Original Article

Childhood nephritic syndrome Clinical manifestations and histopathlogical spectrum

Nariman-F.-Ahmed* FICMS
Raghad Ibrahim** FICMS

Fac Med Baghdad 2007; Vol. 49, No.3
Received Nov. 2006
Accepted April 2007

Summary:

Background: *Nephrotic syndrome in children is a clinical manifestation of different histopathological subtypes.*
Objectives: *The objectives were to study the different histopathological subtypes of idiopathic nephrotic syndrome and to study their clinical and biochemical parameters at the time of diagnosis for children admitted to Children Welfare Teaching Hospital.*
Methods: *A Retrospective study was done on 160 children with idiopathic nephrotic syndrome who were diagnosed and/or treated at Children Welfare Teaching Hospital and were followed up in the pediatric nephrology consultation clinic between April 2004 and April 2006.*
Results: *The study group included 40 children with idiopathic nephrotic syndrome r Who underwent renal biopsy. There were 26(68.7%) males and 14(31.2%) females.*
Age at onset ranged between (1-15) years, median age (3.5) years. Facial oedema was found in 90%, hypertension in 45% patients, gross hernaturia in 27.5 and persistent microhematuria in 45%. Sixteen (40%) patients had focal and segmental glomerulosclerosis on renal biopsy, nine (22.5%) patients minimal change nephrotic syndrome, eight (20%) patients mesangioproliferative glomerulonephritis, and seven (17.5%) patients had membranoproliferative glomerulonephritis.
Conclusion: *Focal and segmental glomerulosclerosis was the most common histopathological subtype in our study group. Further large studies is needed to find out changing trends of histopathology in childhood nephrotic syndrome*
Key words: *Nephrotic syndrome, Children, Histopahological subtypes*

Introduction:

Nephrotic syndrome represents a complex of symptoms caused by increase glomerular permeability to plasma proteins. (1, 2)

Most commonly appears between the age of 2 years and 6 years. (3)

There is variation in different histological type in different population. It could be subdivided into congenital, idiopathic (primary) or secondary nephrotic syndrome. (3) Idiopathic nephrotic syndrome occurs in about 90% of children, it includes mainly three histological types: - (3)
1-minimal change disease, this account for about 85% of nephrotic children, 95% responds to steroid.
2-mesangial proliferations presenting approximately 5% of idiopathic nephrotic syndrome. Approximately 50% of patients with this histological lesion respond to steroid therapy.
3-focaland segmental glomerulosclerosis represents 10% of idiopathic nephrotic syndrome, 20% of patients respond to steroid therapy. 4. Others (ex. Membranoproliferative glomerulonephritis).

Children with onset of nephrotic syndrome between 1 and 8 years of age are likely to have steroid-responsive minimal change disease; therefore steroid therapy may be initiated without renal biopsy. (3)

*Dep. Of pediatrics, Coll. Of Medicine, Univ. of Baghdad
**, Pediatrician, Child welfare Teaching Hospital

Indications of renal biopsy in nephrotic syndrome include: (2) Onset age < 12months or >8 years, macroscopic hematuria. , Hypertension, microscopic hematuria, low plasma C3. Renal failure not attributed to hypovolaemia, steroid resistant and frequent relapses.

Patients and method:

A retrospective study was done on 160 children with idiopathic nephrotic syndrome admitted to Children Welfare Teaching Hospital from April 2004- April 2006. (With age of onset 1-15years), median age 3.5 years.

Secondary and congenital causes of nephrotic syndrome (N.S.) were excluded form the study.
The definitions used to describe patients with nephrotic syndrome in the study (1, 3)
-Nephrotic syndrome: The presence of protienuria>1 g/m2 /day, plasma albumin <25g/l, hypercholesterolemia and oedema.
- Remission: Urine (trace, negative or +) for protein on dipstick for 3 consecutive days.
- Steroid responsive: - Remission achieved with steroid therapy a lone - Relapse: 3+ to 4+ proteinuria plus oedema
- Frequent relapses: Four or more relapses within any 12 months period.
- Steroid dependent: - Patients who relapse while on alternate day steroid therapy or within 28 days of stopping predinsolon.
- Steroid resistance: Failure to achieve response in spite of 8 weeks predinsolone 60mg/m2/day.
- Hypertension: is defined as average systolic or

diastolic blood pressure greater than or equal to 95th percentile for age and sex measured on at least three separate occasions.

