Original Article

Nutrition-Focused Physical Examination for Detecting Protein Energy Wasting in Children with Chronic Kidney Disease

Abstract

Introduction: There is a need to explore less laborious point-of-care assessment tools to diagnose protein energy wasting (PEW) in children with chronic kidney disease (CKD). This cross-sectional study was undertaken to assess the profile of specific nutrition-focused physical examination (NFPE) and mid-arm muscle area (MAMA) in children with CKD and determine their role in the diagnosis of PEW. **Methods:** PEW criterion was applied to all eligible children and MAMA was derived from mid-arm circumference and triceps skin fold thickness. NFPE signs examined were muscle wasting (MW) and subcutaneous fat loss (FL). **Results:** One hundred and twenty-six children with CKD (86 in CKD stages 2–4 and 40 on dialysis) were studied. PEW was prevalent in 41.8% children with CKD2-4 and in 72.5% on dialysis. In children with CKD 2–4, low MAMA, MW, and FL were significantly associated with PEW with an odd's ratio of 5.3 (1.55,18.30), 10.6 (3.8,29.8), and 10.5 (3.7,29.2) respectively (P = <0.001). Similarly, in children on dialysis, low MAMA, MW, and FL were more likely to be associated with PEW with an odd's ratio of 17 (2.2,127.7); P = 0.017, 16.6 (3,90.8); P = 0.001 and 19 (2.1,170.3); and P = 0.009, respectively. MW demonstrated high sensitivity and specificity [80.6 and 72%, respectively, with a positive predictive value (PPV) of 67.4%] to diagnose PEW in the CKD 2-4 group and in those on dialysis [86.2 and 72.1%, respectively, with PPV of 89.3%]. **Conclusion:** Clinical signs based on NFPE are useful in detecting PEW in children with CKD2-4 and in those on dialysis.

Keywords: *Anthropometry, children with CKD, NFPE, PEW*

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Introduction

Undernutrition is known to occur in children with chronic kidney disease (CKD) and kidney failure (KF) and is governed by complex interactions between appetite, inflammation, dietary nutrient intake, comorbidities, increase energy expenditure, and metabolic rate. Protein energy wasting (PEW) is a distinct entity coined to describe the clinical consequences of anorexia, loss of muscle mass, and increased energy expenditure in the background of uremia.[1] In 2014, a revised criterion adapted from adult criterion was proposed for children that included five criteria – body mass index (BMI), mid-upper arm circumference (MUAC), biochemical measures [serum albumin, cholesterol, transferrin, C-reactive protein], reduced appetite, and short stature.[2] The chronic kidney disease in children (CKiD) study reported PEW to be present in 7–20%, which varied based on the number of criteria used.[2] Another study from a low middle income country revealed a higher burden of PEW in children with CKD 2–5 including those on dialysis and observed that anthropometry and appetite were more useful parameters compared to biochemical measures of assessment.[3] The diagnosis of PEW demands adequate facilities for blood tests and involves high costs. This could be a barrier for prompt diagnosis of PEW in under resourced regions. This calls for a need to explore point-of-care assessment tools to predict the risk of PEW that can be undertaken by health care professions, trained nurses, and dieticians.

Loss of muscle mass is a critical component of PEW. The CKiD study underscores the utility of MAC in assessing the severity of muscle loss and reports MAC to be associated with reduction in estimated glomerular filtration rate.[2] While MAC is a surrogate parameter for both muscle and fat loss, there is need to explore the role of a parameter that reflects muscle

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loss like mid-arm muscle area (MAMA) in these children. However, anthropometry parameters are known to have gaps in accuracy with questionable reliability in those with edema and bone deformities. A nutrition-focused physical examination (NFPE) serves as an important component of nutritional assessment, endorsed by the Accreditation Council for Education in Nutrition and Dietetics, that detects presence of fat loss (FL), muscle wasting (MW), and edema.[4,5] These simple bedside physical signs, though proposed for the assessment of nutrition in children, have not been studied in children with CKD.[6] This study was undertaken primarily to assess the profile of specific NFPE signs and MAMA in children with CKD (including dialysis). In addition, the role of NFPE as a point-of-care assessment in the diagnosis of PEW was studied.

