Original article

Nephrotic syndrome in Nepalese children: clinical profile, histopathology and outcome in a tertiary care center of Nepal.

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Abstract

Introduction: The demographic, clinical features, steroid response, histopathology and complications of all children diagnosed with nephrotic syndrome at Tribhuvan University Teaching Hospital over a 3-year period.

Methods: A retrospective study was conducted among patients who were admitted in the Pediatrics ward of Tribhuvan University Teaching Hospital with the diagnosis of Nephrotic syndrome from April 2010 to April 2013.

Results: During the study period from 2010 April to 2013 April, there were total of 80 patients admitted with the diagnosis of nephrotic syndrome. There was male preponderance with sex ratio 1.28:1. Mean age of patient at first episode was 8.51±4.33 years. Among the admitted patients, 48.8% (41) of children had single episode whereas steroid resistance was observed in 16.2% (13) of patients. Hematuria and hypertension were present in 21.2% (7) and 50% (40) of patients respectively. Renal dysfunction was present in 21.2% (17). Pneumonia was the most common complications 18.8% (15), followed by UTI 8.8%(7), spontaneous bacterial peritonitis 3.8% (3) and acute renal failure 7.5% (8). Two patients had multiple complications. Alternative therapies were used in 25% (20) of patients and cyclophosphamide was used most commonly as alternative therapy which was used in 17.4% (14). Most common histopathological diagnosis was FSGS 30.3% (10) followed by MPGN 15.5% (5), SLE nephropathy 15.5% (5) and IgA nephropathy 15.5% (5)

Conclusion:

The clinical course of childhood NS in Nepal is similar to the developed world. Differences at Presentation included older age and increased prevalence of microscopic hematuria, hypertension.

Key words: childhood; nephrotic syndrome; histology, outcome.

Introduction

Childhood nephrotic syndrome (NS) is a common renal disease all over the world. Idiopathic nephrotic syndrome is the most common form of NS in children with the potential of progression to end stage renal disease (ESRD).[1] However, the disease incidence and prognosis vary greatly with geography. Estimates on the annual incidence of nephrotic syndrome ranges from 20-70 per million children, and prevalence from 12-16 per 100,000 [2]. However, the incidence in the Indian subcontinent is estimated at 90 to 100 per million population.[3] There is epidemiological evidence of a higher incidence of nephrotic syndrome in children from south Asia (Pakistani, Indian, and Bangladeshi)[4,5,6,7] and Arab children.[8] Several studies in past had concluded that outcome of nephrotic syndrome, responsiveness to steroid and pathological type varies greatly in different races.[9,10] Whether these disparities result from genetic differences, local environmental influences, or a complex interplay between the two is unclear.

There is paucity of literature regarding the clinical spectrum of childhood NS among Nepalese children. The aim of the present study is to describe the demographic, clinical features, steroid response, histopathology and complications of all children diagnosed with nephrotic syndrome in Nepal. Knowledge of these parameters could have therapeutic and preventive relevance. Therefore, the present study was conducted.

Methods

A retrospective study was conducted among patients who were admitted in the Department of Pediatrics at Tribhuvan University Teaching Hospital with the diagnosis of Nephrotic syndrome from April 2010 to April 2013. Nephrotic syndrome was diagnosed on the basis of heavy proteinuria (40 mg/m2/hr in children), hypoalbuminemia (<2.5 g/dL), edema, and hypercholesterolemia exceeding 220 mg/ dL[11]. The hospital records were reviewed for demographic data, clinical features, age at first episode, presence of hypertension, hematuria, complications, biochemical finding, histopathology. The details of clinical course and alternative treatment modalities were recorded from their follow up record at pediatric nephrology clinic. The definitions Nephrotic syndrome remission, relapse, steroid dependence and resistance used in the department were according to that given by Indian Academy of Pediatrics.[12]

