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Original Research Article

SPECTRUM OF INFECTIONS IN CHILDREN WITH PRIMARY NEPHROTIC SYNDROME IN A TERTIARY CARE CENTRE

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ABSTRACT

Background: Primary nephrotic syndrome (NS) is a common chronic kidney disorder in children, characterised by proteinuria, hypoalbuminaemia, hyperlipidaemia, and oedema. Children with NS are prone to various infections that can worsen outcomes and increase morbidity and mortality. Understanding the infection patterns in this population is crucial for better management. The objective is to assess the spectrum of infections in children diagnosed with primary nephrotic syndrome. **Materials and Methods:** A retrospective observational study was conducted over six months at a tertiary care centre. The medical records of 61 children aged 1–12 years with primary nephrotic syndrome were reviewed. Data on clinical presentation, laboratory parameters, infection type, treatment, and outcomes were collected and analysed. **Result:** The study included 61 children with primary nephrotic syndrome (57.3% males, mean age 5.7 ± 3.2 years). Infections were found in 36.1% of patients, with urinary tract infections (9.8%), pneumonia (6.5%), and peritonitis (3.2%) being the most common. Fever was present in 90.9% of infected cases. Infected children had a longer hospital stay (10.2 ± 3.4 days) than non-infected (6.1 ± 2.8 days, $p < 0.05$). Mortality occurred in 6.5%, all in infected children, with no significant differences in age, illness duration, or steroid use between groups. **Conclusion:** Infections are common in children with primary nephrotic syndrome, primarily affecting the urinary and respiratory tracts. Early detection and management of infections are vital for reducing complications, hospital stays, and mortality.

INTRODUCTION

Nephrotic syndrome (NS) is one of the most common chronic kidney disorders in children. It is clinically characterised by heavy proteinuria, hypoalbuminaemia, hyperlipidaemia, and oedema. Although NS can affect individuals of any age, it is more frequently observed in children than adults. The disease often follows a relapsing and remitting course, where the initial response to treatment is followed by a symptom-free period and subsequent relapses, particularly with swelling of the body. These cycles may persist for months to years in some children, posing significant challenges for both the patient and their families. The primary pathophysiological mechanism in most cases is the effacement of podocyte foot processes without evidence of glomerular deposits or inflammation on histology.[1]

Despite this, the glomerular filtration rate, which reflects the kidney's filtering ability, remains preserved in the majority of children with primary NS.[2] Based on the initial steroid response, NS is classified as steroid-sensitive nephrotic syndrome (SSNS) or steroid-resistant nephrotic syndrome (SRNS). A considerable proportion of children with SSNS may experience frequent relapses or become steroid-dependent, necessitating repeated courses of steroids or alternative immunosuppressive therapies.[3]

Children with NS are vulnerable to several complications, including infection, venous thromboembolism (VTE), and acute kidney injury (AKI). While the clinical significance of infections and VTE is well recognised, the epidemiology and outcomes of AKI in this population remain unclear.[4] Infections are a leading cause of morbidity and mortality in children with NS, as they may trigger relapses, hinder steroid responsiveness, and prolong hospitalisation.[5] In the absence of prompt and appropriate treatment, infections can be fatal. Prior to the widespread use of corticosteroids and antibiotics, mortality in children with NS was as high as 40%,

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with nearly half of these deaths attributed to preventable infections.[6]

Viral upper respiratory tract infections have been reported to precede up to 50% of paediatric NS cases, possibly due to a non-specific immune response or cross-reacting antibodies.[7] This has raised interest in the potential role of other infections, such as urinary tract infections (UTI), diarrhoea, peritonitis, and skin infections, in modifying disease activity. Key risk factors for infection include urinary losses of immunoglobulins and complement factors B and I, presence of oedema, and immunosuppression due to corticosteroids or cytotoxic drugs.[8,9]

Major infections reported in NS include peritonitis, pneumonia, UTI, cellulitis, meningitis, and tuberculosis.[10,11] Pneumococcal infections are among the most common invasive bacterial infections in NS. However, limited data are available on the incidence, patterns, and associated factors of infections in children with NS. In this context, the present study aimed to assess the spectrum of infections in children with primary nephrotic syndrome.

MATERIALS AND METHODS

This hospital-based retrospective observational study included 61 children from the Paediatric Outpatient Department (OPD) and the Paediatric Intensive Care Unit (PICU) of the Department of Paediatrics at Tirunelveli Medical College and Hospital, Tirunelveli, over a six-month period from July 2022 to December 2022. The study was approved by the Institutional Ethics Committee, and informed consent was obtained from all parents of the children when necessary.

Inclusion and Exclusion Criteria

The study included children aged between 1 and 12 years who were diagnosed with nephrotic syndrome and were either brought to the outpatient department or admitted to the inpatient department of our hospital. Children aged < 1 year or > 12 years, those with congenital nephrotic syndrome, and those presenting with features of nephritis or secondary nephrotic syndrome were excluded.

