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Functional Abnormalities of the Kidney and Urinary Tract in Malnourished Children in Zagazig University Hospitals

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ABSTRACT

Background: Obstructive uropathies, tubular diseases, and chronic kidney disease (CKD) are among the many renal disorders that malnutrition is frequently associated with. However, there is little information about the frequency of renal and urinary tract issues in underweight kids. **Objective:** The aim of the current study was to identify the anomalies of the functioning kidney and urinary tract in hospitalized children with malnutrition.

Patients and methods: A cross-sectional study was conducted on 48 kids diagnosed to have malnutrition in the Pediatric Nutrition Unit at Zagazig University Hospitals, from February 2019 to May 2020. All cases underwent thorough history taking, physical examinations, and laboratory tests to detect functional abnormalities including serum NGAL, eGFR, blood urea, serum creatinine, serum electrolytes and also urine analysis. Abdominal ultrasound was done for all patients to detect any structural abnormalities.

Results: Anthropometric measurement of our patients showed that there were distributions of weight, height, chest, head, and mid-arm circumferences as 6.96 (SD 2.21), 73.41 (SD 13.1), 44.9 (SD 4.67), 44.47 (SD 4.89) and 12.24 (SD 1.62), respectively. overall mean serum NGAL was 183.8 (SD 8.63) with 62.5% abnormal, while overall mean GFR was 65.89 (SD 29.8) ml/min/1.73m2 with 60.4% abnormal, 29.2% were abnormal regarding urea, 47.9% abnormal regarding creatinine, 4.2% had pus in urine analysis and overall, 62.5% had functional outcome. Seven cases with structure abnormality were found in our study, 1 case with nephrocalcinosis and 6 cases with echogenic kidney and overall, 14.6% had structural abnormalities. **Conclusion:** Children who were underweight frequently had functional renal problems. Functional malnutrition is linked to disorders of the kidney and urine system.

Keywords: Functional kidney, Malnutrition, Children, Cross sectional study, Zagazig University.

INTRODUCTION

The term "malnutrition" covers a wide range of conditions characterized by inadequate food intake and/or increased catabolic losses. It has been applied to the undernutrition of Marasmus and Kwashiorkor seen in developing nations. In the industrialized world and increasingly in the developing world, it has also been used to treat obesity, a condition brought on by overeating. It has also been used to describe states of insufficient food intake that are associated with shortages of certain vitamins and minerals [(1)].Children who are seriously unwell frequently experience malnutrition, especially those who are younger than 2 years old. As indicated by higher morbidity, mortality, and length of stay, it is linked to poor outcomes (LOS). Malnutrition is still one of the world's main public health issues, especially in southern Asia and sub-Saharan Africa [(2)].

Children who have functional kidney abnormalities face serious issues. Recurrent urinary tract infections, growth failure, edoema, proteinuria, and hematuria are possible outcomes. These conditions necessitate hospitalisation for diagnostic procedures and medicinal or surgical therapy. Some congenital anomalies, such as the posterior urethral valve, primary vesicoureteral reflux, and hypo-dysplastic/multi-cystic diseases, can lead to end-stage renal disease (ESRD) and chronic kidney disease (CKD). Dialysis or a kidney transplant are necessary treatments for certain illnesses [(3)].

The main issues in the pediatric age group are anatomical and functional urinary tract abnormalities [(4)]. Proteinuria, edema, development failure, recurrent infections, and hematuria may arise from these, necessitating hospitalization for research and medical or surgical treatment [(5,6)]. Malnutrition has been linked to a number of renal illnesses, either directly or indirectly through secondary kidney issues or initial dietary deficiencies. Most malnutrition in impoverished nations is primary, although hospitalized children have been found to have a wide range of secondary malnutrition prevalence (6%–51%) [(7,8)].

It's critical to discover reversible causes of advanced chronic renal disease in malnourished children as well as kidney disease and anomalies the urinary system. It can be difficult to tell when renal problems are brought on by hunger or vice versa. While the history and outward symptoms of kidney diseases include obstructive uropathies, functional problems like hypoplastic kidneys, tubular anomalies, and low-grade vesicoureteral reflux are more specific reflux can occasionally go undetected and manifest as malnutrition and growth failure [(5)]. **Van De Voorde *et al.*** [(3)] have demonstrated that malnutrition is a common factor in other renal conditions including

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CKD, obstructive uropathies, and tubular disorders (like renal tubular acidosis and Bartter syndrome).

