



STUDY OF CLINICAL AND ETIOLOGICAL SPECTRUM OF INFECTIONS IN NEPHROTIC SYNDROME

Paediatrics

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ABSTRACT

Nephrotic syndrome is a common renal disorder. The pattern of infections and the spectrum of infectious agents in these children are different in different geographical region of India. This study is conducted to look for the pattern of infections in children with nephrotic syndrome admitted under tertiary care hospital for appropriate management of these children and to institute preventive measures. This study was a record based observational study conducted from Dec 2022 to Jul 2024 in the Department of Paediatrics, at tertiary care centre among Children between 1 year to 14 years fulfilling the KDIGO Criteria for nephrotic syndrome. Total 150 children with nephrotic syndrome were included in the study with mean age was 7.25 ± 3.89 years & majority were aged between 6-10 years with male predominance. About 40% had past history of infection. About 64% children had >10 days of hospital stay & 36% had <10 days of hospital stay. Majority of children 99.33% were discharged & only one child died. Partially immunized children, raised haematocrit value, raised CRP level & Sr. albumin level had significantly higher risk of infection in children with nephrotic syndrome. The children with infection & nephrotic syndrome had significantly longer hospital stay ($p < 0.05$). The high prevalence of infections across different socioeconomic and age groups suggests that nephrotic syndrome patients remain vulnerable throughout the disease course, whether during initial attacks or relapses. Tailored infection control measures, alongside continuous patient and caregiver education, are essential to improve outcomes in this population.

KEYWORDS

Children, Nephrotic Syndrome, IFRNS, FRNS

INTRODUCTION

Nephrotic syndrome is a common renal disorder. Its evolution from Hippocrates over 1000 years have undergone recent advances and effective treatment introduction during the 1900's. The advent of immunosuppressants, antibiotics and immunomodulators have brought in significant changes to the curve of mortality and morbidity in NS. Steroids used in the treatment of nephrotic syndrome was first isolated in 1936 and cortisone synthesis was attempted in 1946. ISKDC established in 1965 formulated definitions, pathogenesis and recommendations for management and therapy of Nephrotic syndrome which are standard protocols even today.[1]

It is the most common disease of kidney in childhood with an incidence of 2-16.9 per 1 lakh population. The incidence is 20-70 cases per million in western countries, while in Asian countries the incidence is around 90-160 per million population.[2]

Without adequate medical therapy, nephrotic children are more susceptible to mortality, more due to bacterial infection. Before the time of corticosteroids and antibiotic treatment, about 40% of children expired and 50% of these deaths were due to infection.3 Recently it has been proved that at least 50% of the active cases in paediatric onset NS are initiated by a common viral URTI, which may be secondary to nonspecific response of the host to infection more than the reaction generated to the virus itself or their antibody.[3]

Children diagnosed with nephrotic syndrome (NS) are exposed to multiple sources of infectious complications resulting in increased morbidity and further subsequent complication.[4] Children with nephrotic syndrome who respond to therapy have an 80-90% possibility of having one or more activates. 50% of those that have activity are infrequent relapses and can be managed with short courses of prednisone.[3]

In Nephrotic Syndrome due to alterations in both cellular and humoral mechanism d/t urinary loss of Ig, properdin factor B (opsonin), immunosuppressive therapy, malnutrition, edema and ascites as a potential culture medium and defective cell mediated immunity is responsible for increased infections in Nephrotic Syndrome. [5] The various infections involved are Pneumonia, UTI, Septicaemia, SBP, cellulitis, abscesses, pulmonary TB. These infections cause significant

morbidity and mortality. ARTI and UTI are the most frequent infectious triggers of relapse.

Immunosuppression may mask typical clinical presentation of infections in Nephrotic syndrome and proper management might get delayed. The pattern of infections and the spectrum of infectious agents in these children are different in different geographical region of India. This study is conducted to look for the pattern of infections in children with nephrotic syndrome admitted under tertiary care hospital for appropriate management of these children and to institute preventive measures.

