Primary Nephrotic Syndrome of Childhood (Twenty Two Years Experience)

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Introduction

Nephrotic syndrome (NS) is a relatively common disease in childhood with an estimated annual incidence of 2 to 7 new cases per 100,000 children and a prevalence of 16 cases per 100,000 younger than 18 years of age (1,2). Primary NS (PNS) is classified into minimal change disease (MCD), focal glomerulosclerosis (FGS), membranoproliferative glomerulonephritis (MPGN), mesangioproliferative glomerulonephritis (MePGN), IgM nephropathy (IgM N) and membranous glomerulonephritis (MGN). Minimal change disease and the others might have a similar presentation, but clinical course, response to therapy, long-term prognosis for the progression of end stage renal disease are different. The aim of this study is to report the frequency, initial clinical and laboratory features, clinical course and prognosis of different types of PNS in Turkish children.

Patients and Methods

This study presents a retrospective analysis of Turkish children with PNS up to 16 years of age who were diagnosed between the dates of January 1981 – May 2003. Nephrotic syndrome was defined as heavy proteinuria (urine protein excretion > 40 mg/m² per hour) with associated edema and hypoalbuminemia. Patients with underlying secondary causes such as hepatitis B and C, sickle cell disease or lupus nephropathy and congenital NS were excluded. At the time of initial evaluation a history was taken, physical examination was performed. Laboratory evaluation including urinalysis, 24-h protein excretion, serum levels of urea, creatinine, cholesterol and albumin were recorded. In addition, clinical course and final outcome for each patient were evaluated. Hypertension was defined as the presence of systolic and/or diastolic blood pressure above 95th percent for age and sex. End stage renal disease (ESRD) was defined as serum creatinine greater than 5 times the age related normal upper limit or the need for dialysis therapy. The patients were treated with prednisone (2 mg/kg/day, max 80 mg/day) for 4-6 weeks, followed by single and lower doses, on alternate days, for additional weeks. The medication was then gradually discontinued within 2 or 3 months. Response to the therapy was classified according to the definitions from International Study of Kidney Disease in Children (ISKDC) (3). Steroid-resistant patients and some patients with frequent relapses received cyclophosphamide or cyclosporine therapy. Renal biopsy was performed in the following situations: 1. age of onset younger than one year and older than 7 years; 2. unusual clinical features (macroscopic hematuria, persistent hypertension) and/or laboratory abnormalities (hypocomplementemia, abnormal renal function); 3. steroid non-responsive or dependent patients. Materials of kidney biopsy were examined by light and immunofluorescence microscopy. Patients were classified as MCD, FGS, MPGN, MePGN, IgM N and MGN. In addition, patients were divided into two groups as MCD and non-MCD.

Statistical analyses were performed using the Statistical Package for Social Science (SPSS) for Windows. Data from groups of patients were calculated as mean±SD or as percentages. P< 0, 05 was considered statistically significant. Comparisons between groups were performed with Student's t-test for continuous data and chi-square test or Fisher's exact test for categorical data.

Results

Among 102 children, 56 (55%) were male, 46 (45%) were female. Mean age of the study group was 64±45 months (ranged 8-168 months). The follow up period was 56±50 months. Fifty-six (55%) patients were diagnosed as MCD with their initial presentations, laboratory features, the clinical course and renal biopsy findings (4 patients) in suspicious cases. Renal biopsy was performed in all the 46 (45%) patients a group which we describe as ''non-MCD group''.

Table 1 shows the distribution of histopathologic diagnoses and Table 2 shows the distribution of demographic, clinical and laboratory data.

Further evaluation of different histopathological diagnosis of the patients revealed that the age at presentation of the patients with MPGN were older than the patients with MCD (124±40 months vs. 34±19 months, p<0,001) and the patients with FGS (124±40 months vs. 55±47 months, p=0,001). It was also noted that 75 % of the patients with MPGN were older than 9 years and 75 % of the patients with MCD were younger than 5 years of age.

Family history for renal diseases as nephrotic syndrome or chronic renal failure was found in 8 children all were included in non-MCD group.

During follow up, ESRD developed in 11 children, 6 with MPGN and 5 with FGS.

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Table 1. Distribution of histopathologic diagnosis

Renal pathology	n (50)	(%)
MPGN	19	(38)
FGS	11	(22)
MePGN	7	(14)
MGN	5	(10)
IgM N	4	(8)
MCD	4	(8)

MPGN: Membranoproliferative glomerulonephritis, FGS: Focal Glomerulosclerosis,
MePGN: Mesangioproliferative glomerulonephritis, MGN: Membranous glomerulonephritis,
IgM N: IgM nephropathy, MCD: Minimal Change Disease

Table 2. Distribution of demographic, clinical and laboratory data from patients with MCD and non-MCD groups

	MCD group N=56	Non-MCD group N=46	p
Age (months)			
Mean±SD	41±24	93±50	<0,001
Hypertension			
n (%)	7 (12)	17 (37)	0,007
Hematuria			
n (%)	11 (19)	36 (78)	<0,001
Level of serum creatinine (mg/dl)			
Mean±SD	0,49±0,24	1,19±1,69	<0,001
Hypocomplementemia			
n (%)	1 (2)	11 (24)	0,005

Discussion

Minimal change disease is the most common cause of PNS in children. The frequency of MCD was reported in 55 to 77% of nephrotic children (ISKDC) (4). The frequency of MCD is 55% in our series. This relatively low frequency might be because of the location of our hospital being as a third step health care center where complicated patients are referred for renal biopsy.

Our results show that MPGN is the predominant histopathological type in our patients with PNS. Similar results were reported from Nigeria (5). In contrast, other studies from USA, India and S. Arabia have reported that FGS was the most common histopathological subtype in PNS of childhood (4, 6, 7, 8). The differences between different populations could be related with ethnic, genetic and/or environmental factors.

MCD carries a favorable long-term outcome. Whereas, non-MCD usually bears a poor prognosis and requires more aggressive therapy. The results of our study have shown that certain demographic, clinical and laboratory features at presentation might be predictable for prognosis in childhood PNS. The mean age of MCD group was younger than non-MCD (3, 5 years of age vs. 8 years of age). Detailed evaluation of different histopathological subtypes revealed that the mean age of patients with MPGN were found to be 2 times higher than the mean age of patients with FGS (10 years of age vs. 4, 5 years of age). Thus age seems to be an independent predictor for the prognosis of PNS in childhood.

In addition, the presence of hypertension, hematuria and hypocomplementemia in MCD group was significantly lower.

In conclusion, younger age of onset, absence of hematuria, hypertension, hypocomplementemia and renal failure at presentation could be interpreted as indicators of a favorable prognosis in childhood PNS.

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