The aim of the current study was to identify the anomalies of the functioning kidney and urinary tract in hospitalized children with malnutrition.

PATIENTS AND METHODS

A cross-sectional study was conducted on 48 kids diagnosed to have malnutrition in the Pediatric Nutrition Unit at Zagazig University Hospitals, from February 2019 to May 2020.

Inclusion criteria: Aged from 2 to 40 months, and both sexes were included. Patients met the criteria for acute malnutrition, which included weight for height, failure to thrive, or bilateral pitting edema, and z-score <-3, mid arm circumference z-score <-3 [9]. Patients admitted for the first time at the Nutrition Unit of Zagazig University Hospitals.

Exclusion criteria: Any kids with known kidney issues or symptomatic congenital kidney and urinary tract anomalies (CAKUT), as well as functional abnormalities (CKD, glomerular or tubular disorders, urinary tract infections), were disqualified. Children with malnutrition who were readmitted for a variety of issues or who left before the lab workup was finished were omitted.

All these patients underwent complete history taking and physical examination, By calculating serum Neutrophil Gelatinase-Associated Lipocalin, the functional state of the kidneys was evaluated (NGAL), Samples for NGAL assay were obtained from patients and separation of plasma was done by centrifugation: 1500xg at 4°C for 15 min. Plasma was then taken out and put into a new polypropylene tube. The transferred plasma was again centrifuged at 1500xg for 15 minutes at 4°C to remove any traces of white blood cells. Human NGAL ELISA Kit, DPG NGAL, Diapharma Group, West Chester, USA), glomerular filtration rate (eGFR), and urinalysis for signs of proteinuria, hematuria, pyuria, and culture were used to measure NGAL in research. The Schwartz formula was used to calculate the estimated glomerular filtration rate (eGFR) [eGFR= 0.413 × (height in cm/serum creatinine in mg/dl)] (Schwartz et al., 2009), with k= 0.413, as suitable for standard creatinine. Functional renal status was divided into normal and subnormal categories based on eGFR, with eGFR less than 90 ml/min per 1.73 m2 being categorised as subnormal. Based on the degree of the eGFR drop, four further subgroups of subnormal eGFR were identified (60 – 90 ml/min per 1.73 m2 is mildly decreased, 30-59 ml/min per 1.73 m2 is moderately decreased, 15-29 ml/min per 1.73 m2 is severely decreased and less than 15 ml/min per 1.73 m2 is renal failure).

Laboratory procedures were preformed including complete blood count (CBC), creatinine (Cr) (by Jaffey's method), urea and serum electrolytes (Na, K, Ca, Mg and Ph) .Kidney size, echogenicity, hydronephrosis, hydroureter, and cysts or stones in the kidneys and urinary system were all examined by ultrasonography (US) of the kidneys, ureter, and bladder (KUB).

Functional abnormality was characterized as aberrant NGAL levels in the blood and low GFR (<90 ml/min/1.73 m2) or urinary tract infection, tubular, glomerular abnormalities (such proteinuria), etc.

On pre-made tables, information comprising sociodemographics, observable consequences like pneumonia and diarrhea, physical findings like anthropometry, edema, and MUAC (mid upper arm circumference), as well as laboratory results, were gathered.

Ethical Consideration:

The protocol for this study was approved by the Institutional Review Board [IRB] and the Local Ethics Committee at the Faculty of Medicine, University of Zagazig. Written informed consent was obtained from parents or guardians of all participants. This study was executed according to the code of ethics of the World Medical Association (Declaration of Helsinki) for studies on humans.

Statistical Analysis

Microsoft Excel software was used to code, enter, and analyze historical data, basic clinical examinations, laboratory investigations, and outcome measurements. Statistical Package for Social Sciences (SPSS, version 20.0) program was then used to import the data and perform the analysis. Qualitative data were defined as numbers and percentages. Quantitative data were tested for normality by Kolmogorov-Smirnov test. Normal distribution of variables was described as mean and standard deviation (SD), and non-parametric data was summarized as median and range.

RESULTS

Table 1 summarizes age and gender data of the studied patients.

Table (1): Age and sex distribution among studied groups.