Methods

This cross-sectional study was undertaken in children aged 2–18 years with CKD stages 2–4 and those on dialysis (for at least 1 month). The analysis reported here is a subset of an ongoing larger single-center study on PEW in children with CKD undertaken from April 2017 to June 2021. Recruitment of children was done at the pediatric CKD clinic of a tertiary care hospital. Those with bony deformities (in whom height could not be accurately recorded), sick children or those admitted in hospital within the last 1 month, and those who did not give consent for venipuncture for the study were excluded. Institutional ethical approval and informed consent from parents of children were obtained.

Diagnosis of PEW: Diagnosis of PEW was based on criteria used in the CKiD study.[2] Criteria included (a) biochemical parameters of serum cholesterol <100 mg/dL, serum albumin <3.8 g/dL, serum transferrin <140 mg/dL, and C reactive protein >3 mg/L; (b) BMI for height age <5th centile, a marker of body mass; (c) MUAC <5th centile, a marker of muscle mass; (d) decreased appetite; and (e) short stature defined by height for age <3rd centile. Based on the number of criteria that each subject fulfilled, children were stratified as "Minimal PEW," defined as fulfilling any parameters in two or more criteria of (a) through (e) or "Standard PEW" defined as any parameter fulfilled in three or more criteria or "Modified PEW" defined as fulfilling any parameter of the ≥3 or more criteria with short stature. For the purpose of this study, children were grouped into – a) those with PEW (who fulfilled any of the stratified categories) and b) those without PEW.

Body weight and height were recorded using a digital weighing scale (Tulaman Pvt. Ltd, India) to the nearest 0.05 kg and height recorded by a stadiometer (Standard steel, India) to the nearest 0.1 cm. Height for age percentile was calculated using reference charts of Indian Academy of Pediatrics.[7] BMI (weight in kg/height^2) for height age (age at which the child's current height is at 50th centile) was calculated using CDC charts.[8] MUAC was measured using a nonmetal measuring tape to the nearest 0.1 cm and interpreted using reference charts based on centiles with a cut off of fifth centile being provided.[9] The assessment details of appetite and biochemical criteria are available in a previous study.[3]

Additional measures and nutrition-focused physical examination signs

MAMA was derived from MUAC and expressed in millimeter (mm) using the formula: MAMA (mm^2) = [MUAC (mm) –∏ T]^2/ 4∏.[9] Skin fold thickness was recorded to the nearest millimeter with a Holtain Tanner skinfold calipers having a pressure of 10 g/mm^2 of contact surface area and a dial graduation of 0.2 mm. Triceps skinfold thickness (T) was measured over the left arm triceps muscle half way between elbow and acromial process of the scapula with the skinfold parallel to the longitudinal axis of the upper arm. MAMA was interpreted using reference charts based on centiles and a measure of <5th centile for age and gender was considered a surrogate for MW.[9] Subjective global nutritional assessment (SGNA) was undertaken in all children recruited. Parameters of NFPE [loss of subcutaneous fat, MW, and edema] were studied based on specific signs described under SGNA.[10]

Physical examination findings [Table 1] specific to subcutaneous fat loss (FL) were identified on cheeks, ribs, and buttocks, and findings for MW were looked for over the clavicle, shoulder, scapula, thigh, knee, and calf.[10] After examining for FL and MW in all areas, subjectively the degree of fat or wasting was rated as follows: If the signs are present in some areas and not noted in other areas, then the child falls into "moderate malnutrition"; if severe signs are present in all or most areas, it is "severe malnutrition," and if no signs are present, it is "no malnutrition." The presence of edema was examined over ankle and sacrum. A single assessor blinded to the biochemical and mid-arm circumference measures of the child performed these assessments.

Statistical analysis

Data were analyzed using IBM SPSS statistics for windows, Version 24.0 (Armonk, NY: IBM Corp.). All categorical data were summarized using frequency and percentages and continuous data expressed as mean (standard deviation) or median (Interquartile range) based on the distribution. To study the association between nutritional parameters and PEW, student's *t*-test, Chi-square test, or Fisher's exact test were used. The factors associated with PEW were studied using logistic regression. The diagnostic ability of other parameters of undernutrition compared to PEW was assessed by calculating diagnostic estimates. The *P* value was considered significant at 5% level of significance for all comparisons.

