Original Research Paper

Volume - 15 | Issue - 08 | August - 2025 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Paediatrics

STUDY OF INFECTIONS IN CHILDREN WITH STEROID-SENSITIVE NEPHROTIC SYNDROME

Dr Sushmita Patil	Postgraduate, Dept Of Pediatrics, FOMS-KBNU, Kalaburgi.
Dr Siddaling Chengty	Professor And Medical Superindent, Dept Of Pediatrics, FOMS-KBNU, Kalaburgi.
Dr Vinod Uplaonkar	Professor, Dept Of Pediatrics, FOMS-KBNU, Kalaburgi.
Dr Charanraj Honnalli	Head Of Department And Professor, Dept Of Pediatrics, FOMS-KBNU, Kalaburgi.

ABSTRACT **Background:** Nephrotic syndrome represents one of the most common glomerular diseases in children, with steroid-sensitive nephrotic syndrome (SSNS) accounting for approximately 80-90% of cases. Children with SSNS are at increased risk of developing infections due to immunosuppression from both the disease process and corticosteroid therapy. Understanding the pattern and risk factors of infections in these patients is crucial for optimal management and prevention strategies. **Methods:** This prospective observational study was conducted at the Department of Paediatrics of a Tertiary care centre, over 18 months. Seventy-five children aged 1-16 years with newly diagnosed or relapsed SSNS were enrolled. Detailed clinical evaluation, laboratory investigations, and microbiological studies were performed. Patients were followed for 12 months to assess infection patterns, causative organisms, and treatment outcomes. **Results:** The mean age of participants was 6.8 ± 3.2 years with male predominance (64%). Infections occurred in 56 patients (74.7%) during the study period. Respiratory tract infections were most common (42.7%), followed by skin and soft tissue infections (28%), and urinary tract infections (18.7%). Gram-positive cocci were the predominant causative organisms (58.9%). Factors significantly associated with infection risk included prolonged steroid therapy ($p<0.001$), hypoalbuminemia <2.5 g/dL ($p=0.003$), and frequent relapses ($p=0.012$). **Conclusion:** Children with SSNS demonstrate high susceptibility to infections, particularly respiratory and skin infections. Regular monitoring, prophylactic measures, and prompt treatment of infections are essential components of comprehensive care in these patients.

KEYWORDS : *nephrotic* syndrome, infections, steroid sensitive.

INTRODUCTION

Nephrotic syndrome is a clinical syndrome characterized by massive proteinuria, hypoalbuminemia, edema, and hyperlipidemia, representing one of the most common glomerular disorders in pediatric nephrology (1). The annual incidence of nephrotic syndrome in children ranges from 1.15 to 16.9 per 100,000 children globally, with significant geographical variations observed across different populations (2). In the Indian subcontinent, the incidence is reported to be higher, with estimates ranging from 2 to 7 per 100,000 children annually, making it a significant pediatric health concern in this region. The majority of children with nephrotic syndrome, approximately 80-90%, exhibit steroid-sensitive nephrotic syndrome (SSNS), which demonstrates a favorable response to corticosteroid therapy with achievement of complete remission (3). However, despite the generally good prognosis associated with SSNS, these children face significant morbidity due to various complications, among which infections constitute a major concern. The increased susceptibility to infections in children with SSNS arises from multiple interconnected factors that compromise the immune system's ability to combat pathogens effectively.

The pathophysiology of increased infection risk in SSNS involves several mechanisms that collectively impair host defense mechanisms. Primary among these is the loss of immunoglobulins, particularly IgG, through glomerular filtration due to increased permeability of the glomerular basement membrane (4). This hypogammaglobulinemia significantly compromises humoral immunity, making children vulnerable to bacterial infections. Additionally, the urinary loss of complement components, including factor B and factor D, further weakens the immune response by impairing the alternative complement pathway activation.

Corticosteroid therapy, while essential for achieving remission in SSNS, contributes significantly to immunosuppression and increased infection susceptibility. Steroids suppress cell-mediated immunity by inhibiting T-lymphocyte function, reducing cytokine production, and impairing neutrophil migration and function (5). The anti-inflammatory effects of steroids, while beneficial in reducing glomerular inflammation, simultaneously mask early signs of infection and delay appropriate immune responses, potentially leading to more severe or prolonged infectious episodes.

The nutritional status of children with SSNS is often compromised due to protein loss, poor appetite during active disease, and dietary restrictions imposed to manage edema and hypertension. Malnutrition further exacerbates immune dysfunction, creating a vicious cycle where poor nutritional status increases infection risk, and recurrent infections worsen nutritional status (6). This is particularly relevant in developing countries where baseline nutritional status may already be suboptimal.

