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Original Article

Prevalence of Different Clinical Variants of Nephrotic Syndrome in Children 1–18 Years of Age in Tertiary Care Hospital of North India

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Abstract

Introduction: Childhood nephrotic syndrome has an incidence of 90–100 per million population of India. This study was conducted with the primary objective of studying the prevalence of different clinical variants of childhood nephrotic syndrome (new-onset steroid-sensitive nephrotic syndrome/infrequent relapsing nephrotic syndrome [IFRNS]/frequently relapsing nephrotic syndrome [FRNS]/steroid-dependent nephrotic syndrome [SDNS]/steroid-resistant nephrotic syndrome [SRNS]), while the secondary objectives were to estimate the prevalence of use of steroid-sparing drugs in those with FRNS and SDNS.

Materials and Methods: A retrospective study of all patients referred to renal diseases clinic at Government Medical College, Jammu, was done. Records of 61 children of 1–18 years of age fulfilling the International Study of Kidney Disease in Children criteria for nephrotic syndrome attending to our nephrology clinic were reviewed over 1 year period. Standard definitions for new-onset nephrotic syndrome, IFRNS, FRNS, SDNS, and SRNS were used. Steroid-sparing drugs used were levamisole in FRNS and low-dose SDNS whereas cyclophosphamide, mycophenolate mofetil (MMF), and tacrolimus in high-dose SDNS.

Results: Among nephrotic syndrome, patients mean age of presentation was 5.95 years, with M: F ratio of 1.77:1. Infrequent relapsers (27.9%) were the most prevalent clinical variant followed by steroid-dependent nephrotic syndrome (24.6%) and new-onset nephrotic syndrome (21.3%). Prednisolone alone was successful in achieving remission in 50.8% of total cases and less commonly involving use of other immunosuppressants with prednisolone such as levamisole (23%), cyclophosphamide (9.8%), and tacrolimus in (3.3%). However, prednisolone in combination with cyclophosphamide and then MMF was used in 14 (23%) in an aim to achieve full remission, but full remission was achieved in 48 (78.7%).

Conclusion: In the present study, clinical profile of children with nephrotic syndrome was concordant with typical nephrotic syndrome in children. Pattern of nephrotic syndrome differs in our population in terms of increased number with SDNS and response to treatment did not differ significantly from other studies.

Key words: Frequent relapsers, Infrequent relapsers, Mycophenolate mofetil, Steroid dependence, Steroid resistance

INTRODUCTION

Childhood Nephrotic Syndrome is an important chronic disease in children. Incidence is reported to be 2–3/100000 children in western countries while as its incidence is slightly higher (9–10/100000) in indian children and its prevalence is 12–16/100000 children [1]. Nephrotic syndrome, as we know it today, is a combination of proteinuria, hypoalbuminemia, hyperlipidemia, and edema[2], a concept that took some time to be developed. Interestingly, the effective treatments became available only recently in the mid 1900s, with the advent of steroids, antibiotics, diuretics, and other immunomodulators. Even today, there is a gap in our understanding of the etiology(s) of nephrotic syndrome of childhood, and better treatments are still required in the more resistant forms. The syndrome manifests with varied clinical and

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pathological states. Corticosteroids remain the mainstay for treatment of nephrotic syndrome. Based on the response to corticosteroids, children with Nephrotic syndrome segregate into steroid-sensitive group that has a good long term prognosis but risk of frequent relapses/dependence and steroid resistant group that has poor outcomes despite immunosuppression.[2] Response to medications is quite variable with some children requiring further course of steroid sparing agents , while others achieve complete remission after the course of prednisolone. Steriod sparing agents , such as levamisole, cytotoxic agents like cyclophosphamide, Mycophenolate mofetil, calcineurin inhibitors and rituximab are often used to induce or maintain remission with mixed results[2].

This study was undertaken to assess the demographic and clinical profile, prevalence of different clinical variants of childhood Nephrotic syndrome and role of immunosuppresants in achieving remission in our centre as no such data is available from our demographic settings.

MATERIALS AND METHODS

A retrospective study of all patients referred to renal diseases clinic at Government Medical College, Jammu, was done. Records of 61 children in the age group of 1–18 years of age fulfilling the International Study of Kidney Disease in Children (ISKDC) criteria for nephrotic syndrome (NS) attending to our nephrology clinic were reviewed from August 2019 to January 2020.

Inclusion Criteria

- Children 1–18 years with nephrotic syndrome diagnosed as per the ISKDC guidelines (nephrotic range proteinuria with spot urine PCR of >−2, hypoalbuminemia <2.5 g/dl, hyperlipidemia (serum cholesterol >200 mg/dl), and edema.

