Original Article http://journals.sbmu.ac.ir/jpn
https://doi.org/10.22037/jpn.v9i3.34122

Kidney Size Assessment in Children with Severe Acute Malnutrition Under 5 Years of Age: A Comparative Study

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Abstract

Background and Aim: Malnutrition is a common disorder worldwide. Growth of visceral organs is affected by various factors including nutrition. Kidney size is an important parameter to assess renal growth. Kidney size in malnourished children is not well studied. We compared kidney size between severe acute malnourished (SAM) and normal children.

Methods: This prospective case control study was carried out at a tertiary care center in North India. Children with SAM (n=124) were enrolled as cases and 86 age and sex matched healthy children were enrolled as controls. All children were subjected to anthropometric and sonographic kidney size measurement. Various renal size parameters were compared between cases and controls. Linear correlation coefficients of kidney dimensions with anthropometric parameters were derived. P-values <0.05 were considered significant.

Results: The kidney length was significantly lower in malnourished cases compared to healthy controls. There was no difference in renal width and combined kidney volume (CKV) between the two groups. However, renal depth, combined relative kidney volume, CKV/body height ratio, and CKV/BSA ratio were significantly higher in malnourished child compared to healthy controls. Kidney size parameters (kidney length, width, depth, CKV) had significant correlations with anthropometric measurements in both groups but the correlations were stronger in healthy controls compared to malnourished children.

Conclusion: Malnourished children had a significantly smaller kidney length. This point should be remembered while evaluating kidney size in these children to avoid unnecessary invasive investigations.

Keywords: Malnutrition; Child; Kidney size; Ultrasonography.

Received: February, 2021
Revised: March, 2021
Accepted: May, 2021

Conflict of interest: The authors declare no conflict of interest.
Please cite this article as: Kumar P, Gupta S, Mehta AJ, Athwani VK. Kidney Size Assessment in Children with Severe Acute Malnutrition Under 5 Years of Age: A Comparative Study. J Ped Nephrol 2021;9(3):1-7.
https://doi.org/10.22037/jpn.v9i3.34122

Introduction

Somatic growth is an important indicator of health in children. Kidney size is an important parameter in the evaluation of renal growth in children. Measurement of renal dimensions provides an opportunity to evaluate whether renal growth is satisfactory in a child (1). When evaluating renal abnormalities such as atrophy, hypoplasia, hypertrophy or other malformations, kidney size is an important parameter. Ultrasonography is the preferred method for assessment of renal size in children due to lack of radiation exposure and availability (2). Malnutrition is a widespread disorder in children worldwide, especially in developing countries like India. It is a well-known fact that growth of visceral organ is affected by various factors including nutrition. Poor renal growth may have some long-term consequences, including increased risk of hypertension or a tendency to develop chronic kidney disease (3-5). Presently there are only few studies on kidney size in Indian children (6-9); moreover, no data is available for kidney size in malnourished Indian children. Therefore, this study was conducted to investigate the effect of malnutrition on kidney size in the children under 5 years of age.

Methods

This study was conducted in the pediatrics department of a tertiary care center in North India during

July 2013 to June 2015. Severe malnourished (SAM) children aged 6-60 months were enrolled as cases, and well-nourished age and sex matched children presenting for routine checkup/mild illnesses/immunization were enrolled as controls. Children with anatomical abnormalities, i.e., hydronephrosis, vesicoureteral reflux (VUR), and nephrolithiasis, children with major congenital malformations, chronic disease or urinary tract infections (UTI), renal failure, preterm/post-term children and those who were small/large for gestational age (SGA/LGA) were excluded from the study. SAM was defined as per WHO diagnostic criteria for SAM if any of the following was observed: (a) weight-for-height below -3 standard deviation of the median WHO growth reference; (b) visible severe wasting; (c) presence of bipedal edema; or (d) mid upper arm circumference below 11.5cm (10).

The primary objective was to compare kidney size between SAM and normal children. The secondary objective was to find out kidney size predictors in malnourished children in terms of anthropometric measurements. The calculated sample size was 86 patients in each arm with a study power of 90% and α-error of 0.05 assuming a standard deviation of 10 mm^3 in the kidney volume and a minimum difference to be detected of 5 mm^3. The study was approved by the Institutional Research Review Board and informed written consent was obtained from the guardians of all eligible participants.

