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Article *in* Asian Journal of Medicine and Health · June 2017

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Demographic, Clinical and Therapeutic Characteristics of Children Aged 0-15 years with Nephrotic Syndrome: A Retrospective Study of the Komfo Anokye Teaching Hospital, Kumasi, Ghana

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Authors' contributions

This work was carried out in collaboration between all authors. Authors RCB, ALB and RKDE designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors KOD and EOA managed the analyses of the study. Author RCB managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJMAH/2017/33270
Editor(s):
(1) Atanu Bhattacharjee, Department of Pharmacognosy, NGSM Institute of Pharmaceutical Sciences, Karnataka, India.
Reviewers:
(1) Gérard Coulibaly, University of Ouagadougo, Burkina Faso.
(2) Rodolfo A. Valtuille, Salvador University, El Salvador.
(3) Souilmi Fatima-Zohra, University Sidi Mohamed Benabdallah, Fes, Morocco.
Complete Peer review History: http://www.sciencedomain.org/review-history/19621

Original Research Article

Received 7th April 2017
Accepted 8th June 2017
Published 20th June 2017

ABSTRACT

Background: Nephrotic syndrome is a common childhood renal disease globally with a penchant for the early years of life and has generated a lot of interest among paediatricians and nephrologists.
Aim: This study aimed to determine the clinical, therapeutic and socio-demographic features of

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children with nephrotic syndrome at the Komfo Anokye Teaching Hospital (KATH) in Kumasi, Ghana.

Methodology: Hospital-based single-center study conducted from December 2015 to May 2016 among children with nephrotic syndrome at the Child Health Department of the Komfo Anokye Teaching Hospital (KATH) in the Ashanti Region of Ghana. Retrospective data of 172 patients admitted from January 2011 to January 2015 was used. Socio-demographic and laboratory data (biochemical and serological) of participants were retrieved from the laboratory database while clinical information (family history, past medical records, and symptoms) was retrieved from the patients' records.

Results: Of the 172 participants sampled, 112 (65.1%) were males and 60 (34.9%) were females. The mean ages of the males and the females were similar (6.56 ± 3.25 vs 6.80 ± 3.19; p = 0.647). Interestingly, majority of the males 49 (68.1%) and the females 23 (31.9%) were within the age group 4-7 years. Compared to females, more male participants had ascites [17 (81.0%) vs 4 (19.0%)], and bilateral nephromegaly [13 (76.5%) vs 4 (23.5%)]. On clinical examination, the commonest conditions among the males and the females were hypertension [44 (25.6%)] followed by glomerulonephritis [31 (18.0%)] and then infection [15 (8.7%)]. The least condition on clinical examination among the participants was hepatomegaly [2 (1.2%)] which was seen more in the males [2 (100%)] than the females. Participants presented with more generalized body swellings [122 (70.9%)], facial puffiness [105 (61.0%)], and symptoms of infection [101 (58.7%)]. Hematuria [3(1.7%)] was uncommon among the participants and was lower in the males [1(33.3%)] than the females [2(66.7%)]. Most participants had undetermined steroid response with males dominating. Males were more sensitive to steroids than females.

Conclusion: Nephrotic syndrome was common among males aged 4-7 with low social class. Renal impairment, generalized body swelling, facial puffiness, symptoms of infection and hypertension were the commonest clinical manifestations. Males were more steroid sensitive than females.

Keywords: Nephrotic syndrome; clinical; demographic; children; Ghana.

1. INTRODUCTION

Nephrotic syndrome is characterized by heavy proteinuria, hypoalbuminemia, generalized oedema, hyperlipidaemia, lipiduria and sometimes thrombotic and thromboembolic complications [1,2]. The refractory form of this condition can progressively lead to chronic kidney disease (CKD) [3,4]. Nephrotic syndrome can be idiopathic with unknown etiology or can be precipitated by drugs, infections and by systemic diseases like systemic lupus erythematosus, diabetes mellitus, amyloidosis and cancers [3]. Idiopathic nephrotic syndrome has an incidence and prevalence of 1-7 and 16 per 100,000 children respectively [5]. Except for the clinical characteristics of the disease and the therapeutic interventions which greatly affects a child's development and quality of life, the long-term outcome of nephrotic syndrome is generally favorable [6]. Hospital attendance and admission is common in patients with this condition mostly due to laboratory investigations and to cater for complications that may arise [4].

