RESULTS OF RENAL BIOPSY IN CHILDREN WITH NEPHROTIC SYNDROME AT TRIPOLI CHILDREN HOSPITAL

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ABSTRACT

Nephrotic syndrome is an important renal disorder in children. The role of renal biopsy in children with nephrotic syndrome is controversial, especially in children with frequent relapses or steroid-dependent nephrotic syndrome. The aims of this study are to verify indications of renal biopsy in children with nephrotic syndrome, to identify patterns of glomerular disease and its corresponding outcomes. This is a descriptive study reviewed retrospectively a 25 renal biopsies from children with nephrotic syndrome who followed up in nephrology unit at Tripoli Children Hospital from Jun. 1995 to Jan. 2006. Children with either steroid resistant or steroid dependent who underwent renal biopsy were included. Twenty five of children (14 male and 11 female) with nephrotic syndrome were included. The mean age 5.2±4.6years (range was from 1-14 years). 14(56%) children were steroid resistant and 11(44%) children were steroid dependent. Minimal-change disease (MCD) accounted for 12(48%) children, focal and segmental sclerosis (FSGS) was accounted for 10(40%) children and 3**(**12%) children accounted for other histopathological types. 7(87.5%) of children with FSGS had progressed to end stage renal disease. Steroid resistant was the main indication for renal biopsy in children with nephrotic syndrome. There was increased frequency of FSGS nephrotic syndrome among children with steroid resistant type with poor outcomes.

KEY WORDS: Nephrotic syndrome, Renal biopsy, Minimal change disease, Focal segmental glomerulosclerosis.

INTRODUCTION

Minimal change disease (MCD) is the most frequent lesion associated with idiopathic nephrotic syndrome in children[(1)]. In 1970, the International Study of Kidney Disease in Children (ISKDC) reported an increased frequency of MCD than focal segmental glomerulosclerosis (FSGS) and other renal pathology. On the basis of data from the ISKDC conducted in 1978, it has been accepted that MCD is by far the most frequent lesion associated with idiopathic nephrotic syndrome in children and adolescents, accounted for 77% of cases in all biopsies performed in children while FSGS represented nearly 8-10%[(2)]. However, recently several reports have been noted that there is an increase trend of FSGS in both children and adults who were biopsed for their nephrotic syndrome to rates as high as 50%[(3,4)]. The role of the renal biopsy in children with nephrotic syndrome is controversial, especially in patients with frequent relapses or steroid dependent nephrotic syndrome[(5)]. Steroid resistant still remain the main indication for renal biopsy in children with nephrotic syndrome[(6)]. Certain clinical features are consider to be atypical in steroid sensitive nephrotic syndrome these include, extreme of age (less than 1 years, or greater than 12 years), persistent hypertension, persistent renal impairment, gross hematuria and low plasma complement concentration[(7)]. It is well recognized that FSGS in children with idiopathic nephrotic syndrome carries poor prognosis. Although initially considered a resistant lesion but the data suggest that more aggressive therapies can induce a response in more than 50% of patients[(8,9,10,11)]. Our objectives are to verify the indications of renal biopsy in children with nephrotic syndrome, identifying patterns of glomerular disease frequency as well as their outcomes.

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PATIENTS AND METHODS

A retrospective review was conducted of children with idiopathic nephrotic syndrome who underwent percutaneous renal biopsy from Jun, 1995 to Jan, 2006. The study include children with steroid resistant nephrotic syndrome and children with steroid dependent who presented with atypical presentation which include Age (less than 2 years and more than 10 years), persistent hypertension, renal function impairment persistent hematuria and decrease serum complement.

At presentation, they were evaluated for hypertension, hematuria, renal function status and serum complement. After discussion with parents, kidney biopsy was performed in all patients. The procedure done in Tunisia or Jordan. The specimens had examined by light microscopy, Immunoflourenscnce stained and electron microscopy. Minimal change disease was diagnosed by normal glomeruli on light microscope, lack of immuno deposit on Immunoflourenscnce and foot process effacement by electron microscope.