Exclusion criteria

- Children whose records were not complete were excluded from the study
- Children with secondary causes of nephrotic syndrome were excluded from the study.

Written informed consent was taken from parent/guardian of each child before including them in study. Thorough history, detailed examination, and clinical assessment including anthropometry and blood pressure were noted during evaluation. Laboratory values were acquired for confirmation of our diagnosis and for renal dysfunction. A retrospective study of all patients referred to renal diseases clinic at Government Medical College, Jammu, was done. Our medical college runs special clinic for patients with nephrotic syndrome every Wednesday 3–5 pm. Monthly follow-up of all patients is done. All patients referred to special clinic are investigated for proteinuria. Complete clinical examination is done to rule out complications. Biannually, all children undergo ophthalmic examination to screen for the development of cataract. Period of review was for the year 2019. Review was done from special clinic cards used for documentation of visits of patients in renal disease special clinic. Variables assessed were sex distribution, age at presentation for first attack, duration of edema, steroid responsiveness, and use of steroid-sparing agents. Biopsy was performed on five patients with steroid-dependent nephrotic syndrome (SDNS) and steroid-resistant nephrotic syndrome. Histopathology was suggestive of minimal change disease in two and focal segmental glomerulosclerosis in three.

All analyses were carried out using statistical software, SPSS, after data collection.

RESULTS

The present study consists of 61 cases of nephrotic syndrome attending our Pediatric Nephrology Special clinics in the Department of Pediatrics, GMC, Jammu, over a period of 1 year.

Inclusion and Analytical Sample Flow

A total of 61 cases of nephrotic syndrome were studied in 1 year period from January 2019 to December 2019. Table 1 shows that 63.93% of children were in the age group of 3–9 years and the age ranged from 1 to 16 years with mean

Table 1: Profile of patients with nephrotic syndrome

Variable	Number	Percentage	Mean±SD
Age in years			
0–3	9	14.75	5.95±3.47
3–6	21	34.42	
6–9	18	29.50	
9–12	8	13.11	
12–15	3	4.91	
≥15	2	3.27	
Sex			
Male	39	63.9	
Female	22	36.1	
Duration of nephrotic syndrome in years			
≤1	15	24.59	3.20±2.54
1–3	27	44.26	
3–6	12	19.67	
6–9	6	9.83	
>9	1	1.63	
Duration of edema in weeks			
≤1	31	50.81	1.67±0.96
1–2	23	37.70	
>2	7	11.47	

SD: Standard deviation

age of the onset of nephrotic syndrome as 5.95 years. Male-female ratio was 1.77:1. Mean height of patients was 104.21 ± 19.87 cm (71–163) and the mean weight was 20.15 ± 9.38 kg (9–50). Mean duration of nephrotic syndrome in years was 3.20 ± 2.54 years and mean duration of edema in weeks was 1.67 ± 0.96.

Table 2 shows that infrequent relapsers accounted for maximum number of cases 27.9% followed by SDNS 24.6% and new-onset NS – 21.3%.

Table 2 also shows that prednisolone alone was successful in achieving remission in 50.8% of total cases and less commonly involving use of other immunosuppressants with prednisolone such as levamisole (23%), cyclophosphamide (9.8%), and tacrolimus (3.3%). However, prednisolone in combination with cyclophosphamide and then MMF was used in 14 (23%).

Table 2: Clinical types and use of immunosuppressants in patients of nephrotic syndrome

Clinical types	Number	Percentage
SSNS		
New-onset NS	31	21.3
IFRNS	14	27.9
FRNS	6	19.7
SDNS	8	24.6
SRNS	2	6.6
Immunosuppressants		
PRED		50.8
P+LEV		23.0
P+CYP		9.8
P+MMF		13.1
P+TAC		3.3

SSNS: Steroid-sensitive nephrotic syndrome, SRNS: Steroid-resistant nephrotic syndrome, IFRNS: Infrequent relapsing nephrotic syndrome, FRNS: Frequently relapsing nephrotic syndrome, SDNS: Steroid-dependent nephrotic syndrome, MMF: Mycophenolate mofetil

Table 3: Results of biochemical tests in patients of nephrotic syndrome

Variable	Number	Percentage	Mean±SD (range)
Serum albumin			
≤1.5	17	27.86	1.78±0.46 (0.80–3.5)
1.5–2.5	43	70.49	
2.5–3.5	1	1.63	
Serum cholesterol			
200–300	12	19.67	392.09±105.81 (223–712)
300–400	21	34.42	
400–500	21	34.42	
>500	7	11.47	
Serum creatinine			
<0.5	17	27.86	0.68±0.93 (0.20–7.70)
0.5–1.00	41	67.21	
≥1.00	3	4.91	
BUN			
<20	23	37.70	31.60±2.69 (6.00–177.00)
20–40	26	42.62	
40–60	6	9.83	
≥60	6	9.83	

SD: Standard deviation, BUN: Blood urea nitrogen

Table 3 shows that Mean serum albumin, cholesterol, creatinine, and blood urea nitrogen in the study group were 1.78, 392, 0.68, and 31.60, respectively. Mean spot urine protein-creatinine ratio values were 8.48 accounting for approximately 23% of cases.