Table 1: Assessment of subcutaneous fat loss and muscle wasting in SGNA[8]. FL: Subcutaneous fat loss; MW: Muscle wasting, MN: Malnutrition

Sites	Methods	Severe MN	Moderate MN	No MN
FL				
Facial cheeks	Palpate cheeks	Hollow	Flat	Full
Biceps/Triceps	Arm bent, pinch fat (without muscle) and roll between fingers	Very little space between fingers	Some space between fingers	Thick fold of fat tissue between fingers
Ribs	Child pressing hand against a solid object	Depression between ribs apparent	Depression between ribs not apparent	Chest is full
Buttocks	Child standing	Wasted and baggy	Slight curve but not round	Round
MW				
Clavicle	Look for prominence of clavicle	Prominent and protruded	Some protrusion	Visible but not prominent
Shoulder	Position arms at side and look for bone prominence	Shoulder to arm joint is square, bones and acromion prominent	Shoulder not square but acromion mildly prominent	Round and curved at shoulder and able to grasp muscle tissue at shoulder joint
Scapula	Push hands against solid object and look for prominence of bones	Bone prominent, muscle wasting around is seen as depressions	Variable wasting around scapula bone	Bone not prominent, no depressions
Thigh	Child sits, prop leg up on low furniture, grasp quadriceps	Quadriceps can be squeezed, hollow inner thigh	Inner thigh depression present	Firm quadriceps and no depressions
Knee	Knee propped up after sitting	Knee is square and prominent, no muscle mass	Knee bone is noticeable, little muscle around	Knee bone not prominent, muscle prominent
Calf	Grasp calf muscle to assess amount of tissue	Flat, thin and no shape	Some shape	Bulb shape and firm

Results

Eighty-six children with CKD stages 2–4 (50% males) and 40 on dialysis (60% males; 5 on hemodialysis and 35 on peritoneal dialysis) were studied. The median age (IQR) of those with CKD 2–4 and those on dialysis were 120.5 months (87,162) and 123.5 months (86,153.5), respectively. The median duration of CKD was 12 months (3,44) and duration on dialysis was 7.5 months (3,18). Most common etiology of CKD and kidney failure was congenital anomalies of kidney and the urinary tract (62%).

Profile of PEW, MAMA, and NFPE signs in children with CKD stages 2–4 and on dialysis

PEW was noted to be higher in those on dialysis compared to CKD 2-4 [29 (72.5%) vs 36 (41.8%) P = 0.001]. Among the anthropometry parameters of PEW, the proportion of children with short stature, low MUAC, and low BMI were comparable between those with CKD 2-4 and those on dialysis. Low MAMA was significantly higher in children with CKD 2-4 compared to those on dialysis [64 (77.1%) vs 22 (55%), P = 0.01] respectively. Both moderate and severe MW were observed in a significantly higher proportion of those on dialysis compared to CKD 2-4 (17 (42.5%) vs 32 (37.2 %) and (11 (27.5%) vs 11 (12.7%), P = 0.048). Severe FL was significantly higher in children on dialysis compared to those with CKD 2-4 ((9 (22.5%) vs 4 (4.6%), P = 0.009). Edema was more commonly present in those on dialysis compared to those with CKD 2-4 [19 (47.5%) vs 3 (3.5%), P =<0.001].

Association of MAMA and NFPE parameters with PEW [Table 2]: In both groups of CKD 2-4 and dialysis, age, gender, duration of CKD/dialysis, and etiology of CKD were not significantly associated with PEW. However, low MAMA, MW, and FL were associated with the presence of PEW in both the groups. In children with CKD 2–4, low MAMA, MW, and FL were significantly associated with PEW with an odd's ratio of 5.3 (1.55,18.30), 10.6 (3.8,29.8), and 10.5 (3.7,29.2), respectively (P =<0.001). Similarly, in children on dialysis, low MAMA, MW, and FL were associated with PEW [Table 2].

