J Ped Nephrol
Journal of Pediatric Nephrology
2025. Volume 13

Research Paper

Clinicopathological Profile and Outcomes of Idiopathic Steroid-resistant Nephrotic Syndrome in Children: A Single Centre Experience

Amrita Ray[1], Mrinal Kanti Das[1], Koushik Bhattacharjee[2*], Keya Basu[3]

1. Department of Pediatric Medicine, IPGMER SSKM Hospital, Kolkata, India.
2. Department of Nephrology, IPGMER SSKM Hospital, Kolkata, India.
3. Department of Pathology, IPGMER SSKM Hospital, Kolkata, India.

Use your device to scan and read the article online

Citation Ray A, Kanti Das M, Bhattacharjee K, Basu K. Clinicopathological Profile and Outcomes of Idiopathic Steroid-resistant Nephrotic Syndrome in Children: A Single Centre Experience. Journal of Pediatric Nephrology. 2025; 13:E47919. https://doi.org/10.22037/jpn.v13i1.47919

https://doi.org/10.22037/jpn.v13i1.47919

Article info:
Received: 12 Jan 2025
Accepted: 17 Mar 2025
Publish: 25 May 2025

Corresponding Author:
Koushik Bhattacharjee, Associate Professor.
Address: Department of Nephrology, IPGMER SSKM Hospital, Kolkata, India.
E-mail: doc.koushikbhattacharjee@gmail.com

ABSTRACT

Background and Aim: Wide variations exist regarding different histopathological types and treatment outcomes of idiopathic steroid-resistant nephrotic syndrome (iSRNS) in children. This study has been conducted to evaluate clinicopathological profile and short-term outcomes of iSRNS in children and to analyze predictive factors for outcomes.

Methods: This cross-sectional observational study was conducted at a tertiary care hospital in eastern India over a period of 18 months. Children with iSRNS aged 2–12 years, with an available renal biopsy report, for whom treatment was started within six months, were included. Data were collected at baseline and at 6 and 12-24 months.

Results: Of the 40 children with iSRNS (mean age: 1 year and 4 months; male: female ratio: 1:1), 30% and 70% respectively had hematuria and hypertension at the onset of nephrotic syndrome. Late SRNS was more common (55%) than initial SRNS (45%). Before the development of late SRNS, the percentages of steroid-dependent, infrequent relapsing and frequent relapsing nephrotic syndrome were 45.4%, 41% and 13.6%, respectively. Focal segmental glomerulosclerosis (62.5%), minimal change nephrotic syndrome (32.5%), and IgM nephropathy (5%) were the prevalent renal biopsy findings, with no association to the clinical features or renal parameters. 75% of participants received cyclosporine, and the rest received tacrolimus. The percentages of complete remission, partial remission and no response at 6 months were 70%, 12.5% and 17.5%, respectively; and at the end of 12–24 months they were 80%, 0% and 20%, respectively. No predictive factors for outcome were found.

Conclusion: The present study explored the complex nature of iSRNS in children. Development of SRNS cannot be predicted by any clinicopathological factors. Early age at onset of NS and the presence of hypertension are likely indicators of subsequent development of SRNS. A large percentage of iSRNS achieved complete remission with effective therapies available in the era of modern medicine.

Keywords: Nephrotic syndrome, Idiopathic, Steroid resistant, Children

J Ped Nephrol
Journal of Pediatric Nephrology

Introduction

Nephrotic syndrome (NS) is considered to be one of the most prevalent childhood glomerular disorders, with an estimated annual incidence in children under 16 years of age of 2 to 7 per 100,000 [1]. NS is defined is defined as heavy proteinuria (proteinuria >40 mg/m²/hr or 1 g/m²/24 hr or first morning protein-to-creatinine ratio ≥2 g/g or ≥3+ on dipstick) and clinical findings arising from the large urinary losses of protein, namely hypoalbuminemia (≤3 g/dL), edema, and hyperlipidemia (cholesterol >200 mg/dL) [2, 3].

