Epidemiology and Clinicopathologic Characteristics of Childhood Nephrotic Syndrome in BeninCity, Nigeria

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Abstract

Medical records of 58 children, 38 (65.5%) males and 20 (34.5%) females with nephrotic syndrome (NS) admitted to the paedlatric wards of the University of Benin Teaching Hospital (UBTH) Benin-City, Nigeria, between January, 1991 and December, 1995 were reviewed. The aim of the study was to document the epidemiologic as well as certain clinico-pathologic characteristics of the disease in Benin-City. More males than females (ratio of 1.9:1) and older children (meant (SEM) 8.2+0.5 years; range 2-15 years) were affected. About 62% of the patients were aged 7 years and above. There was a high incidence of hypertension (41.4%) and microscopic haematuria (60%) in the patients. Hypercholesterolaemia and hypoalbuminaemia were seen in only 21.6% and 30.2% of evaluated patients respectively. Hypercholesterolaemia and hypoalbuminaemla as diagnostic criteria for NSin our locale may not be very useful. About 51.7% of patients responded to the initial course of prednisolone, out of whom 43.3% relapsed (26.7%) frequently and 16.7% infrequently. Mortality rate was 6.9%. Urinary tract infection (UT!) occured in 44.8% of the patients and was caused largely by Staphylococcus aureus and untyped coliform organisms (JPMA 48:235,1998).

Introduction

Nephrotic syndrome (NS) is a leading cause of childhood morbidity worldwide[1-3]. In Nigeria, it is a leading renal cause of paediatric admissions outside urinary tract infection (UT!) and post streptococcal glomerulonephritis[2,4]. Most caucasian series report NS as a disease of pre-school aged children with peak age incidence of 2-3 years, affecting more males than females[1,5]. Seventy to 90% of such cases are due to minimal change lesions in which hypertension, haematuria and poor response to steroid therapy are uncommon[1-6]. However, different epidemiologic pattern and histologic variants have been reported from Nigeria and some parts of Africa[7,8].

In most centres in developing countries lacking facilities for renal biopsy, dialysis and renal transplantation rational management is based on knowledge of relevant epidemiologic data which are known to vary from one area to another. Incidentally, most Nigerian studies have emanated from units outside the south- south zone[4,7] to which Bemn-City belongs.,There is therefore, paucity of such data in ourcentre as with similarcentres inthirdworld. The study was undertaken to document the epidemiology of NS in Bemn-City, noting areas of similarities and pecularities in relation to other reports.

Methodology

Medical record of all children managed for NS at the Paediatric wards of the University of Bemn Teaching Hospital (UBTH), Benin- City, Nigeria between January, 1991 and December, 1995 were retrospectively analysed. Parameters documented were age, sex, results of urinalysis, 24 hour urine protein estimation, serum creatinine, serum protein and cholesterol, Others were urine culture results, response to steroid therapy, occurrence of relapse, follow-up and treatment durations, hypertension and

in-vitro anti-microbial sensitivity pattern of cultured organisms to selected antibiotics. Complications and outcome were also recorded. NS as diagnosed in the presence of generalised oedema, massive proteinuria, (urinazy protein loss inexcess of 0.05-0.1 g/kg body weight/day)[9] and variably hypoalbuniinaemia or hyperlipidaemia or both.

As part of the initial evaluation following admission, clinical features and laboratory parameters already outlined were routinely documented. On the confirmation of diagnosis patients were placed on 4-6 weeks course of prednisolone unless where absolutely contraindicated; following which response to steroid was determined. Patients who were hypertensive received a- methyldopa or hydralizine or both while treatment for urinary tract infecion (UT!) was ultimately guided by in-vitro culture and antimicrobial sensitivity reports. Other complications were addressed as they occurred. Follow-up notes were also reviewed.

The student t-test orChi-square test were used to test the significance of observed means where necessary.

Results

Fifty-eight of 63 patients with NS were eventually assessed as case notes for 5 (7.9%) were not available or grossly incomplete. The 58 patients were made up of 38 (65.5%) males and 20 (34.5%) females, giving a male to female ratio of 1.9:1. Mean age and standard error of mean (SEM) of the children was 8.2±0.6 years. For males the mean (SEM) age was 8.3±0.6 years in comparison with 8.0±0.9 years for females. The age range was 2-15 years. Over 62% of the patients were aged 7 years and above. Age and sex distribution of the patients is shown in Table I.

