

Research Article**Incidence and Profile of Infections in Pediatric Nephrotic Syndrome: Experience from Northeast India****Dr. Sanjib Kumar Debnath¹, Dr. Nitu Bikomiya Deori², Dr. Bhaskar Debnath³**

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Abstract

Introduction: Children with nephrotic syndrome are at elevated risk of infections due to immune dysfunction related to the disease process and immunosuppressive therapy. These infections contribute substantially to morbidity and mortality. This hospital-based cross-sectional study was conducted in the Department of Pediatrics, Silchar Medical College and Hospital, to evaluate the incidence and clinical spectrum of infections in children with nephrotic syndrome.

Methods: The study included 180 children aged 2–12 years with nephrotic syndrome admitted from March 2023 to February 2024. Data were collected on demographic profile, clinical presentation, type of nephrotic syndrome, infection patterns, and outcomes. Investigations included complete hemogram, serum albumin, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and cultures of blood, urine, ascitic fluid, or pleural fluid as indicated. Data were analyzed using SPSS software, with $p < 0.05$ considered statistically significant.

Results: The mean age was 5.13 ± 2.30 years; 56.7% were below 5 years, and 60% were male. The spectrum of infections included upper respiratory tract infection (48.3%), urinary tract infection (20.6%), pneumonia (12.2%), acute gastroenteritis (11.1%), sepsis (5.6%), spontaneous bacterial peritonitis (4.4%), measles (1.1%), varicella (1.1%), cellulitis (0.6%), and pulmonary tuberculosis (0.6%). URTI and UTI were the most common infections in first-episode and

infrequent relapsers, respectively, while spontaneous bacterial peritonitis was significantly more frequent among frequent relapsers. Low serum albumin, elevated CRP, and raised ESR were significantly associated with poor outcomes. Eight children (4.4%) died during hospitalization, mainly due to sepsis and spontaneous bacterial peritonitis.

Conclusion: Infections significantly influence the course and outcomes of childhood nephrotic syndrome. Regular monitoring of serum albumin and inflammatory markers may help identify high-risk patients and allow timely initiation of preventive and therapeutic interventions. These findings support incorporating routine infection surveillance and albumin monitoring into standard care protocols for hospitalized children with nephrotic syndrome.

Keywords: childhood nephrotic syndrome, infections, relapse, spontaneous bacterial peritonitis

1. Introduction

Nephrotic syndrome is marked by edema, significant proteinuria ($>1 \text{ g/m}^2/\text{day}$; $>40 \text{ mg/m}^2/\text{hr}$), and low serum albumin levels ($<3 \text{ g/dL}$) [1]. It is one of the most prevalent kidney conditions in children [2,3]. Nearly 95% of pediatric nephrotic syndrome cases are primary with unknown etiology. The remaining cases are caused by renal involvement in various systemic conditions such as amyloidosis, hepatitis B, Henoch-Schönlein purpura (HSP), and systemic lupus erythematosus (SLE). Rarely,

congenital forms occur, such as Finnish type nephrotic syndrome[4].

On kidney biopsy, minimal change disease (MCD) accounts for 80%, focal segmental glomerulosclerosis (FSGS) for 7–8%, and mesangioproliferative glomerulonephritis for 7–8%[1]. The annual incidence of idiopathic nephrotic syndrome in children varies from 1.4 to 6.1 per 100,000 children depending on ethnic origin, with a global incidence of approximately 2.92 per 100,000 children per year[5,6]. Incidence is notably higher in Asia (particularly southern and eastern Asia) at 6.1 per 100,000 children per year compared to Europe, North America, and Oceania (2.4, 2.15, and 1.4 per 100,000 children per year, respectively)[6].

Complications of nephrotic syndrome can be categorized as disease-related or drug-therapy-related. Disease-related complications include infections, thromboembolism (pulmonary embolism and venous thromboembolism), cardiovascular disease, anemia, hypovolemic crisis, acute kidney injury, and metabolic disorders such as hypothyroidism, hypocalcemia, and bone disease[7]. Sinha et al. in their 2021 revised guidelines for steroid-sensitive nephrotic syndrome noted that infections account for major complications, with 19–44% of hospitalizations attributed to infections[1,8].