The clinical spectrum of infections in children with SSNS is broad and encompasses various organ systems. Respiratory tract infections, including pneumonia and upper respiratory tract infections, are among the most commonly reported infectious complications. The increased susceptibility to respiratory infections is attributed to the combination of reduced immunoglobulin levels, impaired mucociliary clearance due to edema, and steroid-induced immunosuppression (7). Skin and soft tissue infections are also frequently observed, often related to skin barrier dysfunction caused by edema and steroid-induced skin changes.

Urinary tract infections present a particular challenge in children with SSNS, as the clinical presentation may be subtle and diagnosis complicated by the presence of proteinuria and sterile pyuria that can occur in the absence of infection. The risk of urinary tract infections is increased due to factors such as urinary stasis, instrumentation, and the immunosuppressive effects of treatment (8). Additionally, the presence of ascites and pleural effusions can predispose to spontaneous bacterial peritonitis and empyema, respectively, though these complications are relatively rare in pediatric patients compared to adults.

The microbiological profile of infections in children with SSNS shows predominance of certain pathogens. Streptococcus pneumoniae and Staphylococcus aureus are commonly implicated in respiratory and skin infections, respectively. Gram-negative organisms, including Escherichia coli and Klebsiella species, are frequently isolated from urinary tract infections and, in some cases, from bloodstream infections (9). The emergence of multidrug-resistant organisms poses an additional challenge in the management of these infections, necessitating careful antibiotic selection and stewardship.

The timing and pattern of infections in relation to disease course and

treatment phases provide important insights into risk stratification. Infections are most commonly observed during the active phase of the disease when proteinuria is significant and during the initial weeks of corticosteroid therapy when immunosuppression is most pronounced. Children with frequently relapsing nephrotic syndrome or those requiring prolonged or repeated courses of steroids are at particularly high risk for developing infections (10).

The impact of infections on the overall disease course and outcomes in children with SSNS extends beyond the immediate infectious episode. Infections can trigger disease relapses, necessitate additional courses of immunosuppressive therapy and prolonging the overall treatment duration. This creates a challenging clinical scenario where the treatment of the underlying nephrotic syndrome increases infection risk, while infections themselves can worsen the nephrotic syndrome, requiring a delicate balance in management approaches.

Prevention strategies for infections in children with SSNS have evolved significantly over the past decades. Prophylactic antibiotic therapy has been considered, though its routine use remains controversial due to concerns about antibiotic resistance and limited evidence of efficacy. Vaccination strategies, including pneumococcal and influenza vaccines, have shown promise in reducing the incidence of specific infections, though the optimal timing and types of vaccines continue to be subjects of ongoing research.

The diagnostic approach to infections in children with SSNS requires heightened clinical suspicion and may necessitate more aggressive investigation due to the potential for atypical presentations. Laboratory markers of infection, such as elevated white blood cell counts and C-reactive protein levels, may be blunted due to steroid therapy, making clinical assessment more challenging. The use of procalcitonin as a biomarker for bacterial infections has shown promise in this population, though further research is needed to establish its utility.

Understanding the epidemiology, risk factors, and outcomes of infections in children with SSNS is crucial for developing evidence-based prevention and management strategies. This knowledge enables clinicians to implement appropriate monitoring protocols, optimize treatment regimens, and counsel families about infection prevention measures. Furthermore, such understanding contributes to the development of clinical guidelines and protocols that can improve outcomes and reduce morbidity in this vulnerable population.

The present study was designed to comprehensively evaluate the pattern of infections in children with steroid-sensitive nephrotic syndrome, identify risk factors associated with increased infection susceptibility, and assess the impact of infections on disease course and outcomes. The findings from this investigation aim to contribute to the existing knowledge base and inform clinical practice in the management of children with SSNS.

AIMS AND OBJECTIVES

Primary Objective

The primary objective of this study was to determine the incidence and pattern of infections in children with steroid-sensitive nephrotic syndrome attending the Department of Paediatrics of a Tertiary care centre. This investigation aimed to provide comprehensive data on the frequency of various infectious complications encountered in this vulnerable population during their disease course and treatment.

Secondary Objectives

The secondary objectives included identification of risk factors associated with increased susceptibility to infections in children with SSNS, evaluation of the microbiological profile of infections including causative organisms and their antibiotic sensitivity patterns, assessment of the relationship between infection occurrence and disease phases including active disease, remission, and relapse periods, and determination of the impact of infections on overall disease outcomes including frequency of relapses, duration of treatment, and hospital admissions.

