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SPECTRUM AND OUTCOMES OF INFECTIONS IN CHILDREN WITH NEPHROTIC SYNDROME

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Abstract

Objective: To determine the spectrum and outcomes of infections in children with nephrotic syndrome and to evaluate their association with disease characteristics.

Study Design: Descriptive cross-sectional study.

Place and Duration of Study: Conducted at University of Child Health Sciences, The Children's Hospital, Lahore from January 2022 to July 2022.

Methodology: A total of 155 children diagnosed with nephrotic syndrome were enrolled using non-probability consecutive sampling. Demographic and clinical data, including type of nephrotic syndrome, relapse status, and laboratory parameters, were recorded. Infections were identified based on clinical features and laboratory investigations, and categorized into respiratory tract infections, urinary tract infections, peritonitis, sepsis, and others. Microbiological profiles were documented where available.

Results: The mean age of patients was 6.8 ± 3.2 years, with a male predominance. Respiratory tract infections were the most common (36.1%), followed by urinary tract infections (24.5%) and peritonitis (16.1%). Gram-negative organisms, particularly *Escherichia coli*, were the most frequently isolated pathogens. A majority of infections occurred during relapse (62.6%). Hospitalization was required in 58.7% of cases, while 14.8% required intensive care.

Conclusion: Infections are common in children with nephrotic syndrome and are strongly associated with disease activity and adverse outcomes. Early detection, appropriate management, and preventive strategies are essential to reduce morbidity and improve clinical outcomes.

Keywords: Nephrotic syndrome, infections, children, peritonitis, urinary tract infection, outcomes.

INTRODUCTION

One of the most frequent chronic kidney diseases in children is nephrotic syndrome, and its manifestation is excessive proteinuria, hypoalbuminemia, edema, and hyperlipidemia [1]. Even though most of the cases are of an idiopathic nature and can be treated effectively using corticosteroids, children with nephrotic syndrome are still highly prone to infections, which are a major cause of morbidity and mortality [2]. This is because of the altered immune status of such patients, the loss of immunoglobulins and complement factors, and the immunosuppressive effects of steroid therapy, which predispose them to a broad range of infections [3]. The infections of children with nephrotic syndrome may affect a variety of organ systems, although the most frequent presentations are peritonitis, respiratory tract infections, urinary tract infections, cellulitis, and sepsis [4]. One of the most dangerous and life-threatening complications, which used to be one of the most severe among these, is spontaneous bacterial peritonitis [5]. The probability of infection is especially high during relapses, when proteinuria is highest and immune impairment is most severe. Also, long-term or regular administration of corticosteroids and other immunosuppressants further predisposes to common and opportunistic pathogens [6].

The range of causative organisms has also changed over time, with a focus on Gram-positive organisms like Streptococcus pneumoniae giving way to more Gram-negative bacteria and increasingly resistant strains. This dynamic microbiological profile, along with regional differences in pathogen distribution and antimicrobial resistance patterns, underscores the importance of local data to inform empirical treatment and preventive

measures [7]. Infections in this high-risk group should be detected early and treated appropriately to improve outcomes. Clinical manifestations of infections in children with nephrotic syndrome are mild and self-limiting diseases, and serious complications that may lead to hospital admission, intensive care, or even death [8]. Infections can also lead to recurrence, prolonged hospitalization, and high health care costs. Although treatment has improved, complications associated with the infection remain a significant clinical challenge, especially in low- and middle-income countries where access to health care resources might be limited [9].

In addition to clinical manifestations, the pathophysiology underlying the increased risk of infection in nephrotic syndrome is complex [10]. Deficiency of immunoglobulin G in the urine results in loss of humoral immunity, whereas a reduction in complement protein levels (especially factors B and D) inhibits opsonization and clearance of bacteria. Edematous tissues can also serve as a favorable environment for bacterial growth, and a low intravascular volume can hamper the proper trafficking of immune cells [11]. In addition, T-cell impairment and cytokine modulation have been reported, further contributing to a general state of immunosuppression. The other notable issue is the effect of the nutritional status and socioeconomic aspect on infection susceptibility [12]. The chronic illnesses of the children also result in malnutrition that further undermines immune defenses and predisposes children to recurrent infections [13]. Resource-constrained environments may increase the risk of infections and worsen outcomes due to delayed healthcare-seeking behavior, poor hygiene, and limited access to vaccinations. These aspects all lead to inconsistencies in the patterns and outcomes of infections across populations [14].

