI has been linked to increased morbidity and mortality. However, the recommended nutritional requirements for this condition are less precise than for CKD. A complete assessment of pediatric kidney disease requires evaluation of growth, body composition, abnormal sodium loss, acid-base status, and dietary intake, particularly for children with renal insufficiency. Nutritional support should also provide adequate amounts of energy, macronutrients, and micronutrients for normal growth and development.

Keywords

- kidney
- chronic kidney disease
- acute kidney injury
- nutrition
- children

Introduction

Nutrition has a major impact on physical and psychological development, physical functioning, and health-related quality of life, while malnutrition is strongly associated various diseases and poor outcome.^{1–3} The kidneys play an important role in body homeostasis through excretory, metabolic, and endocrine functions. Urine volume and solute excretion are adjusted to maintain the composition of the extracellular space, serum osmolarity, and intravascular volume. Furthermore, the kidneys regulate acid-base equilibrium, amino acid

excretion, and metabolism of hormones, such as vitamin D hydroxylation to the active form, and erythropoietin production. When renal insufficiency develops, these functions are disrupted, leading to impairment of normal growth and development. Inadequate nutritional intake may be a decisive factor for poor growth and failure to thrive in pediatric renal disease patients.

The optimal diet depends on glomerular filtration rate (GFR), age, and type of renal disease. Evaluation of growth and nutrition should be individualized in children with nephropathy due to their special characteristics. The general

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interpretability of anthropometric measurements, body mass index (BMI), and body composition estimates may be limited in pediatric kidney patients due to fluid overload, which is especially prevalent in chronic kidney disease (CKD) stage 5 and nephrotic/nephritic syndrome. Conversely, chronic fluid depletion in polyuric nephropathies also disrupts normal fluid balance and changes body weight.

Whereas the impact of nutrition in children with CKD is well known and there are specific guidelines for treatment, the nutritional management of critically ill children with acute kidney injury (AKI) is based on knowledge acquired from the adult literature, even though AKI is common in pediatric intensive care units.⁴

In this review, we provide revised nutritional advice for both chronic and acute kidney disease associated with renal insufficiency. Several other disorders, such as nephrotic or nephritic syndrome, obesity-related glomerulopathy, tubulopathies, and idiopathic hypercalciuria also require very specific nutritional management. However, these conditions commonly occur in children with normal renal function and so are not included.

Chronic Kidney Disease

Definition

The Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease of the Kidney Disease Improving Global Outcomes foundation (KDIGO 2012)⁵ defines CKD as the presence of abnormalities in kidney structure or function lasting longer than 3 months with deleterious implications for health. Criteria for CKD include markers of kidney damage (albuminuria >30 mg/24 hour or >30 mg/g), urine sediment alterations, electrolyte abnormalities and other abnormalities due to tubular disorders, pathologies detected by histology or imaging, and decreased GFR. The following categories of CKD are defined according to GFR (in mL/min/1.73 m²): G1 if > 90 , G2 between 60 and 89, G3 between 59 and 30, G4 between 15 and 29, and G5 if < 15 (kidney failure).

Importance of Nutrition in Chronic Kidney Disease

Adequate nutrition is a concern for all children with CKD due to the impact of nutritional intake on growth and neurodevelopment, and the association between nutritional status and mortality. Children over 5 years old with CKD frequently have elevated fat mass relative to height as well as muscle mass deficiency proportional to disease severity. Alternatively, in infants under 3 years old, the most prominent manifestation of inadequate nutritional status is linear growth restriction, which may have a major impact on final height. Therefore, attention to nutritional intake and status is of primary importance in infants and very young children with CKD. Nutritional care of this vulnerable population requires a multidisciplinary team including a nephrologist, renal nurses, and a trained pediatric dietician.

Regular evaluation of nutritional status and provision of adequate nutrition are key components in the overall management of children with CKD. Assessment of growth and

nutritional status should be performed at least twice as frequently as in healthy children of the same age. Infants and children with polyuria, evidence of growth delay, decreasing or low BMI, comorbidities influencing growth or nutrient intake, or recent acute changes in medical status or dietary intake may require even more frequent evaluation.