Ability of MAMA, MW, and FL parameters to diagnose PEW in children with CKD 2–4 and dialysis: The specificity and sensitivity of MAMA to diagnose PEW was 93.9% vs 47.1% in CKD 2-4 and 90% vs 58.6% in the dialysis group, respectively. MW demonstrated 80.6% sensitivity and 72% specificity [positive predictive value (PPV) of 67.4%] to diagnose PEW in the CKD 2–-4 group. In the dialysis group, MW also showed 86.2% sensitivity and 72.1% specificity to diagnose PEW [PPV of 89.3%]. Similarly, combining parameters of MW with FL demonstrated 80.6% sensitivity and 72% specificity for diagnosis of PEW in CKD 2–4 [PPV

Table 2: Association of MAMA and NFPE parameters (MW: muscle wasting; FL: Subcutaneous fat loss) with PEW in children with CKD2-4 and on dialysis. PEW- (PEW absent) PEW+ (PEW present

Parameters	CKD2-4 (*n*=86)				Dialysis (*n*=40)			
	PEW-	PEW+	OR (95% C.I)	*P*	PEW-	PEW+	OR (95% C.I)	*P*
MAMA *n*(%) *n*=83								
<5th centile	3 (6.1)	16 (47.0)	5.3 (1.55,18.30)	<0.001	1 (9.0)	17 (58.6)	17 (2.2,127.7)	0.017
>5th centile	46 (93.8)	18 (52.9)	Ref		10 (90.1)	12 (41.3)	Ref	
MW *n*(%) *n*=86								
Absent	36 (83.7)	7 (16.2)	10.6 (3.8,29.8)	<0.001	8 (66.7)	4 (33.3)	16.6 (3,90.8)	0.001
Present	14 (32.5)	29 (67.4)	Ref		3 (10.7)	25 (89.2)	Ref	
FL *n*(%) *n*=86								
Absent	42 (77.7)	12 (22.2)	10.5 (3.7,29.2)	<0.001	10 (50)	10 (50)	19 (2.1,170.3)	0.009
Present	8 (25)	24 (75)	Ref		1 (5)	19 (95)	Ref	

of 67%] and 86.2% sensitivity and 72.7 specificity in the dialysis group [PPV of 89.3%].

Discussion

This cross-sectional study reports a high burden of PEW in children with CKD, including those on dialysis. Importantly, this is one of the few studies in children with CKD that explores the role of NFPE – a noninvasive, cost-effective clinical tool to detect PEW. The findings of this study highlight the utility of NFPE parameters of MW and FL in the diagnosis of PEW in these children. MAMA found to have a low sensitivity to diagnose PEW in both groups. On the other hand, MW as a single parameter proved to have a high sensitivity and specificity to diagnose PEW in children with CKD and those on dialysis.

Muscle and fat loss leading to cachexia can result from undernutrition and chronic inflammatory states. The process involves gluconeogenesis, breakdown of adipocytes, release of acute phase reactants, and inflammatory cytokines that facilitate muscle degradation.[11] Further, there is evolving evidence to suggest that specific biomarkers like leptin, 25 hydroxyvitamin D levels, and interleukin -1 play a specific role in CKD-related cachexia.[12-14] In pursuit of developing an inclusive criterion reflective of the complex interplay of nutrition and inflammation, the PEW criterion was proposed for adults. Thereafter, the criterion was adapted for use in children with CKD. In contrast to the CKiD study, we have reported the burden of PEW in children from a low middle income country to be as high as 59% in those with CKD2-4 and 58% in those with kidney failure.

Among the five criteria, anthropometry parameters of MAC, BMI, and height were useful to diagnose PEW in children with CKD and kidney failure. MAC and BMI, though cannot differentiate between fat and muscle mass, have been useful anthropometry parameters for PEW assessment in children with CKD.[3,15-17] Though MAC has been noted to be useful for assessment of undernutrition and frailty in these children,[3,18] it is a surrogate parameter that reflects subcutaneous fat tissue, bone, and muscle and may not be an ideal tool to specifically detect MW. The role of MAMA in determining MW or PEW has not been studied in children. In adults with CKD, MAMA was noted to be significantly associated with daily total protein intake.[19] One study from Egypt observed 66% of children on hemodialysis to have reduced muscle mass based on MAMA.[20] We observed low MAMA to be more commonly prevalent in the group with CKD (77%) than in those on dialysis (55%), while low MAC was noticed in lesser proportion of children in both groups (57 and 47.5%, respectively). This could possibly speculate the presence of reduced muscle mass and preserved/increased fat mass in these children. Besides, C-zeroT low MAMA found to have low sensitivity to diagnose PEW in both groups, making it a weak screening tool for PEW. This may be explained by the fact that MAMA reflects the upper-arm regional muscle area that may not be representative of MW present in other areas of the body.