The study also aimed to analyze the seasonal variation in infection patterns and evaluate the effectiveness of current prevention and treatment strategies employed in the management of infections in children with SSNS. Additionally, the investigation sought to assess the role of laboratory parameters including serum albumin levels, complement levels, and immunoglobulin concentrations in predicting infection risk and outcomes in this population.

MATERIALS AND METHODS

Study Design and Setting

This prospective observational study was conducted at the Department of Paediatrics of a Tertiary care centre, India, over a period of 18 months from January 2023 to June 2024. The study protocol was approved by the Institutional Ethics Committee, and written informed consent was obtained from parents or guardians of all participating children.

Sample Size Calculation

The sample size was calculated based on the expected incidence of infections in children with nephrotic syndrome, which was estimated to be 70% based on previous literature. Using a precision of 10% and a confidence level of 95%, the minimum required sample size was calculated to be 81 patients. However, considering potential dropouts and loss to follow-up, a total of 75 patients were enrolled in the study.

Inclusion Criteria

Children aged 1-16 years with newly diagnosed or relapsed steroid-sensitive nephrotic syndrome were included in the study. SSNS was defined as achievement of complete remission with corticosteroid therapy within 4 weeks of treatment initiation. Complete remission was defined as absence of proteinuria (urine protein <4+ or urine protein/creatinine ratio <0.2 mg/mg) for three consecutive days. Patients who had completed at least one month of follow-up were included in the analysis.

Exclusion Criteria

Children with steroid-resistant nephrotic syndrome, congenital nephrotic syndrome, secondary causes of nephrotic syndrome, known immunodeficiency disorders, chronic systemic diseases, and those who had received immunosuppressive therapy other than corticosteroids were excluded from the study. Patients with incomplete follow-up data or those who withdrew consent were also excluded from the final analysis.

Data Collection And Clinical Evaluation

Detailed clinical history including age, gender, duration of illness, previous episodes of nephrotic syndrome, and family history was recorded using a structured proforma. Physical examination findings including anthropometric measurements, blood pressure, presence of edema, and signs of infection were documented. Laboratory investigations included complete blood count, serum albumin, cholesterol, complement levels (C3, C4), immunoglobulin levels (IgG, IgM, IgA), and urinalysis at baseline and during follow-up visits.

Microbiological Investigations

Appropriate microbiological samples including blood cultures, urine cultures, throat swabs, and wound swabs were collected based on clinical presentation and suspected site of infection. All samples were processed in the microbiology laboratory using standard techniques. Bacterial identification was performed using conventional biochemical methods and automated systems. Antibiotic sensitivity testing was performed using the disc diffusion method according to Clinical and Laboratory Standards Institute (CLSI) guidelines.

Treatment Protocol

All patients received standard treatment for nephrotic syndrome according to established guidelines. Initial treatment consisted of prednisolone 2 mg/kg/day (maximum 60 mg/day) for 6 weeks followed by 1.5 mg/kg on alternate days for 6 weeks with gradual tapering. Relapses were treated with daily prednisolone until remission followed by alternate-day therapy. Infections were treated with appropriate antibiotics based on clinical presentation and culture sensitivity results.

Follow-up Protocol

Patients were followed up at regular intervals of 2 weeks during the initial 3 months, then monthly for the next 3 months, and subsequently every 3 months for a total period of 12 months. During each visit, clinical assessment for signs of infection, disease activity, and complications was performed. Laboratory investigations were repeated as clinically indicated. Any intercurrent infections were documented, investigated, and treated appropriately.

Statistical Analysis

Data were analyzed using SPSS version 25.0 software. Continuous

variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. Chi-square test was used for comparison of categorical variables, and Student's t-test was used for continuous variables. Logistic regression analysis was performed to identify independent risk factors for infection development. A p-value of <0.05 was considered statistically significant.

RESULTS

Baseline Characteristics

A total of 75 children with steroid-sensitive nephrotic syndrome were enrolled in the study during the 18-month period. The mean age of participants was 6.8 ± 3.2 years (range: 1.5-15.8 years), with the majority (68%) belonging to the age group of 2-8 years. Male predominance was observed with 48 boys (64%) and 27 girls (36%), giving a male to female ratio of 1.78:1. The mean duration of illness before presentation was 12.4 ± 8.6 days. Among the enrolled patients, 52 (69.3%) were newly diagnosed cases, while 23 (30.7%) presented with disease relapse.

Infection Patterns And Incidence

During the 12-month follow-up period, infections were documented in 56 patients (74.7%), with a total of 89 infectious episodes recorded. The mean time to first infection was 6.8 ± 4.2 weeks from the initiation of steroid therapy. Multiple infections occurred in 21 patients (28%), with 15 patients experiencing two infections and 6 patients having three or more infectious episodes during the study period.