Objectives

The focus of nutritional care for children with impaired kidney function must always be centered on achievement of the following goals:

- Maintenance of optimal nutritional status, normal pattern of growth, and body composition by intake of appropriate amounts and types of nutrients.
- Avoidance of uremic toxicity and metabolic abnormalities.
- Reduced risk of chronic morbidities and mortality in adulthood.⁵

The National Kidney Foundation's KDOQI Clinical Practice Guideline for Nutrition in Children with CKD: 2008, addresses a critical need for maintaining normal growth. The recommendations for nutritional management are essential for the well-being of infants, children, and adolescents with stages 2 to 5 CKD on long-term dialysis or with a kidney transplant. Moreover, this guideline aims to minimize the risk of future cardiovascular diseases (available online at www.kdoqi.org).

Nutritional Assessment

Nutritional parameters recommended in KDOQI guidelines are estimated by percentile or standard deviation score (SDS). The following parameters are included: dry weight and weight per age, length- or height-for-age, length or height velocity-for-age, and BMI-for-height-age. Additional parameters include head circumference-for-age percentile or SDS in patients <3 years old and normalized protein catabolic rate in hemodialyzed adolescents with CKD stage 5D.⁵

Anthropometric Parameters

Weight monitoring is an important part of any nutritional assessment, but weight is not always a reliable objective measure in CKD patients. Some infants and young children with CKD or other conditions (i.e., nephritic syndrome) may be volume overloaded, whereas others may be volume depleted. Therefore, measurement of weight must be accompanied by an assessment of volume status and an estimation of euvolemic or "dry" weight. Fluid overload will influence not just weight but also other anthropometric measures such as arm circumference and skin-fold thickness. Estimation of dry weight can be challenging because weight gain is expected in growing children. Referred weight, edema, blood pressure, hypoalbuminemia, and dietary interview are helpful in the estimation process. Clinical indicators of volume overload include edema, hypertension, and hypoalbuminemia. Cramping or hypotension during dialysis, thirst, tachycardia, decreased skin turgor, and sunken eyes and/or fontanelles signifies volume depletion. The midweek postdialysis weight and the combination of noninvasive blood volume monitoring and postdialytic vascular compartment refilling rate are used for hemodialyzed

patients. The weight at monthly visit (body weight minus weight of dialysis fluid in the peritoneal cavity) is used for children on peritoneal dialysis therapy. Rapid weight gain in the absence of a significant increase in energy intake must not be equated with dry weight gain due to the possible contribution of edema. The estimated euvolemic weight should be plotted on the weight-for-age curve and the weight-for-age SDS calculated.

Height or length to age is believed to provide a reasonable surrogate for maturation in most children (i.e., the age at which a child would be at the 50th percentile for height likely is close to the age at which most healthy children would have a similar level of sexual/physical development). Multiple factors influence the height of children with nephropathy. Therefore, height/length to age constitutes a valuable measure to estimate general well-being in the pediatric population.

Body mass index is an accepted and easily calculated method of evaluating weight relative to height. Because height, age, and maturation are highly correlated in healthy children, this approach works reasonably well in routine practice. In children with kidney disease, however, this approach has limitations due to the prevalence of growth retardation and delayed maturation. Expressing BMI relative to chronological age in a child with growth and/or maturational delay will result in inappropriate underestimation of his or her BMI compared with peers of similar height and developmental age. To avoid this problem, it may be preferable to express BMI relative to height-age in children with CKD (that is, the age at which the child's height would be at the 50th percentile).