Methods: Case records were obtained from the hospital's Medical Records Department, and relevant information was documented using a structured pro forma. Baseline characteristics were recorded, including data from focused history and detailed clinical examinations. All children underwent complete blood count, kidney and liver function tests, lipid profile, and routine microscopic examination of urine. In children with suspected peritonitis, ascitic fluid analysis, including cytology, biochemical tests, and culture, was performed, and cerebrospinal fluid analysis was performed in those with suspected meningitis. Chest radiography, blood cultures, and urine cultures were performed when clinically indicated. This systematic approach ensured a comprehensive evaluation and appropriate identification of infections in children with nephrotic syndrome.

RESULTS

The mean age of the children was 5.7 ± 3.2 years, with a mean disease onset of 5.2 ± 2.1 years and a mean duration of 6.4 ± 3.9 months. The mean weight and height were 18.4 ± 5.1 kg and 112 ± 17.6 cm, respectively. Males constituted 35 (57.3%), rural residents 43 (70.4%), and 23 (37.7%) belonged to the lower socioeconomic class. Initial episodes accounted for 55.72%, followed by IFRNS 15 (24.59%), FRNS/SDNS 8 (13.1%), and SRNS 4 (6.59%). At assessment, 8 (13.1%) were in remission, and 19 (31.1%) had relapsed. Half 34 (55.7%) were previously untreated, while 15 (24.59%) received only prednisolone and 12 (19.6%) received other immunosuppressants with or without prednisolone. Mean haemoglobin was 10.3 ± 2.4 g/dl, serum creatinine 0.62 ± 0.29 mg/dl, serum albumin 1.6 ± 0.43 g/dl, and serum cholesterol 429 ± 158 mg/dl [Table 1].

Table 1: Baseline demographic, clinical, and laboratory characteristics

Parameter (Mean, N (%))		Value
Demographics	Age (years)	5.7 ± 3.2
	Age of onset of disease (years)	5.2 ± 2.1
	Weight (kg)	18.4 ± 5.1
	Height (cm)	112 ± 17.6
	Duration of the disease (months)	6.4 ± 3.9
	Male	35 (57.3%)
	Female	26 (43%)
	Rural inhabitant	43 (70.4%)
	Lower socioeconomic class (Kuppuswamy scale class IV or below)	23 (37.7%)
Type of the disease	Initial episode	34 (55.72%)
	IFRNS	15 (24.59%)
	FRNS/ SDNS	8 (13.1%)
	SRNS	4 (6.59%)
Remission status	Remission	8 (13.1%)
	Relapse	19 (31.1%)
	Initial episode	34 (55.7%)
Treatment received	Previously untreated	34 (55.7%)
	Only prednisolone	15(24.59%)
	Other immunosuppressant ± prednisolone	12 (19.6%)

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Laboratory parameters	Hb (g/dl)	10.3 ± 2.4
	Serum Creatinine (mg/dl)	0.62 ± 0.29
	Serum Albumin (g/dl)	1.6 ± 0.43
	Serum cholesterol (mg/dl)	429 ± 158

Among the study population, urinary tract infection was the most frequent infection, observed in 6 children (9.8%), followed by pneumonia in 4 children (6.5%). Peritonitis and acute diarrhoea were each reported in two cases (3.2%), while cellulitis, typhoid, hepatitis, tuberculosis, meningitis, malaria, and sepsis were each noted in one case (1.63%). No cases of varicella or measles were observed [Table 2].

Table 2: Distribution of infections and associated diseases

Infection/disease	N (%)
Peritonitis	2 (3.2%)
Pneumonia	4 (6.5%)
UTI	6 (9.8%)
Cellulitis	1 (1.63%)
Acute diarrhoea	2 (3.2%)
Typhoid	1 (1.63%)
Hepatitis	1 (1.63%)
Tuberculosis	2 (3.2%)
Meningitis	1 (1.63%)
Varicella	0
Measles	0
Malaria	1 (1.63%)
Sepsis	1 (1.63%)

Among the study participants, fever was the most frequent symptom, observed in 14 (63.6%) cases, followed by abdominal pain and respiratory symptoms in six (27.2%) cases each. Urinary symptoms were present in 4 (18.1%), diarrhoea and/or vomiting in 2 (9%), chills/rigor in 3 (13.6%), hypotension in 2 (9%), and shock in 1 (4.54%). Laboratory findings included leucocytosis in 8 (36.3%), neutrophilia in 7 (31.8%), leukopenia in 4 (18.1%), neutropenia in 3 (13.6%), and thrombocytopenia in 1 (4.54%) patient [Table 3].