Multiple factors predispose children with nephrotic syndrome to infections from encapsulated organisms, including immunosuppressive therapy, presence of generalized edema, urinary loss of immunoglobulins (IgG), and complement factors (factor B)[1,8]. In the presence of edema, large fluid collections may become infected. Stretching of skin can lead to spontaneous breaches allowing bacterial entry. The urinary loss of factor B (alternative complement pathway component) increases susceptibility to infections from encapsulated organisms. Transferrin, an essential innate immune component required for normal lymphocyte function, is also lost in urine[4]. Infection risk increases with disease duration and the

use of immunosuppressive medications. Infections frequently precipitate relapses, which in turn heighten the risk of hospitalization, morbidity, and mortality[8].

This study aimed to determine the incidence and risk factors of infections in hospitalized children with nephrotic syndrome and to evaluate their clinical profile and the association of laboratory parameters with infection outcomes.

2. Materials and Methods

2.1 Study Design and Setting

This hospital-based cross-sectional study was conducted in the Department of Pediatrics, Silchar Medical College and Hospital, Silchar, Assam, from March 2023 to February 2024.

2.2 Study Population

Children aged 2–12 years with clinical manifestations of nephrotic syndrome admitted during the study period were eligible for enrollment.

2.3 Inclusion and Exclusion Criteria

Children fulfilling the Indian Society of Pediatric Nephrology (ISPN, 2021) criteria for nephrotic syndrome were included: edema, heavy proteinuria ($>40 \text{ mg/m}^2/\text{hr}$; $>1 \text{ g/m}^2/\text{day}$), and hypoalbuminemia ($<3 \text{ g/dL}$). Relapse was defined as reappearance of proteinuria (urine protein $\geq 3+$ or urinary protein to creatinine ratio $>2 \text{ mg/mg}$) for three consecutive days in a child who had attained remission.

Children with acute nephritis, secondary nephrotic syndrome, or those admitted for renal biopsy, intravenous cyclophosphamide, or rituximab infusion were excluded.

2.4 Sample Size

Based on Daniel's formula with an expected prevalence of infection of 30% from previous Indian studies[8,9], 95% confidence level, and 7% absolute precision, the minimum sample size was calculated to be 172. Accounting for potential dropouts, 180 children were enrolled.

2.5 Data Collection

After obtaining informed parental consent and institutional ethical approval, data were collected on demographic details, clinical presentation, infection profile, and outcomes.

2.6 Investigations

All children underwent complete blood count, serum albumin, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), serum creatinine, electrolytes, and urine microscopy with culture. Blood cultures, ascitic fluid cultures, pleural fluid cultures, and cerebrospinal fluid cultures were performed when clinically indicated. Additional investigations including Mantoux

test, sputum for acid-fast bacilli (AFB)/CBNAAT, and imaging studies (chest X-ray or abdominal ultrasound) were performed to confirm suspected infections such as pneumonia or peritonitis.

2.7 Statistical Analysis

Data were entered in Microsoft Excel and analyzed using SPSS software (version 21.0). Continuous variables were summarized as mean (standard deviation) or median (interquartile range), and categorical variables as frequencies and percentages. Associations were tested using chi-square or Fisher's exact test, with $p < 0.05$ considered statistically significant.

3. Definitions of Specific Infections

Infection	Definition
Spontaneous Bacterial Peritonitis (SBP)	Acute onset of fever, vomiting, or abdominal pain with ascitic fluid neutrophils $>100/\text{mm}^3$ and/or positive culture[4]
Pneumonia	Fever and cough with tachypnea, chest retractions or crepitations, and radiological confirmation on chest X-ray[1,10]
Upper Respiratory Tract Infection (URTI)	Presence of ≥ 3 of the following: fever, sore throat, runny nose, earache, pharyngeal congestion, tender sinuses, tonsillar enlargement/congestion with or without exudates[10,11]
Urinary Tract Infection (UTI)	Symptoms of UTI with significant bacteriuria ($>10^5$ CFU/mL in clean-catch sample or $>10^4$ CFU/mL in catheterized sample) and pyuria (>10 WBC/ mm^3 in uncentrifuged urine or >5 /high-power field in centrifuged sample)[4]
Pulmonary Tuberculosis	Cough >2 weeks with/without fever, history of contact, positive Mantoux test, suggestive chest X-ray, or positive AFB/CBNAAT[1,12]
Cellulitis	Local erythema, swelling, warmth, and tenderness, with or without fever[12]
Sepsis	Life-threatening organ dysfunction with fever and systemic symptoms; blood culture may be positive or negative[4,12]
Acute Gastroenteritis (AGE)	Change in stool consistency and increased frequency (liquid or watery stool occurring >3 times daily)[13]

4. RESULTS

4.1 Demographic and Clinical Characteristics

Of the 180 children enrolled, the mean age was 5.13 ± 2.30 years, with 56.7% below 5 years and 60% male. The predominant presenting symptoms were edema and decreased urine output (90% each), followed by cough/cold (55.6%).

