CLINICAL AND BIOCHEMICAL EVALUATION OF ATYPICALLY PRESENTED CHILDHOOD NEPHROTIC SYNDROME

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Summary

Nephrotic Syndrome(NS) is an important chronic renal disorder in children characterized by massive proteinuria, hypoalbuminaemia, hypercholesterolaemia and generalized oedema, occasionally with atypical presentation like hypertension, haematuria, low C3 & impaired renal function. This study was conducted with the objective to find out the differences in clinical and biochemical changes & to observe the differences in response to predoisolone between atypical & classical Nephrotic Syndrome. Thirty cases of nephrotic syndrome with atypical presentation of age <2 yrs and >8 yrs associated with hypertension, haematuria, low C3, impaired renal function admitted in the department of Paediatrics, Bangabandhu Sheikh Mujib Medical Unversity, Bangladesh Institute of Child Health, Dhaka & Chittagong Medical College were studied from 15th April, 2003 to 15th September, 2003. Equal number of classical nephrotic syndrome cases were taken as comparator for comparison of clinical features, biochemical behaviour and response to steroid treatment. Age of presentation of the study group ranges from 1 to 15 years with Mean age was 7.50 + 4.45 years with male female ratio 1.72:1. Most (70%) of the study group presented with 2 or more atypical features. Most (60%) of the cases presented at age more than 8 years. Urinary total protein was found to be lower in the study group but the difference from the comparator was not statistically significant (P>0.05%) & the serum cholesterol level was significantly lower (P>0.05) in study group. Focal segmental glomerulosclerosis was the predominant (41.66%) histopathologic finding on biopsy. Response to steroid was significantly poor in the study group(P<0.001). Nephrotic syndrome in children may present with atypical clinical features, abnormal biochemical and histopathological findings with poor response to steroid. All patients of nephrotic syndrome should be screened carefully on the basis of their clinical presentation & biochemical values to identify the atypical cases.

Key words: nephrotic syndrome; proteinuria; oedema

Introduction

Nephrotic syndrome is an important chronic renal disorder in children [1]. It is very important to know about the disease in different dimension due to its chronicity, variable outcome and complexity in management[1]. The incidence of nephrotic syndrome is 1 to 3 per 100000 children [2]. Fifty to sixty percent of total indoor bed in pediatric nephrology unit of Bangabandhu Sheikh Mujib Medical University (BSMMU) is occupied by the patient of nephrotic syndrome [3].

Nephrotic syndrome may be defined as a clinical condition characterized by massive proteinuria (> 40 mg/hr/m^2 determined quantitatively on over night collection), hypoalbominaemia (<2.5 gm/dl), generalized edema and hypercholesterolaemia (>250mg/ dl) [4]. It is more common in boys than in girls (2:1) and most commonly appears between the age of 2 & 6 years [5].

Along with the classical presentation a number of cases present with some atypical presentation (age of onset < 2years or > 8 years, haematuria, hypertension, low C3level and impaired renal function) [6,7]. Outcome of these patients are poor in comparison with the classical presented nephrotic syndrome [8]. There is a shift towards an increasing prevalence of focal segmental glomerulosclerosis over the years in the Indian population with higher prevalence of atypical presentation. This trend has immense therapeutic and prognostic significance[9]. In our country we do not have any actual data regarding the atypical presentation of childhood nephrotic syndrome. The aim of our study to find out the clinical and biochemical changes between atypical and classical nephrotic syndrome and also to observe the difference in response to treatment with initial steroid therapy between the two groups.

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Materials and method

This is a descriptive comparative study and was carried out in The Department of Pediatric Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka.Bangladesh Institute of Child Health, Dhaka. Department of pediatrics, Chitagong Medical College Hospital, Chittagong during the period of 15th April 2003 to 15th September 2003.

Thirty cases of atypical presentation of Nephrotic Syndrome (study group) were included having the following inclusion Criteria [6,7] :

I. Age of onset: Less than 2 years or more then 8 years.

II. Hypertension

III. Hematuria

IV. Low C3

V. Impaired renal function

Any patient presented with Hematuria, Hypertension due to other causes were excluded from the study.

