International Journal of Contemporary Pediatrics
Jamil JI et al. Int J Contemp Pediatr. 2026 May;13(5):717-722
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20261135

Original Research Article

Risk factors for relapse of steroid-sensitive nephrotic syndrome in children

Joheb Imtiaz Jamil[1], Wahida Khanam[1], M. Nazmul Hossain[1], Tanjina Sharifa[1], Mohammad Nasir Uddin[1], Mohammad Ahad Adnan[1]*, Sajia Akhter[2], Ifthakhar Ahmed[1]

[1]Department of Pediatrics, Institute of Child and Mother Health (ICMH), Dhaka, Bangladesh
[2]Department of Pediatrics, 250 Bedded Hospital, Magura, Bangladesh

Received: 26 February 2026
Accepted: 03 April 2026

***Correspondence:**
Dr. Mohammad Ahad Adnan,
E-mail: ahadnann@gmail.com

ABSTRACT

Background: The management of nephrotic syndrome (NS) is often challenged in relapse cases. Authors aimed to find out the risk factors for relapse of steroid-sensitive nephrotic Syndrome.
Methods: This cross-sectional study was carried out in the department of pediatrics, ICMH, Dhaka, from July 2020 to June 2021. A total of 40 admitted as well as follow-up relapse cases of steroid-sensitive NS were enrolled and proceeded to clinical and laboratory evaluation.
Results: The mean onset of NS was 3.86±2.35 years. Frequently relapsing NS (FRNS) was found in 14 (35.0%) cases and infrequently relapsing NS (IFRNS) was 26 (65.0%) cases. The majority of children responded within 7 days to initial steroid therapy (75% in IFRNS group and 50% from FRNS group); again, 50% of children with FRNS needed a longer time (≥7 days) to respond to initial steroid therapy. RTI and UTI were higher in FRNS, whereas viral fever and diarrhea were higher in IFRNS. The age of onset of NS, mean serum albumin, serum cholesterol and serum creatinine were not statistically significant compared with the type of relapse. Time needed to respond with initial steroid therapy at 1st attack of NS had a statistically significant difference when compared with the type of relapse in children with SSNS.
Conclusions: RTI and UTI were seen to occur in higher frequency in relapse cases of NS. A longer time taken to achieve remission during the first episode was significantly associated with FRNS.

Keywords: Nephrotic syndrome, Relapse, Remission, Renal function, Steroid

INTRODUCTION

NS is the most common kidney disease in childhood. Globally, the reported incidence of NS is 2-3/100000 children per year.[1] As defined by the International Study of Kidney Disease in Children (ISKDC), NS is characterized by proteinuria (>40 mg/m^2/h), hypoalbuminemia (<2.5 g/dl), edema and usually hypercholesterolemia >200 mg/dl.[1-3] Based on the pattern of response to corticosteroids, NS is subdivided into steroid-sensitive NS (SSNS) and steroid-resistant NS (SRNS). Fortunately, 80% of the children with idiopathic NS show remission of proteinuria following treatment with corticosteroids and are classified as 'steroid-sensitive' (SS) and they usually have minimal change disease on histopathology.[3] Among patients with SSNS, the clinical course can be variable with differing relapse rates and overall dependence on steroid administration. The majority of children with NS relapse within the first six months of initial therapy. Approximately 30% of children experience only one attack and get cured after a single course of steroid therapy.[4] It is estimated that approximately 50% of patients with SSNS will have a frequently-relapsing (FR) and/or steroid-dependent course.[5] The biological basis for the pattern of response to corticosteroids remains unknown. The definitive

reason why some patients respond to corticosteroids and others do not escapes explanation, but proposed mechanisms underlying the pathogenesis of SSNS have sought to clarify this variability in the pattern of response. Shalhoub (1974) proposed that SSNS is the result of a primary T-cell dysfunction.[6] Subsequent studies have explored changes in T-cell surface expression, function and cytokine release in the setting of nephrotic syndrome; experimental recapitulation of these findings in multiple studies has been lacking.[7,8] The other mechanisms for SSNS propose the 'structural defects of the podocyte' or 'increased glomerular permeability' due to differential expression of circulating factors, e.g., vascular endothelial growth factor (VEGF), interleukin-13 (IL-13), interleukin-18 (IL-18), tumor necrosis factor alpha (TNFα), etc.[9,10]

Although there is a high initial response rate to steroids and a favorable prognosis in children with SSNS, relapses may occur in 60% to 90% of the initial responders, which can lead to increased morbidity, complications and decreased quality of life. When the disease progresses to frequent relapses, it is often accompanied by steroid dependence in about 20% to 60% of patients.[11] Relapses are also associated with the risk of complications such as sepsis, thrombosis, dyslipidemia and malnutrition. Children with FRNS are also at high risk of facing significant adverse effects of steroid therapy, as they need repeated courses of steroids for treatment.