In this study renal biopsy was done for nephrotic patients with clinical and biochemical parameters suggest a diagnosis other than minimal change disease (ex.

hypertension, gross hematuria, persistent microscopic hematuria, impaired renal function) or if child fails to respond to steroid therapy. The study group included 40 children with idiopathic nephrotic syndrome who under went biopsies.

Percutaneous renal biopsy was done under ultrasound gaiud, patients were given diazepam (0.2mg/kg), and trucut needle gage 18 was used. The sample taken was preserved in formalin 20% and sent for histopathology study to be evaluated by light microscopy.

Results:

Percutaneous renal biopsy was performed in 40 of 160 patients with idiopathic nephrotic syndrome. There were 26(68.7%) males and 14(31.2) females. With age of onset ranged between (1-15 years), median age 3.5 years Focal and segmental glomerulosclerosis (FSGS) was the most common histopathological subtype, occurring in 16 of 40 children (40 %).other subtypes included minimal change disease(MCD) in 9 children(22.5 %), mesangioproliferative glomerulonephritis (Mesp.GN) in8 children(20%),and membranoproliferative glomerulonephritis (MPGN) in 7 children (17.5 %). Table No. (1)

Table (1) distribution of histopathological subtypes of idiopathic nephrotic syndrome among 40 patients underwent renal biopsy

Histopatlohogical lesions	Male No. (%)	Female NO. (%)	Total No. (%)
Minimal change disease	6(15)	3(7.5)	9(22.5)
Focal segmental ghomerulosclerosis	11(27.5)	5(12.5)	16(40)
Mesa ngioproli ferative glomerulonephritis	4(10)	4(10)	8(20)
Membranoprolifera tive glomerulonephritis	5(12.5)	2(5)	7(17.5)
Total	26(65)	14(35)	40(100)

Regarding clinical and biochemical parameters: Facial oedema was found in 36(90 %) patients, hypertension in18 (45 %) patients, gross hematuria in 11(27.5 %) patients and persistent microscopic hematuria in 18(45 %) patients. Table No. (2)

Table (2) clinical and biochemical parameters of the patients according to their histopathological subtypes

Histopathological Lesions	Facial oedema No. (100%)	Hypertension NO. (100%)	Gross Hematuria No. (100%)	Microhematur No. (100%)
Minimal change disease	9(22.5)	2(5)	2(5)	4(10)
Focal segmental ghomerulosclerosi	14(35)	8(2.2)	5(12.5)	7(17.5)
Mesangioprolifera tiv+ glomerulonephritis	7(17.5)	4(l)	2(5)	3(7.5)
embranoproliferati glomerulonephritis	6(15)	4(10)	2(5)	4(10)
Total	36(90%)	18(27.5)	11(27.5)	18(27.5)

Among 7 steroid sensitive nephrotic patients 43 % had minimal change disease (MCD), 28.5% had mesangioproliferative glomerulonephritis (Mesp.GN) and28.5% had membranoproliferative glomerulonephritis (MPGN). No patient with focal and segmental glomerulosclerosis (FSGS) had response to steroid. Table No. (3 Among 14 steroid dependent nephrotic patients 28 % had minimal change disease (MCD), 43 % had Focal and segmental glomerulosclerosis (FSGS), 14.25 % had mesangioproliferative glomerulonephritis (Mesp.GN) and] 4.25 % had membranoproliferative glomerulonephritis (MPGN). Table No. (3) Among 19 patients % who failed to respond to steroid, 10.5 % had minimal change disease(MCD), 50.6 % had Focal and segmental glomerulosclerosis (FSGS) , 21 % had mesangioproliferative glomerulonephritis (Mesp.GN) and 15.7 % had membranoproliferative glomerulonephritis (MPGN) . Table No. (3)

Table (3) distribution of histopathological lesion according to steroid responsiveness

Histopatlohogical Lesions	Steroid Responsive No. (%)	Steroid Depended No. (%)	Steroid Resistant No. (%)
Minimal change disease	3(43)	4(28)	2(10.5)
Focal segmental ghomerulosclerosis	0	6(43)	10(50.6)
Focal segmental ghomerulosclerosis	2(28.5)	2(14.5)	4(21)
Membranoproliferative glomerulonephritis	2(28.5)	2(14.5)	3(15.6)
Total	7(17.5)	14(35)	19 (47.5)

