Study of Spectrum of Histopathological Findings in Childhood Nephrotic Syndrome In Tertiary care Hospital

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Abstract

Background: The overall prevalence of Nephrotic syndrome (NS) in childhood is approximately 2-5 cases per 100000 children. The cumulative prevalence rate is approximately 15.5 cases per 100000. Steroid responsive minimal change nephrotic syndrome (MCNS) is most common variety and has good prognosis. Separation of MCNS from Non-MCNS is important.

Aim: This study was undertaken to evaluate the histopathological diagnosis of Non-MCNS diseases.

Methods: This study was done in Dept of Paediatrics, KIMS, Hubli during January 2011 to December 2013. All children between 0 to 12 years, who fulfilled diagnostic criteria of nephrotic syndrome, and had indications for renal biopsy were taken into study. Their demographic, clinical, laboratory and histopathological data were retrieved from files and original renal biopsy forms.

Results: Fourteen children with idiopathic nephrotic syndrome (INS) were analysed during the period. There were 9 boys (64%), 5 girls (36%). M:F= 2.5:1. No patients of congenital NS were present. In children who underwent biopsy, 42.5% were infrequent relapses followed by 21.42% were frequent relapses and steroid dependent. Among 14 children who underwent biopsy 6 had hypertension (42%), 5 had hematuria (35%) and 3 (21.42%) were steroid dependent. The most common histopathological subtypes in 14 children were Minimal change disease (MCD)- 5(35.71%) followed by IgA Nephropathy-4 (28.57%) and 2(14.28%) were focal segmental glomerulosclerosis (FSGS).

Conclusion: Our results indicate MCD to be the most common histopathological variety in INS, followed by IgA Nephropathy and FSGS. Most children respond to therapy and achieve remission and have a better long term prognosis. Properly indicated renal biopsy has diagnostic and prognostic value in children.

Key words: Minimal change disease; Focal segmental glomerulosclerosis; idiopathic nephrotic syndrome

Introduction

Nephrotic syndrome is characterized by nephrotic range proteinuria and the triad of clinical findings associated with large urinary losses of protein: hypoalbuminemia, edema, and hyperlipidemia. Approximately 90% of children with nephrotic syndrome have idiopathic nephrotic syndrome. Idiopathic nephrotic syndrome (INS) is associated with primary glomerular disease without evidence of a specific systemic cause. Idiopathic nephrotic syndrome includes multiple histological types: minimal change disease (MCD), mesangial proliferation, focal segmental glomerulosclerosis (FSGS), membranous nephropathy, and membranoproliferative glomerulonephritis. Nephrotic syndrome (NS) may also be secondary to systemic diseases. The overall prevalence of NS in childhood is approximately 2-5 cases per 100000 children. The cumulative prevalence rate is approximately 15.5 cases per 100000[1,2].

In nephrotic syndrome prognosis is difficult. Conventional investigations yield little information of prognostic value. Even the blood urea and the glomerular filtration rate are often misleading. Children with onset of nephrotic syndrome between 1

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and 8 years of age are likely to have steroid-responsive MCNS and best long term prognosis. So the separation of MCNS from others is important[3,4,5]. Children with features of Non-MCNS (gross hematuria, hypertension, renal insufficiency, age <1 yr or >8 yr) should be considered for renal biopsy before treatment. Hence, the aim of the present study was to evaluate the histopathological diagnosis of Non-MCNS diseases.

Materials and Methods

This study was undertaken in Dept. of Pediatrics, KIMS, Hubli from January 2011 to December 2013 and children were of 0 to 12 years of age.

Nephrotic Syndrome consisted of nephrotic range proteinuria defined as protein excretion of > 40 mg/sq.m/hr or a first morning protein:creatinine ratio of >2-3 : 1, edema and hypoalbuminemia (serum albumin level <2.5 g/dl).

Steroid dependency was defined as relapse while on alternate-day steroid therapy or within 28 days of completing a successful course of prednisone therapy.

Frequent relapsers were patients who respond well to prednisone therapy but relapse ≥4 times in a 12-month period.

Steroid resistants were who fail to respond to prednisone therapy within 8 weeks of therapy.

Following informed consent, ultrasonography (USG) guided renal biopsy was done in the following situations[1,2,6]:

- Age of onset between <1 yr or >8yr
- No response to 8 weeks of prednisolone therapy
- Frequent relapse, steroid dependent
- Persistent hematuria
- Renal insufficiency

A detailed history was taken, clinical examination and urine analysis data were entered in predesigned proforma.

USG guided renal biopsy was performed on all after informed and written consent. Two renal biopsy materials of 5 mm length, one in formalin, and one in normal saline were sent for light microscopy and immunofluorescence examination.

Results

Children between 0-12 years of age were included in the study. A total of 14(n) children were studied. Mean age of presentation was 7.93 +/- 3.67 years. There were 9 boys (64%), 5 girls (36%). M:F= 2.5-1. (Table 1)

Table 1. Age and gender distribution

	<1year	1-8years	>8years
Male	0	4	5
Female	0	3	2
Total	0	7	7
%	0	50	50

Male: Female: 2.5:1

In children who underwent biopsy, 42.85% were infrequent relapses followed by 21.42% were frequent relapses and steroid dependent. Among 14 children who underwent biopsy 6 had hypertension (42%), 5 had hematuria (35%) and 3 (21.42%) were steroid dependent (Table 2).

Table 2. Clinical state of the patients

	No. of children	%
Frequent relapsers	3	21.42
Infrequent relapsers	6	42.85
Steroid dependent	3	21.42
Steroid resistant	1	7.14

The most common histopathological subtypes in 14 children were Minimal change disease - 5 (35.71%) followed by IgA Nephropathy - 4 (28.57%) and 2 (14.28%) were FSGS (Table 3, Table 4).

Table 3. Histopathological findings on immunofluorescence

	No. of children	%
Minimal change disease	5	35.71
IgA nephropathy	4	28.57
FSGS	2	14.28
FGS	1	7.14
OTHERS*	2	14.28

*Mild mesangial proliferation with patchy tubular atrophy, Mild proliferative with no chronic tubulo interstitial change

Table 4. Histopathological findings and its distribution

		MCD	IgAN	FSGS	FGS	Others
AGE	<1 year	-	-	-	-	-
	1-8 years	2	2	1	1	1*
	>8 years	3	2	1	0	1+
Hypertension		1	0	2	1	2
Hematuria		0	3	1	1	0
Steroid dependent		2	1	0	0	0
Steroid resistant		0	0	0	0	1*

* Mild mesangial proliferation with patchy tubular atrophy

+ Mild proliferative with no chronic tubulo interstitial change

Discussion

The treatment of nephrotic syndrome in children is often challenging[7]. Approximately 10-20% of children with NS are classified as having Steroid resistant nephrotic syndrome (SRNS). The treatment of steroid dependent and frequent relapsers is challenging and there always is a risk of adverse reaction to immunosuppressive drugs. Because of risk of complication due to side effects of prolonged treatment with immunosuppressive drugs[8] and risk of progressive renal disease, reports have suggested that the outcome can be predicted from the clinical response to steroids and has best prognostic value. Renal biopsy has definite role and is of significant prognostic value.

Our study throws light on the spectrum of histopathology findings in Idiopathic Nephrotic Syndrome (INS). Our results indicate MCD to be the most common histopathological variety in INS, followed by IgA Nephropathy and FSGN.

Most children respond to therapy and achieve remission and have a better long term prognosis.

Properly indicated Renal biopsy has diagnostic and prognostic value in children.

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