Relapses are often triggered by upper respiratory or gastrointestinal infections.[2] There are several risk factors for relapse based on some previous studies.[12-14] Including age, sex, nutritional status, hypertension, hematuria, creatinine level, infections at the time of diagnosis of NS, time to achieve remission during the first episode and duration of the interval between remission and first relapse. If the risk factors for relapses could be predicted at the onset of disease, it would lead to better long-term management of the disease. This study aimed to identify the risk factors of relapses in SSNS in children.

METHODS

This cross-sectional study was conducted at department of Pediatrics at ICMH, Dhaka, from July 2020 to June 2021. All FRNS and IFRNS cases, from 1 to 14 years of age, admitted in ward as well as those who came to follow up clinic were enrolled in the study. Children with prior incomplete data, congenital NS, steroid-resistant NS and secondary forms of NS were excluded.

The prevalence of relapse cases of NS at any time of the year is undetermined to date. Hence, from all relapse cases admitted in ICMH during this study period, as per availability and according to the inclusion criteria, a total of 40 cases were taken purposively in this study. A pre-tested, semi-structured questionnaire was used to collect data. After taking informed consent, a detailed history regarding the current attack and previous attacks was recorded.

Statistical analyses were carried out using SPSS version 23. The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Chi-Square test was used to analyze the categorical variables. Student's t-test was used for continuous variables. P values <0.05 were considered statistically significant. The protocol was approved by the Institutional Review Board (IRB) of ICMH. Informed written consent was taken before starting the interview.

RESULTS

Among 40 cases of SSNS with relapse, 26 (65%) cases had IFRNS and 14 (35%) had FRNS. Almost two-thirds (65%) of children belonged to the age group≥1-6 years and 35% belonged to the age group>6-14 years (Figure 1). Mean age was found to be 5.38±2.76 years. The study observed female predominance with a male-to-female ratio of 1:1.35 (Figure 2).

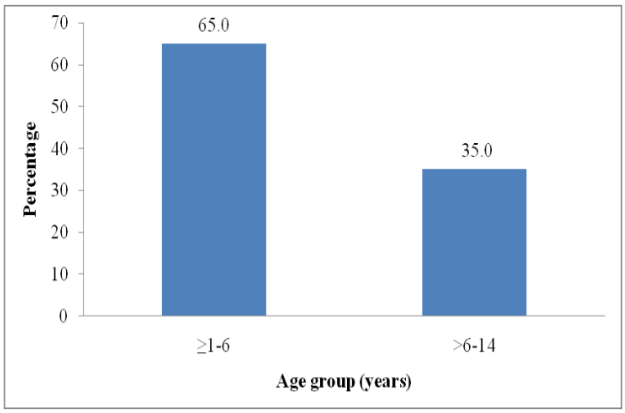

Figure 1: Age group distribution of the studied children.

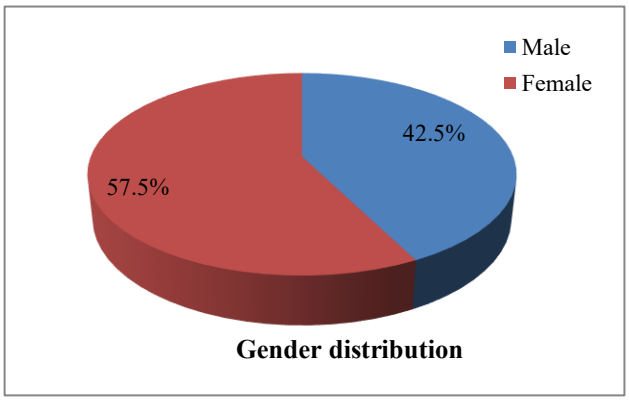

Figure 2: Gender distribution of the studied children.

Most of the children, 28 (70.0%), came from rural areas. Most of the mothers (32, 80.0%) were housewives. Among the fathers, 10 (25.0%) were businessmen.

