

Nutritional Assessment of Children with Nephrotic Syndrome Attending a Tertiary Health Facility: A Case Control Study

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ABSTRACT

Introduction: There is increased risk of protein energy malnutrition in children with nephrotic syndrome. Children with nephrotic syndrome are prone to both macro and micronutrient deficiency and are at risk of poor growth, muscle mass depletion and cognitive impairment. There are few works on assessing the nutritional status of children with nephrotic syndrome in Nigeria and sub-Saharan Africa.

Objectives: To assess the nutritional status of children with nephrotic syndrome attending the Nephrology Clinic of the Lagos State University Teaching Hospital, Ikeja, Lagos.

Method: A prospective, case-control study carried out between October 2017 and April 2018. Children with diagnosis of nephrotic syndrome were enrolled. The controls were apparently healthy children who presented to the outpatient general paediatric clinic for minor illnesses. Anthropometric parameters such as weight, height, waist to hip circumference were taken and weight to height, body mass index, weight to age, height to age were calculated. Socio-demographic information such as age, sex, religion of parents, social class were documented. Serum albumin levels were taken as well.

Result: A total of 61 subjects with nephrotic syndrome were recruited. 41(67.2%) of studied subjects were males and 20(32.8%) were females with male to female ratio of 2:1. The median age of

studied subjects was 72 months (80.7±42.2 months, mean ± SD). For the controls, a total of 27 children were recruited. 20 (74.1%) were males with a male to female ratio of 1.3:1 and the mean age was 80±46.4 months. The mean weight of the studied subjects was 25.13±10.45kg with a median of 23kg and in the controls, mean weight of all was 26.06±11.25kg. The mean height of subjects with nephrotic syndrome was 119.1±22.1cm and in control group 123±25.1cm. The mean body mass index in all subjects was 17.1±2.6kg/m² while in control group 16.4±2.23kg/m². Weight for age(WFA) Z score assessment was done in studied subjects not more than 10 years (120 months). 2 (4.08%) had low weight for age, in 42 (85.7%) the WFA was normal and 5(10.2%) were overweight. Compared to the controls with maximum age of 120 months (21 subjects), all except one overweight subject had normal weight for age z-score. Height for age in 7 subjects (11.5%) was <-2 to -3 which depicts stunting. 2 subjects (3.27%) were very stunted with height for age values of <-3. The remaining subjects (85.2%) had normal height for age. All control cases had normal height for age. There was a positive relationship between the use of steroid and stunting (p= 0.004). Waist to Hip ratio values between the two groups (Cases and controls) showed that the cases were more likely to have a high value compared with the controls (p=0.001).

Conclusion: Children with nephrotic syndrome are indeed prone to growth impairment with associated risk of cardiovascular morbidities. Careful attention to use of simple measurements can promptly identify

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the risk and disease modifying treatments can be instituted early.

INTRODUCTION

Nephrotic syndrome is a renal disease characterized by constellation of symptoms primarily due to increased glomerular permeability.¹ The incidence of nephrotic syndrome is 2-7 per 100,000 children in developed countries.² In Nigeria, nephrotic syndrome is a common renal manifestation in children. In a study by Ladipo et al³ in Lagos, Nigeria, the commonest cases of children admitted for renal diseases was nephrotic syndrome which accounted for 22.8% of admissions for renal abnormality.

There is increased risk of protein energy malnutrition in children with nephrotic syndrome.⁴ Children with nephrotic syndrome are prone to both macro and micronutrient deficiency and are at risk of poor growth, muscle mass depletion and cognitive impairment.⁵ Nutritional impairment in nephrotic syndrome occurs from the disease process, poor dietary intake and steroid therapy. It is a major contributor to increased morbidity and mortality in affected children.

Nutritional assessment and maintenance of adequate nutrition is essential in children with nephrotic syndrome. Nutrition affects growth, neurocognitive and pubertal development.^{6,7} The importance of assessment of nutritional status of children with renal diseases by paediatric nephrologists was reported by Montalvo-Vilvar and co-researchers.⁸ Nutrition is a modifiable risk factor for mortality and should be routinely monitored in children with renal abnormalities. The authors assessed the nutritional status of 214 subjects aged two to sixteen years with renal diseases at National kidney and transplant Institute in Philippines. 109(50.9%) of the subjects had nephrotic syndrome. Subjects between 2 and 9 years that had malnutrition and were stunted mostly had nephrotic syndrome.