Children aged 6-60 months presenting to our centre were assessed for enrolment as case or control as per inclusion and exclusion criteria. The children were subjected to detailed history and examination and managed as per the institutional protocol.

Anthropometric Measurements: All children were weighed in minimal clothing using an electronic weighing scale. The length of the children <2yrs was measured by placing the child in an infantometer and the measurement was done from the top of the head to the sole of the foot with the patient lying on the back with the hip and knees extended. The height of the children >2yrs was measured in the standing position using a stadiometer from the top of the head to the sole of the feet with the back against the stadiometer and head erect while the patient was facing forward and looking straight. The mid upper arm circumference (MUAC) was measured using a non-stretchable tape at the midpoint between the acromion and olecranon processes in the left arm. Length/height and MUAC were recorded up to one decimal place. All anthropometric measurements were done twice by one observer and the average measurement was taken.

Kidney size measurement: The kidney size was measured by ultrasonography (Toshiba Nemio SSA-550A) using a 3.75MHz sector probe with an accuracy of 0.1 mm. All measurements were done by one radiologist with the patient in the supine position or in lateral decubitus position. The kidney length (KL), width, and depth were measured for both kidneys. All measurements were obtained prospectively on static original ultrasound images using electronic callipers at the time of scanning. The maximum length of each kidney was measured between the uppermost edge of the upper pole and the lowest edge of the lower pole.

Kidney volume (cm^3) =mean length ×mean width × mean depth × 0.523 (1).

Left and right kidney volumes were added for the combined kidney volume (CKV). Relative kidney volume (RKV) was calculated as CKV/body weight (cm^3/kg).

The Du Bois and Du Bois equation was applied for body surface area (BSA) calculation (m^2: BSA=height (cm)$^{0.725}$ × weight (kg)$^{0.425}$×0.007184] (11). Kidney volume/ height and kidney volume/BSA ratios were also calculated.

Statistical analysis: The data were collected and compiled into MS Excel spread sheets. Continuous variables were summarized as mean and standard deviation and analyzed using unpaired t test. Categorical variables were summarized as proportion (%) and analyzed using Chi-Square test. Pearson's correlation analysis was used to determine correlations between different variables. P-values <0.05 were considered significant. All analyses were performed using the SPSS software version 21.0.

Results

During the study period, 255 severely malnourished children were admitted to our institute and 131 malnourished children were excluded for various reasons. Cases and controls were age and sex matched but weight, height, BSA, MUAC and BMI were significantly higher in controls than in cases (Table 1).

Table 1: Baseline characteristics of study population

Characteristics	Cases (N=124)	Controls (N=86)	p-value
Male:Female (Ratio)	77:47 (1.64)	61:25 (2.44)	0.239
Age; (months) Mean±SD	24.99± 16.93	28.35± 17.1	0.161
Weight; (Kg) (Mean±SD)	7.48± 2.59	12.28± 3.66	0.000
Height; (cm) (Mean±SD)	75.45± 12.26	86.89± 13.25	0.000
BSA; m^2 (Mean±SD)	0.39± 0.10	0.53± 0.12	0.000
MUAC; cm (Mean±SD)	11.0± 1.2	13.7± 0.8	0.000
BMI; Kg/cm^2 (Mean±SD)	13± 2.9	16± 1.2	0.000

Anthropometric measurements were similar in male and female participants in case and control groups. Right and left kidney sizes were similar in cases and controls (Table 2) and there was no gender difference in kidney size in the two groups ($p>0.05$). KL was significantly lower in malnourished children compared to healthy controls.

There was no difference in renal width and CKV between the two groups. However, renal depth, combined RKV, CKV/body height ratio and CKV/BSA ratio were significantly higher in malnourished children compared to healthy controls (Table 3).

Kidney length, width, and depth, CKV, and CKV/body height ratio had a significant correlation with body height, BSA and weight in healthy controls. There was a moderate positive correlation with body height, BSA and weight. In malnourished children, the kidney size parameters i.e. kidney length, width, and depth, CKV, combined RKV, and CKV/BSA ratio had a significant correlation with body height, weight and BSA. Significant correlation coefficients are summarized in (Table 4).