Almost two-thirds (26, 65.0%) of children came from the lower middle-income group (Table 1). The majority (33, 82.5%) of the children with SSNS had a history of onset of NS at ≥1-6 years and only 7 (17.5%) children had onset of NS beyond 6 years. The mean onset of NS was 3.86±2.35 years. All (100%) children had bed side urine for albumin positive, 26 (65.0%) had cough, 21 (52.5%) had fever, 18 (45.0%) had facial swelling, 7 (17.5%) had dysuria, 4 (10.0%) had generalized swelling, 3 (7.5%) had swelling of legs and 2 (5.0%) children had diarrhea (Table 2).

Table 1: Socio-demographic characteristics of the study children (n=40).

Socio-demographic characteristics	Frequency	%
Residence		
Urban+Slum	12	30.0
Rural	28	70.0
Mother's occupation		
Housewife	32	80.0
Self-employed	2	5.0
Day labour	2	5.0
Garments worker	4	10.0
Father's occupation		
Service	8	20.0
Business	10	25.0
Living abroad	4	10.0
Small trader	1	2.5
Day labour/rickshaw puller	6	15.0
Farmer	2	5.0
Others	9	22.5
Socio-economic status		
Low	5	12.5
Lower middle	26	65.0
Upper middle	8	20.0
Upper	1	2.5

Table 2: Clinical presentation during the current attack of NS (n=40).

Clinical presentation	Frequency*	%
Bedside urine for albumin	40	100.0
Cough	26	65.0
Fever	21	52.5
Swelling of the face	18	45.0
Dysuria	7	17.5
Generalized swelling	4	10.0
Swelling of legs	3	7.5
Diarrhoea	2	5.0

*Multiple response.

Table 3: Association with serum albumin, cholesterol and creatinine level at 1st attack of NS with the type of relapse (n=40).

Biochemical variables	Type of relapse				P value
	Frequent relapse (n=14)		Infrequent relapse (n=26)		
	Mean	±SD	Mean	±SD	
Serum albumin (gm/dl)	2.12	±0.66	1.90	±0.44	0.216
Serum cholesterol (mg/dl)	417.50	±93.93	451.26	±85.42	0.257
Serum creatinine (mg/dl)	0.68	±0.38	0.67	±0.33	0.893

P<0.05 was significant.

No hypertension was noted in any case of relapse. Mean serum albumin, serum cholesterol and serum creatinine levels at 1st attack of NS had no statistically significant difference when compared with the type of relapse in

children with SSNS (Table 3). Age of onset of NS was not a statistically significant factor for relapse (Table 4). Time needed to respond with initial steroid therapy at 1st attack of NS had a statistically significant difference when compared with the type of relapse in children with SSNS (Table 5). Among various infections, RTI and UTI were higher in the FRNS group of SSNS. Viral fever and diarrhea were found in infrequent relapse, but not in the frequent relapse group. Regarding the type of infection, the difference was not statistically significant (Table 6).

Table 4: Association with age of onset of 1st attack and type of relapse (n=40).

Age of onset of NS (in years)	Type of relapse				P value
	Frequent relapse (n=14)		Infrequent relapse (n=26)		
	N	%	N	%	
≥1-6	11	33.3	22	66.7	0.470
>6-14	3	42.9	4	57.1	

P<0.05 was significant.

Table 5: Association of time needed for response to steroid therapy at 1st attack of NS with type of relapse (n=40).

Time needed to respond with initial steroid therapy (days)	Type of relapse				P value
	Frequent relapse (n=14)		Infrequent relapse (n=26)		
	N	%	N	%	
≤7	07	50.0	23	76.7	0.011
>7	07	50.0	03	23.3	

P<0.05 was significant.

Table 6: Association of the type of infection in the current attack with relapse of NS.

Type of infection in the current attack	Type of relapse				P value
	Frequent relapse (n=14)		Infrequent relapse (n=26)		
	N	%	N	%	
RTI	10	38.5	16	61.5	0.364
UTI	4	44.4	5	55.6	
Viral fever	0	0.0	3	100	
Diarrhea	0	0.0	2	100	

RTI=Respiratory tract infection, UTI=Urinary tract infection, P<0.05 was significant.