Objective

To determine the spectrum and outcomes of infections in children with nephrotic syndrome and to evaluate their association with disease characteristics.

METHODOLOGY

This was a cross-sectional descriptive study conducted at University of Child Health Sciences, The Children's Hospital, Lahore from January 2022 to July 2022. . A total of 155 pediatric patients diagnosed with nephrotic syndrome were included in the study. Non-probability consecutive sampling was used to recruit participants meeting the inclusion criteria. The study involved children between the age of 1 and 14 years with a diagnosis of nephrotic syndrome (new diagnosis or relapse). Both male and female patients who arrived with a clinical or laboratory evidence of infection during the illness were eligible to be included. Children with secondary nephrotic syndrome or congenital nephrotic syndrome and children with underlying chronic systemic disorders, including malignancy, congenital immunodeficiency, or chronic liver disease, were excluded. Patients with incomplete medical records were also excluded from the study.

Data Collection

With the consent of the institutional ethical review committee, 155 patients who met the inclusion criteria were recruited. Parents or guardians were informed about it and gave informed consent. A structured proforma was used to collect the data. Demographic variables (age, gender, and socioeconomic status) were documented. Clinical data entailed the type of nephrotic syndrome (new onset, relapse, steroid-dependent, or steroid-resistant), length of illness, and history of treatment. Infection data were recorded (e.g., type of infection (e.g., peritonitis, respiratory tract infection, urinary tract infection, cellulitis, sepsis), location of infection, microbiology results, and management received). Laboratory results, including complete blood count, serum albumin, urine protein level, and culture reports, were documented. Outcomes were hospitalization requirement, hospital stay duration, complications, infection recurrence, and death.

Data Analysis

All data were entered and analyzed using SPSS version 25. Quantitative variables such as age and hospital stay duration were reported as mean ± standard deviation or median (IQR), as appropriate. Qualitative variables, such as gender, infection type, and outcomes, were presented as frequencies and percentages. Stratification was performed by age, gender, type of nephrotic syndrome, and type of infection to control for confounding variables. A p-value ≤0.05 was considered statistically significant.

RESULTS

Data were collected from 155 patients, with a mean age of 6.8 ± 3.2 years. The majority of patients were in the 1–5 year age group (40.0%), followed by 6–10 years (37.4%) and 11–14 years (22.6%). There was a male predominance (59.4% males vs 40.6% females). Regarding disease type, relapse was the most common presentation (50.3%), while 26.5% were new onset cases.

Table 1: Baseline Demographic and Clinical Characteristics (n = 155)