Table I. Age and sex distribution of patients with nephrotic syndrome.

Age (yrs.)	Males	Females	Total	%
<1	-	-	-	-
1-3	2	4	6	10
4-6	12	4	16	28
7-9	12	4	16	28
10-12	5	5	10	17
13-15	7	3	10	17

Selected Clinical Features

Twenty-four (41.4%) of the patients had hypertension during the initial course of evaluation. Nineteen (79.2%) of these were males, 5 (20.8%) females, while 16(66.7%) were aged 7 years and above.

Table II. Relationship between age and selected clinical features of nephrotic syndrome.

Parameter	Age <7 years	Age >7 years	P value
Hypertension (n=58)			
Present	8	16	>0.05
Absent	14	20	
Microscopic haematuria (n=50)			
Present	10	20	>0.05
Absent	10	10	
Urinary tract infection (UTI) (n=58)			
Present	6	20	>0.05
Absent	16	16	

The relationship between age group and hypertension is shown in Thble II while that between hyertension, haematuria and steroid responses is depicted in Table III.

Table III. Steroid response and certain clinical features in children with nephrotic syndrome.

	Steroid responsive	Steroid Non-responsive	P value
Hematuria (n=50)			
Yes	10	13	>0.05
No	20	7	
Hypertension (n=57)			
Yes	13	10	>0.05
No	17	18	
UTI (n=57)			
Yes	12	14	>0.05
No	18	14	

No patient presented with macroscopic haematuria. However, urine microscopy results were available

for 50 patients of whom 30 (60.0%) had microscopic haernaturia. Fourteen (46.7%) of these patients had hypertension.

Laboratory parameters

Serum cholesterol results were available for 51 (87.9%) patients. Mean (±SEM) serum cholesterol was 217.91±6.86 mg/cl! and only 11(21.6%) had levels inexcess of 250 mg/dl. The mean serum cholesterol for males (2 13.0±9.9 mg/dl) was not significantly different from that of females (233.7±9,4 mg/dl, P>0.05). The meanurinary protein loss in24 hourswas 2.4±0.3 gm/rn . Mean 24- hour urinary protein loss in males (2.7±0.4 gm/rn2) was not significantly different from that of females (2.0±0.1 gm/m2). Mean serum creatinine in 54 patients, for whom record were available was 1.13±0,04 mg/dl. Mean values for males (1.05±0.06 mg/dl) was not significantly different from that of females (1.27±0.05 mg/dl), (P>0.05). Mean serum albumin and globulin were 2.69±0.10 and 2.58±0.11 mg/dl respectively. The sex differences in the mean serum albumin and globulin is shown in Table IV.

Table IV. Sex distribution of some biochemical parameters in patients with nephrotic syndrome (mean±SEM).

Mean value	Males	Females	Both sexes
Serum cholesterol (mg/dl)	213.00±9.91	223.72±9.40	217.91±6.86
24 hour urinary protein (gm/m^2/day)	2.68±0.40	2.00±0.10	2.41±0.30
Serum albumin (mg/dl)	2.48±0.11	3.03±0.17	2.69±0.10
Serum globulin (mg/dl)	2.63±0.13	2.66±0.19	2.58±0.11
Serum creatinine (mg/dl)	1.05±0.06	1.27±0.05	1.13±0.04

Clinical course of nephrotc syndrome

Of' the 58 patients, 30(51.7%) responded to 4-6 weeks course of prednisolone with 13 (43.3%) of them achieving response after three weeks of therapy. Twenty-eight (48.3%) were steroid resistant. Twelve (40%) of the steroid responsive patients remained symptom-free during the follow-up period (mean, 7,4±1.2 months). Four (13.3%) required steroid to remain symptom-free, while 13 (43.3%) relapsed. Eight (26.7%) and 5 (16.7%) respectively relapsed frequently and infrequently. One (3.3%) of the steroid responsive patients was lost to follow-up soon after discharge. The relationship between haematuria, presence of UTI, hypertension and steroid responsiveness is shown in Thble III. Two (3.4%) patients each died of septlcaernia and suspected thrombo-embolic phenomena.