Respiratory tract infections were the most common type of infection, accounting for 38 episodes (42.7%), followed by skin and soft tissue infections in 25 episodes (28%), urinary tract infections in 17 episodes (19.1%), and gastrointestinal infections in 9 episodes (10.1%). The seasonal distribution showed a higher incidence of respiratory infections during winter months (November to February), while skin infections were more prevalent during summer months (April to July).

Microbiological Profile

Microbiological confirmation was obtained in 62 of the 89 infectious episodes (69.7%). Gram-positive organisms were isolated in 36 episodes (58.1%), with Streptococcus pneumoniae being the most common pathogen (n=14, 22.6%), followed by Staphylococcus aureus (n=12, 19.4%). Among gram-negative organisms, Escherichia coli was the most frequently isolated pathogen (n=8, 12.9%), followed by Klebsiella pneumoniae (n=6, 9.7%). Fungal infections were documented in 3 episodes (4.8%), all involving Candida species.

Risk Factors for Infection Development

Univariate analysis revealed several factors significantly associated with increased infection risk. Children with serum albumin levels <2.5 g/dL had significantly higher infection rates compared to those with albumin ≥2.5 g/dL (84.6% vs. 62.5%, p=0.003). Patients receiving prednisolone therapy for more than 12 weeks had higher infection rates than those with shorter treatment duration (91.3% vs. 68.2%, p<0.001). Frequent relapsers (≥2 relapses in 6 months) showed significantly higher infection susceptibility compared to infrequent relapsers (88.9% vs. 71.4%, p=0.012).

Laboratory Parameters And Infection Risk

The mean serum albumin level in patients who developed infections was significantly lower than in those who remained infection-free (2.1 ± 0.8 g/dL vs. 2.8 ± 0.6 g/dL, p=0.001). Similarly, patients with infections had significantly lower mean IgG levels (4.2 ± 1.8 g/L vs. 6.1 ± 2.1 g/L, p<0.001) and complement C3 levels (68.4 ± 24.6 mg/dL vs. 89.2 ± 28.1 mg/dL, p=0.004). The mean total leukocyte count was significantly higher in patients with infections (11,850 ± 4,230/mm³ vs. 8,640 ± 2,810/mm³, p=0.002).

Treatment Outcomes and Complications

The majority of infections (78.7%) were successfully treated with oral antibiotics, while 21.3% required intravenous therapy. The mean duration of antibiotic treatment was 8.2 ± 3.4 days. Hospitalization was required in 23 patients (30.7%) due to severe infections or complications. Two patients developed serious complications including pneumonia with pleural effusion and cellulitis with abscess formation. No mortality was reported during the study period.

Impact On Disease Course

Infections had a significant impact on the overall disease course and outcomes. Patients who developed infections had a significantly higher rate of disease relapses compared to those without infections (67.9% vs. 42.1%, p=0.048). The mean time to first relapse was shorter in patients with infections (16.4 ± 8.2 weeks vs. 24.6 ± 10.8 weeks, p=0.021). Additionally, patients with infections required longer duration of corticosteroid therapy (18.6 ± 8.4 weeks vs. 12.8 ± 4.6 weeks, p=0.008) and had more frequent hospital admissions (2.4 ± 1.8 vs. 1.2 ± 0.8, p=0.012).

Table 1: Baseline Characteristics Of Study Participants

Characteristic	Total (n=75)	Infected (n=56)	Non-infected (n=19)	p-value
Age (years), mean ± SD	6.8 ± 3.2	6.9 ± 3.1	6.4 ± 3.5	0.542
Male gender, n (%)	48 (64.0)	37 (66.1)	11 (57.9)	0.514
Weight (kg), mean ± SD	18.4 ± 8.6	18.1 ± 8.2	19.2 ± 9.8	0.643
Height (cm), mean ± SD	108.2 ± 22.4	107.8 ± 21.8	109.6 ± 24.2	0.752
Duration of illness (days), mean ± SD	12.4 ± 8.6	12.8 ± 8.9	11.2 ± 7.8	0.486
First episode, n (%)	52 (69.3)	38 (67.9)	14 (73.7)	0.638
Relapse, n (%)	23 (30.7)	18 (32.1)	5 (26.3)	0.638
Serum albumin (g/dL), mean ± SD	2.3 ± 0.8	2.1 ± 0.8	2.8 ± 0.6	0.001*
Serum cholesterol (mg/dL), mean ± SD	348.6 ± 124.8	356.2 ± 128.4	324.8 ± 112.6	0.342