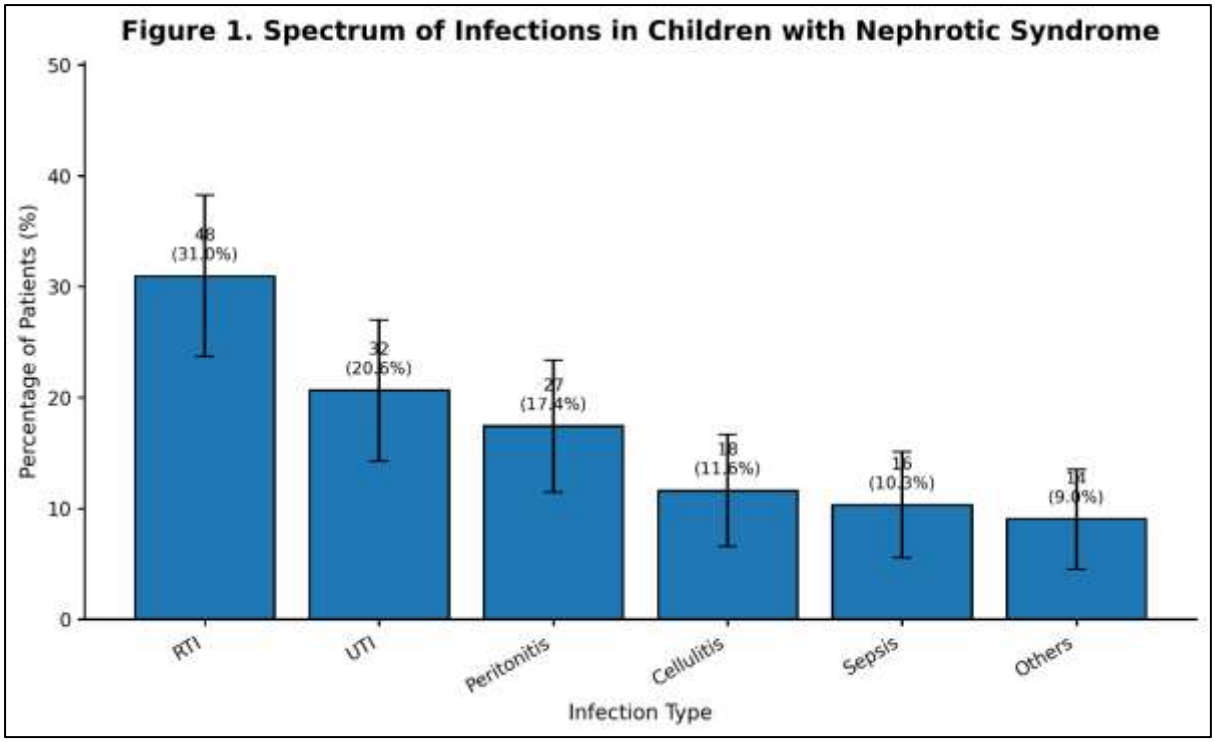
Variable	Category	n (%) / Mean ± SD
Age (years)	—	6.8 ± 3.2
Age Group	1–5 years	62 (40.0%)
	6–10 years	58 (37.4%)
	11–14 years	35 (22.6%)
Gender	Male	92 (59.4%)

	Female	63 (40.6%)
Type of Nephrotic Syndrome	New onset	41 (26.5%)
	Relapse	78 (50.3%)
	Steroid dependent	23 (14.8%)
	Steroid resistant	13 (8.4%)

The spectrum of infections showed that respiratory tract infections were the most frequent, affecting 31.0% of patients, followed by urinary tract infections (20.6%) and peritonitis (17.4%). Cellulitis (11.6%) and sepsis (10.3%) were less common but clinically significant, while other infections comprised 9.0%. The microbiological profile revealed a predominance of Gram-negative organisms, with *Escherichia coli* being the most common isolate (24.5%), followed by *Streptococcus pneumoniae* (17.4%) and *Staphylococcus aureus* (16.1%). *Klebsiella* species accounted for 13.5%, while other organisms made up 28.5%, reflecting a diverse infectious etiology.

Table 2: Spectrum of Infections (n = 155)

Infection Type	**n (%)**
Respiratory tract infections	48 (31.0%)
Urinary tract infections	32 (20.6%)
Peritonitis	27 (17.4%)
Cellulitis	18 (11.6%)
Sepsis	16 (10.3%)
Others	14 (9.0%)
Organism	
Escherichia coli	38 (24.5%)
Streptococcus pneumoniae	27 (17.4%)
Staphylococcus aureus	25 (16.1%)
Klebsiella species	21 (13.5%)
Others	44 (28.5%)



Clinical outcomes indicated that a large proportion of patients required hospitalization (72.3%), and 11.6% needed ICU admission, highlighting the severity of infections. The mean hospital stay was 6.2 ± 3.1 days. Infection-triggered relapse was observed in 44.5% of patients, demonstrating a strong link between infections and disease activity.