The role of ethnicity in the epidemiology of nephrotic syndrome has been mentioned in several studies [7] with reported incidence being higher in South Asian children than children in Europe and North America [8,9]. Ethnicity may also affect the histopathological presentation of the condition and response to immuno-suppressive steroid therapy [10,11].

Most studies conducted on nephrotic syndrome in sub-Saharan Africa described the clinical and pathological course [11,12], and the pattern of steroid sensitivity [13] with inconsistent findings. In addition, data on the demographic and clinical characteristics (including steroid sensitivity pattern) of Ghanaian children with nephrotic syndrome remain scanty. Thus, this study sought to investigate the clinical, therapeutic and the socio-demographical features of children with nephrotic syndrome at the Komfo Anokye Teaching Hospital (KATH) in Kumasi in the Ashanti region of Ghana.

2. MATERIALS AND METHODS

2.1 Study Design/Area

This retrospective hospital-based single-center study was conducted from December 2015 to May 2016 among children with nephrotic syndrome at the Child Health Department of the

Komfo Anokye Teaching Hospital (KATH) in Kumasi in the Ashanti Region of Ghana. The hospital offers both general and specialist care services in internal medicine, physiotherapy, general surgery, anaesthesia, oncology, paediatrics, obstetrics and gynecology, dental, ear, eye, nose and throat (DEENT) care and serves as the main referral facility for the Ashanti, Brong Ahafo, and the Northern Regions of the country.

2.2 Ethical Considerations

The study was approved by the Institutional Review Board of the University of Cape-Coast (IRB-UCC) and authorities of KATH (RD/CR16/016).

2.3 Inclusion and Non-inclusion Criteria

Data of participants aged between 0-15 years who presented with nephrotic syndrome within a stipulated period of 4 years were included in the study. However, we excluded children with nephrotic syndrome whose folders did not have adequate information (i.e. all the clinical, sociodemographic characteristics) on the condition.

2.4 Study Population/Data Collection

Retrospective data of 172 patients with nephrotic syndrome (112 males and 60 females) were obtained manually from the laboratory database. Data of in-patients spanning the period January 2011 to January 2015 were included in this study. Nephrotic syndrome is a condition characterized by heavy proteinuria, hypoalbuminemia (serum albumin <2.5 g/dl), hyperlipidemia (serum cholesterol >200 mg/dl), and edema [2]. Nephrotic range proteinuria is when there is early morning urine protein of 3+/4+ (on dipstick or boiling test), spot protein/creatinine ratio >2 mg/mg, or urine albumin excretion >40 mg/m^2/hr (on a timed-sample). Accurate quantitative assessment of proteinuria, including 24-h urine protein measurement is not often necessary. To clarify the course of nephrotic syndrome the following definitions are used: Remission: Urine albumin nil or trace (or proteinuria <4 mg/m^2/hr) for three consecutive early morning specimens. Relapse: Urine albumin 3+ or 4+ (or proteinuria >40 mg/m^2/hr) for three consecutive early morning specimens, having been in remission previously. Frequent relapses: Two or more relapses in initial 6 months or more than three relapses in any 12 months. Steroid dependence: Two consecutive relapses when on alternate day steroids or within 14 days of its discontinuation. Steroid resistance: Absence of remission despite therapy with daily prednisolone at a dose of 2 mg/kg per day for 4 weeks [2].