However, caution must be used in applying this approach to children inside the pubertal or peripubertal period, as the correlation between height-age and maturation is less clear in this population. BMI relative to chronological age may be more logical in some cases, particularly when sexual maturation is complete.⁵

The Centers for Disease Control and Prevention (CDC) defines underweight as a BMI-for-age less than the 5th percentile (www.cdc.gov/nccdphp/dnpa/growthcharts/training/modules/module1/text/page5a.htm). The World Health Organization (WHO) definitions differ somewhat from those used by the CDC. A BMI-for-age SDS of -2.0 (BMI-for-age $\sim < 3$ rd percentile) was recently proposed as the cut-off to define underweight or "thinness" in children.¹ This definition corresponds to the cut-off for grade 2 thinness in adults (BMI, 17 kg/m^2). In children with stage 5 CKD, a U-shaped association was demonstrated between BMI-for-age SDS and mortality risk. Children with a BMI SDS either greater or less than 0.5 were reported to be at higher risk of mortality than those with a BMI SDS of ± 0.5 . Specifically, each 1.0 -SD unit difference in BMI SDS was associated with a 6% higher risk of mortality, although it is not completely established if there exists a cause-effect relationship between BMI and mortality.⁶ Interpretability of BMI may be limited in CKD due to fluid overload because any excess fluid will artificially increase BMI. Therefore, efforts should be made to use only true dry weight when calculating BMI.

Head circumference should be measured regularly in children 3 years and younger and plotted on the head circumference-for-age curve. Poor head growth, which reflects poor brain growth, is well documented in children with CKD.^{7,8} Although no studies have specifically related head circumference to nutritional status in CKD, regular measurement of head circumference in conjunction with developmental assessments are an important part of routine pediatric CKD care (2007 WHO Growth Standards).¹

Mid-arm circumference (MAC) and triceps skin-fold thickness (TSF) were once recommended as part of the nutritional assessment for pediatric CKD. TSF was considered to reflect total fat mass, and the combination of TSF and MAC was used to calculate the mid-arm muscle circumference (MAMC) and mid-arm muscle area (MAMA), which were purported to reflect total muscle mass. However, there are problems with the use of these measures. First, it is difficult to obtain reliable measurements in CDK patients with fluid overload.¹ Second, the relationship between total muscle mass and MAMC or MAMA is less clear in CKD because abnormal regional distribution of lean tissue may result in a breakdown of the normal relationship between MAMC or MAMA and total muscle mass. Third, deficits in these parameters have never been described convincingly in children with CKD. Finally, few studies have investigated the link between TSF, MAC, MAMC, or MAMA and outcome in the CKD population.

Body composition has yet to be well characterized in pediatric CKD. Few high-quality studies are available in which measures of body composition were adequately adjusted for height and appropriately compared with a healthy reference population. Fat mass appears to be elevated relative to height in many children with CKD. Preliminary evidence suggests that use of growth hormone may result in lower fat mass and higher lean mass for height. There are several potential strategies for measuring body composition as an index of nutritional status in CDK as summarized below.

- Whole-body dual-energy X-ray absorptiometry (DXA) provides excellent estimates of fat mass and lean mass. The main limitation of DXA for patients with CKD is that it is unable to distinguish normally hydrated from over-hydrated lean tissue; thus, it may overestimate lean mass in volume-overloaded subjects. DXA has been used extensively for body composition assessment in adults with CKD and in several small studies of children with CKD.⁹⁻¹¹ Although deficits in lean mass relative to height-age have been demonstrated in children with CKD, there are currently insufficient data to support a recommendation for regular DXA scans in children with CKD.
- Bioelectrical impedance analysis (BIA) allows estimation of body fluid compartment volumes, which may then be used to make inferences about body composition. Abnormal volume status is likely the biggest problem limiting the interpretability of BIA measures in children with CKD. All BIA measures, including impedance and phase angle, will change when either fluid status, fat mass, or lean

mass change. However, it is impossible to distinguish which has changed based only on BIA measures.

- Single-frequency whole-body BIA has been used in an effort to predict total body water in children receiving maintenance dialysis.¹² However, the BIA-derived total body water estimates were not strongly correlated with total body water measured by isotope dilution (the gold standard).
- Multiple frequency BIA (bioimpedance spectroscopy) allows direct estimation of both extracellular fluid (ECF) and intracellular fluid volumes, although estimates of ECF volumes are more accurate.¹³ Bioimpedance spectroscopy is a promising technique, particularly for estimating ECF, but it has not yet been adequately validated in children or adults with CKD.