Discussion

In children, ultrasonography, intra-venous-pyelogram (IVP), dimercaptosuccinic acid (DMSA) scan, computerized tomography (CT), and magnetic resonance imaging (MRI) are used to assess the kidney size. Sonography is a universal method of assessing renal size as it is safe, non-invasive and inexpensive compared to other methods. Moreover, this examination is real-time, tri-dimensional, independent of organ function, and phase of respiration (6).

Malnutrition is a major public health problem throughout the developing world. In India, Almost half of the children under age five years (48%) are chronically malnourished (13). Knowledge of the kidney size in these children may prevent additional invasive imaging procedures, including renal scanning and voiding cysto-urethrography, to exclude hypoplastic–dysplastic kidney. This may further decrease morbidity and mortality due to a poor immune system.

Only a few studies have investigated the effect of malnutrition on the kidney size (1,14). In the present study, we compared kidney size between severe acute malnourished children and age and sex matched healthy children. For exact quantification of the effect of malnutrition on the kidney size, we excluded children with anatomical abnormalities, i.e., hydronephrosis, VUR, renal scarring, major congenital malformations, chronic disease, UTI, and renal failure. K Mishra et al found that the mean CKV was significantly lower in SGA newborns (13.85 ± 4.02 cm^3) compared to AGA infants (16.88 ± 4.53 cm^3) ($p<0.001$) (15). Similarly, Giapros V et al reported that twin SGA infants born prematurely were unable to achieve catch-up in KL in the first 24 months of life (16).

Schmidt et al studied kidney growth in premature children and found that they had smaller kidneys compared to mature children at all ages (0, 3, 18 months) without any significant catch-up growth (17). Therefore, preterm/post-term children and those who were small/large for gestational age were also excluded to remove the effect of extreme weight differences related to birth weight. Aydin Ece et al (1) studied the effect of malnutrition on kidney size in marasmic children. Their study group consisted of 74 malnourished and 47 healthy children. Both groups were statistically similar in

Table 2: Comparison of right and left kidney size between cases and controls

	Cases (N=124)			Controls (N=86)		
Kidney Parameters	**Right Kidney**	**Left Kidney**	**p-value**	**Right Kidney**	**Left Kidney**	**p-value**
Length; Mean±SD (mm)	55.27±9.01	56.57±9.55	0.271	60.18±7.29	62.29±7.52	0.064
Width; Mean±SD (mm)	26.67±3.92	27.39±4.58	0.185	26.59±4.63	27.17±4.83	0.423
Depth; Mean±SD (mm)	28.42±4.57	29.34±4.64	0.117	26.16±4.26	26.8±4.31	0.329
Kidney Volume; Mean±SD (cm^3)	22.57±6.70	24.32±9.13	0.087	22.56±8.28	24.5±9.27	0.150
Relative Kidney Volume; Mean±SD (cm^3)	3.20±1.31	3.49±1.47	0.098	1.86±0.55	2.01±0.56	0.081
Kidney Volume/Body Height Ratio; Mean±SD (cm^3/cm)	0.30±0.11	0.32±0.12	0.099	0.25±0.07	0.28±0.08	0.069
Kidney Volume/BSA Ratio; Mean±SD (cm^3/m^2)	59.5±22.11	64.24±23.41	0.102	42.2±11.51	45.6±12.03	0.060