Hematological evaluation showed mean hemoglobin 12.15 g/dL, total leukocyte count (TLC) $15,133/\text{mm}^3$, and platelets $3.89 \text{ lakh}/\text{mm}^3$. Leukocytosis ($>12,000/\text{mm}^3$) was present in 71.7% and anemia (hemoglobin $<11.5 \text{ g/dL}$) in 32.2%. Raised ESR ($>30 \text{ mm/hr}$) and CRP ($>1 \text{ mg/dL}$) were noted in 84.4% and 58.3%, respectively.

Hypoalbuminemia was nearly universal (mean 1.94 g/dL ; 98.3% $<3 \text{ g/dL}$), with hypercholesterolemia present in 99.4% (mean 377.2 mg/dL). All children had heavy proteinuria; pyuria was present in 11.7%. Urine cultures were sterile in 81.7%, with *E. coli* (11.7%) being the commonest isolate. Blood cultures were sterile in 97.3%, with occasional isolates of *Streptococcus pneumoniae*, MRSA, and *Klebsiella pneumoniae*. Ultrasound was normal in 60%, while ascites was seen in 33.9%.

In terms of disease classification, infrequent relapses were most common (54.4%), followed by first episode (27.8%) and frequent relapses (16.1%).

4.2 Infection Profile

Upper respiratory tract infection (URTI) was the leading infection overall, occurring in 48.3% of

cases, followed by urinary tract infection (UTI) in 20.6%, pneumonia in 12.2%, acute gastroenteritis (AGE) in 11.1%, sepsis in 5.6%, spontaneous bacterial peritonitis (SBP) in 4.4%, measles in 1.1%, varicella in 1.1%, cellulitis in 0.6%, and pulmonary tuberculosis in 0.6%.

Among first-episode cases, UTI predominated (38.0%), followed by URTI (30.0%) and pneumonia (14.0%). In children with infrequent relapses, URTI was the leading infection (56.1%), while in frequent relapsers, URTI (44.8%) and SBP (13.8%) were significantly more frequent ($p=0.01$). Spontaneous bacterial peritonitis was exclusive to the frequent relapse group.

4.3 Ascitic Fluid Analysis

Ascitic fluid in suspected SBP cases consistently showed neutrophilic leukocytosis. Only two cases yielded positive cultures, with *E. coli* and *Streptococcus pneumoniae* identified as the causative organisms.

4.4 Clinical Outcomes and Mortality

Pediatric intensive care unit (PICU) transfer was required in 13.9% of cases. Mortality was 4.4% ($n=8$), occurring mainly in children with spontaneous bacterial peritonitis progressing to sepsis and multiorgan failure. Poor outcomes (death or PICU transfer) correlated significantly with lower serum albumin and higher CRP/ESR values ($p<0.001$), underscoring hypoalbuminemia as a key risk factor for severe infections.

Table 2 Distribution according to infection profile in different clinical type (N=180)

Infection	1st episode (N=50)	Frequent relapse (N=29)	Infrequent relapse (N=98)	Steroid dependence (N=13)	Steroid resistance (N=2)	Complicated relapse (N=7)
Pulmonary TB	0(0.0%)	0(0.0%)	1(1.0%)	0(0.0%)	0	0
URTI	15(30.0%)	13(44.8%)	55(56.1%)	7(53.8%)	0	0
Pneumonia	7(14.0%)	4(13.8%)	9(9.2%)	2(15.4%)	1(50%)	1(14.3%)
UTI	19(38.0%)	6(20.7%)	12(12.2%)	4(30.8%)	0	2(28.6%)
AGE	6(12.0%)	3(10.3%)	11(11.2%)	2(15.4%)	0	0(0.0%)
SBP	0(0.0%)	4(13.8%)	3(3.1%)	0(0.0%)	0	4(57.1%)
Sepsis	2(4.0%)	3(10.3%)	3(3.1%)	1(7.7%)	0	5(71.4%)
Measles	1(2.0%)	0(0.0%)	1(1.0%)	0	0	0
Varicella	0(0.0%)	0(0.0%)	2(2.0%)	0	0	0
Cellulitis	0(0.0%)	0(0.0%)	1(1.0%)	0	0	0
Skin infection	1(2.0%)	1(3.4%)	3(10.3%)	0	0	0