DISCUSSION

Out of 40 children, most of the children (70.0%) came from rural areas. Almost two-thirds (65.0%) of children came from lower-middle income group family. In their study, Minj et al reported that 48 patients (60.0%) were from the lower socioeconomic strata, 22 (27.5%) were from the upper-middle class and 10 (12.5%) were from lower middle strata.[15] A study done by Sarker et al found similar results with 59% of cases from lower, 39% from middle and 2% from upper socioeconomic strata.[16] He also reported that 60% of the subjects in his study came from rural areas, 35% from urban areas and the remaining 5% from urban-slum areas. Their finding regarding residence and socio-economic status were similar and consistent with our findings. Another study done by Uwaezuoke et al reported a lower incidence of the disease in lower socioeconomic strata.[17] This variation could be due to bias in the patient selection criteria.

This study showed that almost two-thirds (65.0%) of children belonged to the age group ≥1-6 years and 35% belonged to the age group ≥6-14 years. The mean age was found to be 5.38±2.76 years. Albar et al reported that the majority of children (66.2%) in their study were 5 years of age or more (ranging from 1.4 to 17.5 years).[18] The mean age of presentation with relapse in nephrotic syndrome in his study was 4.37±2.32 years. Minj et al observed maximum number of patients (58.7%) were less than or equal to 6 years of age.[15] This result was similar to the study. Again, another study done by Ali et al revealed that the most common age-group at presentation was 1-5 years in Saudi children, comprising a total of 51 patients (63.7%) out of 80 cases.[19] Similar study done by Sarker et al, (2012) found that, out of 100 patients, the majority (67%) were between 2-6 years of age with a mean age of 5.3±2.1 years.[16] The age predominance of <6 years was also noticed in the study done by Andersen et al, (2010).[20] Ali et al in their study of Sudani children with NS reported that the mean age at presentation was 5.2±3.5 (range 1.5–16) years.[21] The age spectrum was variable, with 42.4% of patients being in the age range of 1–5 years. The male-to-female ratio in the study was 1:1.35. Balaji et al observed there were 97 male children (60.6%), 63 female children (39.4%), with a male-to-female ratio of 1.5:1 in their study.[14] Albar et al observed mostly boys (66.2%), with a male: female ratio of 1.95:1.18 Minj et al, (2019) observed a greater male

preponderance (66.3%) in his study as compared to females (33.8%); the ratio being 1.96:1.[15]

Similar finding of male predominance was observed in the studies done by Rahi et al, Ali et al and Noer et al who obtained the ratios of (M: F-1.5:1), (M: F-2.2:1) and (M: F- 3.5:1) respectively.19,22,23 Ali et al reported that out of 460 children admitted with idiopathic NS, 330 (71.7%) had SSNS.[21] Of them, 220 (66.7%) were males and 110 (33.3%) females, with a male-to-female ratio of 2:1. However, the study findings went in contrast with their findings regarding gender and it might be due to coincidence. The current study showed that the majority (82.5%) of children reported the age of onset of NS within ≥1-6 years. The mean age of onset of NS was found to be 3.86±2.35 years. Usually, the typical age of onset of minimal change NS is 2-6 years of age. Minj et al reported 81.25% of their study population had an age at first onset of ≤6 years and 18.75% had an age at first onset of>6 years.[15] Ali et al observed that the mean age of onset of the disease was 5.4±3.57 years in their studied children.[21] All these findings supported the study findings. Balaji et al observed that the mean serum albumin was 2.3±0.344 gm/dl.[14] Ali et al reported serum cholesterol was elevated in all patients (mean 347.34±117.87 mg/dl) and elevated serum creatinine in 7.27% (mean 1.4±0.35 mg/dl) in their study.[21] Clinical characteristics of minimal change nephrotic syndrome (MCNS) include hypoalbuminaemia and hyperlipidaemia and our findings correlated with the above findings.

The present study showed that three-fourths (75.0%) of children needed ≤7 days to respond with initial steroid therapy. The mean time to respond with initial steroid therapy was 6.52±2.71 days. Balaji et al reported that the children who took more than 14 days to achieve remission during the first episode experienced frequent relapse.[14] In his study, Minj et al observed that among children treated with 8 weeks of steroid therapy in the first episode of NS, 35 (92.1%) had frequent relapses and only 3 (7.9%) had infrequent relapses.[15]

The study showed that frequent relapse was found in 14 (35.0%) and infrequent relapse was found in 26 (65.0%) cases. Minj et al studied a total of 80 children with a relapse of nephrotic syndrome.[15] Out of them, 50 (62.5%) had frequent relapses and 30 (37.5%) had infrequent relapses. Ali et al showed 37.3% of their study population had frequent relapses.[21] However, other studies reported a lower rate of infrequent and frequent relapses; Mishra et al reported that 59.3% had relapses (52% infrequent, 7.3% frequent and 0.6% steroid-dependent).[24] Noer et al reported 63.6% had relapsing NS, including 50.5% infrequent and 13.3% frequent relapses.[23] However, the difference among these findings was out of control; it might be due to the natural history of the disease itself and the genetic predisposition of the patients.