Idiopathic NS, being the most common form (85-90%), has a favorable response to corticosteroids. Approximately 10–15% of childhood idiopathic NS remain initially unresponsive or later develop steroid-resistance [4]. In steroid resistant NS (SRNS), there is an absence of remission after therapy with daily prednisolone at a dose of 2 mg/kg or 60 mg/m² for 4 weeks [5], with a recent modification of duration to 6 weeks [6]. It is reported that 36–50% of children with SRNS progress to end-stage kidney disease (ESKD) within 10 years [7, 8]. The most common spectrum of renal biopsy in children with SRNS includes focal and segmental glomerulosclerosis (FSGS), minimal change disease (MCD), and diffuse mesangial proliferation (DMP) [9, 10]. Mutations in podocyte-associated genes are also detected in 10–30% of non-familial SRNS [11-13].

Inhibitors of the renin-angiotensin-aldosterone system and calcineurin inhibitors (CNI) remain the most important treatment options of patients with non-genetic forms of idiopathic SRNS. Around 50–70% of non-genetic SRNS cases achieve complete or partial remission with available therapies [4]. Furthermore, SRNS patients with a multidrug-resistant phenotype do not respond to immunosuppressive therapies, such as CNIs, prednisolone, and rituximab [14].

Considering the wide variations in the prevalence of different histopathological types of idiopathic SRNS and, accordingly, the treatment outcomes, we proposed to conduct this study, which is rarely done from this region (West Bengal) of eastern India, unlike other parts of our country.

Hypothesis of the study

Older age at onset, nephritic-nephrotic clinical profile and initial idiopathic SRNS (iSRNS) in children are more prevalent in FSGS, but short-term treatment outcomes are better in non-FSGS pathology.

Materials and Methods

This hospital-based cross-sectional observational study was conducted in the Department of Pediatric Medicine at IPGME&R/SSKM Hospital, Kolkata, and was approved by the Institutional Ethics Committee. Follow-up cases of iSRNS aged 2-12 years attending the department of pediatric medicine of IPGME&R and SSKM Hospital, for whom treatment was started within six [6] months, satisfying the inclusion and exclusion criteria, were included in the study after obtaining written informed consent/assent from guardians/parents and patients, as appropriate. Adequate prior medical records and renal biopsy report (light microscopy and immunofluorescence microscopy) were available for all study participants. The duration of the study was 16 months (Figure 1).

Primary objectives

a) To determine the frequency of different histopathological types of iSRNS in children with steroid resistance.

b) To identify the mean age at onset of illness and the mean age at diagnosis of iSRNS of different histopathological variants and their correlations with haematuria and/or hypertension.

c) To analyze the short-term outcomes of treatment at 6 months in terms of complete remission (CR), partial remission, (PR) and no response (NR) in different histopathological types of iSRNS.

Secondary objective

To determine the long-term renal outcomes who completed 12 months or more of treatment at the time of enrollment in the study, during the current follow-up, in terms of CR, PR, NR; persistent HTN; eGFR; and course of disease.

Those with secondary NS, NS complicated with hepatitis B and hepatitis C and HIV, reflux nephropathy, family history of NS, congenital NS or NS with syndromic presentation, genetic study report suggestive of a significant pathogenic variant, features of chronic kidney disease (CKD) at the beginning of SRNS treatment, renal biopsy performed outside IPGME&R, and cases where

parents or patients did not give consent/assent were excluded from the study.

The pre-structured proformas were completed using relevant clinical history, physical examination findings, and laboratory investigations at baseline and during follow-up. The course of disease and response to treatment at the end of 6 months and at the time of inclusion in the study, with mention of the treatment regimen and total duration of treatment, were also recorded.

Blood investigations included serum urea, creatinine, and albumin. Detailed urine examination with dipstick for albumin, blood, leukocyte esterase, and/or urinary protein/creatinine ratio, microscopical examinations, culture and sensitivity when required. Percutaneous ultrasound-guided renal biopsy was routinely performed with a semi-automated biopsy gun under sedation and/or local anesthesia by the nephrologist in the Department of Nephrology, and the biopsied tissue processing and examination were done in the Renal Histopathology Unit under the Department of Pathology with light microscopy (LM) and immunofluorescence (IF) microscopy.