Table 3: Comparison of various kidney size parameters between cases and controls

	Right Kidney			Left Kidney		
Kidney Parameters	**Cases (N=124)**	**Controls (N=86)**	**p-value**	**Cases (N=124)**	**Controls (N=86)**	**p-value**
Length; Mean±SD (mm)	55.27±9.01	60.18±7.29	0.000	56.57±9.55	62.29±7.52	0.000
Width; Mean±SD (mm)	26.67±3.92	26.59±4.63	0.893	27.39±4.58	27.17±4.83	0.738
Depth; Mean±SD (mm)	28.42±4.57	26.16±4.26	0.000	29.34±4.64	26.8±4.31	0.000
Kidney Volume; Mean±SD (cm^3)	22.57±6.70	22.56±8.28	0.992	24.32±9.13	24.5±9.27	0.889
Relative Kidney Volume; Mean±SD (cm^3)	3.20±1.31	1.86±0.55	0.000	3.49±1.47	2.01±0.56	0.000
Kidney Volume/ Body Height Ratio; Mean±SD (cm^3/cm)	0.30±0.11	0.25±0.07	0.001	0.32±0.12	0.28±0.08	0.001
Kidney Volume/ BSA Ratio; Mean±SD (cm^3/m^2)	59.5±22.11	42.2±11.51	0.000	64.24±23.41	45.6±12.03	0.000
KIDNEY PARAMETERS	**Cases (N=124)**		**Controls (N=86)**		**p-value**	
Combined Kidney Volume; Mean±SD (cm^3)	46.89±17.46		47.06±17.31		0.945	
Combined Relative Kidney Volume; Mean±SD (cm^3)	6.45±2.63		3.87±1.09		0.000	
Combined Kidney Volume / Body Height Ratio; Mean±SD (cm^3/cm)	0.62±0.22		0.53±0.15		0.001	
Combined Kidney Volume/ BSA Ratio; Mean±SD (cm^3/m^2)	123.7±44.53		87.8±23.05		0.000	

Table 4: Linear correlation coefficients (r) of kidney size with anthropometric measurements in cases and controls

Kidney parameters	Cases (N=124)			Controls (N=86)		
	Body Weight	Body Length	BSA	Body Weight	Body Length	BSA
Right Kidney Length	0.366	0.433	0.412	0.620	0.629	0.632
Right Kidney Width	0.382	0.352	0.380	0.363	0.432	0.399
Right Kidney Depth	0.267	0.230	0.261	0.662	0.722	0.696
Left Kidney Length	0.347	0.426	0.395	0.699	0.706	0.710
Left Kidney Width	0.284	0.226	0.266	0.499	0.552	0.530
Left Kidney Depth	0.312	0.261	0.300	0.618	0.655	0.641
Combined Kidney Volume	0.415	0.400	0.422	0.689	0.733	0.718
Combined Relative Kidney Volume	-0.416	-0.298	-0.381	NS	NS	NS
Combined Kidney Volume/Body Height Ratio	NS	NS	NS	0.405	0.448	0.429
Combined Kidney Volume/BSA Ratio	-0.214	-0.232	-0.233	NS	NS	NS
All 'r' value shown are significant as p-value <0.05, NS = non-significant						

terms of age and sex but malnourished children had significantly lower weight, height, BMI, BSA, MUAC and skin-fold thickness compared to healthy subjects ($p<0.001$). There were no significant differences in anthropometric parameters between male and female malnourished children ($p>0.05$). These findings are almost similar to our results. In the present study, KL was significantly lower in malnourished child compared to healthy controls, but no difference was seen in renal width, CKV between the two groups. In a study by Aydin Ece et al, malnourished children had significantly lower KL, parenchymal width, and CKV compared to healthy controls (1).

According to Pantoja ZR et al., obese patients had significantly larger KL compared to normal-weight patients ($P<0.01$) (18). In our study, renal depth, combined RKV, CKV/body height ratio, and CKV/BSA ratio were significantly higher in malnourished children compared to healthy controls. Similarly, Aydin et al found that combined RKV and renal volume/BSA ratio of malnourished children was significantly higher compared to the control subjects. However, there was no difference in depth of right kidney, width of both left and right kidneys, and mean CKV/body height ratio between malnourished children and control subjects (1). Morrison et al showed higher relative kidney weight in malnourished children on autopsy (14).

All parameters of the right and left kidneys in cases and controls were similar in the present study. A review of the literature showed conflicting results related to right and left kidney size. However, most of the studies investigating Indian children have reported similar results (6,7,9) except one study (8). In most of the studies (2,19-22) conducted outside India, the left KL was more than the right KL while one study reported different results (23). In a Turkish study by Aydin Ece et al (1), all measurements of the left kidney were larger than those of the right kidney in healthy controls; in this study, the length, depth, width, parenchymal width and volume of the left kidney were larger than those of the right kidney in malnourished children.

The present study found no difference in kidney size according to gender in healthy and malnourished children. Although body proportion and rate of general somatic growth are strikingly different between boys and girls, their KLs did not display significant difference in most of Indian children studies (6-9).