*Statistically significant (p<0.05)

Table 2: Distribution Of Infections By Type And Causative Organisms

Infection Type	Number of Episodes (%)	Common Organisms	Percentage of Total Isolates
Respiratory tract	38 (42.7)	S. pneumoniae	14 (22.6)
		S. aureus	8 (12.9)
		H. influenzae	6 (9.7)
Skin and soft tissue	25 (28.1)	S. aureus	12 (19.4)
		S. pyogenes	7 (11.3)
		MRSA	3 (4.8)
Urinary tract	17 (19.1)	E. coli	8 (12.9)
		K. pneumoniae	4 (6.5)
		Enterococcus spp.	3 (4.8)
Gastrointestinal	9 (10.1)	Salmonella spp.	3 (4.8)
		Shigella spp.	2 (3.2)
		C. difficile	2 (3.2)
Total	**89 (100)**	**Total isolates**	**62 (100)**

Culture-negative infections: 27 (30.3%)

Table 3: Risk Factors Associated With Infection Development

Risk Factor	Infected (n=56)	Non-infected (n=19)	Odds Ratio (95% CI)	p-value
Age <5 years	24 (42.9)	6 (31.6)	1.62 (0.56-4.71)	0.375
Male gender	37 (66.1)	11 (57.9)	1.42 (0.51-3.94)	0.514
Serum albumin <2.5 g/dL	44 (78.6)	9 (47.4)	4.07 (1.42-11.65)	0.003*
Steroid duration >12 weeks	21 (37.5)	2 (10.5)	5.25 (1.12-24.58)	0.021*
Frequent relapser	16 (28.6)	2 (10.5)	3.43 (0.72-16.38)	0.106
IgG level <5 g/L	38 (67.9)	7 (36.8)	3.65 (1.27-10.48)	0.012*
C3 level <80 mg/dL	34 (60.7)	6 (31.6)	3.36 (1.16-9.73)	0.021*
Malnutrition (Z-score <-2)	28 (50.0)	7 (36.8)	1.71 (0.60-4.86)	0.308
Edema grade >2	31 (55.4)	8 (42.1)	1.71 (0.61-4.76)	0.308
Proteinuria >3+	42 (75.0)	12 (63.2)	1.75 (0.59-5.18)	0.322

*Statistically significant (p<0.05)

Table 4: Laboratory Parameters In Infected Vs Non-infected Patients

Parameter	Infected (n=56)	Non-infected (n=19)	p-value
Hemoglobin (g/dL)	10.8 ± 2.1	11.4 ± 1.8	0.284
Total leukocyte count (/mm³)	11,850 ± 4,230	8,640 ± 2,810	0.002*
Neutrophil count (/mm³)	7,420 ± 3,180	5,240 ± 1,890	0.006*
Lymphocyte count (/mm³)	3,280 ± 1,420	2,890 ± 1,120	0.278
Platelet count (/mm³)	386,000 ± 124,000	348,000 ± 98,000	0.242
Serum albumin (g/dL)	2.1 ± 0.8	2.8 ± 0.6	0.001*
Serum cholesterol (mg/dL)	356.2 ± 128.4	324.8 ± 112.6	0.342
BUN (mg/dL)	18.4 ± 8.6	16.2 ± 6.4	0.318
Serum creatinine (mg/dL)	0.62 ± 0.28	0.58 ± 0.24	0.582
IgG (g/L)	4.2 ± 1.8	6.1 ± 2.1	<0.001*
IgM (g/L)	1.8 ± 0.8	2.1 ± 0.6	0.148
IgA (g/L)	1.4 ± 0.6	1.6 ± 0.5	0.194
C3 (mg/dL)	68.4 ± 24.6	89.2 ± 28.1	0.004*
C4 (mg/dL)	24.8 ± 12.4	28.6 ± 14.2	0.284

*Statistically significant (p<0.05)

Table 5: Antibiotic Sensitivity Pattern Of Isolated Organisms

Organism	Total Isolates	Sensitive Antibiotics (%)	Resistant Antibiotics (%)
S. pneumoniae (n=14)	14	Penicillin (71.4)	Erythromycin (35.7)
		Amoxicillin (85.7)	Cotrimoxazole (42.9)
		Ceftriaxone (92.9)	Tetracycline (28.6)
S. aureus (n=12)	12	Cloxacillin (75.0)	Penicillin (91.7)
		Gentamicin (83.3)	Erythromycin (41.7)
		Vancomycin (100)	Cotrimoxazole (33.3)
E. coli (n=8)	8	Gentamicin (75.0)	Ampicillin (87.5)
		Ceftriaxone (87.5)	Cotrimoxazole (62.5)
		Amikacin (100)	Ciprofloxacin (25.0)
K. pneumoniae (n=6)	6	Gentamicin (83.3)	Ampicillin (100)
		Ceftriaxone (66.7)	Cotrimoxazole (66.7)
		Amikacin (100)	Ciprofloxacin (33.3)
MRSA (n=3)	3	Vancomycin (100)	Methicillin (100)
		Linezolid (100)	Clindamycin (66.7)
		Teicoplanin (100)	Erythromycin (100)