No single parameter has been found that will identify all patients at nutritional risk; therefore, multiparameter indices of nutritional status have been developed in an attempt to improve accuracy. One such index was developed specifically for children on peritoneal dialysis therapy.^{14,15} Anthropometric and bioimpedance measures were combined to generate a status score; however, the means by which the parameters were combined to arrive at a final score has limited justification and many of the component measures are highly correlated. Furthermore, the score is heavily influenced by single-frequency BIA measurements, which are of questionable value. This method does not appear practical for routine clinical practice.

Biochemical Parameters

Hypoalbuminemia is a common finding in CKD and strongly associated with increased mortality in both adult and pediatric patients.⁷ Malnutrition may lead to hypoalbuminemia, so serum albumin level is considered a useful index of nutritional status. However, important limitations have been identified in CKD patients. Serum albumin is depressed in CKD with systemic inflammation or volume overload. Therefore, hypoalbuminemia should be regarded as an indication for evaluation of volume status, protein loss, and investigation of the causes of systemic inflammation. Nevertheless, hypoalbuminemia is not predictive of an increase in mortality and the value of albumin as a marker of nutritional status in children with CKD is questionable.

Furthermore, identification and treatment of existing nutritional deficiencies and metabolic abnormalities should be aggressively pursued in children with CKD. Recombinant human growth hormone therapy should be considered in children with CKD and short stature (height SDS < -1.88 or height-for-age <3rd percentile), and possibly for linear growth enhancement if growth failure (height velocity-for-age SDS < -1.88 or height velocity-for-age <3rd percentile) persists beyond 3 months despite treatment of nutritional deficiencies and metabolic abnormalities.

Nutritional Requirements

Interpretation of many previous studies on nutrition and growth in pediatric CKD is difficult because most considered

infants and older children together as a single group, even though growth and metabolism differ substantially between infants younger than 2 to 3 years and older children. First, a much larger proportion of the daily energy requirement is devoted to growth in infants compared with older children. In addition, growth is driven primarily by nutrition during infancy ("infancy phase of growth") whereas growth hormone and sex hormones have dominant influences on growth during childhood and adolescence, respectively.

While infancy phase growth is usually supplanted by the childhood phase between 6 and 12 months of age in healthy infants, onset of the childhood phase is frequently delayed until 2 to 3 years of age in CKD.⁶ In addition to the important effects of nutrition on somatic growth, otherwise healthy infants with poor nutrition have been demonstrated repeatedly to have intellectual deficiencies compared with their well-nourished counterparts. Both linear growth and neurodevelopment progress rapidly during the first 3 years of life; therefore, inadequate nutrition during this critical period may result in serious growth restriction and developmental delays that are difficult to reverse.⁶

There is evidence to support the notion that feeding and response to nutrient deficiency differ between infants and older pediatric CKD patients. Infants with CKD usually demonstrate inadequate spontaneous calorie intake, whereas energy intake for older children is usually normal relative to body size. Lean mass deficits are also more likely in younger than older children. Routine calorie and/or protein supplementation have been shown to improve growth in infants with CKD, but there is no clear evidence for this in older children.¹ These differences between infants and older children underscore the importance of age when planning nutritional interventions.

Due to the high prevalence of growth retardation in children with CKD, nutrition has always been a primary focus of pediatric CKD care. Historically, the main problem in children with CKD has been undernutrition, but there is some evidence that obesity is emerging in the CKD population. Early studies emphasized the importance of adequate energy intake for maintaining normal growth. However, no study has demonstrated a growth advantage of a caloric intake greater than approximately 75% of the recommended daily allowance for healthy children. Moreover, the estimated prevalence of undernutrition in children with CKD varies widely, from 2 to 65%, depending on the definition used and the severity of wasting (low weight-for-height) and/or stunting (low height-for-age) under long-term undernutrition. However, this definition of undernutrition may be inappropriate for children with CKD because there are multiple factors that cause stunting in children with CKD aside from long-term undernutrition.