Standard definitions related to childhood onset NS were used in this study. CR was defined as the first morning urine protein-to-creatinine ratio (uPCR) <0.2 (mg/mg) or negative or trace proteinuria on dipstick for three consecutive days. Partial remission (PR) was defined as first morning uPCR >0.2 to <2 (mg/mg) and, if available, serum albumin >3 g/dL (30 g/L) [15].

Statistical analysis

Data were tabulated in Microsoft Excel and analyzed with SPSS software, version 24. Continuous variables were presented with Mean±SD. Categorical variables were presented with frequency and percentage. The chi-square test and one-way ANOVA were used for statistical analysis. P≤0.05 was considered statistically significant.

Results

We evaluated 40 children with iSRNS. The mean age of the study participants was 1 year 4 months, with an equal male-to-female ratio (1:1) (Table 1). Among the 40 individuals studied, the most common age group for onset of NS was 13-24 months, representing 55% of cases, followed by 25-48 months, accounting for 25%. The remaining cases were evenly split between onset occurring at ≤12 months and >48 months, each representing 10% of the total. The most prevalent age range for SRNS onset was 13-24 months, constituting 45% of cases, followed by 25-48 months, making up 35%. The least common age groups for SRNS onset were ≤12 months and >48 months, each representing 7.5% and 12.5% of cases, respectively.

Among the SRNS children, 30% (n=12) had hematuria, while hematuria was absent in 70% (n=28) at the onset of NS. At initial presentation 72.5% (n=29) of iSRNS cases were diagnosed with hypertension, while 27.5% (n=11) did not exhibit hypertension. Among the 40 study participants, 92.5% (n=37) did not have a family history of NS, while only 7.5% (n=3) had a positive family history. Among the 40 SRNS children, 45% (n=18) exhibited initial SRNS, while 55% (n=22) had late SRNS. Among the 22 patients with late SRNS, 3 patients (13.6%) had frequently relapsing NS (FRNS), while 9 patients (41%) had infrequently relapsing NS (IFRNS), and the largest group, comprising 10 patients (45.4%), had steroid-dependent NS (SDNS).

Table 1. Association of different parameters with kidney biopsy findings

Parameters		No. (%)			P
		FSGS	IgM Nephropathy	MCNS	
Hematuria	Yes	7(58.3)	2(16.7)	3(25)	0.082
	No	18(64.3)	0(0)	10(35.7)	
Hypertension	Yes	17(58.6)	2(6.9)	10(34.5)	0.565
	No	8(72.7)	0(0)	3(27.3)	
Creatinine (mg/dl)	>0.6	4(80)	0(0)	5(20)	0.657
	<0.6	21(60.0)	2(5.7)	12(34.3)	

FSGS: Focal and segmental glomerulosclerosis; MCNS: Minimal change nephrotic syndrome.

J Ped Nephrol
Journal of Pediatric Nephrology

Table 2. Correlation of the outcome at 6 months with different parameters

Parameters		Mean±SD/No. (%)			P
		Complete Remission	Partial Remission	No Remission	
Age of onset of NS (m)		30.11±4.41	22.29±5.35	42±15.06	0.368
Age of onset of SRNS (m)		34.71±4.4	34.29±9.95	43.2±15.34	0.777
Baseline serum albumin (g/dL)		2.09±0.06	2.01±0.13	2.04±0.04	0.825
Baseline cholesterol (mg/dL)		350.75±21.13	470.57±51.54	355.4±50.11	0.060
Baseline creatinine (mg/dL)		0.5±0.02	0.54±0.05	0.56±0.1	0.601
Kidney biopsy pattern	FSGS	17(60.7)	2(40)	6(85.7)	0.440
	IgM nephropathy	2(7.1)	0(0)	0(0)	
	MCNS	9(32.1)	3(60)	1(14.9)	

FSGS: Focal and segmental glomerulosclerosis; MCNS: Minimal change nephrotic syndrome.