Laboratory data (biochemical and serological) of patients were retrieved from the laboratory database. Also, past medical history, family history, social class, radiology (ultrasound), clinical examination history, presenting symptoms and response to steroid therapy information were retrieved from the patients' clinic files and follow-up reports. Steroid therapy records of participants were also retrieved and classified into three groups: Steroid-Sensitive Nephrotic syndrome (SSNS), Steroid Dependence Nephrotic Syndrome (SDNS) and Steroid Resistance Nephrotic Syndrome (SRNS).

Steroids are used in the management and treatment of nephrotic syndrome. This results in a decrease in the proteinuria and the risk of infection as well as a resolution of the edema that characterizes the condition [14]. The first treatment which lasts for 4-8 weeks involves prednisone prescribed at 60 mg/m² of body surface area/day. The dose is reduced to 40 mg/m² for another 4 weeks. In the case of a relapse patients or children are treated with prednisolone 2 mg/kg/day till urine tests negative for protein. Then, 1.5 mg/kg/day for 4 weeks. Patients who relapse frequently are treated with cyclophosphamide or nitrogen mustard or cyclosporin or levamisole. Patients respond to prednisolone in several ways.

Steroid sensitive patient refers to the one who responds to the corticosteroids in the first 8 weeks of treatment. This is demonstrated by a strong diuresis, disappearance of edemas, and a negative test for proteinuria in three urine samples taken during the night.

Steroid resistant patient has proteinuria which persists after the 8-week treatment. The lack of response to steroid therapy is indicative of the severity of the glomerular damage, which could develop into chronic kidney disease.

In the steroid tolerant patient there is hypertension, weight gain, aseptic or avascular necrosis of the hip or knee, cataracts and embolisms.

The steroid dependent patient reports with proteinuria when the dose of corticosteroid is decreased or there is a relapse in the first two weeks after treatment is completed.

2.5 Statistical Analysis

Data was analyzed with SPSS version 16 (SPSS Inc. Chicago). Independent t-test was used to compare mean scores between two groups. One-way ANOVA was also employed to compare the mean scores of more than two groups and P < 0.05 was interpreted as statistically significant.

3. RESULTS

The mean ages of the males (6.56 ± 3.25) and the females (6.80 ± 3.19) were similar (P = 0.647). Majority of the males 49 (68.1%) and the females 23 (31.9%) were found within the age group 4-7 years. There was no significant difference between the males and the females with respect to social class (P = 0.128), locality (P = 0.303), past medical history (P = 0.858), family history of nephrotic syndrome (P = 0.955), steroid response (P = 0.062) and viral hepatitis infection (P = 0.252) [Table 1].

The males had lower systolic blood pressure (P=0.264) and diastolic blood pressure (P = 0.484) than the females however, the difference was not significant. The blood pressure categories showed the highest incident of optimal blood pressure in the males (63.4%) than the females (36.6%). The means of serum potassium (5.74 ± 1.10) and urea (8.90 ± 1.32) were higher in the males than the females while serum sodium (136.07 ± 6.17), creatinine (141.07 ± 34.94), albumin (22.40 ± 10.41), total cholesterol (19.22 ± 10.47) and calcium (2.14 ± 0.55) were higher in the females than the males. However, the differences were not significant (P>0.05) [Table 2].

Table 1. Demographic and clinical characteristics and steroid response of children with nephrotic syndrome