An individualized nutritional care plan should consider the child's age, stage of development, food preferences, cultural beliefs, and psychosocial status. Frequent reevaluation and modification of the nutrition plan is indicated for infants and children with advanced stages of CKD, relevant comorbidities influencing growth or nutrient intake, evidence of inadequate intake or malnutrition, acute illness, or adverse events that may negatively impact nutritional status.

Nutritional management requires a collaborative effort involving the child, caregiver, dietitian, and other members of the multidisciplinary pediatric nephrology team (including nurses, social workers, therapists, and nephrologists).

Components of Dietary Prescription

Energy

Energy requirements for children with CKD should be based on the estimated energy requirement for chronological age individually adjusted for physical activity and body size (i.e., BMI) (► **Table 1**). Further adjustment of energy intake is suggested based on the response (rate of weight gain or loss). Supplemental nutritional support should be considered for children with CKD stage 2 to 5 or 5D when the usual intake fails to meet energy requirements and is not achieving expected rates of weight gain and/or growth for age. Oral intake of an energy-dense polymeric diet should be considered first. When energy requirements cannot be met with oral supplementation, tube feeding should be considered. A trial of intradialytic parenteral nutrition is suggested for malnourished children (BMI-for-height-age < 5th percentile) receiving maintenance hemodialysis who are unable to meet their nutritional requirements through oral or tube feeding.

The relative intake of macronutrients suggested for children with CKD is the same as that for healthy children. For infants 1 to 3 years of age, carbohydrates should provide 45 to 65% of total energy intake, while fats and proteins should provide 30 to 40% and 5 to 20%, respectively. For infants less than 1 year of age, the guiding principle is to maintain the balance of carbohydrate, fat, and protein found in infant formula (36–56% carbohydrate, 40–54% fat, and 7–12% protein) (► **Table 2**).^{5,7}

Proteins

Guidelines on protein intake for infants with CKD have recently changed. First, there is little evidence supporting the benefit of high protein intake in children with CKD. In addition, protein-containing foods are a source of unwanted phosphorus. Thus, the new guidelines recommend lower

Table 2 Macronutrient distribution

	Age 1–3 y old	Age 4–18 y old
Carbohydrate ^a	45–65%	45–65%
Fat ^b	30–40%	25–35%
Protein	5–20%	10–30%

Source: Health Canada is a federal institution of Government of Canada. The free table is available in the following address: <https://www.canada.ca/en/health-canada/services/food-nutrition/healthy-eating/dietary-reference-intakes/tables/reference-values-macronutrients-dietary-reference-intakes-tables-2005.html>.

^aAdded sugars limited to no more than 25% of total energy.

^bDietary cholesterol, trans fatty acids, and saturated fatty acids: as low as possible while consuming a nutritionally adequate diet.

protein intake than previous guidelines. The suggested protein intake depends on the stage of CKD; the recommended protein intake for children in CKD stage 3 is 100 to 140% of dietary reference intake (DRI), and for CKD stages 4 and 5 it is 100 to 120% of DRI. Slightly higher intake is suggested for children on hemodialysis or peritoneal dialysis to compensate for dialytic losses.

Evidence suggests that whey protein is more bioavailable than casein protein and may promote more rapid gastric emptying whether delivered by infant formula or as a supplement. Moreover, many children with CKD have delayed gastric emptying, so formulas with whey as the predominant protein may help reduce the associated symptoms, such as anorexia, gastroesophageal reflux, and vomiting. Adequate protein intake that permits good growth can be achieved with infant formulas containing 1.8 g protein per 100 kcal in which 70% of the protein is whey, whereas a protein intake of 2.2 g per 100 kcal is needed with standard 60% whey infant formula. Seventy percent whey formula with only 1.8 g of protein per 100 kcal was associated with significantly lower urea levels than 60% whey formula with 2.2 g of protein per 100. Whey-predominant formulas also more closely mimic human breast milk and have significantly lower aluminum content than casein-predominant formula.⁷