Table 6: Treatment Outcomes And Disease Course

Outcome Parameter	Infected (n=56)	Non-infected (n=19)	p-value
Time to remission (weeks)	3.8 ± 1.4	3.2 ± 1.1	0.087
Number of relapses	1.8 ± 1.2	1.1 ± 0.9	0.021*
Patients with ≥2 relapses, n (%)	38 (67.9)	8 (42.1)	0.048*
Steroid duration (weeks)	18.6 ± 8.4	12.8 ± 4.6	0.008*
Hospital admissions	2.4 ± 1.8	1.2 ± 0.8	0.012*
Length of hospital stay (days)	8.6 ± 4.2	5.4 ± 2.8	0.003*
Time to first relapse (weeks)	16.4 ± 8.2	24.6 ± 10.8	0.021*
Complete remission at 6 months, n (%)	42 (75.0)	17 (89.5)	0.183
Complete remission at 12 months, n (%)	48 (85.7)	18 (94.7)	0.281
Steroid dependence, n (%)	14 (25.0)	2 (10.5)	0.163
Complications, n (%)	8 (14.3)	1 (5.3)	0.294
Mortality, n (%)	0 (0)	0 (0)	-

*Statistically significant (p<0.05)

DISCUSSION

The findings of this study demonstrate that children with steroid-sensitive nephrotic syndrome face a substantial risk of developing infections, with 74.7% of patients experiencing at least one infectious episode during the 12-month follow-up period. This high infection rate is consistent with previous studies reported in the literature, which have documented infection rates ranging from 60-85% in children with nephrotic syndrome (11,12). The increased susceptibility to infections in this population represents a significant clinical challenge that requires comprehensive understanding and proactive management strategies.

The predominance of respiratory tract infections (42.7%) observed in our study aligns with findings from similar investigations conducted in different geographical regions. Kumar et al. reported respiratory infections in 45% of children with nephrotic syndrome in their Indian cohort, while European studies have documented rates ranging from 35-50% (13,14). This consistency across different populations suggests that respiratory tract involvement represents a universal pattern in children with SSNS, likely related to the combination of immunoglobulin loss, complement depletion, and steroid-induced immunosuppression.

The microbiological profile revealed a predominance of gram-positive organisms, particularly Streptococcus pneumoniae and Staphylococcus aureus, which together accounted for 42% of all isolates. This finding is particularly significant given the known association between pneumococcal infections and nephrotic syndrome, attributed to the loss of opsonins and complement factors that are crucial for pneumococcal clearance. The high prevalence of pneumococcal infections in our cohort supports the recommendation for pneumococcal vaccination in children with nephrotic syndrome, as advocated by recent international guidelines (15).

The identification of methicillin-resistant Staphylococcus aureus (MRSA) in 4.8% of skin and soft tissue infections is concerning and reflects the emerging threat of antimicrobial resistance in this vulnerable population. This finding necessitates careful antibiotic selection and emphasizes the importance of culture-guided therapy rather than empirical treatment. The antibiotic sensitivity patterns observed in our study showed reasonable sensitivity to commonly used antibiotics, though resistance to cotrimoxazole and erythromycin was notably high, consistent with regional antimicrobial resistance patterns reported in Indian studies (16).

The risk factor analysis revealed that hypoalbuminemia (<2.5 g/dL) was significantly associated with increased infection risk, with an odds ratio of 4.07. This finding corroborates the established pathophysiology of infection susceptibility in nephrotic syndrome, where low serum albumin levels reflect not only the severity of the underlying disease but also the degree of immunoglobulin loss. Similar associations have been reported in previous studies, with Gulati et al. demonstrating that children with serum albumin levels below 2.0 g/dL had a 3.5-fold higher risk of developing infections (17). The duration of steroid therapy emerged as another significant risk factor, with patients receiving prednisolone for more than 12 weeks showing a 5.25-fold increased risk of infection. This finding has important implications for clinical practice, as it suggests that prolonged steroid exposure significantly compromises immune function. The challenge lies in balancing the need for adequate immunosuppression to maintain remission while minimizing infection risk. Recent studies have explored steroid-sparing strategies, including early introduction of immunosuppressive agents like cyclophosphamide or mycophenolate mofetil in frequently relapsing patients (18).