Characteristics	Male (n = 112)	Female (n = 60)	Total (n = 172)	P-value
Age (years)	6.56 ± 3.25	6.80 ± 3.19	6.65 ± 3.23	0.647
Age group n (%)				0.440
≤ 3	25 (71.4)	10 (28.6)	35 (20.3)	
4-7	49 (68.1)	23 (31.9)	72 (41.9)	
8-11	25 (55.6)	20 (44.4)	45 (26.2)	
12-15	13 (65.0)	7 (35.0)	20 (11.6)	
Social class				0.128
Low	86 (68.8)	39 (31.2)	125 (72.7)	
Moderate	26 (56.5)	20 (43.5)	46 (26.7)	
High	0 (0.0)	1 (100)	1 (0.6)	
Locality				0.303
Urban	67 (68.4)	31 (31.6)	98 (57.0)	
Rural	45 (60.8)	29 (39.2)	74 (43.0)	
Pasts medical history				0.858
1st episode	63 (63.6)	36 (36.4)	99 (57.6)	
2nd episode	23 (67.6)	11 (32.4)	34 (19.8)	
3rd episode	7 (58.3)	5 (41.7)	12 (7.0)	
Frequent relapse	19 (70.4)	8 (29.6)	27 (15.7)	
Family history of NS				0.955
Yes	2 (66.7)	1 (33.3)	3 (1.7)	
No	110 (65.1)	59 (34.9)	169 (98.3)	
Steroid response				0.062
Undetermined	53 (61.6)	33 (38.4)	86 (50.0)	
Sensitive	39 (78.0)	11 (22.0)	50 (29.1)	
Resistant	20 (55.6)	16 (44.4)	36 (20.9)	
Viral hepatitis infection				0.252
Negative	104 (63.8)	59 (36.2)	163 (94.8)	
HBV	4 (100)	0 (0.0)	4 (2.3)	
HCV	4 (80.0)	1 (20.0)	5 (2.9)	

NS= Nephrotic syndrome, HBV= Hepatitis B Virus, HCV= Hepatitis C Virus

Though systolic blood pressure and diastolic blood pressure were lower in the SSNS than the SRNS the difference was not significant (P = 0.198). Serum sodium, calcium, and albumin were similar in both SSNS and SRNS. Serum urea, total cholesterol was higher in the SSNS than the SRNS (P>0.05), whereas serum potassium and creatinine were lower in the SSNS than the SRNS (P>0.05) [Table 3].

On radiological examination, acute renal parenchymal disease (18%) and ascites (12.2%) were the most common conditions and were more prevalent among the male participants. Splenomegaly, partial bowel obstruction, hydronephrosis and obstructive uropathy were the least common. Hypertension (25.6%) and glomerulonephritis (18.0%) were the most common presentations on clinical examination.

Table 2. Clinical and biochemical data of children with nephrotic syndrome

Parameters	Male (n = 112)	Female (n = 60)	Total (n = 172)	P-value
Blood pressure (mmHg)				
SBP	113.30 ± 20.62	117.02 ± 20.93	114.6 ± 20.74	0.264
DPB	74.55 ± 17.96	76.70 ± 21.18	75.30 ± 19.11	0.484
Blood pressure categories				0.580
Optimal	52 (63.4)	30 (36.6)	82 (47.7)	
Normal	3 (100)	0 (0.0)	3 (1.7)	
Prehypertension	0 (0.0)	1 (100)	1 (0.6)	
Hypertension				
Grade 1	2 (66.7)	1 (33.3)	3 (1.7)	
Grade 2	1 (50.0)	1 (50.0)	2 (1.2)	
Grade 3	1 (50.0)	1 (50.0)	2 (1.2)	
Biochemical profile				
Sodium (mmol/L)	133.51 ± 12.81	136.07 ± 6.17	134.47 ± 10.86	0.223
Potassium (mmol/L)	5.74 ± 1.10	4.60 ± 0.71	5.30 ± 0.68	0.420
Urea (mmol/L)	8.90 ± 1.32	8.65 ± 1.51	8.88 ± 1.01	0.872
Creatinine (umol/L)	107.84 ± 23.52	141.07 ± 34.94	119.34 ± 19.54	0.420
Albumin (g/L)	20.45 ± 10.40	22.40 ± 10.41	21.12 ± 0.88	0.292
Total Cholesterol	10.05 ± 5.52	19.22 ± 10.47	13.26 ± 3.67	0.236
Calcium (mmol/L)	1.98 ± 0.45	2.14 ± 0.55	2.04 ± 0.06	0.208

SBP= Systolic Blood Pressure, DBP= Diastolic Blood Pressure

Table 3. Biochemical and clinical data of children with nephrotic syndrome in relation to steroid response

