

## Nutrition assessment of children with advanced stages of chronic kidney disease-A single center study

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### Abstract:

**Background:** Malnutrition is a major problem among children with Chronic Kidney Disease (CKD) and it is essential to be recognized as early as possible. Aim of our study was to assess the nutrition status of children with CKD.

**Methods:** Nutrition status of 30 children (1-16 years) with CKD stages III, IV and on peritoneal dialysis was evaluated. Malnutrition risk was assessed by Pediatric Digital Scaled Malnutrition Risk screening Tool (PeDiSMART) score software. Anthropometry was expressed as Z-scores for age and sex. Phase angle (PhA) and body cell mass were assessed by bioelectrical impedance analysis (BIA). Three-day food intake was recorded and analyzed. Biochemical indexes were assessed.

**Results:** Depending on the marker used for assessment 20-40% of our patients were malnourished. Intake/requirements ratio (median) was 86.5% for actual energy intake and 127% for actual protein intake. Multiple regression analysis has shown that the most determinant factor for Mid Upper Arm Circumference (MUAMC) was actual protein intake, Glomerular Filtration Rate (GFR) and age at diagnosis. PhA was mainly affected by GFR and energy intake. Statistically significant inverse correlation was found between PeDiSMART score and PhA ( $p=0.001$ ), MUAMC ( $p=0.008$ ) as well as protein intake ( $p=0.016$ ).

**Conclusions:** A considerable proportion of children with advanced CKD are undernourished. Regular dietitian evaluation based on novel tools as PeDiSMART score and PhA may identify earlier patients at risk for malnutrition. Hippokratia 2014; 18 (3): 212-216.

**Keywords:** malnutrition, anthropometry, phase angle, PeDiSMART score

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### Background

The consequences of chronic kidney disease (CKD) during childhood may affect dramatically the nutrition state and usually lead to reduced growth rate<sup>1-3</sup>. Protein-energy wasting enhanced by metabolic and hormonal imbalances as well as feeding problems are associated with increased morbidity and mortality in children with CKD<sup>4</sup>. Each decrease height standard deviation score (SDS) of 1 is associated to increase of mortality rate by 14%<sup>5</sup>. Early detection and prevention of malnutrition is considered very important because dietary intervention itself is not enough to cease chronic inflammation catabolism or to reverse the decreased growth rate<sup>6-11</sup>. In order to assess its signs as early as possible it is necessary to evaluate nutrition state in a regular basis using evidence based indicators.

Biochemical markers have a poor diagnostic and prognostic accuracy in malnutrition assessment compared to anthropometric measurements<sup>12</sup>. Markers such as pre-albumin and retinol binding protein are not considered reliable as the first is excreted by the kidneys and its concentration can be falsely elevated in patients with advanced kidney disease and both of them are associated

with inflammation<sup>13</sup>. Body mass index (BMI) is recognized as a prognostic indicator of mortality in both adults and children with CKD<sup>14-15</sup>. However its validity, as well as the validity of other anthropometric measurements, is under considerable dispute, mainly because CKD is associated with hydration status imbalances<sup>16,17</sup>. No conventional marker is considered superior to another in assessing body composition among CKD patients.

In our study we aimed to assess the nutrition status of children with advanced stages of CKD using conventional as well as novel nutrition assessment tools.

### Patients & Methods

Thirty children aged 1-16 years (median age 8 years), 20 males and 10 females, with advanced stages of CKD [III, IV and on peritoneal dialysis (PD)] were selected in a CKD pediatric clinic. CKD stages were defined according to Schwartz formula: as stage III estimated glomerular filtration rate (eGFR) 30-59 ml/min per 1.73 m<sup>2</sup>, as stage IV eGFR of 15-29 ml/min/1.73 m<sup>2</sup> and as stage V eGFR of <15 ml/min/ 1.73 m<sup>2</sup>. Six of our patients were polyuric, 5 were oliguric, 2 were anuric and 17 of them had a nor-

mal urine output. Current age at diagnosis and duration of disease were recorded and GFR was calculated according to previous literature<sup>18,19</sup>. Three of our patients were under treatment with growth hormone.

#### *Anthropometry*

Nutrition status was evaluated according to KDOQI (Kidney Disease Outcome Quality Initiative) guidelines<sup>13</sup>. Body weight, height and mid upper arm circumference were measured while z-scores for weight, height, BMI were calculated with the use of software [ANTHRO plus (WHO, Geneva, Switzerland) and EPI INFO (Version 7, CDC, Atlanta, Georgia, 2000)] according to age (height age was also used where necessary according to KDOQI) and sex. Multiple measurements of mid upper arm circumference (MUAC) and triceps skinfold were conducted by an experienced dietitian. Mid upper arm muscle circumference (MUAMC), arm muscle area and arm fat area were calculated.