Among the 40 children studied, the most prevalent biopsy finding was FSGS, accounting for 62.5% (n=25) of cases, followed by minimal change NS (MCNS), which represented 32.5% (n=13), and IgM nephropathy, representing 5% (n=2) (Figure 2).

Table 1 shows the association of different parameters with kidney biopsy findings. The analysis indicated that biopsy findings were as not significantly correlated with hematuria, hypertension, or serum creatinine levels. Of the subjects, 75% (n=30) of iSRNS children received cyclosporin, while 25% (n=10) received tacrolimus.

At the end of 6 months, the majority experienced complete remission, accounting for 70% (n=28) of cases. A smaller proportion of individuals showed no response, constituting 17.5% (n=7) of cases, while 12.5% (n=5) exhibited partial remission. Outcome at 6 months was not significantly associated with any clinical, biochemical, and histopathological findings (Table 2).

The entire study population (n=40) completed 12-24 months of treatment. At the end of 12-24 months, the most common outcome was complete remission, observed in 80% (n=32) of cases, while 20% (n=8) showed

Table 3. Correlation of the outcome at 12-24 months with different parameters

Parameters		No. (%)		P
		Complete Remission	No Remission	
Age of onset of nephrotic syndrome (months)	<12	3(90)	1(3.1)	0.761
	13-24	17(53.1)	5(62)	
	25-48	8(25)	2(25)	
	>48	4(12.5)	0(0)	
Type of (SRNS)	Initial SRNS	15(46.8)	3(37.5)	0.633
	Late SRNS	17(53.1)	5(62.5)	
Kidney biopsy pattern	FSGS	21(65.7)	4(50)	0.429
	IgM nephropathy	2(6.2)	0(0)	
	MCNS	9(28.1)	4(50)	

Abbreviations: SRNS: Steroid-resistant nephrotic syndrome; FSGS: Focal and segmental glomerulosclerosis; MCNS: Minimal change nephrotic syndrome.

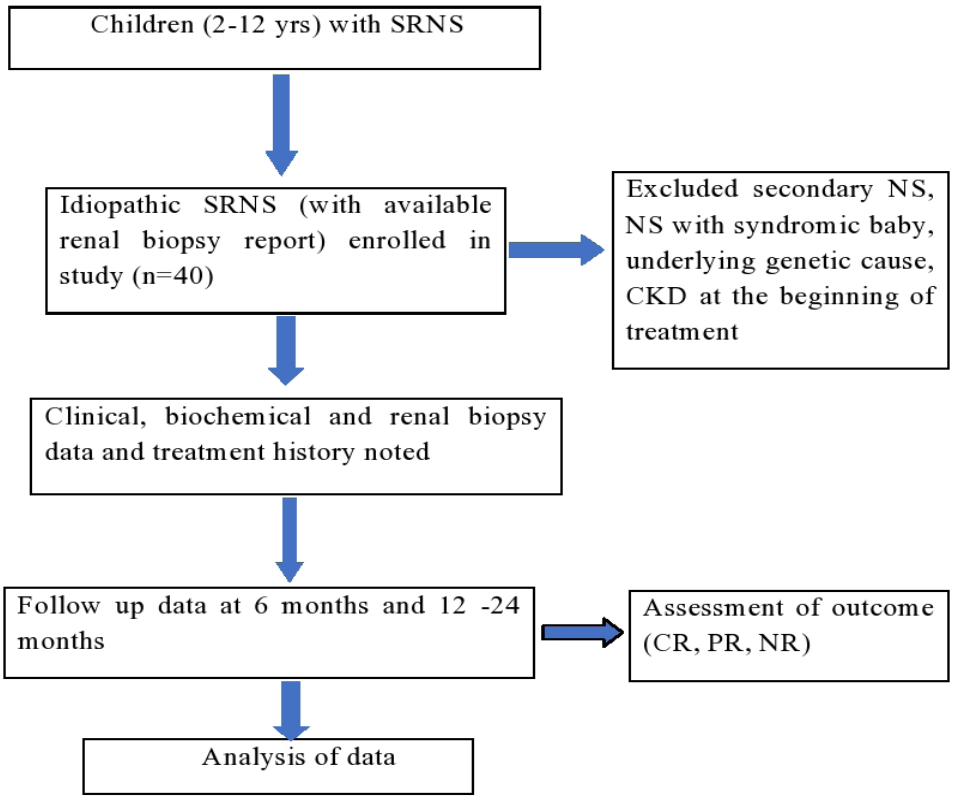

Figure 1. Flow diagram of the study

no response to treatment. We also sought to assess correlations between parameters such as age at onset of disease, type of SRNS, and kidney biopsy pattern with outcomes at 12–24 months (Table 3). However, no statistically significant association was found.