Variable		**Age/ months**	
Mean ± SD		15.89 ± 9.87	
Median (Range)		14.5 (2-40)	
Variable		**N**	**%**
Sex	**Male**	26	54.2
	Female	22	45.8
	Total	48	100

Table 2 summarizes weight, height, head circumference, chest circumference and midarm circumference.

Table (2): Anthropometric measures distribution among studied group.

Variable	Mean± SD	Median (Range)
Weight (kg)	6.96 ± 2.21	7.1 (2.2-11.1)
Height (cm)	73.41 ± 13.1	76.5 (51-94)
Head circumference (cm)	44.9 ± 4.67	45.0 (34-52)
Chest circumference (cm)	44.47 ± 4.89	45.0 (31-53)
Mid arm circumference (cm)	12.24 ± 1.62	12.5 (8.5-15.3)

Table 3 shows that the majority of patients presented with FTT alone. Regarding complications, 12.5% and 18.8% had chest infection and gastroenteritis respectively.

Table (3): History and complication distribution among studied patients.

Variable		N	%
History	**FTT**	43	91.5
	FTT + CP	1	2.1
	Nutritional edema	4	8.3
Complications	**Chest infection**	6	12.5
	Gastroenteritis	9	18.8
	No	33	68.7

Table 4 summarizes the laboratory results of the studied patients.

Table (4): Laboratory distribution among studied group.

Variable	Mean ± SD
HB (g/dL)	12.03 ± 1.58
PLT (10^3/mm^3)	283.25 ± 29.85
TLC (10^3/mm^3)	7.27 ± 1.7
Na (mEq/L)	139.37 ± 5.48
K (mg/dL)	4.64 ± 0.85
Ca (mg/dL)	8.66 ± 0.85
Mg (mg/dL)	2.35 ± 0.44
Ph (mg/dL)	2.66 ± 0.85
Urea (mg/dL)	36.29 ± 2.9
Creatinine(mg/dL)	0.65 ± 0.15
GFR (mL/min/1.73m^2)	65.89 ± 9.8

Table 5 summarizes serum NGAL and functional abnormalities of the studied patients.

Table (5): Serum NGAL and functional abnormalities parameters distribution.

Serum NGAL (ng/mL)			
Mean ± SD		183.8 ± 8.63	
Variable		**N= 48**	**%**
Functional abnormalities	**Absent (<100 ng/mL)**	18	37.5
	Present (>100 ng/mL)	30	62.5

Table 6 summarizes the results of the renal function test.

Table (6): Distribution of the studied patients according to renal function test.

Parameter		N= 48	%
Urea	**Normal**	34	70.8
	Abnormal	14	29.2
Cr	**Normal**	25	52.1
	Abnormal	23	47.9
GFR	**Normal**	19	39.6
	Abnormal	29	60.4
Urine analysis	**Free**	46	95.8
	Pus >100	2	4.2

Table 7 summarizes total structural abnormality of the studied patients.

Table (7): Distribution of the studied patients according to structure abnormalities.

Variable		N= 48	%
Pelviabdominal US	**Free**	41	85.4
	Nephrocalcinosis	1	2.1
	Echogenic kidney	6	12.5

DISCUSSION

The age range was 15.89-9.87, with a minimum age of 2 and a maximum age of 40 months and sex distributed as male 54.2% and female 45.8%. This goes in agreement with **Heird** [10].

Anjum *et al.* [9] examined the incidence of anatomical and functional urinary tract abnormalities in 78 children who were extremely undernourished. The majority of children (79.48%) were under 2 years old, with the mean age being 18 months and 15.53 months.

Height, weight, chest, head, and mid-arm circumferences were also measured allocated according to our patients' anthropometric measurements as 6.96, 73.41, 44.9, 44.47 and 12.24, respectively. This finding agrees with **Shaaban *et al.*** [11]**.** Also, **Anjum *et al.*** [9] found that typical height and weight were 5.69 kg and 68.52 cm, respectively.

In our investigation, the weight to height ratio was abnormal in 100% of the participants. 91.5% of the population were FTT, and 8.3% of them had nutritional edoema. **Anjum *et al.*** [9] discovered that 82% of children with SAM had marasmus, while 18% of children had edematous malnutrition.

The overall test results for 48 malnourished children are displayed. Mean values of urea and creatinine were 36.29 and 0.65 mg/dl, respectively. **Anjum *et al.*** [9] showed laboratory measurements in 78 SAM kids. Mean values of urea and creatinine were 29.0 and 0.68 mg /dl respectively.