#### *Bioelectrical impedance analysis (BIA)*

BIA measurements were also performed (Bodystat Quadscan 4000, Bodystat, Beaconsfield, UK) according to BIA protocol. All continuous ambulatory peritoneal dialysis (CAPD) patients were measured one hour after dialysis so that body fluid compartments were as closer to healthy levels as possible. Phase angle (PhA) as well as body cell mass (BCM) were assessed. PhA percentiles based on healthy children populations are available, but the use of national ranking criteria is considered useful<sup>20-28</sup>. Therefore for the needs of the present study 400 children aged 2-18 were measured with BIA and classification of PhA values to PhA percentiles derived from studies on national pediatric population.

#### *ABN score (Anthropometry, BIA, Nutrition)*

ABN score, a score previously used to assess nutrition status of children with CKD was estimated. The nine anthropometry and BIA parameters (height, weight, BMI, MUAMC, arm muscle area, arm fat area, reactance, PhA and distance) were given scores of 5 for values of  $>0$  SDS, 4 for values of  $\leq 0$  and  $> -1$  SDS, 3 for values of  $\leq -1$  and  $> -2$  SDS, 2 for values of  $\leq -2$  and  $> -3$  SDS and 1 for values of  $\leq -3$  SDS. An average score was calculated for each of the A1 (height, body weight, BMI), A2 (MUAMC, arm muscle area, arm fat area) and BIA (reactance, PhA, distance) groups, and these were summed to obtain the ABN score, which could therefore vary from 3 (worst) to 15 (best)<sup>29</sup>.

#### *Dietary intake*

Three-day energy and protein intake were assessed through 3-day food intake records (2 weekdays and one weekend day included). Patient's parents were given detailed instruction by the dietician to weight (or use measures when weighing was not possible). The analysis was performed using Food Processor software (version 7.40, 1999, ESHA, Portland, OR, USA). Necessary adjustments to include food item analysis, low protein/low phosphorus products as well as local dishes were made. Actual energy intake (%) was defined as energy intake/ calculated individ-

ual energy expenditure\*100 and actual protein intake (%) as protein intake/ calculated individual protein needs\*100. Actual energy and protein intake were assessed the three day food intake records analysis. Energy expenditure and protein needs were calculated according to KDOQI guidelines<sup>13</sup>. Protein/ ideal weight was also calculated.

#### *PeDiSMART score*

Malnutrition risk screening was performed by Pediatric Digital Scaled MAInutrition Risk screening Tool (PeDiSMART) software (2014, Thessaloniki, Greece) which has already been tested in pediatric population<sup>30</sup>. Four parameters were assessed a) nutritional status as derives from weight z-score, b) nutritional intake level, c) symptoms affecting intake and d) overall disease impact. Score range for each parameter was arbitrarily set to 0-4 and there was an adjustment of 2 points for children younger than 1 year, with a total score ranging from 0 to 18.

#### *Biochemical parameters*

Fasting values for urea, creatinine, hemoglobin, TIBC, albumin, total protein and bicarbonate were assessed. Patients were divided into group A (CKD of III and IV stages as defined by GFR levels) and group B (CAPD).

The study has been approved by the Alexander Technological Education Institute of Thessaloniki Bioethics Committee and has been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Patients' parents gave their informed consent prior to their inclusion in the study.

#### **Statistical analysis**

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) for Windows, version 13.5 (SPSS Inc., Chicago, IL, USA). T-test and Mann-Whitney U test were used to compare differences between study groups for parameters with and without normal distribution, respectively. Pearson and Spearman's coefficient of correlation (r) were used to determine the correlations.

Multiple regression analysis with the method of best subsets analysis (after standardization of the values) was also conducted. A p value of  $< 0.05$  was considered to be statistically significant.

#### **Results**

Thirty children aged 1-16 years, 20 male and 10 female, 17 with CKD stages III and IV and 13 on PD were included in this cross sectional study. Median chronological age of our group was 8 years, median age at diagnosis was 1.5 years (range 0-13), median duration of disease was 3 years (range 0.5-15) and median GFR was 16.8ml/min/1.73 m<sup>2</sup> (range 5.7-52.5). No statistical difference between group A and B was found regarding the assessed parameters, apart from blood urea and creatinine related to the disease stage. Therefore the results are presented for all the children together.

Demographic features, and data of anthropometric and BIA measurements, dietary intake and biochemical markers for Group A, Group B and all the children to-

**Table 1:** Median values of Anthropometric, BIA, dietary intake & biochemical parameters of Groups A (stages III&IV, n=17), B (CAPD, n=13) and total (n=30).