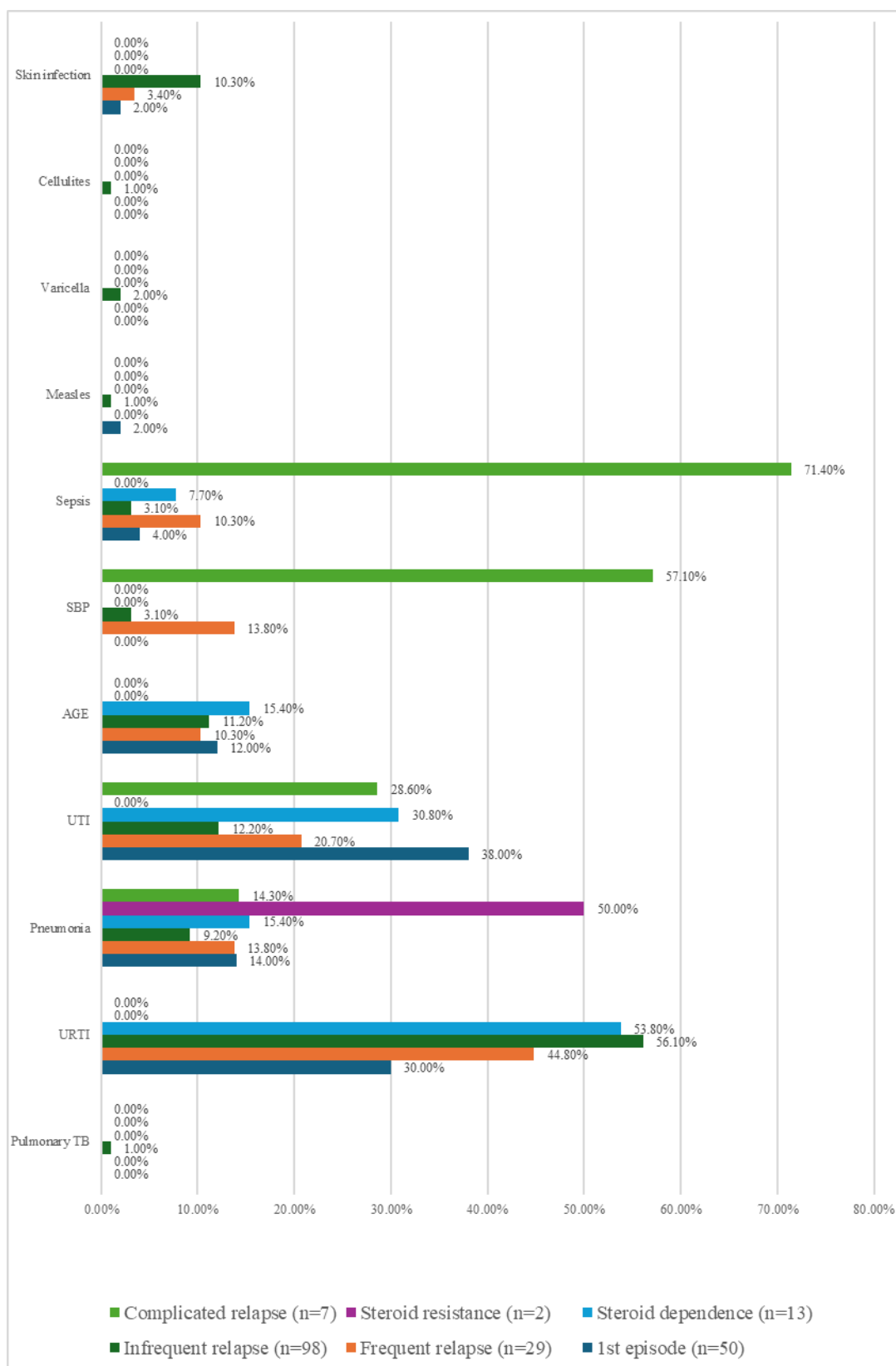


Table 3 Showing SBP association with FRNS

Infection	1st Episode (n=50)	Frequent Relapse (n=29)	p-value
Pulmonary TB	0 (0.0%)	0 (0.0%)	—
URTI	15 (30.0%)	13 (44.8%)	0.18
Pneumonia	7 (14.0%)	4 (13.8%)	1.0
UTI	19 (38.0%)	6 (20.7%)	0.11
AGE	6 (12.0%)	3 (10.3%)	1.0
SBP	0 (0.0%)	4 (13.8%)	0.01
Sepsis	2 (4.0%)	3 (10.3%)	0.35
Measles	1 (2.0%)	0 (0.0%)	1.0
Varicella	0 (0.0%)	0 (0.0%)	—
Cellulitis	0 (0.0%)	0 (0.0%)	—
Skin infection	1 (2.0%)	1 (3.4%)	1.0

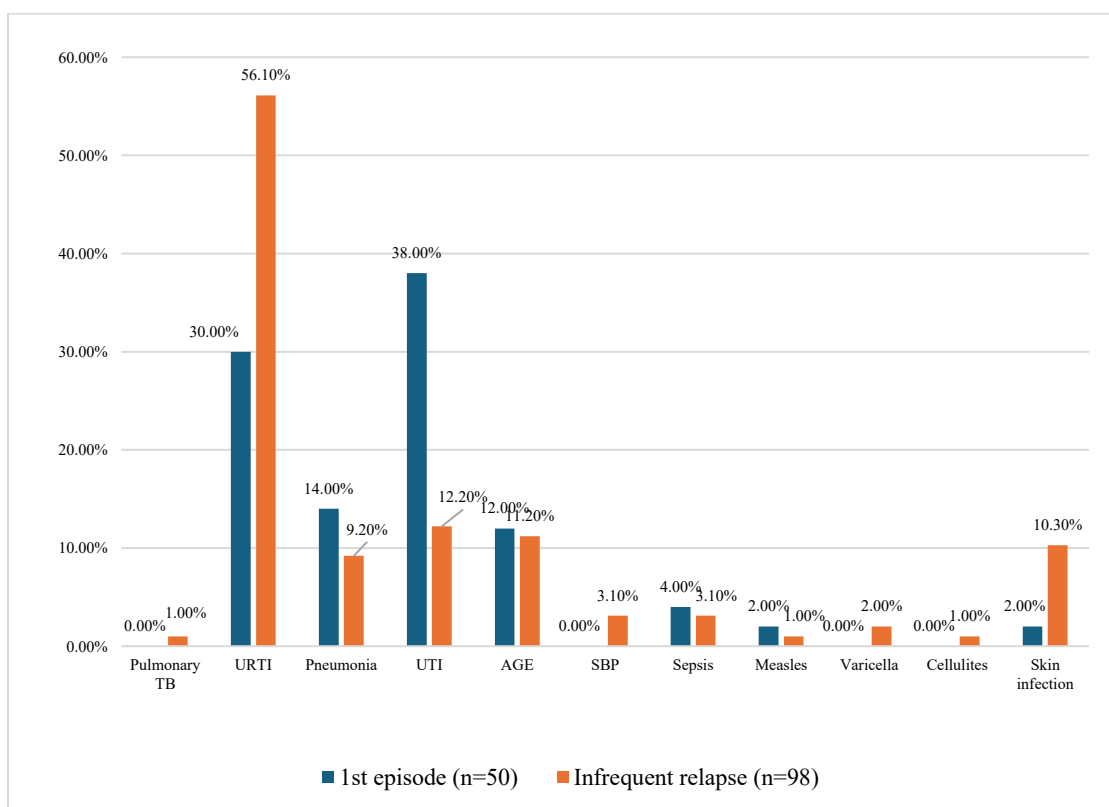


Table 4: Table showing association of UTI with first episode and URTI with infrequent relapse among study population. (N=180)

Infection	1st Episode (n=50)	Frequent Relapse (n=29)	p-value
Pulmonary TB	0 (0.0%)	1 (1.0%)	1.0
URTI	15 (30.0%)	55 (56.1%)	<0.01
Pneumonia	7 (14.0%)	9 (9.2%)	0.37
UTI	19 (38.0%)	12 (12.2%)	0.001
AGE	6 (12.0%)	11 (11.2%)	1.0
SBP	0 (0.0%)	3 (3.1%)	0.55
Sepsis	2 (4.0%)	3 (3.1%)	1.0
Measles	1 (2.0%)	1 (1.0%)	1.0
Varicella	0 (0.0%)	2 (2.0%)	0.55
Cellulitis	0 (0.0%)	1 (1.0%)	1.0
Skin infection	1 (2.0%)	3 (10.3%)	1.0