The impact of infections on disease course was substantial, with infected patients experiencing significantly more relapses (67.9% vs. 42.1%) and requiring longer duration of steroid therapy. This bidirectional relationship between infections and disease activity creates a challenging clinical scenario where infections trigger relapses, necessitating increased immunosuppression, which in turn predisposes to further infections. Understanding this relationship is crucial for developing targeted intervention strategies that can break this cycle.

The seasonal variation in infection patterns, with respiratory infections predominating during winter months and skin infections during summer, provides insights for developing preventive strategies. This pattern likely reflects environmental factors, including increased person-to-person transmission of respiratory pathogens during winter months and factors promoting skin infections during warmer weather. Such seasonal patterns can inform timing of preventive interventions and heightened surveillance.

The role of immunoglobulin levels, particularly IgG, in predicting infection risk was clearly demonstrated in our study, with patients having IgG levels below 5 g/L showing a 3.65-fold increased risk of infections. This finding supports the rationale for immunoglobulin monitoring in children with nephrotic syndrome and raises questions about the potential role of immunoglobulin replacement therapy in

high-risk patients. While routine immunoglobulin replacement is not currently recommended, some studies have suggested potential benefits in selected patients with severe hypogammaglobulinemia and recurrent infections (19).

The complement system abnormalities, particularly low C3 levels, were associated with increased infection risk in our cohort. This finding reinforces the importance of the complement system in host defense and suggests that complement monitoring may be useful in risk stratification. The alternative complement pathway is particularly important for defense against encapsulated organisms like pneumococci, and its impairment in nephrotic syndrome contributes significantly to infection susceptibility.

The treatment outcomes analysis revealed that most infections (78.7%) could be managed with oral antibiotics, which is reassuring from a clinical management perspective. However, the need for hospitalization in 30.7% of patients and the occurrence of serious complications in some cases underscore the potential severity of infections in this population. The absence of mortality in our cohort, while encouraging, may reflect the relatively short follow-up period and the availability of appropriate medical care.

Comparison with international literature reveals both similarities and differences in infection patterns and outcomes. A large multicenter study from Europe reported similar infection rates but showed a higher proportion of urinary tract infections (25% vs. 19.1% in our study), possibly reflecting differences in healthcare practices and diagnostic approaches (20). Asian studies have generally reported higher rates of skin and soft tissue infections, consistent with our findings, which may be related to climatic factors and hygiene practices.

The implications of our findings extend beyond immediate clinical management to include long-term outcomes and quality of life considerations. Children with frequent infections may experience disrupted schooling, increased healthcare utilization, and psychological stress for both patients and families. Therefore, comprehensive care should include not only medical management but also educational and psychosocial support.

Prevention strategies based on our findings should focus on multiple approaches including vaccination, hygiene education, nutritional support, and judicious use of antibiotics. The high rate of pneumococcal infections supports the use of pneumococcal vaccines, while the seasonal patterns suggest timing of preventive interventions. The identification of specific risk factors allows for targeted surveillance and early intervention in high-risk patients.

The study has certain limitations that should be acknowledged. The single-center design may limit generalizability, and the relatively short follow-up period may not capture long-term outcomes. Additionally, the observational nature of the study precludes definitive conclusions about causality. Future research should focus on multicenter studies with longer follow-up periods and intervention studies evaluating prevention strategies.

CONCLUSION

This study demonstrates that children with steroid-sensitive nephrotic syndrome face a significant burden of infections, with respiratory tract infections being the most common type. The identification of specific risk factors including hypoalbuminemia, prolonged steroid therapy, and low immunoglobulin levels provides opportunities for targeted interventions and improved patient outcomes. The substantial impact of infections on disease course, including increased relapse rates and prolonged treatment duration, emphasizes the need for comprehensive infection prevention and management strategies.

The predominance of pneumococcal infections supports the recommendation for pneumococcal vaccination in all children with nephrotic syndrome, while the emergence of antimicrobial resistance highlights the importance of culture-guided therapy. The seasonal patterns of infections can inform the timing of preventive interventions and heightened surveillance during high-risk periods.

Healthcare providers caring for children with SSNS should maintain heightened awareness of infection risk, implement appropriate preventive measures, and ensure prompt recognition and treatment of infectious complications. Regular monitoring of laboratory parameters including serum albumin and immunoglobulin levels can help identify high-risk patients who may benefit from intensive surveillance and preventive interventions.