	Stages III&IV	CADP	All patients
height z-score	-1.15	-1.27	-1.24
weight z-score	-1.07	-1.43	-1.14
BMI z-score	-0.68	0	-0.6
Phase Angle	4.4	3.7	4.3
BCM (kg)	18.45	13.85	16.5
En. Intake (kcal)	1596	1160	1347
Actual En. Intake (%)	86.45	87.55	86.45
Actual Prot. Intake (%)	127	125.6	127
g prot/kg ideal weight	1.71	1.91	1.82
PeDiSMART score	5	5	5
ABN score	12.3	11	12
HB (g/dl)	12.05	11.45	11.9
Urea (mg/dl)	67	80	71
Creatinine (mg/dl)	1.24	5.96	2.62
total protein (g/dl)	7	6,55	6,85
Albumin (g/dl)	4.4	4.3	4.4
TIBC (mg/dl)	250	247	247
HCO <sub>3</sub> (meq/l)	22.5	23.5	22.7

BMI: body mass index, BCM: body cell mass, En: energy, Prot: protein, PeDiSMART: pediatric digital scaled malnutrition risk screening tool, ABN: anthropometry, HB: hemoglobin, TIBC: total iron binding capacity.

gether are shown in Table 1.

Table 2 displays the results of malnutrition detection in our sample as assessed by 6 different markers. According to PeDiSMART Score screening tool 11/30 (37%) were found in risk for malnutrition, 4/11 were in high risk and 7/11 in medium risk for malnutrition. In 7/27 (26%) children % actual caloric intake was below optimal. Correlations are presented in Table 3. Multiple regression analysis has shown that factors significantly associated with MUAMC was % actual protein intake ( $\beta$ : 0.07592,

**Table 3:** Statistical analysis correlations.

	Weight	MUAMC	BCM	Energy intake	Protein intake	PeDiSMART
PhA	r=0.483 p<0.05	r=0.778 p<0.001	r=0.699 p=0.001	r=0.678 p<0.001	r=0.632 p<0.001	r=-0.567 p=0.001
PeDiSMART		r=-0.497 p<0.05			r=-0.461 p<0.05	
Albumin		r=0.562 p<0.05	r=0.591 p<0.05			

PhA: phase angle, PeDiSMART: pediatric digital scaled malnutrition risk screening tool, MUAMC: mid upper arm muscle circumference, BCM: body cell mass.

**Table 2:** Malnutrition-stunting detection results according to anthropometric & bioelectrical impedance analysis markers.

Parameters used to detect malnutrition	Cut of point	Children below cutoff point
Weight z-score	<-2	8/30 (27%)
Height z-score	<-1.88	9/30 (30%)
BMI z-score	<-2	6/30 (20%)
AMA z-score	<-1.6	6/30 (20%)
PhA percentile	<3 <sup>rd</sup> centile	9/30 (30%)
ABN score	<10.33	6/30 (20%)

BMI: body mass index, AMA: arm muscle area, PhA: phase angle.

p=0.006), GFR ( $\beta$ : -0.09473, p=0.003) and age at CKD diagnosis ( $\beta$ : 0.3114, p=0.021). Factors significantly associated with for PhA was GFR ( $\beta$ : -0.04303, p=0.012) and energy intake ( $\beta$ : 0.0010927, p=0.010).

## Discussion

According to our findings 20-30% of our patients are malnourished depending on the marker used for the assessment. Thirty seven percent of our patients are at risk of malnutrition as designated by PeDiSMART score, while 26% of them have an inadequate energy intake. Furthermore multifactorial analysis has shown that MUAMC was most strongly related to %actual protein intake, GFR and age at CKD diagnosis while PhA is mainly affected by GFR and energy intake. The negative correlation found between GFR and PhA as well as between GFR and MUAMC implies in an indirect way that dialysis (which is currently imposed only on lower GFRs), is the most determinant factor for the improvement of the nutrition status.

The small number of patients included in this study as well as the multi diversity of primary disease should be noted. A range of methods are available to assess body composition in children with CKD and assist in malnutrition monitoring. All anthropometric techniques are validated in healthy children, where body composition is considered relatively static. The methodology used in the present study, has certain limitations including the use of bioelectrical impedance and arm indices, that are considered inconclusive and insensitive in small changes as they may overestimate or underestimate nutrition status in a population with volume overload, short stature and delayed puberty or may be

treated with growth hormone, however multi frequency BIA used in the present study is considered more reliable than single frequency BIA. Arm indices are also considered observer depended but accuracy of measurement is increased when conducted by the same experienced personnel when they are performed right after completing dialysis and when evaluation parameters are adjusted to height. Neither BIA nor arm indices measurements are considered part of routine nutrition status assessment.