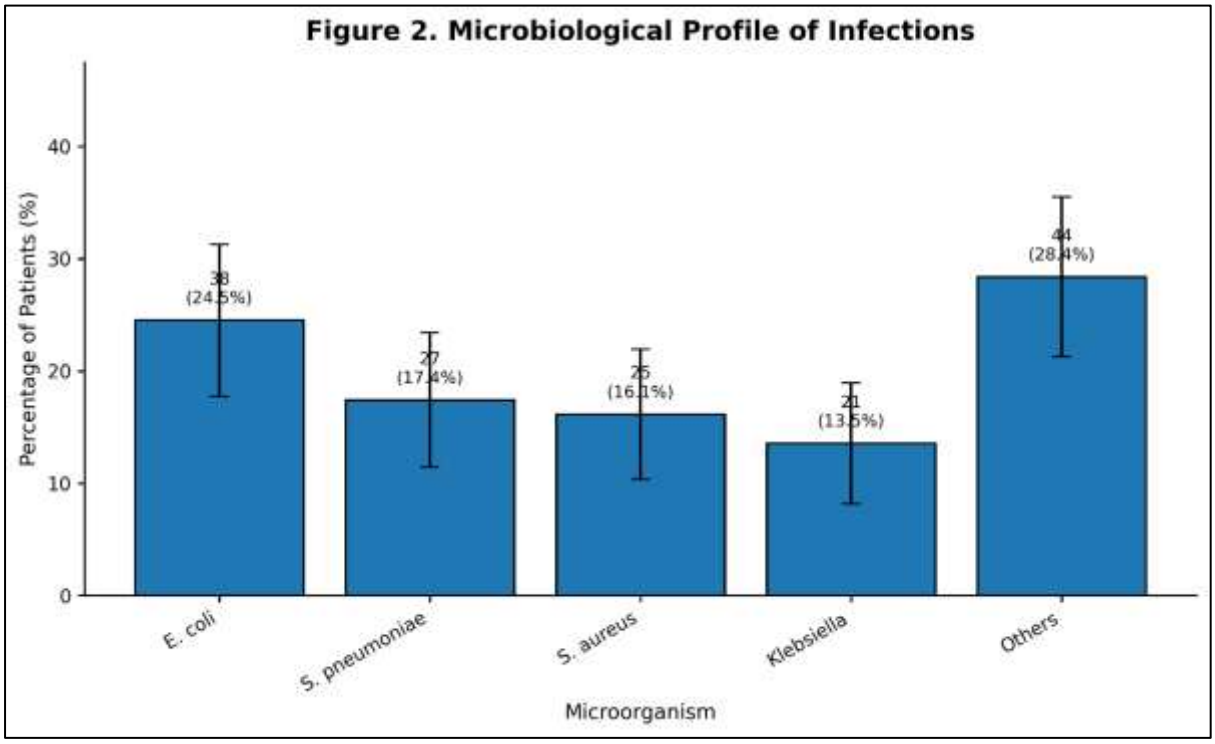
Table 3: Clinical Outcomes (n = 155)

Outcome	**n (%) / Mean ± SD**
Hospitalization required	112 (72.3%)
ICU admission	18 (11.6%)
Mean hospital stay (days)	6.2 ± 3.1
Relapse triggered by infection	69 (44.5%)
Mortality	9 (5.8%)

The association analysis showed that relapse was significantly associated with severe outcomes, occurring in 61.9% of patients with severe outcomes compared to 42.4% without (p = 0.018). Steroid-resistant nephrotic syndrome demonstrated a strong and highly significant association with severe outcomes (17.5% vs 2.2%, p < 0.001). In contrast, steroid-dependent nephrotic syndrome did not show a significant association (14.3% vs 15.2%, p = 0.874).