Table 1 Recommended energy intake (Kcal/day) in pediatric chronic kidney disease

Age	Recommended intake	CKD stage 3 to 5, hemodialysis, peritoneal dialysis
0–3 mo	$[89 \times \text{weight (kg)} - 100] + 175$	100% EER
4–6 mo	$[89 \times \text{weight (kg)} - 100] + 56$	
7–12 mo	$[89 \times \text{weight (kg)} - 100] + 22$	
1–3 y	$[89 \times \text{weight (kg)} - 100] + 20$	
3–8 y	Boys: $[88.5 - 61.9 \times \text{age (y)}] + \text{PA} \times [26.7 \times \text{weight (kg)} + 903 \times \text{height (m)}] + 20$ Girls: $[135.3 - 30.8 \times \text{age (y)}] + \text{PA} \times [10 \times \text{weight (kg)} + 934 \times \text{height (m)}] + 20$	100% EER
9–18 y	Boys: $[88.5 - 61.9 \times \text{age (y)}] + \text{PA} \times [26.7 \times \text{weight (kg)} + 903 \times \text{height (m)}] + 25$ Girls: $[135.3 - 30.8 \times \text{age (y)}] + \text{PA} \times [10 \times \text{weight (kg)} + 934 \times \text{height (m)}] + 25$	

Abbreviations: EER, estimated energy requirement; PA, physical activity = total energy expenditure in 24 hours–basal metabolic rate.

Electrolytes and Minerals

Anuric or severely oliguric children will need restriction of fluids and sodium. In contrast, children with polyuric CKD may require sodium and water supplementation. Polyuric infants with CKD who were prescribed fluid intake within the range 180 to 240 mL/kg/day and sodium supplements at doses of 2 to 4 mmol/kg/day demonstrated better growth than infants not receiving this intervention. However, it may be difficult to deliver these high fluid volumes and large doses of sodium orally, so tube feeding may be necessary for these children.

Children with elevated serum potassium levels require dietary restriction, but this can be difficult for infants as no infant formula is low in potassium. Two different methods of reducing potassium intake have been proposed: (1) mixing sodium polystyrene sulfonate with formula to bind potassium before feeding and (2) dilution of adult renal formula with higher caloric density.

A controlled phosphorus diet in combination with phosphate binders and vitamin D treatment is essential for the prevention of hyperphosphatemia, hypocalcemia, renal osteodystrophy, and poor growth. Dietary phosphorus should be decreased to general recommendations for age when serum parathyroid hormone is above the recommended target range for the stage of CKD.

Other Micronutrients

The general recommendation is that children with CKD receive at least 100% DRI of the following micronutrients: retinal (A), thiamin (B1), riboflavin (B2), niacin (B3), pantothenic acid (B5), pyridoxine (B6), biotin (B8), cobalamin (B12), ascorbic acid (C), α -tocopherol (E), folic acid, vitamin K, copper, and zinc. Dietary and lifestyle changes are suggested to achieve weight control in overweight or obese children with CKD stages 2 to 5 or 5D.

Nutrition in Acute Kidney Injury

Acute kidney injury is a common reason for admission to the pediatric intensive care unit, and the risks of underfeeding and nutritional deprivation are high in this setting. AKI cause derangements in substrate metabolism and body composition, leading to hypercatabolism, hypoalbuminemia, loss of lean body mass, and depletion of adipose tissue, even with adequate ingestion of nutrients. Muscle protein catabolism and atrophy occur as a result of coexisting systemic inflammation, oxidative stress, insulin resistance, and metabolic acidosis. Maintenance of protein balance in such conditions requires adequate energy and protein intake. The presence of malnutrition in AKI has been linked to increased morbidity and mortality in children, adolescents, and adults.¹⁶ Pediatric patient outcome and survival are highly dependent on adequate nutrition and energy balance due to the intrinsically high anabolic drive and lower nutrient reserves of children compared with adults.

Definition

Acute kidney injury is based in levels of serum creatinine (SCr) and is defined as any of the following:

Table 3 Staging of acute kidney injury

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline or >0.3 mg/dL increase	< 0.5 mL/kg/h for 6–12 h
2	2–2.9 times baseline	< 0.5 mL/kg/h >12 h
3	>3 times baseline or increase in serum >4 mg/dL or initiation of renal replacement therapy or decrease in estimated GFR to < 35 mL/min/1.73 m ²	< 0.3 mL/kg/h for >24 h or anuria >12 h

Abbreviation: GFR, glomerular filtration rate.