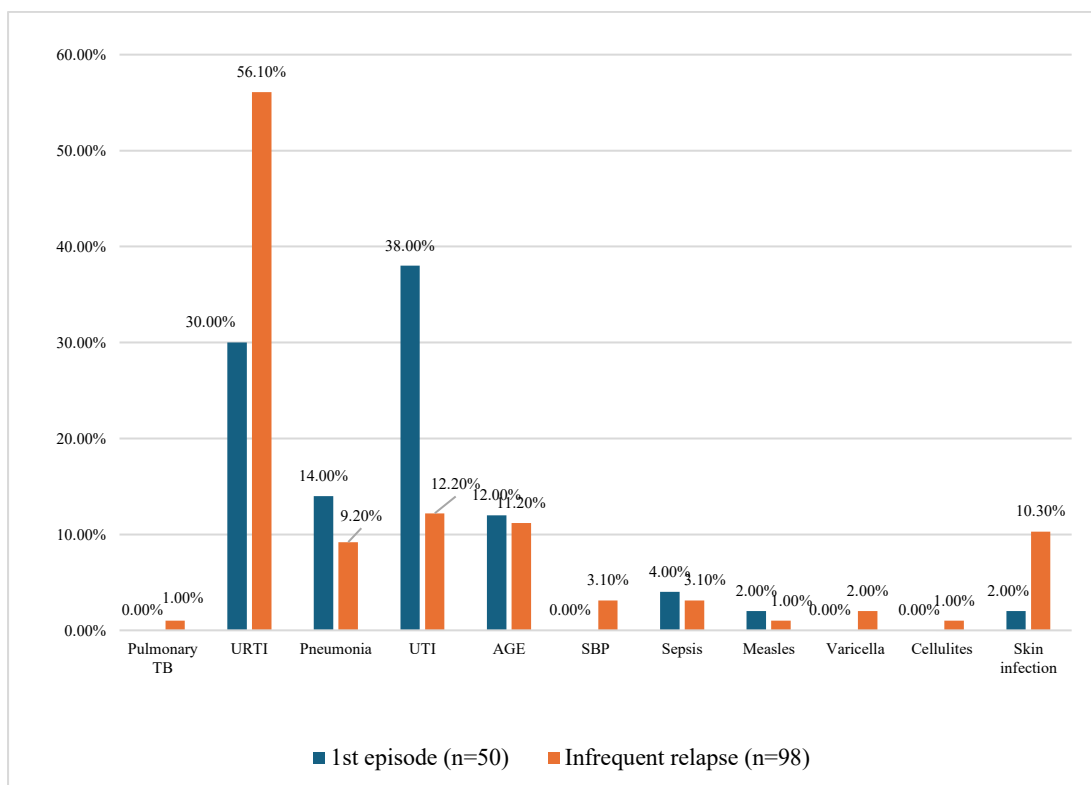
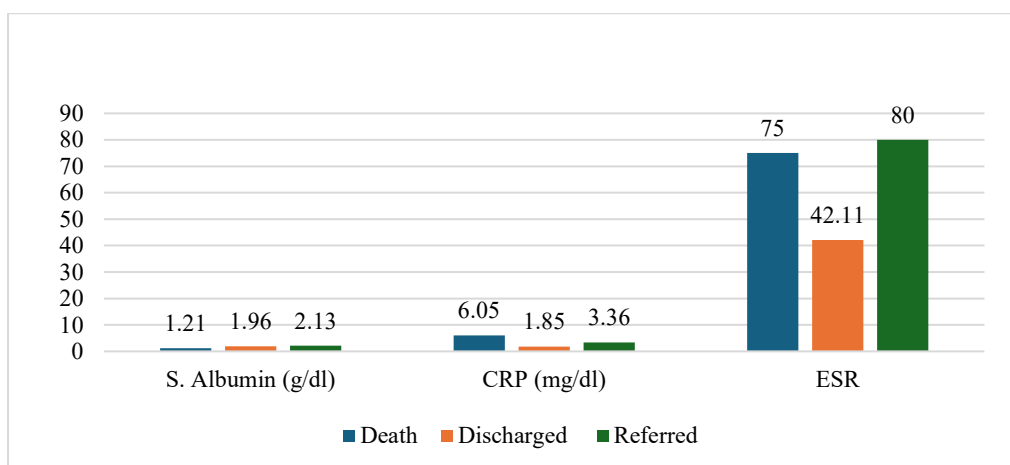