Discussion

Children with iSRNS present a complex clinical scenario, often necessitating a multifaceted approach for optimal management. The study aimed to comprehensively identify the intricate interplay of clinico-pathological and prognostic factors inherent in this subset of patients.

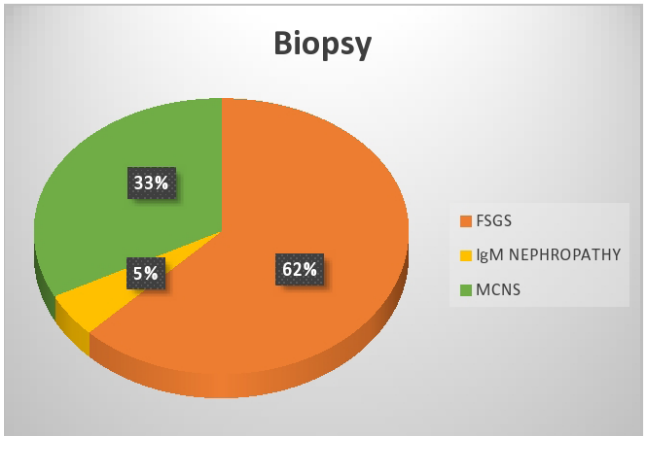

Figure 2. Spectrum of renal biopsy findings

J Ped Nephrol
Journal of Pediatric Nephrology

Among the 40 children studied, the most prevalent age of onset of NS and was between 13 and 24 months, and this age range was also the most prevalent for onset of SRNS. The male-to-female ratio in the study population was 1:1, indicating no gender predisposition for SRNS in children. In a study of childhood NS from Eastern Asia, the male-to-female ratio was 1.9, and approximately 50% of children were <5 years old at diagnosis [16].

In the present study, the children's clinical profile showed that 30% had hematuria and 72.5% had hypertension. In the study by Pokrajac et al., among all SRNS patients, 12(54.5%) had arterial hypertension and 14(63.6%) had microhematuria at presentation [17]. Using logistic regression analysis, they showed that only the presence of hematuria was associated with a higher relative risk of developing resistance to corticosteroid therapy, a result that was statistically significant, while no relation was seen with hypertension.

Also, 45% of the current study population exhibited initial SRNS, while 55% had late SRNS. Results from other studies show similar findings, with late SRNS slightly more prevalent than initial SRNS [18].

In our study, the most prevalent biopsy finding was FSGS (62.5%); followed by MCNS (32.5%) and IgM nephropathy (5%). Comparisons with existing literature revealed mixed results. While a few studies observed a higher proportion of MCD compared to FSGS [18], the study by Banaszak and Banaszak documented an increasing incidence of FSGS and a decline in the incidence of MCD [19]. Increases in steroid resistance in this study were attributed, in part, to the rising incidence of FSGS. FSGS, being the most common histopathological finding in children with SRNS, was also reported in an Indian study in 2005 [20].

Some studies have shown significant differences in clinical characteristics of primary glomerular diseases. In the study by Takaya Ozeki et al., the clinical manifestations of FSGS were compared with MCNS using data from the Japan Renal Biopsy Registry, including both pediatric and adult populations and about 30,949 cases. They showed that the characteristics of nephrotic FSGS and MCNS in biopsy were significantly different. FSGS cases were older on average, had a higher prevalence of hypertension on antihypertensive drugs (56.2 vs 28.7%), and lower eGFR (53 vs 72 mL/min/1.73 m^2). FSGS patients also had a higher prevalence of hematuria (52.9 vs 29.8%) [21]. In our study, no statistically significant association was observed between biopsy findings and hematuria and/or hypertension. This could be due to the small sample size and the possibility of unsampled FSGS among those with MCNS on biopsy, as electron microscopy findings were not available on renal biopsy.