Table 3: Clinical and laboratory features of infected cases

Parameters	N (%)
Fever	14 (63.6%)
Chills/rigor	3 (13.6%)
Abdominal pain	6 (27.2%)
Diarrhoea and/or vomiting	2 (9%)
Urinary symptoms (dysuria, increased frequency)	4 (18.1%)
Respiratory symptoms (Cough and/or breathing difficulty)	6 (27.2%)
Shock	1 (4.54%)
Hypotension	2 (9%)
Leucocytosis	8 (36.3%)
Neutrophilia	7 (31.8%)
Leukopenia	4 (18.1%)
Neutropenia	3 (13.6%)
Thrombocytopenia	1 (4.54%)

Among children with infection (N=22) and without infection (N=39), there were no significant differences in mean age (5.61 ± 3.14 vs. 5.73 ± 3.27 years), age at disease onset (3.84 ± 2.37 vs. 4.03 ± 2.45 years), or disease duration (6.7 ± 4.1 vs. 6.2 ± 3.7 months). The distributions of disease type, remission status, and treatment received were comparable between the groups ($p > 0.05$). Mortality occurred in 9.09% of infected cases, with no deaths in the noninfected group. Mean hospital stay was significantly longer in the infection group (12.2 ± 3.6 vs. 8.3 ± 2.9 days, $p < 0.001$) [Table 4].

Table 4: Comparison of clinical profile, treatment, and outcomes with and without infection

Parameters		Infection (N = 22)	Without infection (N = 39)	p value
Age (years), mean ± SD		5.61 ± 3.14	5.73 ± 3.27	>0.05
Age of onset of disease (years), mean ± SD		3.84 ± 2.37	4.03 ± 2.45	>0.05
Duration of the disease (months), mean ± SD		6.7 ± 4.1	6.2 ± 3.7	>0.05
Male, N (%)		15(42.8%)	20 (57.1%)	>0.05
Type of the disease	Initial episode, N (%)	9 (40.9%)	22 (56.4%)	>0.05
	IFRSSNS, N (%)	6 (27.2%)	9 (23%)	>0.05
	FRNS or FDNS, N (%)	4 (18.18%)	5 (12.8%)	>0.05
	FRNS, N (%)	3 (13.6%)	3 (7.6%)	>0.05
	Initial episode, N (%)	9 (40.9%)	25 (64.15%)	>0.05

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Remission status	In remission, N (%)	4 (18.1%)	5 (12.85%)	>0.05
	In relapse, N (%)	9 (40.9%)	9 (23%)	>0.05
Treatment status	Previously untreated, N (%)	9(43.2%)	25 (64.1%)	>0.05
	Treated with only prednisolone, N (%)	6 (24.3%)	9(23%)	>0.05
	Treated with another immunosuppressive agent, prednisolone, N (%)	7 (32.4%)	5 (12.85%)	>0.05
Short-term outcome	Mortality, N (%)	2 (9.09%)	0	---
	Duration of hospital stay in days, mean ± SD	12.2 ± 3.6	8.3 ± 2.9	<0.001

Urinary tract infection was the most common infection, seen in 2 (33.3%) initial and 4 (66.6%) non-initial episodes (9.8%). Pneumonia occurred in one (25%) initial and three (75%) non-initial episodes (6.5%), while peritonitis, acute diarrhoea, and tuberculosis were each noted in one (50%) initial and one (50%) non-initial episode (3.2%). Cellulitis, typhoid, hepatitis, meningitis, malaria, and sepsis were reported in one case each (1.63%), with malaria limited to the initial episode. No significant differences were observed between the groups ($p > 0.05$) [Table 5].

Table 5: Distribution of specific infections in initial and non-initial episodes of NS

Infection/disease	N (%) seen in the initial episode of NS	N (%) seen in non-initial episode	Total N (%)	P value
Peritonitis	1 (50%)	1 (50%)	2 (3.2%)	>0.05
Pneumonia	1 (25%)	3 (75%)	4 (6.5%)	>0.05
UTI	2 (33.3%)	4 (66.6%)	6 (9.8%)	>0.05
Cellulitis	0	1 (100%)	1 (1.63%)	>0.05
Acute diarrhoea	1 (50%)	1 (50%)	2 (3.2%)	>0.05
Typhoid	0	1 (100%)	1 (1.63%)	---
Hepatitis	0	1 (100%)	1 (1.63%)	---
Tuberculosis	1 (50%)	1 (50%)	2 (3.2%)	>0.05
Meningitis	0	1 (100%)	1 (1.63%)	---
Malaria	1 (100%)	0	1 (1.63%)	---
Sepsis	0	1 (100%)	1 (1.63%)	----