Table 5: Comparison of Laboratory Parameters with Clinical Outcomes in Study Population (n=180)

Laboratory Parameter	Death	Discharged	p-value
CRP (mg/dL)	6.05±2.11	1.85±1.53	<0.001
Serum Albumin (g/dL)	1.21±0.15	1.96±0.35	<0.001
ESR (mm/hr)	75.0±12.55	42.11±16.46	<0.001



5. DISCUSSION

5.1 Demographic and Epidemiological Profile

The demographic characteristics in our study were consistent with established trends reported in previous Indian studies. The mean age of 5.13 years and male predominance (60%) reflect the typical epidemiological pattern of childhood nephrotic syndrome. Alwadhi et al.[10] reported a similar mean age of 6 years with a male-to-female ratio of 3.3:1, while Senguttuvan et al.[14] observed a mean age of 5.95 years and a ratio of 1.6:1. These findings demonstrate that nephrotic syndrome predominantly affects younger male children, a pattern consistently observed across different regions of India. Comparable demographic trends were also noted by Ajayan et al.[15], further validating the age and sex distribution identified in the present study.

5.2 Infection Profile and Clinical Spectrum

In the present study, the commonest infections overall, across first episodes and relapses, were URTI (47.2%), followed by

UTI (20.5%), pneumonia (11.4%), and acute gastroenteritis (11.4%). Among first-episode cases, UTIs were the most prevalent infection (38.0%), followed by URTI (30.0%) and pneumonia (14.0%). During relapses (including both frequent and infrequent relapses), URTI remained the most common infection (54.3%), followed by pneumonia (10.2%) and UTIs (14.2%).

Several Indian studies have documented varying infection profiles in children with nephrotic syndrome. Gulati et al.[9] reported urinary tract infection (13.7%) as the most frequent, followed by tuberculosis (10.4%) and peritonitis (9.1%), with UTIs predominating during first episodes and peritonitis and tuberculosis during relapses. Senguttuvan et al.[14] observed UTIs (46%), peritonitis (25.8%), and respiratory infections (13.5%) as common, while Alwadhi et al.[10] found infections in 83.8% of nephrotic episodes, mainly upper respiratory infections (28%), UTIs (22.8%), and peritonitis (15.8%). Ajayan et al.[15] noted peritonitis (37.8%) and pneumonia (35.1%) as the leading infections, and Kalra et al.[16] reported respiratory infections, UTIs, and sepsis as predominant, with UTIs

common in first episodes and respiratory tract infections during relapses. Kumar et al.[8] observed peritonitis (24%), pneumonia (18%), and UTIs (15%) as major infections. Consistent patterns regarding the predominance of respiratory and urinary tract infections were observed across studies from different parts of India by Alwadhi et al., Senguttuvan et al., and Kalra et al. Our findings are consistent with these results, particularly regarding the predominance of respiratory infections during relapse episodes. In contrast, Gulati et al.[9] reported a higher incidence of tuberculosis, while Ajayan et al.[15] and Kumar et al.[8] found peritonitis to be the leading infection.

5.3 Urinary Tract Infections in First Episode

Urinary tract infection was significantly more common during the first episode of nephrotic syndrome (38% in our study), consistent with the findings of Sreenivasa et al.[13], who reported UTI in 40% of first-episode cases, predominantly caused by *E. coli*. Similarly, Kriti Mohan et al.[17] observed a higher occurrence of UTI during the initial episode compared to relapses. In contrast, Gulati et al.[9] reported greater association during relapses.

5.4 Upper Respiratory Tract Infections and Relapse

Upper respiratory tract infections (URTIs) were the most frequent infection among children with infrequent relapses of nephrotic syndrome in our study. This finding aligns with previous studies by MacDonald et al.[18], Alwadhi et al.[10], and Ajayan et al.[15], which consistently identified respiratory infections as major triggers for relapse. Similarly, Shatha Hussain Ali et al.[19] reported that respiratory infections accounted for one-third of relapses in steroid-sensitive nephrotic syndrome.

