Research Paper

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Clinico-pathological Spectrum and treatment response of Atypical Nephrotic syndrome

Medical Science

KEYWORDS : Atypical nephrotic syndrome, steroid response, clinical course, renal biopsy

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ABSTRACT

Introduction and objectives: nephrotic syndrome (NS) is one of the common problems in children. Aim of the study to find out the prevalence, clinical course and treatment response in atypical NS. Atypical nephrotic syndrome includes extremities of ages (< 1yr & >10yr), hypertension, low C3 levels, haematuria, impaired renal dysfunction. Materials and methods: Patients with nephrotic syndrome children from 1 year to 14 year age were evaluated for presence of atypical features (any one of the features) were included and studied for the clinical course and treatment response were followed-up, analyzed and compared with other NS patients. Results: Prevalence of atypical NS is 16.9% with male predominance and in mostly in older children. Most common clinical course of atypical NS was Infrequent Nephrotic Syndrome (IFRNS), but most of Steriod Resistant Nephrotic syndrome (SRNS) patients had atypical NS. Response to steroid was only 50% in Atypical NS, and the need for combination therapy was high in case of atypical NS (30%).Renal biopsy findings of atypical NS showed MCD (50%) followed by FSGS (30%). Conclusion: Incidence of the atypical nephrotic syndrome was alarmingly high. Most of the atypical cases presented after 10 years of age. Nearly half of atypical NS needs an alternative immunosuppressive therapy with or without steroids. Most of the SRNS patients had an atypical presentation.

Introduction

Nephrotic syndrome (NS) is one of the common problems in pediatric population1). Incidence of nephrotic syndrome is 2-7 per lakh population; prevalence is 12-15 per lakh population2). Nephrotic syndrome may be defined as a clinical condition with presence of massive proteinuria, edema, hypoalbuminemia and hypercholesterolemia. Atypical presentation of nephrotic syndrome includes age <1 and > 10 yrs of age, hypertension, low C3 levels, impaired renal function and haematuria along with other features. The outcome of the atypical presentation (i.e. response to steroids) was poor when compared with normal presentation. In India, there is an increasing trend of FSGS due to increase in atypical presentation3). In this study we are assessing the incidence, presentations treatment response and complications of atypical NS.

Aim of the study

1. To calculate the prevalence of the atypical NS.
2. To find the clinical course of atypical NS.
3. To find out the treatment response of atypical NS

Materials and methods:

All children (aged 1 month -14 yr) attending general pediatrics and pediatric nephrology clinic at SVPPGIP, SCB medical college, Cuttack from Jan 2009 to Dec 2013. Those children with features of nephrotic syndrome like massive proteinuria (> 40 mg/ m2/hr or 1gm/ m2/24hr), edema, hypoalbuminemia (<2.5 m/ dL) and hypercholesterolemia (> 250 m/dL) were included and assessed for the presence of atypical presentation like low C3 levels, impaired renal function, haematuria, hypertension and including age of 1st attack (<1 yrs and >10 yrs of age). Presence of any one of the above features will be taken as the atypical presentation and after informed consent from the parents or guardians; they were grouped into atypical group and the rest as another group. The treatment response and clinical course of both groups were assessed for the atypical Nephrotic syndrome group and other nephrotic group. Those children were followed up for 12 months to assess the clinical course. Patients attending at least 2 follow-ups were only included into the study. The children who were lost for the follow up were excluded. The results were obtained, analyzed and discussed using simple statistics and student t test.

Secondary causes of NS and other causes of edema, hypoalbuminemia, hypertension, haematuria were ruled out before including into the study. Both microscopic (> 5 RBCs/ HPF in urine routine) and macroscopic haematuria were included. Hypertension was considered when systolic pressure is more than 95 percentile for that particular age, sex of the patient. Investigations like complete blood count, urine routine, serum electrolytes creatinine and urea cholesterol C 3 levels chest X-ray USG ANA ds-DNA were done in those study population. Renal biopsy were based on the Indian society of pediatric nephrology guidelines, we could do biopsy in only 30 cases, after informed consent. Clearance of proteinuria (i.e. protein/creatinine ratio < 0.2) was considered as adequate steroid response after the treatment. All children were studied for the treatment response.