Associated Complications

The commonest complication seen in the patients with NS was urinaiy tract infection (UT!). There were 35 episodes of UT! in 26 (44.8%) patients caused largely by Staphylococcus aureus (48.8%) and untyped coliform organisms which showed high in-vitro resistance to commonly used antibiotics including ampicillin and nalidix acid. Other complications noted in the patients are depicted in Table V.

Table V. Complications found in children with nephrotic syndrome.

Complications	No. of episodes	%
Urinary tract infection	25	63
Peritonitis	5	9
Skin sepsis	10	18
Septicaemia	2	4
Thromboembolism	2	4
Acute renal failure	1	2
Chronic renal failure	1	2

Discussion

NS was responsible for 0.23% of paediatric admissions to the University of Benin Teaching Hospital, Bemn-City over the five years study period, giving a yearly incidence of 46 per 100,000 admitted children in comaprison to the 2:100,000 childhood population as reported from Western Europe[1]. The higher incidence in our study may be due partly to the fact that the work was hospital based.

The finding of male Preponderance in the study is in agreement with most reports[1,3,5]. However, the mean age at presentation of 8.2±0.5 years is at variance withreports from caucasian series that NS is a disease of pre-school aged children[1,9]. Nonetheless, the finding is inconsonance withthat of Adhikari et al in South Africa that noted a peak age of presentation of 7- 8 years. Unlike what one observes in Western Europe, it is likely that most patients may have had non-minimal histologic lesions known to occur frequently after 6 years of age[1]. In support of this view is the high prevalence of hypetension and haematuria in our study. These features are uncommon in children with minimal change lesion[9,10].

The high prevalence of hypertension in the study does not correspond with the low prevalence rate (9-35%) reported in caucasions[9]. Similarly, microscopic haematuria was found in 60% of 50 patients evaluated. This finding also differs from the 25% prevalence rate noted in three common histologic lesions by Rance et al[9]. The high prevalence of haematuna and hypertension may also be related to the probable secondaiy NS found in these patients.

Hypercholesterolaemiawas not acommonfeature in the study as only 11(17.5%) patients had serum cholesterol in excess of 250 mg/dl. The finding is at variance with another report which noted that 95% of children with minimal change lesion and 60% of children with other histologic type had hypercholesterolaemia[11]. Abdur Rahman et al[12] also found high incidence of hypercholesterolaemia in their series from Nothern Nigeria. Blood cholesterol levels are intricately linked with food intake, hormonal status and blood levels of albumin with which it has a reciprocal relationship[10]. The relatively high levels of serum albumin noted in the study and a possible dietary factor may explain the rarity of hypercholesterolaemia in the study. Consequently hypercholesterolaemia may not be an important feature in the diagnosis of NS in our locality.

In the study, mean serum albumin was unexpectedly normal which could imply that the protein predominantly lost in urine of these patients is non-albumin. Caution is therefore required, especially in

similar socio-economic setting, on the reliance of hypo-alburninaemia for thediagnosis of childhood NS. The mean serum creatinine 1.13±0.04 mg/dl (range 0.20-1.60 mg/dl) was normal. Only 32% of cases had abnormally high serum creatinine. This finding is comparable to the 25% incidence for elevated serum creatinine in children with minimal change NS[1].

No two patients from the same family was seen throughout the study period in comparison with the 6% familial occurrence reported by Mattoo et al[5] in Saudi children with NS. Only 51.7% of our patients responded to 4-6 week course ofprednisolone with 35% doing so after three weeks of therapy. Corresponding figures for patients with minimal change lesion are 73-94% and 70% respectively[1]. Mattoo et al[5] in their histologically heterogenous group reported 90% response to initial course of steroid and 45% relapse rate. Corresponding figures in our study are 51.7% and 43.3%. The differences in the histologic types seen in these series may explain the varying responses and relapse rates between the studies. The low mortality rate in children with NS documented by other workers[6] and ascribed to increased use of antibiotics is confirmed by this study.

As noted by Gulati et al[13] urinary tract infection (UT!) caused largely by staphylococcus aureus and untyped coliform organisms, was the commonest complications seen in these children with NS. Other complications included skin sepsis, septicaemia and peritonitis. NS is known to be associated with impaired immunologic functions[6] that make them susceptible to the infections.

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