Biochemical parameters, including serum albumin, cholesterol, and creatinine showed no statistically significant association with outcomes. Kashif et al. showed similar results [22]. They did not find any statistically significant associations between various biochemical parameters and outcomes of NS, which is in accordance with the observations of our study.

Seventy-five percent (75%) of SRNS patients were treated with cyclosporin, while 25% were treated with tacrolimus in this cohort. After 6 months, 70% of cases achieved CR, while PR and no response were seen respectively in 12.5% and 17.5% of participants. Similar findings were shown in another study where calcineurin inhibitors (CNIs) were used in 86.8% of the children, and response rates with cyclosporine and tacrolimus for CR were 80% and 73.7%, respectively, with median (IQR) time to response being 3 (2–4) months [18]. In some studies, the percentage of CR and PR achieved with CNI was respectively 30–40% and 60–80% [6]. In our study, the percentage of CR was relatively higher.

The analysis of the current study indicated no statistically significant difference in biopsy findings among different outcomes at 6 months (P=0.440). In the study by Watanabe et al., they concluded that if CR was achieved, FSGS and MCNS in children may constitute a single disease spectrum, because the long-term outcomes were favorable irrespective of histology [23].

In our study, no significant difference was observed in remission rates between cyclosporin and tacrolimus. Similar to our observations, Liu et al. in their study observed that tacrolimus, compared with cyclosporine, showed little or no difference in the number who achieved complete or partial remission [24].

At 12-24 months of treatment, the most common outcome was CR (80%), and 20% patients showed no response to treatment. Among those with CR, 40.6% (n=21) exhibited FSGS, 6.2% (n=2) showed IgM nephropathy, and 28.1% (n=9) had MCNS. The analysis revealed no statistically significant difference in biopsy findings based on remission status (P=0.646). The type of resistance, whether early or late, did not reveal any statistically significant difference in remission status (P=0.957). Straatmann et al., in a study conducted on patients diagnosed with idiopathic NS and subsequent late SRNS, concluded that most patients with late SRNS responded to immuno-

suppressive therapy by reduction or resolution of proteinuria and preservation of renal function [25]. Few studies on SRNS in children showed that CNIs work best when used in combination with steroids [26].

Conclusion

The majority of patients with childhood iSRNS had onset of NS and onset of steroid resistance within 2 years of age, with an equal male-to-female proportion. The majority of children with idiopathic SRNS had hypertension at the onset of nephrotic state. Late steroid resistance is slightly more common than initial SRNS. SDNS is the most common presentation before developing steroid resistance. FSGS was found to be the most common renal biopsy finding among patients with childhood SRNS. The present study showed a significant proportion of patients experienced complete remission within six months of treatment, with most maintaining remission at 12- to 24-month follow-up. This highlights the effectiveness of current treatment modalities in managing NS and the importance of ongoing monitoring and personalized care for long-term remission. Renal biopsy findings were not significantly associated with clinical and renal parameters at baseline. The short-term outcome of iSRNS in children was not significantly influenced by any baseline clinical features, laboratory values, or renal biopsy findings.

Overall, the present study underscores the complex nature of NS management, necessitating a multifaceted approach that considers individual patient characteristics, disease severity, and treatment response patterns. Moving forward, further research is warranted to elucidate additional factors influencing treatment response and long-term prognosis, ultimately facilitating the development of more tailored and effective therapeutic strategies for patients with SRNS.

Limitations of the study

Despite sincere efforts, the present study has lacunae. The sample size was small. The study was conducted in a single centre. It was carried out in the state's premier referral center with an advanced nephrology department, so referral bias cannot be ruled out.

Ethical Considerations

Compliance with ethical guidelines

This study was approved by the Institutional Ethics Committee, IPGME&R/SSKM Hospital, Kolkata , India (Code: IPGME&R/IEC/2022/505).