Out of 61 cases, one case expired during the study period.

Table 4 shows the status of patients at follow-up. About 78.7% (48) of patients achieved full remission.

DISCUSSION

Patients with NS lose massive amounts of protein in urine, leading to hypoproteinemia, hyperlipidemia, and edema.[1] In this study, we analyzed 61 patients of NS over 1 year, 39 were male, and 22 females with M: F ratio of 1.77:1. In our report, 3–6 years age group constituted maximum number of cases with mean age of 5.95 ± 3.47 years. The mean age was similar to that reported in other studies. In a study by Sahana,[3] mean age at presentation was 7.4 years. In their study, 65% of the subjects belonged to 6–12 years of age followed by 1–5 years (31%). Pandya and Mehta[4] reported mean age as 4.08 years and Kiran and Kumar reported the mean age at presentation as 6.7 years.[5] There were 73 (68.2%) males and 34 (31.7%) females with a male-female ratio of 2.1:1. Sahana[3] found that 76% of the subjects were males while 24% were female with male-to-female ratio of 3.27:1 suggesting a male preponderance. Pandya and Mehta and Kiran and Kumar also observed male predominance in their studies.[4,5] These observations are similar to data available from other centers. The mean age of presentation was similar to other studies. A study in Auckland observed mean age at diagnosis as 5.4 years.[6] A single-center study done in Iran reported mean age of presentation as 4.87 years.[7] According to observational studies, the prevalence of nephrotic syndrome in children has a 2–1 male-to-female ratio. Other studies report an incidence of 1.45–1.9/1.

In our study, infrequent relapse NS accounted for maximum number of cases 27.9% followed by SDNS 24.6% of cases

Table 4: Results of clinical and biochemical remission in cases

Variable	Number	Percentage
Remission		
Full	48	78.7
Partial	8	13.1
No	5	8.2

and new-onset NS – 21.3%. Majority of patients were steroid sensitive 68.9% and steroid dependence was seen in 24.6%, whereas steroid sensitivity documented in earlier studies by Pandya and Mehta[4] was 88.1% and steroid dependence was observed in 8.4% of patients, but our results are in concordance with the prevalence of steroid-sensitive nephrotic syndrome in the literature and other studies.[3] The study conducted by Safaei and Maleknajed demonstrated steroid sensitivity in 66%, steroid resistance in 20.5%, and steroid dependence in 13.5%. Among patients with steroid-sensitive NS, 37% were non-relapsers, 38.8% frequent relapsers, and 26.4% infrequent relapsers.[7]

Prednisolone alone was successful in achieving remission in 50.8% of total cases. Other immunosuppressants used with prednisolone were levamisole (23%), cyclophosphamide (9.8%), and tacrolimus (3.3%). However, prednisolone in combination with cyclophosphamide and then MMF was used in 14 (23%) to achieve complete remission.

However, only 78.7% (48) of patients achieved full remission in our study and 13.1% achieved partial remission and 5 out of 61 patients (8.2%) never achieved remission and were biopsied and two patients were found to be having minimal change disease and three patients had underlying focal segmental glomerulosclerosis. Alhassan *et al*.[8] studied 25 nephrotic patients to determine the patterns in children with NS. The male-to-female ratio was 2:1. Twenty-three (92%) patients were sensitive to the first steroid course and two were steroid resistant, and both of them proved to have focal segmental glomerulosclerosis. Of those who responded, 6 patients (24%) remained in remission, while 17 (68%) patients became steroid dependent. Regarding SDNS, 7 (41%) patients showed infrequent relapsers and 10 (59%) had frequent relapses. Our findings were consistent with the previous studies.

CONCLUSION

In the present study, clinical profile of children with nephrotic syndrome was concordant with typical nephrotic syndrome in children. Pattern of nephrotic syndrome differs in our population in terms of increased number with SDNS and response to treatment did not differ significantly from other studies. However, long-term follow-up with more number of patients is required to substantiate the pattern of disease in our setup.

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