Thirty cases of classically presented Nephrotic Syndrome were included in the control group

Inclusion Criteria of control group [4] : The admitted cases of nephrotic syndrome having the following criteria :

1. Age 2 yrs to 8 yrs
2. No hypertension
3. No hematuria
4. Normal C3
5. Normal renal function.

Patients presented with oedema due to other causes and secondary causes of Nephrotic syndrome e.g. SLE were excluded from the study.

After taking informed consent form the parents about the motive of the study, a detailed history was taken and clinical examination was done. Bedside heat coagulation test of urine was done in each case for gross assessment, following investigations were done to confirm the diagnosis for both cases and controls.

Urine routine and microscopic examination,culture with colony count and sensitivity test, estimation of 24hrs. urinary total protein, complete blood count, serum total protein, serum albumin, albumin globulin ratio, serum cholesterol, blood urea, serum creatinine, electrolytes, serum C_3 and C_4 level, HBsAg, chest X-ray and Ultra sonogram of Kidney Urinary Bladder region. Other investigations like ANA, DS-DNA was done as per indication.

Renal biopsy is indicated in atypically presented nephrotic syndrome[1]. But in this study renal biopsy was performed only in 12 cases. We failed to do in another 8 cases due to uncontrolled hypertension. In rest of the cases, consent was not found from the guardians.

Hematuria was considered in presence of both microscopic and macroscopic hematuria[7].

Hypertension was considered as systolic and or diastolic blood pressure above 95th centile for the age of the patient. Poor renal function was determined on the basis of more than upper limit of age matched serum creatinine level.

For this study, only urine culture proven cases were takan as urinary tract infection.

Peritonitis was diagnosed on the basis of clinical findings, e.g. abdominal pain, tenderness, ascites, absent or sluggish bowel sound, leucocytosis with or without positive peritoneal fluid and blood culture.

Respiratory tract infection was considered on the basis of clinical findings, e.g. fever, cough, sore throat, dyspnea, positive chest findings, with of without radiological evidence.

The patients of both groups were treated with oral prednisolone 60mg/m^2/day in 3 divided doses for 6 weeks following by prednisolone 40 mg/m^2/day in single dose every alternative day for 6 weeks in initial attack.

Oral Prednisolone 60 mg/m^2/day in 3 divided doses until urine protein free for 3 consecutive days, followed by alternate day prednisone 40 mg/m^2 given as single morning dose for 4 weeks in relapse cases.

Statistical analysis

Data was processed checked and initially bivariated, analysis was done between case and control. The result was compared using student 't' test for unpaired data $p \leq .05$ was taken as significant.

Results

A total 60 patients of nephrotic syndrome were studied .where 30 patients were taken as study group, who presented with atypical presentation of nephrotic syndrome and 30 of them were taken as comparator group who were presented with classical presentation of Nephrotic syndrome.

The range of age in the study group was 1 year to 15 years, with the mean age of 7.50 ±4.45 years (±SD) (Table I).

The age of comparator group ranges from 2 years 3 month to 7 years, with the mean age of 3.90 ± 1.61 years (±SD). Majority (88.67%) of the comparator group were found between 2 to 6 years.

Sex distribution of the study group was 19 male and 11 female with the male-female ratio 1.72:1. In comparator group, 18 were male and 12 were female with male-female ratio 1.5:1 (Table I)

Age of onset of the study group below 2 years were 5 (16.67%), 2 to 8 years 7(23.33%), more than 8 years 18(60%). Hematuria 19(63.63%), Hypertension 9(30%), Low C3 7(23.33%) and poor renal functions 8(26.67%) were common presentations of the study group (Table II).

The presentation of study group with 1 of 5 features of atypical presentation of nephrotic syndrome were 9(30%), with 2 feature were 9(30%),with 3 features were 9(30%) and with 4 features were 2(6.7%) with all 5 features was 1 (3.33%) (Table III).

The comparison of 24 hours urinary total protein (UTP)/m2/day, serum albumin level g/1 and serum cholesterol level mg/d1 between study and comparator group shown (Table IV).

Mean 24 hours UTP /m2/day in study group was 2.96 ± 0.21 /m2/day (±SE) and in comparator group mean 24 hours UTP/m2/day was 3.07 ± 0.18(±SE). (Table IV).

Means serum albumin level in study group was found 17.00 ± 0.66g/1 (±SE), in comparator group mean serum albumin level was 16.73 ± 0.64g/1(±SE), (Table IV).