In idiopathic FSGS, the glomeruli show mesangeal proliferation and segmental scaring on light microscope, Immunoflourenscnce show IgM and C3 staining in area of segmental sclerosis. By electron microscope show segmental scaring of glomerular tuft with obliteration of glomerular capillary lumen. FSGS was diagnosed when at least one glomerulus demonstrate segmental sclerosis on light microscope.

A diagnosis of steroid resistant was made if there is no response to 4-week course of prednisone at a dose of 60 mg/m2/day. Steroid dependent was defined as development of 2 consecutive relapses during steroid therapy or within 2 wk of its cessation. Hypertension was defined as a blood pressure consistently above 95th centile for height, age and sex. Hematuria and proteinuria are assessed by dipstick urine analysis.

STATISTICS ANALYSIS

After data collected they were coded and transferred into the Statistical Package for the Social Sciences (SPSS), version 12. Results are expressed as either means ± SD or percentage. The statistical tools used like frequencies, ratio, and chi-square test. The level of significance was set at P value < 0.05 in all cases.

RESULTS

This study provided the histopathological classification of nephrotic syndrome in children followed up in Tripoli Children Hospital over a period of 10 years (1995-2006) on a total 25 renal biopsies, 14(56%) were males and 11(44%) were females. The mean age 5.2 ± 4.6years (range was from 1-14 years). The mean period before biopsy was 15.8 mo (range 1-84 mo) and mean follow up duration (6.5 ± 3.1) years range (2-11) years.

The indications of renal biopsy were as following 14(56%) were steroid resistant and 11(44%) were steroid dependent as shown in (table 1).

(Table 1) Indications of renal biopsies

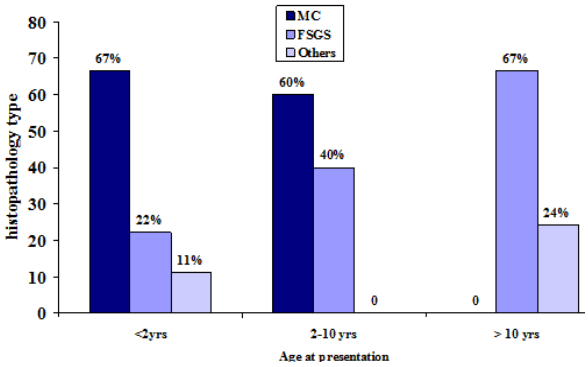
Type	MCD (%)	FSGS (%)	Other pathology	Total (%)
Steroid resistant	4(28.6)	8(57.1)	2(14.3)	14(56)
Steroid dependent	8(72.1)	2(18.2)	1(9.1)	11(44)
Total	12(48)	10(40)	3(12)	25(100)

MCD minimal change disease, FSGS focal segmental glomerulo-sclerosis SR steroid resistant, SD steroid dependent.

Other histopathology accounted for 3(12%) which include lupus nephritis in one case, IgA nephropathy in one child and mesangio proliferative glomerulosclerosis (MPGN) in one child.

At presentation 12(48%) of these children had presented with typical presentation and 13(52%) had presented with atypical presentation. The atypical presentation include extreme of age, hypertension, hematuria, renal impairment, low serum complement.

When compare age at presentation versus histopathology types of nephrotic syndrome 9(36%) children were less than 2 years of age, 10(40%) children are between 2-10 years of age and 6(24%) are more than 10 years of age as shown in (figure 1).



(Figure 1) age at presentation n versus type of histopathology types

When compare MCD with FSGS and other histopathology types, children MCD were younger at diagnosis than FSGS and other pathology (2.9yeares versus 7 and 8.7 years), boys were more likely to be MCD than FSGS (64.3% versus 28.6%) and steroid resistant children were more likely to be FSGS than MCD while steroid dependent were more likely to be MCD than FSGS as shown in (table 2).