The NFPE is a comprehensive approach that includes visual and tactile assessments for muscle and fat loss in children. Areas of the body that reflect MW and FL are specific and mutually exclusive. While muscles that best represent wasting are quadriceps, deltoids, temporalis, pectoralis, trapezius, supra and infraspinatus, and gastrocnemius, FL is well identified over the triceps, mid axillary line, iliac crest, buttocks, below ribs, and face.[10] In infants and toddlers, differentiating fat and muscle loss could be a challenge. The youngest child in this study being 7 years of age was not a limitation to undertaking NFPE. The pediatric specific NFPE provides guidance on the body areas that need to be examined for MW (temple, clavicle, shoulder, scapula, thigh, knee, and calf) and FL (face, arms, chest, and buttocks). Prominent bone structure at the clavicle, shoulder, scapula, knee sites, and flat or hollow areas in the upper or lower legs suggests that MW and hollow facial cheeks, depressions between ribs, and flat buttocks are key signs of FL. Our findings reveal severe MW and FL to be predominantly evident in children on dialysis. The parameters of FL, MW, and edema are components of NFPE that are incorporated into the SGNA. Signs of MW and FL were seen to highly correlate with the severity of SGNA rating of malnutrition in adults and children.[20,21]

In the context of CKD, edema is a known confounding factor for nutritional assessment in CKD. Edema could be a result of protein losses through PD, proteinuria in those with underlying glomerular disease, and fluid retention. However, despite moderate edema being present in the majority, severe FL and MW were observed in about one-fifth to one-fourth of the cohort, respectively. Interestingly, low MAC was more commonly noted in children on dialysis compared to those with CKD 2–4 despite 47.5% of them presenting with edema. These findings suggest that certain physical findings may still be useful even in the presence of edema in a population with a high burden of undernutrition.

The clinical skill of NFPE is underutilized by clinicians, nurses, and dieticians in routine care of children with CKD. Some of the key reasons relate to lack of training and limited awareness of the tool and time constrains. Dieticians and nurses trained in adult related NFPE may find it unfamiliar to undertake such an assessment in children.[22] NFPE has received attention especially in the past few years and has been included in the training curriculum for registered dieticians. Hands on workshops and efforts to include NFPE into telehealth services are gaining momentum.[23-27] A recent global survey on kidney nutrition care reveals low implementation of formal nutrition assessment for patients with CKD across the globe.[26] Empowering registered dieticians and nurses with methodical training for the point-of-care assessment of nutrition status is critical.[28,29] NFPE is one such tools that have the potential for use at any level of health care delivery.

This is one of the very few studies that focused on the role of NFPE to identify undernutrition and PEW in children with CKD. The high burden of PEW in this population makes it feasible to study surrogate assessment tools. As a point-of-care assessment tool, NFPE could be easier compared to interpretation of BMI/MAMA using reference charts indexed to age/gender and height. Identifying specific signs for individual compartments of muscle and fat loss through NFPE provides added benefit as BMI cannot differentiate muscle from fat tissue. However, small sample size with small numbers in each of the categories of PEW limited further analysis of exploring the role of NFPE in detecting severity of PEW. Importantly, implementation of NFPE could be time consuming and demanding patient cooperation and trained assessors.

Conclusion

Clinical signs of MW and FL based on NFPE have a diagnostic ability to identify children with PEW. These findings reiterate the importance and relevance of NFPE in the assessment of children with CKD. Besides, NFPE has the potential to be instituted by trained nurses and dieticians as a point-of-care assessment for PEW in any health care context.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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