The recommended measurements for nutritional assessment in children with renal diseases include review of dietary intake, assessment of serum albumin, height or length (and SD score), estimated dry weight, weight/height index, skin fold thickness, mid upper arm circumference, and head circumference in children aged three years and below.⁴

With careful search, no report has been published on nutritional assessment of children with nephrotic syndrome. This study aimed to assess the nutritional assessment of children with nephrotic syndrome that attends the nephrology clinic of a tertiary institution in Lagos state, Nigeria using some of the recommended tools. The result of this study will hopefully reiterate the need for routine nutritional assessment in children with nephrotic syndrome for early identification, treatment and counselling on nutritional rehabilitation that can contribute to reduction in mortality.

SUBJECTS AND METHODS

The present study was a prospective, case control study. The study was carried out at the nephrology clinic and outpatient unit of Lagos State University Teaching Hospital, (LASUTH) Ikeja, Nigeria. LASUTH is a major referral centre from both government and private hospitals within Lagos state and its environs. The nephrology unit in the department of paediatrics in LASUTH is an established unit with paediatric nephrologists.

The study was carried out between the period of October 2017 to April 2018. It involved questionnaires to ascertain biodata and sociodemographic factors of the subjects. Anthropometric data taken were estimated dry weight, height, blood pressure, waist and hip circumference. Body mass index, weight z score, height z score, weight for age, height for age, BMI for age and waist to hip ratio were all calculated. Serum albumin was also measured.

Eligible subjects were children with nephrotic syndrome diagnosed using clinical and laboratory (generalised oedema, serum protein creatinine ratio greater than 2.0, dipstick urine protein of at least 3 pluses, serum albumin less than 2.5g/dL and elevated triglyceride of greater than 200mg/dL. The controls were apparently healthy children that visited the hospital for a minor complaint.

Parental socio-economic stratification was carried out using Oyediji classification.⁹ It was determined using maternal education, maternal occupation, paternal education and paternal occupation. Classes 1 and 2 were classified as upper, 3 as middle and 4 and 5 as lower social classes.

Weight for age (WFA) assessment was done for subjects 10 years and below. Low weight for age

was classified according to WHO with Z score of <-2.0. Normal and overweight children were classified as Z score between -2.0 and +2.0 and >+2.0 respectively. Height for age (HFA) was assessed in all subjects. Subjects with HFA Z score <-3 were classified as very stunted and those <-2 to -3 as stunted. Wasting was classified using BMI for age in all subjects with Z score <-2 as wasting, between -2 and +1 as normal, >+1 to +2 as overweight, +2 to +3 as obese and 3+ and above as severely obese.

Weight and height of eligible subjects were measured using a weighing scale. Body weight was recorded to the nearest 0.1kg with subjects' barefoot and wearing light clothing. The measured weights were the dry weights. This was clinically assessed in euvoaemic subjects in the absence of oedema. The height was measured with subjects standing barefoot and looking forward. The shoulders, buttocks and heels touched the vertical surface of the stadiometer and the head of each subject was in a Frankfurt plane. It was ensured that the measuring arm rested on the crown of the head and height value was read to the nearest 0.1cm. Waist circumference was measured using an inelastic tape measure in subjects two years and above. Waist circumference land mark was midpoint between the edge of the iliac crest and the lower margin of the last palpable rib. Hip circumference was measured at the largest circumference of the buttocks. Steps taking were according to WHO recommendation.¹⁰ Waist to hip ratio was subsequently calculated in subjects two years and above.

Analysis was done using Statistical Package for Social Sciences software 20.0 version. Patients' demographics will be represented as frequency and percentages. Tables and figures were used to represent those variables as appropriate. Continuous variables were summarized using mean and standard deviation while non-parametric data was summarized using median. Comparison between qualitative data was done using chi square or Fisher exact test. Comparison between numeric parameters like social groupings and anthropometric data were analyzed using Pearson correlation. BMI classification and social groupings were analyzed using ANOVA. HFA classification and duration on steroid use grouping was done using Kruskal Wallis. Probability values less than 0.05 were considered statistically significant.