The average hemoglobin in our study was 12.03±1.58 G/dl. Mean sodium level was 139.37. The average potassium level was 4.64 while the average calcium level was 8.66, Magnesium levels averaged 2.35 and phosphorus levels averaged 2.66. **Anjum *et al.*** [9] revealed that 9 (10%) kids and 8 (10%) kids had hyponatremia (11.5%) had low potassium. Metabolic acidosis, or 10.8% of patients had abnormally low serum bicarbonate levels, and 12.8% had excessive bicarbonate levels (metabolic alkalosis) in 2 (2.5%) cases.

In our study, we depend on serum NGAL as a sensitive biomarker of acute kidney injury to detect functional abnormalities of the kidney and we found that overall mean serum NGAL was 183.8 with 62.5% abnormal, while overall mean GFR was 65.89 ml/min/1.73m2 with 60.4 abnormal, 29.2% were abnormal regarding urea, 47.9% abnormal regarding Cr and overall 62.5% had functional outcome. Seven cases with structure abnormality was found in our study, one case with nephrocalcinosis and 6 cases with echogenic kidney (4 cases grade I and 2 cases grade II) and overall 14.6% had structural abnormalities.

Anjum *et al.* [9] discovered that 57 (73%) had structural (n=46, 80.7%) or functional (n=7) problems (n=11, 19.3%) whereas 21 (26.92%) The structural and functional status of youngsters was normal. The average eGFR was 71.45 ml/min/1.73m2 and it was normal (>90 ml/min/1.73m2) in 21 (27%) children. Based on eGFR, the severity of functional renal impairment is 27 (34.61%) children's eGFR ranged from 30 to 59 ml, although 12.38% of them had substantial functional impairment (GFR<30 ml/min/1.73 m^2).

In the study of **Gopal *et al.*** [12], it was determined that UTI was discovered in 11.34% of malnourished children and that there was no difference in incidence across different levels of malnutrition.

In our study, we detect 2 cases of UTI with 4.2 % of the malnourished children. **Ardissino *et al.*** [13] said it is unexpected that more than 80% of children have functional renal impairment. There are several things that could account for this. The most significant is that, even despite the fact that nephron development is complete by 35–36 weeks, glomerular and tubular development lasts until the age of 18 months, and GFR keeps increasing until adult levels by the age of two years. Participants using techniques for assessing serum creatinine and GFR, concomitant illnesses (20–52%), dehydration (52%), low birth weight and preterm histories (12%), and dehydration are additional factors that may contribute to subnormal GFR.

Our study showed no significant correlation except for significant negative correlation between serum NGAL and GFR. Group with abnormalities was significantly associated with higher serum NGAL, urea, creatinine and lower GFR.

Multivariate logistic regression revealed that the only significant independent predictor was GFR.

After stabilizing from acute kidney injury, investigations for structural and functional abnormalities of the urinary system may have been conducted difficulties, according to findings of substantial infection complications, hematological abnormalities, and electrolyte abnormalities [12].

In our analysis, we found 6 cases complicated by chest infection (12.5%) and 9 cases complicated by acute gastroenteritis.

Anjum *et al.* [9] detected in children with malnutrition, the urinary system has a high a significant percentage of anatomical anomalies and a frequency of functional problems.

In the course of our research, we discovered that the malnourished kids tended to have more functional kidney abnormalities and less structural abnormalities.

Limitations of the study are a small sample size, a lack of follow-up after the patient has stabilized, and the treatment of infections and dehydration. The findings from this study, which involved a single location, might not be applicable to other situations. Yet, we firmly feel that our findings are significant for identifying structural and functional problems in malnourished children. As we lack follow-up information, it is therefore challenging to determine if this subnormal GFR is a sign of CKD or merely a temporary decline in renal function brought on by one or more reversible causes, such as dehydration and sepsis.

CONCLUSION

Prior malnutrition is common among infants and children admitted to hospitals, as evidenced by low weight and reduced levels of plasma proteins on admission. Combined clinical, anthropometric and laboratory parameters are needed for appropriate nutritional assessment of these patients. We discovered that children who were underweight frequently had functional renal problems. So, we can draw the conclusion that functional Malnutrition is linked to disorders of the kidney and urine system.

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