5.5 Spontaneous Bacterial Peritonitis in Frequent Relapsers

In our study, spontaneous bacterial peritonitis (SBP) was identified as a major infection among children with frequently

relapsing nephrotic syndrome (FRNS), where ascitic fluid cytology fulfilled diagnostic criteria with or without culture positivity. Ascitic fluid culture showed bacterial growth in two cases, yielding *Streptococcus pneumoniae* and *Escherichia coli* as the causative organisms. Similar findings were reported by Alwadhi et al.[10], who found *S. pneumoniae* as the predominant pathogen in 15.8% of cases, and by Kumar et al.[8], who also identified *S. pneumoniae* as the leading organism in both blood and ascitic fluid cultures. Senguttuvan et al.[14] observed peritonitis in 25.8% of infections, with *E. coli* and *Klebsiella* being more frequent, while Ajayan et al.[15] reported *S. aureus* and *E. coli* as common isolates, with culture positivity in only 18.3% of cases. Similarly, Hingorani et al.[20] highlighted the frequency of culture-negative peritonitis, often due to prior antibiotic use. Our findings align closely with these studies, reaffirming *S. pneumoniae* and *E. coli* as the principal pathogens in SBP and emphasizing the need for prompt empirical antibiotic coverage targeting these organisms.

5.6 Role of Hypoalbuminemia as a Risk Factor

Low serum albumin emerged as a major risk factor for infections in children with nephrotic syndrome, particularly those presenting with severe infections requiring intensive care. This finding is consistent with Kumar et al.[8], who reported serum albumin <1.5 g/dL as a significant predictor of peritonitis and UTI, and Behera et al.[21], who also identified hypoalbuminemia as a key determinant of infection risk in steroid-sensitive nephrotic syndrome. Sreenivasa et al.[13] noted a strong link between hypoalbuminemia and severe infections such as sepsis. These consistent findings across multiple studies reinforce the role of low serum albumin as a primary risk factor for infections in nephrotic syndrome. Routine monitoring and early correction of hypoalbuminemia may therefore be essential to reducing infection-related morbidity and improving clinical outcomes in this vulnerable population.

5.7 Mortality and Severe Outcomes

In the present study, mortality was observed in 4.4% of children with nephrotic syndrome, primarily due to severe infections such as spontaneous bacterial peritonitis and sepsis progressing to multiorgan failure. *Streptococcus pneumoniae*, *E. coli*, *Klebsiella*, and MRSA were the main organisms isolated in fatal cases. These findings highlight the critical role of bacterial infections, particularly SBP, in determining poor outcomes. Comparable mortality rates have been reported in previous studies. Ajayan et al.[15] documented a 5.9% mortality rate, predominantly from sepsis and peritonitis, while Kumar et al.[8] reported a 2.5% mortality, mainly linked to sepsis-related multiorgan failure. Our results align closely with these studies, reaffirming that life-threatening infections remain a major cause of death in nephrotic syndrome.

5.8 Regional Variation and Study Implications

Variations in infection patterns and outcomes may be attributed to differences in patient populations, environmental conditions, disease severity, and local management practices. These variations likely reflect regional differences, microbial patterns, and evolving treatment practices, reinforcing the importance of routine urine microscopy and culture at initial presentation for early detection and management. Such comparisons highlight the need for region-specific infection surveillance and early intervention strategies to improve outcomes in children with nephrotic syndrome.

5.9 Limitations

This study has several limitations. First, the patients' cumulative steroid dose and additional immunosuppressant therapy were not assessed, making it impossible to correlate cumulative steroid exposure with infection patterns and relapse characteristics. Second, the lack of long-term follow-up of the study population limits our ability to evaluate persistent infections, the influence of infections over time on disease progression, and the potential for late-onset

complications. Third, as a cross-sectional study design, causality cannot be inferred regarding the relationships between infections and relapses, although clear associations are demonstrated.

6. CONCLUSION

This study establishes that infections remain a significant complication in children with nephrotic syndrome, greatly contributing to morbidity and mortality. Upper respiratory and urinary tract infections were the most prevalent, followed by pneumonia and spontaneous bacterial peritonitis. The results emphasize the importance of prompt detection and management of infections, particularly in children with low serum albumin and raised inflammatory markers. The consistent infection burden across all clinical forms highlights the critical need for routine monitoring, preventive strategies, and caregiver education. Regional epidemiological differences further stress the value of locally adapted infection control measures and surveillance protocols to improve prognosis in pediatric nephrotic syndrome. These findings support incorporating routine infection surveillance and albumin monitoring into standard care protocols for hospitalized children with nephrotic syndrome.

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