RESULTS

A total of 61 subjects with nephrotic syndrome were recruited. 41(67.2%) of studied subjects were males and 20(32.8%) were females with male to female ratio of 2:1. The minimum and maximum age of subjects was 19 months and 192 months respectively. The median age of studied subjects was 72 months (80.7±42.2 months, mean±SD).

For the controls, a total of 27 children were recruited. 20 (74.1%) were males with a male to female ratio of 1.3:1. The minimum and maximum age of the controls was 16 months and 168 months respectively. The mean age was 80±46.4 months.

Socioeconomic classes of subjects with nephrotic syndrome according to Oyedeji classification showed that majority of studied subjects were in the upper class 1 and 2(52.4%). 37.7% of caregivers were in the middle class while 9.8% belongs to the lower socioeconomic class.

Majority of the caregivers' ethnicity was Yoruba (72.1%). A total of 14(23%) of subject hail from Igbo tribe. Other minority tribe represented were Urhobo, Edo and Cotonou in the city of Benin Republic.

A higher percentage of subjects had diagnosis of nephrotic syndrome made between 13 and 60 months (49.2%). In 25 subjects (41%) the diagnosis was made between 61 and 120. In 3 subjects each (4.9%), the diagnosis was in subjects less than 12 months and above 120 months respectively.

A larger percentage of the studied subjects were on steroid medication (81.9%) compared to 11 subjects (18%) of them that were not on steroid medication. Amongst subjects on steroid medication, 22(14.2%) have been on the medication for at most one year while 85.8% have had it for over one year. In all, 52 (85.2%) had steroid sensitive NS. 6 (9.8%) and 2 (3.3%) had steroid resistant and frequent relapse NS respectively.

The mean weight of the studied subjects was 25.13±10.45kg with a median of 23kg. Mean weight for boys and girls is 25.6±10.6kg and 24.1±10.3kg respectively. In the controls, mean weight of all was 26.06±11.25kg. The mean weight was 25.3±11.3kg and 28.2±11.6kg in boys and girls controls respectively. The mean height of subjects with nephrotic syndrome was 119.1±22.1cm. The mean height for boys and girls were 119.2±21.9cm and 118.9±23.1cm respectively. In the controls, the mean height was