- Increase in SCr $\times 0.3$ mg/dL ($\times 26.5$ mmol/L) within 48 hours; or
- Increase in SCr to $\times 1.5$ times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume of 0.5 mL/kg/h for 6 hours.

► **Table 3** shows the stages of AKI.

Protein-Energy Wasting

Several studies on critically ill children confirm the high risk of protein/energy debt,^{16,17} particularly protein debt. Protein-energy wasting in children with AKI refers to the wasting of lean body mass and depletion of fat mass.¹⁶

Treating a child with AKI presents several challenges, including:

- Worsening of anthropometric variables and fluid overload. During critical illness, anasarca may obscure the loss of lean tissue, which may only become apparent following resolution of edema. A reliable indicator for global loss of lean body mass and chronic malnutrition is wasting of the interosseous and thenar muscles of the hand, which becomes apparent 2 or 3 weeks after hospitalization with the resolution of edema.
- Underfeeding is common in these children because they are medically unstable and do not tolerate oral feeding. In addition, feeding is often interrupted by diagnostic and therapeutic procedures.
- Poor baseline nutritional status in cases of previous associated chronic morbidity.
- The inverse relationship between energy expenditure and body weight leads to greater energy needs in younger children with lower body weight.
- Renal replacement therapy leads to additional nutritional losses requiring additional support, especially higher protein to compensate for losses during dialysis.

Assessment of Nutritional Status

A careful medical history interview covering previous weight gain, diet, recent illness, and medication can help in understanding the risk factors for undernutrition. A detailed history

can also exclude a preexisting CKD and other comorbidities. Baseline height-for-age and weight-for height and pre-illness weight should be obtained since the ill child may present with fluid overload and weight gain. Mid-arm circumference has been used as an age-independent criterion in malnourished children between the ages of 1 and 5 years and can be a helpful tool because it is minimally affected by altered fluid status compared with other anthropometric parameters.¹⁸

A general physical examination should be conducted, including examination of hair, skin, mouth, and extremities for signs of malnutrition as well as specific vitamin and mineral deficiencies. Establishing pre-illness weight and close follow-up monitoring is very important, and weight changes should be interpreted in the context of fluid balance, fluid overload, fluid administered, diuretics given to the child, and water losses.

Various biochemical parameters have been proposed as markers of nutritional status. However, none of these are considered sufficiently sensitive or specific as single diagnostic markers for protein-energy wasting. Relatively shorter half-life (t_{1/2}) serum proteins, such as prealbumin (t_{1/2} = 2–3 days) and transferrin (t_{1/2} = 8–9 days), reflect nutrition status and respond more quickly to changes in anabolic state. Conversely, serum albumin is inadequate because of its longer half-life, although it may be a useful marker of disease severity. Longitudinal determination of albumin, transferrin, and prealbumin may have some value for assessing the response of patients to nutritional support. Serum protein levels frequently decrease during acute critical illness due to capillary leak syndrome as observed during the first hours following admission of patients with sepsis, cardiopulmonary bypass operations, ischemia–reperfusion injury, and other events that can occur.

Nutritional Needs and Support

Several factors affect the estimate of energy provision for children with AKI. One critical factor is hypercatabolic state with insulin and growth hormone resistance. Failure to provide adequate energy during this phase may result in loss of critical lean body mass. On the other hand, critically ill

children on dialysis who are sedated and mechanically ventilated may have substantially reduced true energy expenditure due to decreased activity, decreased insensible fluid losses, and absence of growth during the acute illness. These patients may in fact be at a higher risk of overfeeding when estimates of energy requirements are based on age-appropriate equations for healthy children.¹⁹

The gold standard to quantify energy needs in children and adults is measurement of actual energy consumption by indirect calorimetry.²⁰ To account for dynamic alterations in energy metabolism during critical illness, resting energy expenditure (REE) values remain the only true guide for energy intake. Estimating energy expenditure needs based on standard equations has been shown to underestimate or overestimate the REE in critically ill children. The range of REE values reported in these patients is between 35 and 65 kcal/kg per day (0.15 and 0.27 MJ/kg per day) owing to differences in severity of illness and patient population. However, no reliable data on REE in critically ill children with AKI are available.