DISCUSSION

In our study, most children were of preschool or early school age, with a slight male predominance and a majority from rural areas. Over one-third were from lower socioeconomic backgrounds. More than half presented with their first episode, while the rest had relapsing or steroid-resistant disease patterns. At assessment, a minority were in remission, and nearly one-third had relapsed after treatment. More than half were untreated, while the others received corticosteroids alone or in combination with immunosuppressants. Anaemia, hypoalbuminaemia, and marked hypercholesterolaemia were common, whereas renal function was generally preserved. Similarly, Mekonnen et al. reported that 56.3% of children were younger than eight years, with males constituting 59.22%, and the majority lived in rural areas.[12]

Sinha et al. classified children with steroid-sensitive nephrotic syndrome as infrequent relapsers (48.2%), frequent relapsers or steroid-dependent (42.1%), and late steroid resistance (9.7%).[13] Das et al. found that 60.4% of children had not received prior immunosuppressive therapy, 27% were on steroids alone, and 12.5% received other immunosuppressants.[14] Laboratory values, including haemoglobin, serum creatinine, albumin, and cholesterol, were within expected ranges. It describes the demographic and clinical profiles of children with nephrotic syndrome, which is consistent with prior studies.

Our study showed that the most common infections were urinary tract infections and pneumonia, followed by peritonitis and acute diarrhoea. Less frequent infections included cellulitis, typhoid, hepatitis, tuberculosis, meningitis, malaria, and sepsis, with no cases of varicella or measles reported. Similarly, Moorani et al. found that acute respiratory infections were the most common, followed by skin infections, diarrhoea, urinary tract infections, and peritonitis.[15] In a study by Lebel et al., serious bacterial infections were identified in 14.6% of hospital admissions, mostly pneumonia, sepsis, and urinary tract infections.[16] Mekonnen et al. reported that parasitic infections 11 (10.67%) were the most frequent, followed by urinary tract infections 9 (8.73%), peritonitis 8 (7.76%), and pneumonia 8 (7.76%).[12] Infections in nephrotic syndrome commonly involve the respiratory and urinary tracts across multiple populations.

In our study, fever, abdominal pain, respiratory, and urinary symptoms were the most frequent clinical features observed. Laboratory findings often show abnormalities in white blood cell counts, with both increases and decreases. Similarly, Krishnan et al. reported fever 38 (82.6%) as the leading symptom, followed by abdominal pain, vomiting or diarrhoea, and respiratory symptoms.[17] Their laboratory results showed leucocytosis, neutrophilia, thrombocytosis, and less frequent thrombocytopenia. The clinical presentation and laboratory findings related to infections showed consistent patterns involving fever and changes in white blood cells.

Our study showed that no significant differences were observed between the groups in terms of

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demographic or clinical characteristics. However, patients with infections experienced longer hospital stays and higher mortality rates than those without. Similarly, Singh et al. reported fever 49 (64.5%) as the most frequent symptom, with longer hospital stays 8.71 ± 2.95 days for infected patients, but no demographic differences.[18] Kumar et al. found that infected patients had significantly longer hospitalisations (12 ± 8 days).[19] Lora et al. noted infections in 71.05% of nephrotic syndrome relapses, mainly respiratory and urinary infections.[20] Infections increase hospital stay and mortality risk in nephrotic syndrome, despite similar demographic profiles.

In our study, urinary tract infections and pneumonia were more frequent during non-initial episodes, whereas peritonitis, diarrhoea, and tuberculosis were evenly distributed. Other infections, such as cellulitis, typhoid, hepatitis, meningitis, and sepsis, appeared mainly in non-initial episodes. Similarly, Krishnan et al. reported that 35 (73 %) infections occurred during relapse, with pneumonia and urinary infections predominant, and some infections more frequent in initial episodes.[17] Mantan and Singh found that upper respiratory infections 15 (62.5%), peritonitis (18.5%), and diarrhoea (12%) were common, with most patients achieving remission 27 (60%) after treatment. Infections vary between initial and relapse episodes, affecting disease progression and management.[21] Dakshayani et al. reported a significantly higher mean number of infection-related relapses in frequent relapsers than in infrequent relapsers. Overall, 64.35% of relapses were associated with infections, including respiratory tract infections, gastroenteritis, urinary tract infections, and peritonitis.[3] Frequent relapsers experienced more infection-associated relapses, highlighting infection as a relapse trigger.

Limitations

Being a retrospective, single-centre study with a small sample size limits the generalisability of the findings. Additionally, incomplete records and a lack of long-term follow-up may have affected the accuracy and depth of the infection assessment.

CONCLUSION

Our study highlights that infections, particularly urinary tract infections and pneumonia, are common in children with primary nephrotic syndrome, occurring more often during relapses and are associated with longer hospital stays and higher mortality. Typical features included fever, abdominal pain, and white blood cell changes. Early recognition and prompt treatment are vital for reducing complications, preventing relapses, and lessening the disease burden.

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