Hypertension was defined as blood pressure higher than 95th percentile for sex, age and height.[13] Hematuria was defined as>5 red blood cells/ml in centrifuged urine. Initial renal insufficiency was defined as a reversible increase of the serum creatinine level (100-460 µmol/l) accompanied by a decrease of the glomerular filtration rate according to the Schwartz formula at the time of presentation.[14] Children who responded to the steroid regimen, but had a duration of follow up of less than 6 months were categorized as responders

Our institute is a tertiary care centre which caters exclusively to the large number of referred cases. At the initial visit besides clinical examination, a detailed evaluation of treatment history was carried out to find out the appropriateness of therapy. The initial treatment for nephrotic syndrome at our center comprises of prednisolone at a dose of 60 mg/m2/day for 6 weeks followed by 40 mg/m2 on alternate days for 6weeks as recommended by Cochrane renal group.[15] Those who had received treatment less than above recommendation, before their presentation to our hospital were treated as 1st episode of nephrotic syndrome.

Ethical approval was taken from Institutional Review Board of the Institute of Medicine. SPSS 15 software was used for statistical analysis.

Results

Among the patients admitted during the period of 3 years, there were a total of 80 patients admitted with the diagnosis of nephrotic syndrome. The sex ratio was 1.28:1 with male preponderance (Table 1). Mean age at first episode was 8.51±4.33 years with maximum number of patients (28.8%%) in >12 years age group. (Table1).

Table 1: Patient demographic characteristics.

Total number of patients 80	
Males	45
Females	35
Male-to-female ratio	1.28:1
Mean age at admission	8.96±4.33 years
Mean age at first episode (in years)	8.51±4.33 years
Age range at first episode (6 months–16 years	
Age distributionof first episode,	%(n)
1–4 years	23.8 % (19)
5–8 years	26.2 % (21)
9-12years	21.2 % (17)
>12years	28.8 % (23)

Regarding clinical features (Fig:1), hematuria and hypertension were present in 21.2% (17) and 50% (40) of patients respectively. Renal dysfunction characterized by raised urea and creatinine was present in 21.2% (17).

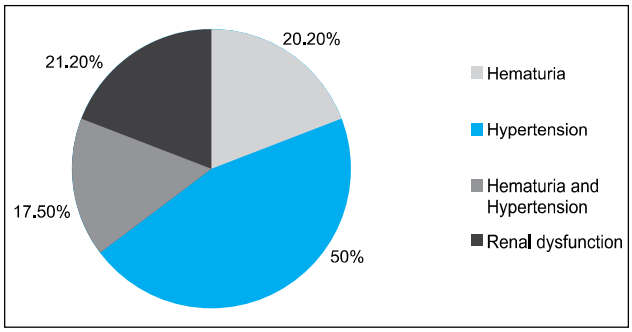

Figure 1: Clinical features in the study population

Complications were present in nearly one third (38.75%) of admissions for NS and infective complication was observed in 32.5% patients. Pneumonia was the most common of complications 18.8% (15), followed by Urinary Tract Infection (UTI) in 8.8% (7), spontaneous bacterial peritonitis(SBP) 3.8%(3) and acute renal failure (ARF) 7.5%(6). Two patients had multiple complications (Fig 2).

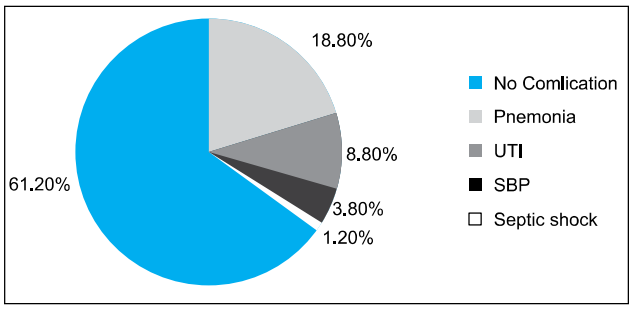

Figure 2: Frequency of complications

85% (68) had idiopathic nephrotic syndrome and 15% (12) had secondary nephrotic syndrome. Among the patients with idiopathic nephrotic syndrome, 83.3% (57) were steroid sensitive and 16.17% (11) were steroid resistant. Among steroid sensitive patients, 68.4% (39)

of children had single episode, 3.5% (2) had frequent relapse, 14.04% (8) had infrequent relapse, 14.04% (8) were steroid dependent. (Fig 3).