Nephrotic syndrome is an immunosuppressive condition and steroid-induced immunosuppression causes recurrent infection. In this study, we observed that RTI and UTI were higher in frequent relapse, whereas viral fever and diarrhea were higher in infrequent relapse, but the difference was not statistically significant (p>0.05). Ali et al observed infections were recorded in 237 (71.8%) patients with SSNS in their study, among them, 49.3% was respiratory infections, 28% UTI and 1.1% peritonitis.[21] The current study showed that mean serum albumin, serum cholesterol and serum creatinine levels in the first attack of NS had no statistical significance when compared with the type of relapse. Sarker et al observed that the mean serum albumin was significantly higher in infrequent relapse than in frequent relapse in their studied children.[16] Mean serum cholesterol and serum creatinine were similar between the two groups.

This study showed that the age of onset of NS was not statistically significant when compared with the type of relapse. Balaji et al observed that the incidence of FR was high in the 1-8 years age group.[14] There were 81 IFR (57.45%) and 60 FR (42.55%); however, the correlation was not statistically significant. Minj et al reported that in the group of children >6 years or older, 48.5% patients had frequent relapses and 51.5% had infrequent relapses; while in the group ≤6 years, 72.3% patients had frequent relapses and 27.7% had infrequent relapses.[15] A statistically significant difference was found in this regard. Children with an age at disease onset ≤6 years were found to have more frequent relapses. Ali et al reported age of onset less than five years was significantly associated with the risk of FR/SD course.[21]

Steroid response pattern to standard prednisolone therapy has immense diagnostic, therapeutic and prognostic value for the treating physician in managing children with Nephrotic syndrome. In this study, the majority of children with infrequent relapse responded to steroid therapy in ≤7 days, whilst children with frequent relapse mostly showed a response in >7 days. (It was found that the length of time required to respond to the first steroid therapy during the first NS attack showed a significant statistical difference (p<0.05) regarding the type of recurrence in children with SSNS). Balaji et al found that the time taken to achieve remission during the first episode of >14 days was significantly associated with frequent relapse (p<0.0001) in their studied children.[14] Minj et al also reported that longer steroid therapy led to frequent relapses. The study finding is also consistent with their findings.[15]

Due to the COVID-19 pandemic situation, the number of hospital admissions was less than usual. Hence, the sample size of the study was relatively smaller, so the result may not indicate the true scenario. The study was done in a single center. So, it does not reflect the whole population of the country. A multi-center study with a large sample size may be undertaken to represent the population of the whole country.