Mean serum cholesterol level in study group was 379.93 ± 22.0 mg/dl (±SE) and in comparator group mean cholesterol level was 438.26 ± 16.74 mg/dl (±SE) (Table IV).

The response of the patients of study group with steroid therapy was 66.67% whereas the response of the patients of control group with steroid therapy was 96.67% (Fig 1). Clinical comparison between steroid responder and steroid resistant cases of study is shown in table VI.

In study group urinary tract infection (UTI) was found n 3 patients (10%) whereas it was in 6 Patients (20%) in comparator group (Table VI). peritonitis was found in study group in 2 patients (6.67%) and in 4 patients (13.33%) in comparator group (Table VI). Cellulites was found in 2 patients of study group (6.67%) and 3 patients of comparator group (10%) (Table VI). Respiratory tract infection was found in 1 patient of study group (3.33%) and 2 Patients of comparator group (6.67%) (Table VI).

Table I : Demographic Profile

Parameter	Case Total (%)	Comparator Total (%)
Age		
<2	5(16.67%)	00
2-8	7(23.33%)	30.(100%)
>8	18(60%)	00
Sex		
Male	19	18 (1.72:1)*
Female	11	12 (1.5:1)*

* Male, Female Ratio

Table II : Showing clinical Presentation of study group

Criteria	Number	Percentage
Age <2years	5	16.67%
Age 2-5 years	7	23.33%
Age >8 years	18	60%
Hypertension	9	30%
Hematuria	19	63.33%
Low C3	7	23.33%
Poor renal function	8	26.67%

Table III : Distribution cases of the according to the presenting features

No. of presenting features	Number	Percentage
1out of 5	9	30%
2 out of 5	9	30%
3 out of 5	9	30%
4 out of 5	2	6.67%
All 5 features	1	3.33%

Table IV: Biochemical values (24 hour UTP, Serum level of Albumin, Cholesterol of patients with Nephrotic Syndrome (Both study and ComparatorGroup)

Level	Study Group N = 30 (Mean ± SE)	Comparator Group N = 30 (Mean ± SE)	p-value
24 hours UTP (gm/sq.m/day)	2.96 ± 0.21	3.07 ± 0.18	>0.05
Serum Albumin (gm/l)	17.00 ± 0.66	16.73 ± 0.64	>0.05
Serum Cholesterol (mg/dl)	379.93 ± 22.2	438.26 ± 16.74	<0.05

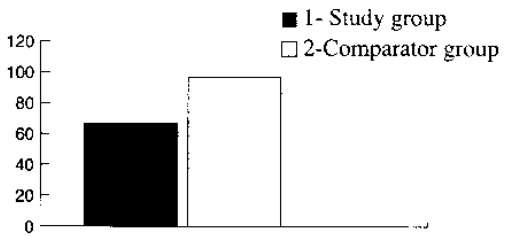

Fig 1: Response to steroid therapy

Table V: Clinical comparison between and steroid responder cases of study group.

Clinical criteria	No. of steroid responder (%)	No. of steroid resistant (%)
Age of onset <2 years (N=5)	3(60%)	2(40%)
Age of onset 2-8 years (N=7)	5(71.5%)	2(28.5%)
Age of onset>8 years (N=18)	12(66.67%)	6(33.33%)
Hypertension (N=9)	5 (55.56%)	4(44.44%)
Hermaturia (N=19)	13(68.43%)	6(31.57%)
Low C3 (N=7)	5(71.5%)	2(28.5%)
Poor renal function (N=8)	4(50%)	4(50%)

Table VI: Complications in patients with nephrotic syndrome (Both study and Comparator Group)

Complication	In study group no (%)	In Comparator group (%)	p-value
UTI	3(10%)	6(20%)	>0.05
Peritonitis	2(6.67%)	4(13.33%)	>0.05
Cellulites	2(6.67%)	3(10%)	>0.05
RTI	1(3.33%)	2(6.67%)	>0.05

UTI: Urinary Tract Infection
RTI: Respiratory Tract Infection

Table VII: Hostopathological findings in the study group (Total no-12)

Histopathological findings	Number	Percetage
Focal segmental glomerulosclerosis(FSGS)	05	41.66%
Minimal change glomerulonephritis(MCNS)	03	25%
Membranoproliferative glomerulonephritis	02	16.66%
Membranous glomerulonephritis	01	8.33%
Diffuse proliferative glomerulonephritis	01	8.33%

Discussion

In this study, to compare the clinical features, biochemical behavior and response to steroid between nephrotic syndrome with atypical presentation and classical presentation, thirty cases of nephrotic syndrome with atypical presentation and thirty cases of nephrotic syndrome with classical presentation were taken.