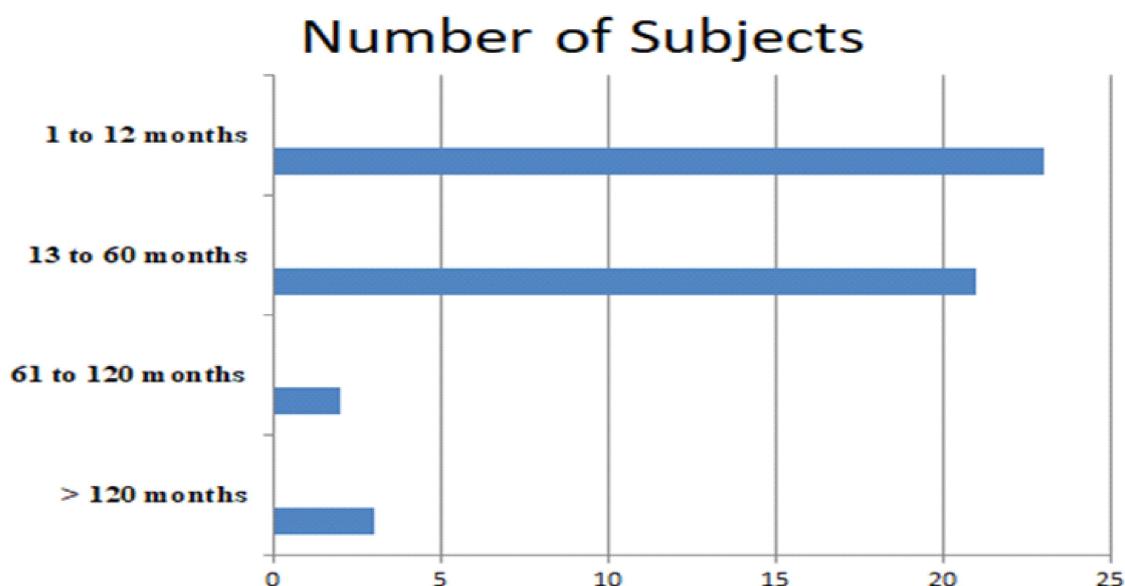


Fig. 1: Duration of steroid therapy in the studied subjects

123±25.1cm. The mean height in boys and girls control subjects was 122.8±26.6 and 126.4±21.8cm respectively.

Mean body mass index in all subjects was 17.1±2.6kg/m². The mean BMI for boys was 17.4±2.39kg/m²; in girls a lower value of 16.5±2.93kg/m² was obtained. In controls, the mean BMI was 16.4±2.23. For boys and girls control subjects, the mean BMI is 16.1±2.16Kg/m² and 17.1±2.38kg/m² respectively.

Weight for age Z score assessment was done in studied subjects not more than 10 years (120 months). 2 (4.08%) had low weight for age, in 42 (85.7%) the WFA was normal and 5(10.2%) were

overweight. Compared to the controls with maximum age of 120 months (21 subjects), all except one overweight subject had normal weight for age z-score. Height for age in 7 subjects (11.5%) was <-2 to -3 which depicts stunting. 2 subjects (3.27%) were very stunted with height for age values of <-3. The remaining subjects (85.2%) had normal height for age. All control cases had normal height for age.

The highest percentage of subjects (40) had normal BMI for age which accounted for 65.6% of studied subjects. 11 (18%) of subjects were overweight while 6(9.8%) were obese. In two subjects each, (3.3%) subjects had wasting and severe obesity. In the controls, 1 subject (3.7%) was

Table 1: Comparison of BMI Z-scoring with the use of steroid in studied subjects

BMI Classification	Steroid Use		Total
	Yes	No	
Wasting	1	1	2
Normal	32	4	37
Overweight	9	3	13
Obese	5	1	6
Severely Obese	2	0	2

BMI: Body Mass Index, $f_x = 4.743$, $p = 0.785$

wasted. Majority (66.7%) had normal BMI for age. 6 (22.2%) and 2 (7.4%) controls were overweight and obese respectively.

49 subjects (80.3%) of subjects are on steroid medication. A higher percentage of subjects have been on steroid for not more than 12 months as shown in figure 1.

In comparing the BMI Z-score classification with the use of steroids, an increase proportion of subjects with obesity were on steroid compared to those not using steroid as shown in table 1. There

was a positive relationship between the use of steroid and stunting as shown in table 2. For subjects on steroid, duration on steroid medication was classified and its relationship with height for age z-score classification is shown in table 3.

All controls had normal height for age compared to the subjects where 7 (11.5%) cases of stunting was depicted in table 4.

In comparing the BMI for age classifications between the cases and the controls, more cases were

Table 2: Relationship between steroid use and Height for age classification of subjects

HFA Classification	Steroid Use		Total
	Yes	No	
Normal	43	7	50
Stunted	5	2	7
Very Stunted	1	0	1

HFA= Height for age; $f_x = 15.182, p = 0.004$

Table 3: Relationship between duration on oral steroid and height for age classification

Duration on steroid (Months)	HFA Classification			Total
	Normal	Stunted	Very Stunted	
1-12	20	2	0	22
13-60	19	2	0	21
61-120 >	1	1	0	2
120	2	1	0	3

HFA= Height for age; $f_x = 27.856, p = 0.06$

Table 4: Comparison of HFA for age in case subjects and controls

HFA Classification	Cases (%)	Controls (%)
Normal	52(85.2)	27(100)
Stunted	7 (11.5)	0(0)
Very Stunted	2 (13)	0 (0)

$f_x = 4.517, p = 0.104$

obese and none in the control had severe obesity as shown in table 5.