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Authors' contributions

Conceptualization: Mrinal Kanti Das; Supervision: Mrinal Kanti Das and Keya Basu; Methodology, formal analysis, and investigation: Amrita Ray; Writing the original draft: Koushik Bhattacharjee; Review and editing: Keya Basu.

Conflict of interest

The authors declared no conflict of interest.

Acknowledgments

The authors are thankful to the support staff of the Department of Pediatric Medicine, Nephrology, and Pathology at IPGME&R/SSKM Hospital, and to all the participants who took part in the study.

References

[1] Eddy AA, Symons JM. Nephrotic syndrome in childhood. Lancet. 2003; 362(9384):629-39. [DOI:10.1016/S0140-6736(03)14184-0] [PMID]

[2] Erkan E. Idiopathic Nephrotic Syndrome In: Kliegman RM, Geme III JW, editors. Nelson textbook of pediatrics.21st ed. Philadelphia: Elsevier Health Sciences; 2019. [Link]

[3] Bagga A, Srivastava RN. Nephrotic syndrome. In: Bagga A, Srivastava RN, editors. Pediatric nephrology. 6th ed. New Delhi: Jaypee; 2016. [DOI:10.5005/jp/books/12792_12]

[4] Tullus K, Webb H, Bagga A. Management of steroid-resistant nephrotic syndrome in children and adolescents. Lancet Child Adolesc Health. 2018; 2(12):880-90. [DOI:10.1016/S2352-4642(18)30283-9] [PMID]

[5] Indian Society of Pediatric Nephrology; Gulati A, Bagga A, Gulati S, Mehta KP, Vijayakumar M. Management of steroid resistant nephrotic syndrome. Indian Pediatr. 2009; 46(1):35-47. [PMID]

[6] Vasudevan A, Thergaonkar R, Mantan M, Sharma J, Khandelwal P, Hari P, et al. Consensus guidelines on management of steroid-resistant nephrotic syndrome. Indian Pediatr. 2021; 58(7):650-66. [DOI:10.1007/s13312-021-2262-y] [PMID]

[7] Mekahli D, Liutkus A, Ranchin B, Yu A, Bessenay L, Girardin E, et al. Long-term outcome of idiopathic steroid-resistant nephrotic syndrome: A multicenter study. Pediatr Nephrol. 2009; 24(8):1525-32. [DOI:10.1007/s00467-009-1138-5] [PMID]

[8] Nourbakhsh N, Mak RH. Steroid-resistant nephrotic syndrome: Past and current perspectives. Pediatric Health Med Ther. 2017; 8:29-37. [DOI:10.2147/PHMT.S100803] [PMID]

[9] Srivastava T, Simon SD, Alon US. High incidence of focal segmental glomerulosclerosis in nephrotic syndrome of childhood. Pediatr Nephrol. 1999; 13(1):13-8. [DOI:10.1007/s004670050555] [PMID]

[10] Gulati S, Sengupta D, Sharma RK, Sharma A, Gupta RK, Singh U, et al. Steroid resistant nephrotic syndrome: Role of histopathology. Indian Pediatr. 2006; 43(1):55-60. [Link]

[11] Sadowski CE, Lovric S, Ashraf S, Pabst WL, Gee HY, Kohl S, et al. A single-gene cause in 29.5% of cases of steroid-resistant nephrotic syndrome. J Am Soc Nephrol. 2015; 26(6):1279-89. [DOI:10.1681/ASN.2014050489] [PMID]

[12] Bierzynska A, McCarthy HJ, Soderquest K, Sen ES, Colby E, Ding WY, et al. Genomic and clinical profiling of a national nephrotic syndrome cohort advocates a precision medicine approach to disease management. Kidney Int. 2017; 91(4):937-47. [DOI:10.1016/j.kint.2016.10.013] [PMID]

[13] Trautmann A, Lipska-Zie¸tkiewicz BS, Schaefer F. Exploring the clinical and genetic spectrum of steroid resistant nephrotic syndrome: The PodoNet Registry. Front Pediatr. 2018; 6:200. [DOI:10.3389/fped.2018.00200] [PMID]