Results

We had around 551 cases of nephrotic syndrome (after excluding the drop-outs) of which Males were 374 and females were 177 with M: F ratio 2.1:1. Out of 551 cases 93 had atypical presentation (i.e.) 16.9% and no significant sex differences in the atypical NS cases. (Table 1) In atypical presentation, most of the cases presented at later age group. (i.e.) 55% of atypical NS presented after 10 years of age. Most common presentation of atypical NS was haematuria. Around 66 % cases had more than one atypical feature. (Table 2) Only 3 cases had a positive family history most common clinical course of atypical NS was IFRNS, but SRNS had more atypical presentation. (Table 3). Only 50% of the atypical group responded to steroids, others required either a combination therapy or an immunosuppresents. Around 30 % cases required multi drug therapy for induction of remission in atypical NS (Table 4). Renal biopsy was done only in selected cases based on the indications. We found 50% of the biopsy population was MCD and the rest 50 % had the features. Out of 15 MCD cases, 9 were males and females 6, most of them are SRNS 9 cases, FRNS and SDNS 3 each, all of the patients presented in the range of 1 -10 yrs (Table 5) Non- MCD conditions had high atypical features.

Table 1. Based on age of presentation
Table 2. Atypical presentation of NS
Table 3. Clinical Diagnosis of nephrotic syndrome
Table 4. Treatment response

Table 5. Comparison of MCD and Non- MCD presentation

Discussion

In our study the mean age of nephrotic syndrome presentation was 5.3 + 3.9 yrs. In comparison with other studies like kumar J et al 7.9 + 5.1 yrs (+ SD)4) and muhamud et al study 7.5 yr + 4.45yr (+ SD)5) we had mean age which was lesser than the comparable group.

Incidence of atypical nephrotic syndrome was around 16.9% in our study. Out of which 55% of atypical cases were more than 10 yr of d age. This shows that more importance of nephrotic syndrome to be given in adolescents. These atypical varieties have lesser steroid response compared to the typical nephrotic syndrome6). As expected the atypical nephrotic syndrome showed male predominance. Male: female ratio in our study was 1.7:1 in atypical group and in rest it was 2.2:1. There was male predominance in other studies also muhumud et al 1.7:15) and 1.5-2:1.7)

Regarding the types of presentation, around 66% cases had more than single symptom which is similar to the muhumd study5) where 70% of cases showing more than 1 feature of atypical presentation. We found haematuria in our study was around 57% cases, which is lesser than the muhamud5) et al 63.6% Ibadin 60%8) and higher than 45 % begum A9) et al studies and another study with 43.8 %4) Hypertension was only 31% cases in our study comparable with muhumud5) 30 % 26.8%4) but not with begum A9) 50% and another study with 41.4%10)

Impaired renal function (i.e.) raised serum urea and creatinine in accordance to the age and sex were observed in 25.3% which is comparable with 26.67 muhumud study5) but was higher in compared with begum A9) 19% and lesser when compared with shrivastav 40 %11) Hypocomplementemia (i.e. low C3 levels) was found in 19 % cases which is slightly high when compared with begum A9)15% and lesser in muhumud5) 23.23% and Geiger eta al 12)

Regarding the clinical course of the atypical nephrotic syndrome, the absolute number of cases were high with infrequent NS but in SRNS the proportion of atypical cases were high around 66% after congenital and infantile ns where 100% cases were atypical Nephrotic syndrome. Family history was positive in only 3 cases out of total atypical cases. Our study shows that the atypical presentation has high proportion of steroid resistant nephrotic syndrome. Out of 93 cases we did renal biopsy in 30 cases others were lost in the follow-up and due to the parent refusal. Renal biopsy showed 50 % of the cases were due to MCD and followed by FSGS which is similar to madani et al 38% 13) but other studies showed most of the cases were due to FSGS like muhumud study 5)41%; kumar et al 38%4) and safei 41%14)

About treatment response around 82% of typical nephrotic syndrome responded only to prednislone which was lesser than the muhumud study 96.67%. Around 13.7% were on combination therapy for the remission. In case of atypical NS only 50 % responded to steroid which was similar to a study where the response was 51.7%11), but in case of muhumud study5) around 66% of cases responded to Steroid therapy. Around 30 % of atypical NS population required multi drug therapy (i.e. combination of prednisolone and immunosuppresents) and rest 20 % responded to various immunosuppresents. The difference in the steroid response of the atypical and another group was statistically significant with p value less than 0.001 (using unpaired student t tests)

Conclusion

Incidence of the atypical nephrotic syndrome was alarmingly high. Most of the Atypical cases presented after 10 years of age. Nearly half of atypical NS needs an alternative immunosuppressive therapy with or without steroids. Most of the SRNS patients had an atypical presentation. Renal biopsy showed mainly MCD in histopathology in our study cohort.

Limitations:

A larger cohort and a longer duration are required. A randomized control trial is required for a better understanding of the atypical nephrotic syndrome

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