Waist to Hip ratio values between the two groups (Cases and controls) showed that the cases were more likely to have a high value compared with the controls as shown in table 6

Serum albumin in subjects with nephrotic syndrome varied between 0.60 to 4.80mg/dL. The mean value is 1.93 ± 0.96 mg/dL. Only 6 subjects with NS had normal serum albumin level and others had hypoalbuminemia at the time of recruitment. In

Table 5: Comparison of BMI for age in case subjects and controls

BMI Classification	Cases (%)	Controls (%)	Total
Wasting	2(3.3)	1 (3.7)	3(3.4)
Normal	37(61.7)	18(66.7)	55(63.2)
Overweight	13 (13)	6(6)	18(19)
Obese	6 (10)	2 (7.4)	8 (9.2)
Severely Obese	2 (3.2)	0 (0)	2 (2.3)

$f_{\chi} = 1.120, p = 0.891$

Table 6: Comparison of waist-hip ratio between the groups (Cases vs Controls)

Subjects	Normal WHR (%)	High WHR (%)	Total (%)
Cases	12 (21.4)	44 (78.6)	56 (%)
Controls	17 (65.4)	9 (34.6)	26

$\chi^2 = 49.514, p = 0.001$

controls, all had normal serum albumin that ranged between 3.59 and 5.12mg/dL with a mean value of 4.35±0.41 mg/dL($f_{\chi} = 59.772, p = 0.001$).

DISCUSSION

Nutritional status is a major determinant of growth and its assessment is essential in children with nephrotic syndrome. A higher risk of poor nutritional status in children with nephrotic syndrome compared with other renal diseases has been documented. Despite this report and the burden of the disease, there is paucity of data on nutritional status in children with nephrotic syndrome.

In the present study, 61 subjects with nephrotic syndrome with 27 controls were recruited. A higher proportion of male in this present study is in keeping with male to female ratio of 2:1 reported by Clark and Barrat.¹¹

The median age at presentation of subjects with NS in the current study was 72 months. Reports have been shown that NS is commoner in children

between the ages of two and six years.^{12,13} A higher proportion of subjects had presentation and diagnosis of NS in the present study. NS has been reported to be commoner in under-5s.¹³

Steroid sensitive NS cases were the most presentation in the present study. Steroid sensitive NS is the commonest form of presentation.¹⁴ The high frequency of relapsing in steroid sensitive NS cases has been reported. In the current study, only 2 subjects (3.28%) had relapse. The fewer cases of relapse compared with a study done in the same region by Esezobor and colleagues¹⁵ is possibly due to the fact that the current study is cross sectional and long-term follow-up is ongoing to see further response to steroid therapy.

Majority of the cases had normal nutritional status (WFA, HFA, BMI for age). This is in keeping with the report by Montalbo-Vilvar et al.⁸ However, the higher occurrence of stunting and obesity in the cases than the controls are worth noting. This finding is commoner in subjects on steroid medication. It is not a surprising finding as these are likely

complications of steroid therapy. This finding further emphasises the need for growth monitoring in children with nephrotic syndrome and those on steroid therapy. Muscle mass depletion and wasting seen in some cases in the present study is also a clinical manifestation of NS.

Abdominal obesity determined by elevated waist to hip ratio is a risk factor for cardiovascular diseases and diabetes. In the present study, a significant proportion of cases had elevated waist to hip ratio compared to the controls. The need for cardiovascular diseases risk and other related illnesses associated with abdominal obesity cannot be over emphasized in children with NS especially those on steroid therapy. In LASUTH, steroid sparing agents are given to frequent relapses and with marked side effects on steroid to avoid the growth impairments following prolong use of the medication.

Hypoalbuminemia is a diagnostic criterion for NS and it's not surprising that majority of the subjects had low albumin levels at the time of recruitment for the present study. Increasing dietary protein has no beneficial effect on serum albumin and can accelerate progression of renal disease.¹⁶ Restriction of protein intake can on other hand result in negative nitrogen balance and malnutrition.¹⁷ Protein diet of 1-2g/Kg body weight per day should be recommended for balanced nutrition and growth.¹⁸

In conclusion, growth impairment is a major challenge in children with nephrotic syndrome. There is need for routine growth assessment, early identification of growth faltering and dietician involvement for nutritional counselling for adequate growth attainment.

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