Discussion:

It is widely accepted that minimal change nephrotic syndrome is the most common cause of nephrosis in children. Children between 1-8 years are very likely to be steroid sensitive minimal change disease (MCD) and so corticosteroid therapy is usually initiated without renal biopsy. (2)

Renal biopsy in our study was done before

treatment for patients presented with clinical features suggest a diagnosis other than (MCD). Although oedema is found in most of the patients, hypertension, gross hematuria and persistent microscopic hematuria was more common in patients with FSGS, a finding which is in consistent with that reported in other Iraqi study. (4)

In this study renal biopsy was performed in 40 out of 160 patients, focal and segmental glomerulosclerosis was the most common histopathological subtype found in 16(40%) patients, followed by minimal change disease in9 (22.5%) patients, mesangioproliferative glomerulonephritis in 8(20%)patients and membranoproliferative glomerulonephritis in7 (17.5%) patients.

Our study group is similar to studies reported. from Iraq and Saudi Arabia with respect to histopathology (5, 6)

While a study from Turkey showed that mesangioproliferative glomerulonephritis was the most common histopathological subtype, followed by membranoproliferative glomerulonephritis. (7)

It has been reported that there are racial and regional differences in. histopathological features and response to steroid therapy in childhood idiopathic nephrotic syndrome. Ramash kumar from India showed an increase incidence of focal and segmental glomerulosclerosis 32% before 1990 versus 38% after 2000. (8)

Recent studies in children shows changing trend of histopathology with increase incidence of focal and segmental glomerulosclerosis during the last decade accompanied by significant decline in the incidence of minimal change disease. (9) In practice the histological category is less important than response to steroid. (2) In our study among 19 patients who failed to respond to steroid, 10.5 % had MCD, 50.6% had FSGS, 21 %had Mesp.GN and 15.7 °/0 had MPGN.While a report from international study of kidney disease in children showed that among 55 patients who failed to respond to steroid45.5% had MCD, 47.5%had FSGS and 7"/o had Mesp.GN.

In conclusion: further large studies are needed in Iraq to find out changing trends of histopathology in childhood nephrotic syndrome, which may have significant implications in the management of childhood nephrotic syndrome in the future.

References:

1- Watson A.R. Idiopathic nephrotic syndrome. In Forfar and Arneil's textbook of pediatric, AGM compel; McIntosh MD. Churchill living stone: 16 editions 2002:968972

2-Clarck A.G., Barratt T.M. steroid responsive nephrotic syndrome.
In: pediatric nephrology, Barratt T.M, MB, FRCS; Avner E.D, MD, Harmon W.E, MD; 5TH edition, 2004: 542-555

3-Richard E. German, M.D, Robert M. Kliegman, MD, Hal B. Jenson, MD. Nephrotic syndrome In: NELSON Textbook of pediatrics. 17th edition: 519: 1753-1757.

4. Izat NF; Idiopathic nephrotic syndrome of childhood and features of relapse. J.Fac.Med (Baghdad), 2003, vol.45, No.1-2

5- Tagreed M. Clinical and histopathological profile of children nephrotic syndrome a thesis submitted to Iraqi commission for medical specialization in partial fulfillment of the requirement for the degree of the Iraqi commission for medical specialization in pediatrics, 2005

6. Kari JA. Changing trends of histopathology in childhood nephritic syndrome in western Saudi Arabia. Saudi j. 2002 Mar; 23(3): 317-21

7-Bircan z. Yavuz A, Katar S, Vitrinet A, Yildirim M.Childhood idiopathic nephritic syndrome in Turkey.Pediatrr.int.2002 Dec; 44(6): 608-11

8-Kaulnar J.Gulati S.Sharma AP.Sharma RK.Gupta RK.I-listopathological spectrum of childhood nephrotic syndrome in India children. Pediatr.Nephrolo.2003 Jul; 18(7): 657-60

9-Dragovic D. Rosenstock JL. What SJ.Panagopoulos G.Devita MV.Michelis MF.Increasing incidence of focal and segmental glomerulosclerosis and an examination of demographic patterns. Clin Nephrolo.2005 Jul; 64(1); 78-9