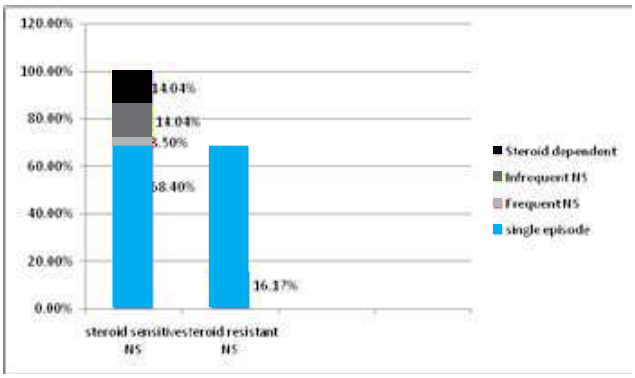

Figure 3: Clinical course of patients

Biopsy was done in 41.2% (33) of total patients. (Tab: 2). Most common histopathological diagnosis was FSGS 30.3% (10) followed by MPGN 15.15% (5), SLE nephropathy 15.15% (5) and IgA nephropathy 15.15% (5). Histologically, 26.2% (21) of patients had primary nephrotic syndrome whereas 15% (12) had secondary nephrotic syndrome. There was no difference of incidence of secondary nephrotic syndrome in two sexes (chi-square test, p 3.04) and with relation to onset at first episode (independent t test, p – 0.6). Analysis of the renal biopsy of patients with steroid resistant group showed that 15.15% (5) patients had FSGS and 15.15% (5) had MPGN and 3.03 % (1) had Membranous GN.

Table 2: The frequency distribution of different histopathological lesions

Pathological lesions	Percentage (Frequency)
Focal segmental glomerulosclerosis (FSGS)	30.3% (10)
Minimal change disease (MCD)	2.5% (2)
Membranoproliferative glomerulonephritis (MPGN)	15.15%(5)
Mesangioproliferative glomerulonephritis (MesPGN)	9.09% (3)
Membranous glomerulonephritis (MGN)	3.03 % (1)
Diffuse proliferative glomerulonephritis	6.06%(2)
IgA nephropathy	15.15%(5)
SLE Nephritis	15.15%(5)
Total	**100%(33)**

Alternative therapies were used in 25% (20) of patients and cyclophosphamide was used most commonly as an alternative therapy in 17.4% (14)(Tab:3).

Table 3. Use of alternative therapies

Drugs	Percentage of cases (N)
Steroids only	75% (60)
cyclophosphamide	15% (12)
cyclosporin	2.5% (2)
levamisole	3.8% (3)
Tacrolimus	1.2% (1)
Levamisole/cyclophosphamide	1.2%(1)
Tacrolimus/cyclophosphamide/ mycophenolate	1.2%(1)

Discussion

This is the first reported largest study of childhood NS in Nepal. This study indicates pattern of nephrotic syndrome in tertiary care referral hospital of Nepal.

In the present study, sex ratio was 1.42:1. NS is more common in male than in females (2:1 to 3:2)[1,11, 16]. Male preponderance with sex ratio of 1.28 to 2:1was also found in other studies done in Tunisie, Nigeria, Saudi Arabia [17-21] Present study also reveals similar sex ratio.

In the present study, majority of patients 28.8 % (23) were in >12 years age group. The most common age of presentation is 2-6yrs11 and occurs in children at a median age of 4 years22. Most of the patients were of this age group was observed in other studies[14, 15, 18] as well. Higher age of presentation in the present study could be due to larger number of referred cases as well as larger number of cases with secondary nephrotic syndrome.