(Table 2) MCD versus FSGS and other histopathology types

Characteristic	MCD	FSGS	Other pathology
No. of children	12	10	3
Mean age at presentation	2.9 ± 2.5 yrs	7 ± 4.8 yrs	8.7± 6.9 yrs
Male: female ratio	3	0.66	0.5
Steroid resistant	23%	61.50%	15.50%
Steroid dependent	75%	16.70%	8.30%

MC minimal change disease, FSGS: focal segmental glomerulonephrosis

Regarding the clinical outcomes of these children a chi-square was done between histopathology types and development of end stage renal failure, no children with MCD advanced to end stage renal failure however 7(87.5%) of children with FSGS progressed to end stage renal failure as shown in (table 3).

(Table 3) Long term follow up

Type	No RF (%)	RF (%)	Total (%)	P value
MCD	12(48)	0(0)	12(48)	0.002
FSGS	3(17.6)	7(87.5)	10(40)	0.001
Others	2(8)	1(4)	3(12)	0.001
Total	17(68)	8(32)	25(100)	

MCD minimal change disease, FSGS: focal segmental glomerulonephrosis, RF: renal failure

DISCUSSIONS

Idiopathic nephrotic syndrome in children has conventionally been associated with minimal change disease. White et al reported that MCNS in up to 90% among all children with idiopathic nephrotic syndrome, FSGS has generally been considered a

relatively infrequent cause[1]. In first ISKDC report (1970) 127 children, MCD was diagnosed in 77%, FSGS in 9% and MPGN in 5% of children who were biopsy prior to treatment[2]. In second ISKDC report (1978) 521 children, FSGS account only for 7%[3]. In recent studies there were increased trends in FSGS as high as 50%[4,12,13]. In this study, there was an increasing trend for FSGS which accounted for 10(40%) in these children who under went renal biopsy while MCD was found in 12(48%). This figure was different from ISKDC previous reports. The increase in frequency of FSGS case is mainly due to highly selectiveness of cases and renal biopsies are not usually preformed in children with idiopathic nephrotic syndrome and being recommended for the small proportion of atypical cases. 57% of children with steroid resistant were FSGS while 72.1% of children with steroid dependent were MCD. Steroid resistant still the most common important indication for biopsy in children with nephrotic syndrome[8] it accounted for 14(56%) in this study. The second indication for renal biopsy was steroid dependent nephrotic syndrome it accounted for 11(44%).

The incidence of MCD has been found to be higher in younger children presented with idiopathic nephrotic syndrome. However FSGS and other renal pathology found to be more in older children. Girls were more likely than boys to develop FSGS and other pathology than MCD these finding was similar to Olivia B et al[10].

Churg et al reported that children with FSGS at time of diagnosis of nephrotic syndrome showed a clinical pattern of rapidly developed steroid resistant and commonly progressed to end stage renal disease (ESRD)[1]. The South west paediatric nephrology study group reported that 21% of children who biopsed for steroid resistant had development of ESRD[15]. In this study there were a high percentage of children who diagnosed as FSGS by renal biopsy progressed to ESRF (87.5%) this high rate may be related to late presentation of these children and late performing a renal biopsy. In many studies including this study MCD had excellent prognosis, the current recommendations of kidney biopsy in childhood idiopathic nephrotic syndrome were put forward to minimize unnecessary kidney biopsies in children with idiopathic nephrotic syndrome.

CONCLUSION

MCD remains the most common histopathological subtype in children with steroid dependent nephrotic syndrome while FSGS is the most histopathological subtype in children with steroid resistant nephrotic syndrome. Most children with steroid resistant due to FSGS progressed to end stage renal disease at the same time no children with MCD progressed to end stage renal disease. Based on these observations, we recommended minimizing renal biopsy in children with steroid dependent nephrotic syndrome. FSGS children were more likely to be girls, older age at presentation and steroid resistant. Children with MCD were more likely to be boys, younger age at presentation and steroid dependent. Renal biopsy should be done as early as possible in children with steroid resistant nephrotic syndrome and more aggressive therapeutic modalities for children with FSGS pathology.

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