CONCLUSION

Children of the younger age group and lower socioeconomic strata were more prone to develop relapse. Among various infections, RTI and UTI were seen to occur in higher frequency in relapse cases of NS. A longer time taken to achieve remission during the first episode was significantly associated with frequent relapse of Nephrotic syndrome.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Johnson RJ, Feehally J, Floege J. Comprehensive clinical nephrology E-Book. Elsevier Health Sciences. 2014.
2. Aier A, Pais P, Raman V. Psychosocial functioning and health-related quality of life in children with nephrotic syndrome: preliminary findings. J Indian Assoc Child Adol Mental Health. 2022;18(4):306-14.
3. Ishikura K, Matsumoto S, Sako M, Tsuruga K, Nakanishi K. Clinical practice guideline for pediatric idiopathic nephrotic syndrome 2013: medical therapy. Clin Exp Nephrol. 2015;19(1):6-33.
4. Esfahani ST, Madani A, Asgharian F, Ataei N, Roohi A, Moghtaderi M, et al. Clinical course and outcome of children with steroid-sensitive nephrotic syndrome. Pediat Nephrol. 2011;26(7):1089-93.
5. Lombel RM, Gipson DS and Hodson EM. Treatment of steroid-sensitive nephrotic syndrome: new guidelines from KDIGO. Pediat Nephrol. 2013;28(3):415-26.
6. Shalhoub R. Pathogenesis of lipoid nephrosis: a disorder of T-cell function. The Lancet 1974;304(7880):556-60.
7. Jamin A, Dehoux L, Dossier C, Fila M, Heming N, Monteiro RC. Toll-like receptor 3 expression and function in childhood idiopathic nephrotic syndrome. Clin Exp Immunol. 2015;182(3):332-45.
8. Berg JG, Weening JJ. Role of the immune system in the pathogenesis of idiopathic nephrotic syndrome. Clin Sci. 2004;107(2):125-36.
9. Clement LC, Avila-Casado C, Macé C, Soria E, Bakker WW, Kersten S, et al. Podocyte-secreted angiopoietin-like-4 mediates proteinuria in glucocorticoid-sensitive nephrotic syndrome. Nature Med. 2011;17(1):117-22.
10. Brenchley PE. Vascular permeability factors in steroid-sensitive nephrotic syndrome and focal segmental glomerulosclerosis. Nephrol Dialy Transplant. 2003;18(6):21-5.
11. Teeninga N, Kist-van Holthe JE, Nauta J. Extending prednisolone treatment does not reduce relapses in childhood nephrotic syndrome. J Am Soc Nephrol. 2012;24:149–59.
12. Constantinescu AR, Shah HB, Foote EF and Weiss LS. Predicting first-year relapses in children with nephrotic syndrome. Pediatrics. 2004;105(3):492-5.
13. Takeda A, Takimoto H, Mizusawa Y and Simoda M. Prediction of subsequent relapse in children with steroid-sensitive nephrotic syndrome. Pediat Nephrol. 2001;16(11):888-93.
14. Balaji J, Kumaravel KS, Punitha P and Rameshbabu B. Risk factors for relapse in childhood steroid-sensitive nephrotic syndrome. Indian J Child Health. 2017;4(3):322-6.
15. Minj SS, Rathi S, Kondekar S and David JJ. Study of risk factors for relapse in frequently versus infrequently relapsing nephrotic syndrome in the 1-18 year age group: a combined prospective, retrospective cohort analytical observational study. Int J Contemp Pediatr. 2019;6(2):803-10.
16. Sarker MN, Islam MMSU, Saad T, Shoma FN, Sharmin LS, Khan HA, et al. Risk factor for relapse in childhood nephrotic syndrome-a hospital based retrospective study. Faridpur Medical College J. 2012;7(1):18-22.
17. Uwaezuoke SN, Okafor HU, Eneh CI and Odetunde OI. The triggers and patterns of relapse in childhood idiopathic nephrotic syndrome: a retrospective, descriptive study in a tertiary hospital, south-east Nigeria. J Clin Nephrol Res. 2016;3(1):1032.
18. Albar H, Bilondatu F, Daud D. Risk factors for relapse in pediatric nephrotic syndrome. Paediat Indonesia. 2018; 58(5):238-41.
19. Ali SH, Ali AM, Najim AH. The predictive factors for relapses in children with steroid-sensitive nephrotic syndrome. Saudi J Kid Dis Transplant. 2016; 27(1):67-72.
20. Andersen RF, Thrane N, Noergaard K, Rytter L, Jespersen B and Rittig S. Early age at debut is a predictor of steroid-dependent and frequent relapsing nephrotic syndrome. Pediat Nephrol. 2010;25(7):1299-304.
21. Ali EM, Elhadi NM, Abdelraheem MB, Ellidir RA. Childhood steroid-sensitive nephrotic syndrome: characteristics and predictors of relapses (A Study at a Single Center in Khartoum). Sudan J Med Sci. 2018;13(3):133-43.
22. Rahi K, Al-Badri AAS, Salih BJ, Hasan FO. Childhood nephrotic syndrome, frequent and infrequent relapses and risk factors for relapses. Iraqi Acad Sci J. 2009;8(3):291-5.
23. Noer MS. Predictors of relapse in steroid-sensitive nephrotic syndrome. Southeast Asian J Trop Med Publ Heal. 2005;36(5):1313-20.
24. Mishra OP, Abhinay A, Mishra RN, Prasad R, Pohl M. Can we predict relapses in children with idiopathic steroid-sensitive nephrotic syndrome. J Trop Pediat. 2013;59(5):343-9.

Cite this article as: Jamil JI, Khanam W, Hossain MN, Sharifa T, Uddin MN, Adnan MA, et al. Risk factors for relapse of steroid-sensitive nephrotic syndrome in children. Int J Contemp Pediatr 2026;13:717-22.