Parameters	Steroid response		P-value
	SSNS (n = 50)	SRNS (n = 36)	
Blood pressure (mmHg)			0.198
SBP	108.22 ± 16.05	113.31 ± 20.27	
DPB	71.50 ± 16.71	75.28 ± 15.43	0.289
Blood pressure categories			0.319
Optimal	27 (54.0)	18 (50.0)	
Normal	1 (2.0)	2 (5.6)	
Prehypertension	0 (0.0)	1 (2.8)	
Hypertension			
Grade 1	0 (0.0)	2 (5.6)	
Grade 2	1(2.0)	1 (2.8)	
Biochemical profile	135.11 ± 5.25	135.79 ± 6.26	
Sodium (mmol/L)			0.671
Potassium (mmol/L)	4.64 ± 0.79	7.01 ± 2.66	0.422
Urea (mmol/L)	7.54 ± 2.00	6.77 ± 1.51	0.773
Creatinine (umol/L)	48.98 ± 9.79	60.89 ± 11.55	0.432
Albumin (g/L)	17.97 ± 9.86	17.43 ± 9.58	0.817
Total Cholesterol (mmol/l)	12.31 ± 5.60	10.64 ± 4.54	0.194
Calcium (mmol/L)	2.01 ± 0.62	2.00 ± 0.42	0.962

SBP= Systolic Blood Pressure, DBP= Diastolic Blood Pressure, SSNS=Steroid Sensitive Nephrotic Syndrome, SRNS=Steroid Resistant Nephrotic Syndrome

Table 4. Frequency of occurrence of some clinical presentations in children with nephrotic syndrome

Characteristics	Male	Female	Total
Radiology examination			
Normal	68 (63.6)	39 (36.4)	107 (62.2)
Acute renal parenchymal disease	21 (67.7)	10 (32.3)	31 (18.0)
Chronic renal parenchymal disease	1 (33.3)	2 (66.7)	3 (1.7)
Ascites	17 (81.0)	4 (19.0	21 (12.2)
Bilateral nephromegaly	13 (76.5)	4 (23.5)	17 (9.9)
Cellulitis of the lower limbs	0 (0.0)	1 (100)	1 (0.6)
Echogenic kidney	3 (100)	0 (0.0)	3 (1.7)
Hepatomegaly	4 (66.7)	2 (33.3)	6 (3.5)
Hydronephrosis	0 (0.0)	1 (100)	1 (0.6)
Obstructive uropathy	0 (0.0)	1 (100)	1 (0.6)
Partial bowel obstruction	1 (100)	0 (0.0)	1 (0.6)
Splenomegaly	1 (100)	0 (0.0)	1 (0.6)
Clinical examination			
Acute Glomerulonephritis	23 (74.2)	8 (25.8)	31 (18.0)
Chronic Glomerulonephritis	5 (29.4)	12 (70.6)	17 (9.9)
Acute renal failure	1 (33.3)	2 (66.7)	3 (1.7)
Chronic renal failure	9 (64.3)	5 (35.7)	14 (8.1)
Hypertension	31 (70.5)	13 (29.5)	44 (25.6)
UTI complications	5 (62.5)	3 (37.5)	8 (4.7)
Hepatomegaly	2 (100)	0 (0.0)	2 (1.2)
FSGS	3 (60.0)	2 (40.0)	5 (2.9)
Infections	13 (86.7)	2 (13.3)	15 (8.7)
Presenting symptoms	68 (64.8)	37 (35.2)	105 (61.0)
Facial puffiness			
Generalized body swellings	81 (66.4)	41 (33.6)	122 (70.9)
Respiratory distress	8 (66.7)	4 (33.3)	12 (6.9)
Abdominal discomfort	54 (71.1)	22 (28.9)	76 (44.2)
Symptoms of infection	65 (64.4)	36 (35.6)	101 (58.7)
Hematuria	1 (33.3)	2 (66.7)	3 (1.7)
Seizures	2 (50.0)	2 (50.0)	4 (2.3)
Fatigue	8 (57.1)	6 (42.9)	14 (8.1)

UTI= Urinary Tract Infection, FSGS= Focal Segmental Glomerulosclerosis

These conditions were more common in males than females. Hepatomegaly (1.2%) was the least common presentation on clinical examination and was more common in males than in females. With regards to the clinical symptoms, participants presented with more generalized body swellings 122 (70.9%), facial puffiness 105 (61.0%), and symptoms of infection 101 (58.7%). hematuria 3 (1.7%) was uncommon among the participants and was lower in the males 1 (33.3%) than the females 2 (66.7%) [Table 4 above].