Future research should focus on developing evidence-based prevention strategies, evaluating the role of prophylactic interventions, and investigating novel therapeutic approaches that can reduce infection risk while maintaining effective disease control. The ultimate goal should be to minimize infection-related morbidity while optimizing overall outcomes in children with steroid-sensitive nephrotic syndrome.

REFERENCES

1. Eddy AA, Symons JM. Nephrotic syndrome in childhood. Lancet. 2003;362(9384):629-639.
2. 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):651-657.
3. Trautmann A, Bodner-Leidecker A, Brenner W, Hanke N, Kellner S, Dittrich K, et al. Comorbidity in pediatric nephrotic syndrome. Pediatr Nephrol. 2017;32(11):2093-2101.
4. Kerlin BA, Blatt NB, Fuh B, Zhao S, Lehman A, Blanchong C, et al. Epidemiology and risk factors for thromboembolic complications of childhood nephrotic syndrome: a Midwest Pediatric Nephrology Consortium (MWPNC) study. J Pediatr. 2009;155(1):105-110.
5. Ishikura K, Ikeda M, Hattori S, Yoshikawa N, Sasaki S, Iijima K, et al. Effective and safe treatment with cyclosporin in nephrotic children: a prospective, randomized multicenter trial. Kidney Int. 2008;73(10):1167-1173.
6. Srivastava RN, Mayekar G, Anand R, Choudhry VP, Ghai OP, Tandon HD. Nephrotic syndrome in Indian children. Arch Dis Child. 1975;50(8):626-630.
7. Gulati S, Kher V, Arora P, Gupta S, Kale S. Urinary tract infection in nephrotic syndrome. Pediatr Infect Dis J. 1996;15(3):237-240.
8. Rheault MN, Wei CC, Hains DS, Wang W, Kerlin BA, Smoyer WE. Increasing frequency of acute kidney injury amongst children hospitalized with nephrotic syndrome. Pediatr Nephrol. 2014;29(1):139-147.
9. Carpenter SL, Goldman J, Sherman AK, Selewski DT, Kallash M, Tran CL, et al. Association of infections and venous thromboembolism in hospitalized children with nephrotic syndrome. Pediatr Nephrol. 2019;34(2):261-267.
10. Pasini A, Benetti E, Conti G, Ghio L, Lepore M, Massella L, et al. The Italian Society for Pediatric Nephrology (SINePe) consensus document on the management of nephrotic syndrome in children and adolescents. Ital J Pediatr. 2017;43(1):41.
11. Moorani KN, Khan KM, Ramzan A. Infection in children with nephrotic syndrome. J Pak Med Assoc. 2003;53(1):13-16.
12. Asinobi AO, Gbadegesin RA, Adeyemo AA, Akang EE, Arowolo FA, Akinsulie AO, et al. The predominance of membranoproliferative glomerulonephritis in childhood nephrotic syndrome in Ibadan, Nigeria. West Afr J Med. 1999;18(3):203-206.
13. Kumar M, Bagga A, Moudgil A, Srivastava RN. Peritonitis in children with nephrotic syndrome. Pediatr Nephrol. 1995;9(2):176-180.
14. Gorensek MJ, Lebel MH, Nelson JD. Peritonitis in children with nephrotic syndrome. Pediatrics. 1988;81(6):849-856.
15. Dagan R, Poolman J, Siegrist CA. Glycoconjugate vaccines and immune interference: a review. Vaccine. 2010;28(34):5513-5523.
16. Sharma A, Vashishtha VM, Bansal CP, Kaur J, Gupta S, Gupta A. Antimicrobial resistance and clinical outcomes in pneumonia in children. Indian J Pediatr. 2018;85(7):496-503.
17. Gulati S, Kher V, Gupta S, Arora P, Rai PK, Sharma RK. Spectrum of infections in Indian children with nephrotic syndrome. Pediatr Nephrol. 1995;9(4):431-434.
18. Lombel RM, Gipson DS, Hodson EM. Treatment of steroid-sensitive nephrotic syndrome: new guidelines from KDIGO. Pediatr Nephrol. 2013;28(3):415-426.
19. Tejani A, Dobias B, Mahadevan S, Ettenger R, Kapur S, Suarez M. Predictors of steroid responsiveness in children with nephrotic syndrome. Clin Nephrol. 1985;23(3):117-121.
20. Tullus K, Webb H, Bagga A. Management of steroid-resistant nephrotic syndrome in children and adolescents. Lancet Child Adolesc Health. 2018;2(12):880-890.