[14] Magnasco A, Ravani P, Edefonti A, Murer L, Ghio L, Belingheri M, et al. Rituximab in children with resistant idiopathic nephrotic syndrome. J Am Soc Nephrol. 2012; 23(6):1117-24. [DOI:10.1681/ASN.2011080775] [PMID]

[15] Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 clinical practice guideline for the management of glomerular diseases. Kidney Int. 2021; 100(4S):S1-S276. [DOI:10.1016/j.kint.2021.05.021] [PMID]

[16] Kikunaga K, Ishikura K, Terano C, Sato M, Komaki F, Hamasaki Y et al. High incidence of idiopathic nephrotic syndrome in East Asian children: A nationwide survey in Japan (JP-SHINE study). Clin Exp Nephrol. 2017; 21(4):651-57. [DOI:10.1007/s10157-016-1319-z] [PMID]

[17] Pokrajac D, Kamber AH, Karasalihovic Z. Children with steroid-resistant nephrotic syndrome: A single -center experience. Mater Sociomed. 2018; 30(2):84-88. [DOI:10.5455/msm.2018.30.84-88] [PMID]

[18] Agrwal S, Mantan M, Dabas A, Batra VV. Childhood steroid-resistant nephrotic syndrome: Long-term outcomes from a tertiary care center. Indian J Nephrol. 2022; 32(4):320-6. [DOI:10.4103/ijn.ijn_258_21] [PMID]

[19] Banaszak B, Banaszak P. The increasing incidence of initial steroid resistance in childhood nephrotic syndrome. Pediatr Nephrol. 2012; 27(6):927-32. [DOI:10.1007/s00467-011-2083-7] [PMID]

[20] Gulati A, Sinha A, Gupta A, Kanitkar M, Sreenivas V, Sharma J, et al. Treatment with tacrolimus and prednisolone is preferable to intravenous cyclophosphamide as the initial therapy for children with steroid-resistant nephrotic syndrome. Kidney Int. 2012; 82(10):1130-5. [DOI:10.1038/ki.2012.238] [PMID]

[21] Ozeki T, Maruyama S, Imasawa T, Kawaguchi T, Kitamura H, Kadomura M, et al. Clinical manifestations of focal segmental glomerulosclerosis in Japan from the Japan Renal Biopsy Registry: Age stratification and comparison with minimal change disease. Sci Rep. 2021 ; 11(1):2602. [DOI:10.1038/s41598-020-80931-9] [PMID]

[22] Kashif AW, Ranjan A, Kalra S, Shravani Uttpal D, Malik A. Clinicopathological spectrum and treatment outcome of idiopathic steroid-resistant nephrotic syndrome in children at a tertiary care center. Med J Armed Forces India. 2022; 78(3):291-5. [DOI:10.1016/j.mjafi.2020.11.004] [PMID]

[23] Watanabe Y, Fujinaga S, Endo A, Endo S, Nakagawa M, Sakuraya K. Baseline characteristics and long-term outcomes of steroid-resistant nephrotic syndrome in children: Impact of initial kidney histology. Pediatr Nephrol. 2020; 35(12):2377-81. [DOI:10.1007/s00467-020-04760-8] [PMID]

[24] Liu ID, Willis NS, Craig JC, Hodson EM. Interventions for idiopathic steroid-resistant nephrotic syndrome in children. Cochrane Database Syst Rev. 2019; 2019(11):CD003594. [DOI:10.1002/14651858.CD003594.pub6] [PMID]

[25] Straatmann C, Ayoob R, Gbadegesin R, Gibson K, Rheault MN, Srivastava T, et al. Treatment outcome of late steroid-resistant nephrotic syndrome: A study by the Midwest Pediatric Nephrology Consortium. Pediatr Nephrol. 2013; 28(8):1235-41. [DOI:10.1007/s00467-013-2483-y] [PMID]

[26] Butani L, Ramsamooj R. Experience with tacrolimus in children with steroid-resistant nephrotic syndrome. Pediatr Nephrol. 2009; 24(8):1517-23. [DOI:10.1007/s00467-009-1220-z] [PMID]