Table 4: Association of Type of Nephrotic Syndrome with Severe Outcomes

Variable	Severe Outcome Present (n=63)	Severe Outcome Absent (n=92)	p-value
Relapse	39 (61.9%)	39 (42.4%)	0.018
Steroid resistant	11 (17.5%)	2 (2.2%)	<0.001
Steroid dependent	9 (14.3%)	14 (15.2%)	0.874



DISCUSSION

The current research measured the range of spectrum and outcome of infection in children with nephrotic syndrome and proved that infections are still a significant burden to morbidity in this group. The results showed that the primary cause was respiratory tract infections, followed by urinary tract infections and peritonitis, with a significant number of patients hospitalized. These findings indicate that the clinical burden of infections in pediatric nephrotic syndrome remains persistent, especially at active disease stages. The infections were mostly observed in children who presented with relapse in this study, and this is in line with the established pathophysiology of nephrotic syndrome. In case of relapse, the heavy proteinuria leads to the loss of immunoglobulins and complement proteins in the urine, impairing humoral immunity. Similar findings have been reported in previous studies, which have identified a higher infection rate during relapse compared to the remitting stage of the disease, underscoring the need to closely monitor patients at this stage. The high infection rate among younger children in this study could also be explained by their relatively weak immune systems and greater exposure to environmental pathogens. The range of infections detected in this research is consistent with previous research, which found that respiratory and urinary tract infections were among the most frequently reported [14]. Nevertheless, the fact that peritonitis and sepsis appeared in a significant percentage of patients highlights the possibility of the development of serious and even life-threatening complications. Previous research has also emphasized spontaneous bacterial peritonitis as a severe complication of nephrotic syndrome, especially in a resource-limited environment where delayed diagnosis and treatment can be experienced [15].

This research revealed a high prevalence of gram-negative organisms, especially Escherichia coli, followed by gram-positive organisms such as Streptococcus pneumoniae and Staphylococcus aureus. This trend toward Gram-negative pathogens has been increasingly reported in the recent literature and may be linked to the widespread use of antibiotics, changing environmental exposures, and evolving resistance patterns [16]. These results have significant consequences for empirical antibiotic therapy, which may need to be extended to high-risk patients. The severity of infections among this group of patients was assessed by the fact that a large percentage of them had to be admitted to the hospital, and a smaller percentage to the intensive care unit [17]. It was also notable that

the mean length of hospital stay was associated with greater healthcare utilization. Notably, almost half of the infections were associated with relapse of nephrotic syndrome, indicating a bidirectional interaction between infection and disease activity. This observation is in line with other studies, which have indicated that infections may cause and make relapses more complex [18].

The results analysis also showed that severe complications had a strong correlation with relapse and steroid-resistant nephrotic syndrome. It is known that children with steroid-resistant disease have long disease courses and are more exposed to immunosuppressive therapy, which can further weaken immune functioning [19]. Past studies have also reported worse outcomes and increased infection-related complications in this patient group, necessitating specific preventive measures. Another significant finding is that the mortality rate was relatively low and clinically significant in this study. Although the treatment has been advanced, the mortality caused by the infection remains an issue, especially in instances of sepsis and late presentation. This highlights the urgency of early identification, timely intervention, and preventive care, such as vaccination and infection control procedures [20].

Limitations

Several limitations of this study must be considered when interpreting the findings. The cross-sectional study design provides only an overview of infection patterns and outcomes, not the ability to determine temporal relationships or causal conclusions regarding infections and disease progression. The research was also conducted at a single tertiary care facility, which may limit the generalizability of the findings to other environments or populations. Non-probability consecutive sampling can introduce selection bias, whereby severe or symptomatic cases are more likely to present to a hospital setting. Also, the use of clinical records and available laboratory data could have led to underreporting or misclassification of some infections, especially when microbiological confirmation was unavailable. The research also lacked long-term follow-up, and therefore, they were unable to determine infection recurrence or long-term consequences, such as the development of steroid resistance or chronic kidney disease.

CONCLUSION

It is concluded that infections are highly prevalent among children with nephrotic syndrome and remain a major contributor to morbidity, particularly during relapse and in steroid-resistant cases. Respiratory tract infections and urinary tract infections constitute the most common spectrum, while severe infections such as peritonitis and sepsis are associated with poorer clinical outcomes and increased healthcare utilization. The findings demonstrate a clear association between infection burden and disease activity, highlighting the need for vigilant monitoring during relapse.

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