4. DISCUSSION

This hospital based single-centre retrospective study described the clinical, demographic and steroid response pattern of Ghanaian children with nephrotic syndrome.

This study showed an obvious male predominance (even though insignificant) in consonance with earlier studies conducted across the globe [3,15-19], but contradicts the findings of studies conducted in Port Harcourt, Nigeria [10] and a recent study in the United States America [20] where there was equal gender distribution. Age 4-7 years as the highest peak age of nephrotic syndrome in this study is in agreement with earlier reports from northern Nigeria, India, Germany [16,21,22], Conversely, studies in Taiwan and Ghana reported lower peak ages of less than 3 years whilst peak ages of 12 years were recorded in studies from

Ghana, Pakistan and USA [3]. This clearly indicates that age as a demographic parameter is an important predisposing factor of nephrotic syndrome.

In keeping with the observation of Gong et al. [23] we identified an association between socioeconomic class and the proportion of participants with nephrotic syndrome. Seeking early and prompt medical attention most especially in private health facilities could account for the lower proportion of the high social class with nephrotic syndrome in this study. However, most of the studied participants were in the moderate (26.7%) and low (72.7%) socioeconomic status, which could be a true reflection of the social status background in Ghana.

In contrast with the findings of Mattoo et al., [24] in a study in Saudi Arabia we observed no relationship between nephrotic syndrome and family history. The higher rate of consanguineous marriages in Saudi Arabia is responsible for this observation [24].

Hepatitis B virus infection and other viral infections have been identified as a cause of childhood nephrotic syndrome. In agreement with findings of studies from Pakistan, Iran and Nigeria we observed a low prevalence of hepatitis B and C among our participants. The low prevalence of hepatitis B observed in our study, however contradicts the 30%, 25.3 and 24% prevalence rates recorded in three studies across northern Nigeria [12,25]. The pattern of hepatitis B observed in this study could be a true reflection of hepatitis B infection among Ghanaian children today.

Our observation of hypertension as the most common condition on clinical examination is in line with documented findings from Ghana [11], Nigeria [12], and the United States of America [3]. Finding hypertension in a patient with nephrotic syndrome on initial diagnosis could help in establishing the type of nephrotic syndrome especially in studies such as ours in which we failed to use microscopy to identify the exact type of nephrotic syndrome. Thus, the observation of acute glomerulonephritis among participants by radiography examination is not surprising.

Renal impairment, generalized body swelling and facial puffiness were the commonest presenting symptoms in this study. Notwithstanding, these findings are less encountered symptoms than what was documented in a prospective study conducted at the University of Nigeria Teaching Hospital [18].

Various studies across the globe have reported different rates of steroid sensitivity ranging from 35-95% [13]. The 29% prevalence of steroid sensitivity is lower than that reported in Nigeria [10,26] Ghana [11] and South Africa [27]. The high age range of our participants (4-7 years), the complicated nature of the condition as well non-compliance with treatment could account for the low prevalence of steroid sensitivity we reported. Our study is limited by our inability to report microscopic (histologic) patterns of nephrotic syndrome in our participants.

5. CONCLUSION

Nephrotic syndrome is a common childhood renal disease in Kumasi. The disease was prevalent among the age category 4-7 especially among those with low social class. Besides, renal dysfunction, generalized body swelling, facial puffiness were the commonest clinical manifestations. A prospective study must be employed in subsequent studies among nephrotic syndrome patients prospective study with histological data that would specify the risk factors for corticosteroid resistance.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this paper.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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