The mean average age of study group was 7.50 ± 4.45 years (±SD) with the range of 1-15 years which correlates with a study done by Kumar J et al[7], where the mean age was 7.9±5.1 years (±SD).

In Comparator group, the mean age is 3.9±1.61 (±SD) which ranges from 2 yr 3 months to 7 years with the peak age of 2-6 years (88.67%) which is in accordance with many studies[5].

There is a consistent male predominance, the male: female ratio being in the range of 1.5-2:1[12], which is very much similar with current study where in study group, male : female ratio is 1.72:1 and in control it is 1.5:1.

In our study, 63.63% patients of study group presented with hematuria which is nearer to an study done by Ibadin et al[13] where hematuria was found in 60% of patient. In one study 'hematuria was found in only 43.8% of patients[7].

In our study, hypertension was found in 30% of patients of study group, which is nearer to a study where it was found in 26.8%[7] and lower than an another where it was found in 41.4%[13].

In current study, renal function detoriation was found in 26.67% of the patients, which is not similar to a parallel study where it was found 40%, done by Shrivastava et al [14].

In our study, low C3 was found in 23.23% of the patients of study group, which correlates with a study done by Geiger et al[15].

Sixty percent of the patients in this study were presented at age more than 8 years of age, which correlates with a study[7]. Seventy percent of the patients presented with two or more features and only 10% of the patients presented with four or more features.

In this study, mean 24 hours UTP level of study group was 2.96 ± 0.21 g/sq.m/24 hours (±SE) and in control group mean was 3.07± 0.18 g/sq.m/24hours (±SE). The difference between two groups is not statistically significant (p>0.05), which correlates with the study of Gulati et al [8].

In our study, mean serum albumin level is 17.00± 0.66g/l (±SE) in study group and mean is 16.73 ± 0.64 g/l (±SE) in Comparator group. The difference between two groups is not signification (P>0.05), which correlates with same study [8].

In the current study, mean srum cholesterol level in the study group is 379.93 ± 22.2 mg/dl (±SE) and in Comparator group mean was 438.28 ± 16.74 mg/dl (±SE). The difference between two groups is statistically significant (P>0.05), which correlates with a study done by Mohammad Alaa Eldin et al[11].

In our study most common histopathological findings was FSGS(41.66%) which is similar with the findings of Kumar et al(38%) & Safaei et al(41%)[17]. MCNS was the second most common findings in our study (25%) which was the commonest finding of Madani et al(38%)[19]. Results of renal biopsy in 138 Turkish children showed that in 49% of cases pathologic findings were compatible with mesangial proliferative glomerulonephritis[18]. In our study, in comparison with other studies in other countries and centers, showed variable histology pattern. It seems that minimal change disease is the most common variation of nephrotic syndrome in children. These differences may be related to racial, genetic and environmental factors.

The response of steroid therapy was found excellent in control group patients in comparison to patients of study group. This difference between the two groups was found statistically highly significant (P>0.001). Here in control group 96.67% of patients responded with steroid therapy, which is in accordance with a study where 95-100% patients responded[6] and similar to another study by Hossain et al in BSMMU[16]. Response of steroid in study group was 66.67%,which is higher than a parallel study where 51.7% patients responded to initial course of steroid[13] and correlates with another study where, done by Gulati S et al[8]. Among the steroid resistant nephrotic syndrome, patient presented with below 2 years of age, hypertension and poor renal function shows poorer response.

Conclusion

The patient with atypical presentation of nephrotic syndrome differs from classical presentation both clinically and biochemically.

It was also noted that the responses of steroid therapy in atypical nephrotic syndrome patients were poor in comparison with the classical presentation.

All patients of nephrotic syndrome should be screened carefully on the basis of their clinical presentation and biochemical values to identify the atypical presentation and should be given special attention regarding management.

Disclosure

All the authors declared no competing interestes.

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