Controversy exists concerning the effect of gender on kidney size. Some foreign studies showed boys had larger kidneys compared to girls (2,20,24) while some other studies found no gender differences (21,22,25). Aydin et al (1) observed no inter-gender difference in kidney size in healthy subjects but male malnourished children had significantly higher left kidney depth, width, volume and relative volume compared to their female counterparts. Schmidt et al reported that boys had significantly larger kidney volumes and larger relative volumes at 0 and 3 months, but not at 18 months of age, compared to girls (17). It is well known that renal size is related to age, weight, and height. A number of studies assessed renal size and volume and their correlation with somatic parameters in children (1,2,7-9,21,24-26). Kidney length followed by renal volume is most studied parameters related to renal size. In the present study, kidney sizes had a significant correlation with body weight, height, BSA in both malnourished and healthy children. In malnourished children, right (r=0.433) and left (r=0.426) KL were best correlated with height followed by BSA (right r=0412, left r=0.395). In healthy children, right KL (r=0.629) was best correlated with body height followed by BSA (r=0.632) while the left KL (r=0.710) was best correlated with BSA compared to height (r=0.706). CKV was best correlated with BSA in malnourished children (r=0.422) but in healthy children it was best correlated with body height (r=0.733). RKV and CKV/BSA ratio were negatively correlated with body weight, height and BSA in malnourished child.

Similar to our study, Aydin et al observed significant correlation between kidney sizes and anthropometric measurements in malnourished children and healthy children. KL was best correlated to body height (r=0.487) followed by body weight (r=0.467) in malnourished children while it was best correlated with weight (r=0.768) followed by body height (0.745) in healthy controls. CKV was best correlated with body height in both groups. RKV had a negative correlation with weight, MUAC and skinfold thickness, but not with height or age of malnourished children (p>0.05). In their study, the authors observed stronger correlations between kidney sizes and anthropometric measurements in healthy control subjects than malnourished children (1), which was similar to our results. Aydin et al concluded that malnourished children had smaller kidney sizes, and body height was the main determinant of the kidney length and volume (1).

In the present study, BMI showed no correlation with kidney length and volume in malnourished children while it had a weak correlation with kidney volume in healthy children. Kim et al found much weaker correlations between BMI and KL or volume compared to height and weight (2). Dinkel et al suggested that determination of renal volume would allow an appropriate estimation of the parenchymal mass in the absence of gross morphological abnormalities such as hydronephrosis, which correlated well with BSA and body weight. (21). Ganesh et al evaluated the correlation between the mean KL and various somatic variables. The results showed that the mean KL had the strongest correlated with height followed by upper thigh (femur) length and chest circumference (9). However, Haugstredts et al reported that KL was best correlated with BSA (25). In a study by Kim et al, bilateral KLs showed the strongest correlation with height and renal volume had the strongest correlation with body weight (2).

Otiv A et al studied the renal size in 1000 normal Indian children aged 1 month to 12 years using sonography. KL had the strongest correlation with body height (r=0.9) and BSA (r=0.89), while renal volume was best correlated with BSA (6). Kim BW et al found that height was the most significant contributing factor to renal growth ($R2=0.636$, $P<0.001$) and concluded that KL was a surrogate to organ growth (26). Schmidt et al studied the effect of lean body mass on kidney size in healthy 10-year-old children and reported that it was the strongest predictor of kidney volume, overruling height, weight and BSA (24).

Conclusion

Malnourished children had smaller kidney lengths than their healthy counterparts. However, RKV, renal volume/BSA ratio and renal volume/body height ratio were higher in malnourished children compared to controls, which could be due to the significant lower weight and height in cases than controls. Kidney size differences of malnourished children should be kept in mind while assessing their renal ultrasound imaging to avoid unnecessary invasive investigations.

A limitation of this study was that it was done in North India. A multicentre study in other regions of the country might improve the precision of the estimates and the generalizability of the results. Another limitation was that renal function measurements were not evaluated in healthy controls and we only evaluated normal kidneys using ultrasound. The potential long-term consequences of poor renal growth, such as increased risk of hypertension or tendency to develop chronic renal insufficiency were not assessed in the present study. More longitudinal studies are needed to investigate these consequences in malnourished children.

Acknowledgments
We are thankful to guardians of children who participated in the study and those who helped us in data collection.

Conflict of Interest
The author declares no conflicts of interest.

Financial Support
The author declares no financial support.

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