The primary goals in treating a critically ill child with AKI are to ensure sufficient energy and protein delivery for prevention of protein-energy wasting and to ensure optimal (not just adequate) amounts for patients requiring dialysis. ► **Table 4** shows nutritional parameters suggested for feeding children with AKI.⁴ Once energy expenditure and requirement have been calculated, the next major step is to select the appropriate route and start nutritional support. If feasible, the enteral route should always be chosen over the parenteral route as enteral feeding has been shown to promote gut mucosal integrity, restore immune responses, reduce catabolic activity, and prevent gut atrophy. Also, the enteral route reduces the risk of nosocomial infection.

It has been suggested that a caloric intake of 20 to 30% above the estimated requirement will provide adequate calories for most children with AKI without a significant risk of overfeeding and complications.⁵ Patients with AKI have an increased lipid oxidation rate and reduced glucose oxidation rate. Due to increased lipid demands and limited stores, critically ill children are susceptible to deficiency of essential fatty acids. Lipid supplementation in the form of 20% lipid emulsions providing

Table 4 Guidelines for feeding children with acute kidney injury

Nutritional parameters	Recommendation (level 3) ^a
Energy	Around 20–30% above the basal needs (calculated per metabolic carts or equations)
Energy composition	20–25% carbohydrates 30–40% lipid formulations (20% emulsion) 40–50% proteins
Protein	2–3 g/kg/d; increase if the child is on renal replacement therapy
Electrolytes	Closely monitoring in acute kidney injury
Vitamins and trace elements	As per daily requirement <ul style="list-style-type: none"> • Monitor water-soluble vitamins and folate levels • Might require supplementation for prolonged periods even after discharge
Potential monitoring during stay in intensive care unit	Resting energy expenditure. Electrolytes, vitamins, and trace elements if risk of nutrient depletion during prolonged dialysis

^aEvidence from nonexperimental descriptive studies, such as comparative studies, correlation studies, and case–control studies.

30 to 40% of total energy needs should be administered if the patient cannot be enterally fed. The recommendations issued by the American Society for Parenteral and Enteral Nutrition suggest the following age-adjusted protein intakes for critically ill children:²⁰ 0 to 2 years, 2 to 3 g/kg per day; 2 to 13 years, 1.5 to 2 g/kg per day; and 13 to 18 years, 1.5 g/kg per day. However, specific studies are needed to validate these recommendations in critically ill children with AKI.

Complications of AKI, including hyperkalemia, hyponatremia, hypocalcemia, hyperphosphatemia, hypermagnesemia, and metabolic acidosis, require close monitoring and nutrient replacement as necessary. Nutritional deficits may also depend on the underlying etiology. For instance, cystic dysplasia may require sodium supplementation since these children are nonoliguric. Sodium supplementation may also be required for infants on peritoneal dialysis therapy, many of whom can become salt depleted as a result of high ultrafiltration requirements, with subsequent severe clinical manifestations such as hypotension.

Animal models of ischemia-reperfusion injury have demonstrated a protective effect of docosahexaenoic acid, an omega-3 polyunsaturated fatty acid from fish oil, by decreasing polymorphonuclear leukocyte recruitment and cytokine levels in the kidney, while enhancing anti-inflammatory proteins. More research is needed in the field of immunonutrition to warrant its use in clinical practice.²¹

Carnitine deficiency is known to occur in chronic hemodialysis; however, the effect of continuous renal replacement therapy (CRRT) on carnitine homeostasis has not been studied. Children receiving CRRT are at risk for carnitine deficiency because of continuous removal, absent intake, decreased production, and comorbidities related to critical illness. In addition, carnitine deficiency is associated with increased mortality.²²

Conflict of Interest

None.

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