In the present study, hematuria was observed in 21.2% (17) of the patient. Hypertension was observed in 50% (40) which is similar to that observed in one study at Nigeria[14, 16]. In contrast hypertension was observed in only (0.5%) of patients in study done at Bangladesh.[18] Similarly, ARF was developed in 17(21.2%).The higher incidences of hypertension and ARF that we observed are possibly related to inclusion of a large number of patients with secondary nephrotic syndrome 12 (15%).

Infection was the most common complication which was observed in 32.5% patients. Other studies reported incidence ranging from 32% to 38%[23, 24]. The commonest major infection was pneumonia 18.8% (15). Incidence of pneumonia among patients with NS ranges from 15% to 55% in Indian studies.[25, 26]. UTI was the second commonest infection in the subjects 8.8%(7). Incidence of UTI among patients with NS ranges from 13.7% to 46 % in studies done in India, Midwestern zone and Nigeria [27,28]. Peritonitis was present in (3.8%) as compared to 1.4% to 16% in other studies[29, 30] These variations probably reflect geographical or socioeconomic heterogeneity of patient populations. Our hospital caters to patients of low socioeconomic status, which explains poor coverage of pneumococcal vaccination (6%). Improving pneumococcal vaccination coverage in NS could be a potentially important strategy to decrease the incidence of major infections.

Table 4: Comparison of our study with other studies in Asia

Study	Country	No of patients with primary NS	Response to steroid therapy	Infrequent relapsers	Frequent relapsers	Steroid dependent
Zaki et al[32]	kuwait	55	84	--	16.6	15.2
Bircan et al[33]	Turkey	114	86.9	21.9	16.7	21.9
Davutoglu et al[34]	Turkey	62	79.8	57.1	-	22.6
Ahmadzadeh et al[35]	Iran	231	87	26.4	34.8	--
Safaei et al[36]	Iran	44	66	26.4	38.8	--
Gulati et al[37]	India	127	82.7	37.9	21.6	18.1
El Sheikh[38]	Saudi Arab	55	89.3	21	45	--
A madani et[39]	Iran	238	81.5	25.1	22.2	27
Our study	Nepal	68	83. 8 %	14.04%	3.5%	14.04%

86.8% (57) of our patients were steroid sensitive which is similar to studies done in other countries as shown in table 4 but is less (94%) than that in ISKDC report.40 In our study 68.4% patients had no relapse which is higher than in other studies. This rate in Ahmadzadeh, Safaei, and El Sheikh studies was 23%, 37% and 38.8%, respectively[35,36,38]. Closer follow up and longer study duration would have increase number of patients with relapse among our study population.

A relatively high proportion 41.2% (33) of the group had a renal biopsy. Most of them were treated earlier by other pediatricians and attended TUTH in case of frequent relapse, steroid dependence or resistance. It has been standard practice in our hospital to perform a biopsy in patients with frequently relapsing or steroid dependent NS prior to commencing alternative immunosuppressive therapy such as cyclophosphamide or cyclosporin A. Biopsy is also done on suspected secondary nephrotic syndrome.

Table 5 demonstrates some major histopathological differences among patient with idiopathic NS compared with studies done in other countries.

Table 5: Histological lesions in idiopathic nephrotic syndrome

Study	Churg et al[41]	Kumar J et al[42]	White et al[43]	Srivastava et al[44]	Our study
No of patients	521	290	145	206	21
MCD	76.4	95 (32%)	77	77	2 (9.5%)
FSGS	6.9	110(38%)	7.5	5	10 (47.6%)
MPGN	7.5	44 (15%)	6	4	5 (23.8%)
MesPGN	2.3	33 (11%)	5.5	5	3 (14.3%)
MGN	1.5	5 (2%)	1.5	1.5	1 (4.7%)
Others	5.4		2.5	7.5	

Conclusion

The clinical course of childhood NS in Nepal is similar to that of the developed world. Older age at presentation and higher incidence of hematuria, hypertension and ARF need to be confirmed by larger studies on idiopathic NS. Wider pneumococcal vaccination coverage in NS could potentially decrease the incidence of major infections in our setup.

Conflict of interest -None

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