Height is perhaps the most reliable marker of growth and a standard way of assessing nutrition status in children with CKD. Children on peritoneal dialysis have lower height z-scores by 1.5 to 2.37 compared to their healthy peers<sup>1-3</sup>. Our patient's median height SDS was -1.24, while 9/30 children were below -2. Lower age at diagnosis is related to malnutrition and has been previously positively correlated to height percentiles lower than normal while low growth rate was associated with disease stage<sup>1-4,31</sup>. This is in agreement with the findings of the present study as MUAMC which is a parameter used to describe nutrition status, was related to age at diagnosis. Muscle and fat deficits, a nutrition state that is typical in CKD, is mainly a result of disease complications.

Reduced growth rates are also attributed mainly to disease complications (hormonal imbalances) reduced energy intake is designated as an independent factor related to growth rate retardation. Energy intake that is lower than 80% of recommended daily allowance (RDA) was related to growth rate reducing<sup>32</sup>. In the present study, 7/27 children (26%) displayed energy intake below optimal. A few studies have assessed energy intake in children with CKD but differences in methodology are complicating any comparison<sup>33-36</sup>. Generally in patients' studies, comparing intake to their individual needs, calculated according the specific condition demands, as is conducted in the present study, is more reliable than comparing to the RDAs. According to the KDOQI guidelines for the calculation of individual energy and protein needs of the CKD pediatric patients<sup>13</sup>, intake/requirements ratio was 86.5% for energy and 127% for protein. Mean energy percent expressed as a percent of RDAs was reported to be from 70.58% to 115% while protein intake was always reported as excessive (up to 255%), with one exception study where protein intake was estimated to be 94% (disease stage was taken into account)<sup>33-36</sup>.

PhA has been previously evaluated as a parameter of nutrition status assessment in adults with CKD. It is considered a useful marker of equal value to other BIA markers, for the detection of malnutrition and monitoring dietary intervention effectiveness<sup>12,16,20</sup>. Its use has also been evaluated in children with CKD by Edefondi et al, who have used PhA percentiles to evaluate the nutrition status of their patients during their first year under CADP<sup>37</sup>. Seventy two percent of their patients were ranked below 3<sup>rd</sup> percentile when evaluated with PhA at the start of their treatment with CADP, a percent which was reduced to 44% and 33% six months and one year after respectively. In the present study 31% of our CADP patients were ranked below 3<sup>rd</sup> percentile, 5/13 children

were in their first year under CADP and the mean dialysis period was 2.7 years. A significant correlation was detected between PhA and conventional, markers such as weight, MUAMC and BCM that are currently used to evaluate nutrition status of patients with CKD<sup>16,38</sup>. BCM and MUAMC were also associated to albumin levels.

Edefondi et al have used dietetic, anthropometric and BIA parameters of children with CKD to calculate ABN score, a score that defines severity of malnutrition from mild to severe PEM (protein energy malnutrition). Forty nine percent (21/43) of their patients on CADP were classified as malnourished with a mean ABN score of  $8.6 \pm 1.3$  (10.33 indicating a state of normal nutrition)<sup>39</sup>. In the present study 6/30 (20%) were found with malnutrition according to ABN with a median score of 9.3. In Edefondi's study a significantly greater proportion of the patients were detected with malnutrition compared to our patients. Twelve out of 21 of their patients with malnutrition, were under CAPD for 24 months, a time limit beyond which a deterioration of nutrition state is reported<sup>39-42</sup>. Interestingly in the present study only 2/6 children under CADP were monitored with malnutrition according to ABN, 3/6 were stage IV and one stage III. Furthermore no statistically significant differences were found between the nutrition status parameters of groups A and B, which indicates that nutrition status deterioration may begin at even earlier stages, however no children of stages I or II CKD were included.

The mean score of PeDiSMART screening tool was 5, indicating mild malnutrition risk. This was expected since PeDiSMART score takes into account additional parameters beyond anthropometric measurements. The negative correlation found between PeDiSMART Score and phase angle, as well as between PeDiSMART Score and MUAMC, reflects that a decrease of lean mass is associated with malnutrition risk as already has been previously demonstrated<sup>32</sup>. Eleven out of thirty (37%) children were at risk of malnutrition, 13% of them at high and 24% at medium risk of malnutrition.

## Conclusion

A significant percentage of our patients with advanced CKD were detected with malnutrition. Most nutritional assessment methods used commonly to other populations are subject to restrictions when applied in CKD patients. Different patterns of malnutrition features are revealed with the use of different methods making interpreting results confusing. However, regular assessment of children with CKD nutrition status is an important parameter of medical nutrition therapy. The use of tools such as PeDiSMART Score and phase angle may attribute in detection of patients at malnutrition risk so that consequent advice may prevent further sequelae, but longitudinal, prospective studies on the association of nutritional markers should be carried out to clarify their value as nutrition status assessment tools.

## Conflict of interest

None declared by Authors.

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