Methodology

This study was a record based observational study conducted from Dec 2022 to Jul 2024 in the Department of Paediatrics, at tertiary care centre among Children between 1 year to 14 years fulfilling the KDIGO Criteria for nephrotic syndrome. Children less than 1 years with Congenital/genetic etiology of nephrotic syndrome, secondary syndrome & children with structural abnormalities of Genitourinary tract were excluded.

This study was conducted after the approval from the clinical ethical committee of the institution, the parents of the children, fulfilling the selection criteria were briefed about the nature of the study and a written informed consent was obtained from the parents/caregivers to participate in the study prior to the enrolment. Parents/caregivers of the children who fulfilled the selection criteria were interviewed and detailed history including demographic details and course of the illness with the treatment history was procured and noted in the proforma. At admission baseline presenting complaints were noted, vitals, anthropometry and detailed examination of the system affected in correlation with the symptoms were made in detail. All the findings were recorded on a pre-designed and pre-tested proforma. Further blood and urine samples were collected for laboratory investigations at admission for the enrolled children. An attempt to delineate the focus of infection based on clinical history and examination was done and appropriate culture samples were sent in addition to routine investigations. All the investigations were processed in the standard lab under tertiary care hospital. All children also screened for infection based on clinical presentation. Urine routine and microscopy, urine-protein creatinine ratio, serum cholesterol, serum albumin Urine heat

test was done for confirmation of nephrotic syndrome. All children also screened with Mantoux test, Gastric Lavage for CBNAAT and Chest X-ray to rule out Latent/ Active TB infection before stating steroids as a standard protocol. Lavage for CBNAAT and Chest x-ray to rule out Latent/ Active TB infection before stating steroids as a standard protocol. Other appropriate investigations were carried out as clinically indicated with respect to organ system involved.

Data was entered systematically in master chart by using MS excel. The data on categorical variables will be presented as n (% of cases) and the values on continuous variables will be presented as Mean $\pm$ Standard deviation (SD). Chi square test will be used for qualitative data. P-values less than 0.05 will be considered to be statistically significant.

RESULTS

Total 150 children with nephrotic syndrome were included in the study with mean age was 7.25 ± 3.89 years & majority were aged between 6-10 years with male predominance. About 40% had past history of infection. Almost 57.35% were completely immunized. About 26.7% were belong to Lower middle SES. About 39.3% were admitted for IFRNS followed by 34% for initial attack. (Table 1) Most common presenting symptom was swelling over body/Facial puffiness/Anasarca (82.66%). (Fig 1) Most children (74.7%) showed raised white blood cell (WBC) counts. Additionally, 62.7% had raised neutrophil counts. ESR values in nephrotic syndrome patients in which 99 patients (66%) have <20 mm/hr & 52% had >6 mg/dl CRP. Mean sr. albumin was 1.742 ± 0.97 g/dl & 41.33% had >1.5 g/dl sr. albumin. About 14% patients have pus cells >10 /hpf. (Table 2)

Out of 84 children with nephrotic syndrome with infection, 35 were culture positive (41.66%). Only one patient was detected with M. Tb in a sputum CBNAAT which was Rifampicin sensitive. (Fig 2) The most common infection was Pneumonia (16.66%), followed by urinary tract infection (UTI) (14%) and septicaemia (10%), AGE (2.66%). Additionally, 44% children showed no signs of infection. (Fig 3)

About 64% children had >10 days of hospital stay & 36% had <10 days of hospital stay. Majority of children 99.33% were discharged & only one child died. (Table 3)

Table 1: Distribution According to Clinic-social Parameter

Clinic-social parameter		Frequency	Percentage
Age (Years)	1-5	52	34.7
	6-10	61	40.7
	11-14	37	24.7
Gender	Male	79	52.7
	Female	71	47.3
Past H/O infection	Present	60	40
	Absent	90	60
Immunization Status	Completely Immunized	86	57.3
	Partially immunized/Unimmunized	64	42.7
SES	Upper	8	5.3
	Upper Middle	36	24
	Lower Middle	40	26.7
	Upper Lower	33	22
	Lower	33	22
Type of Admission	Initial Attack	51	34
	IFRNS	59	39.3
	FRNS	36	24
	Steroid dependent	4	2.66

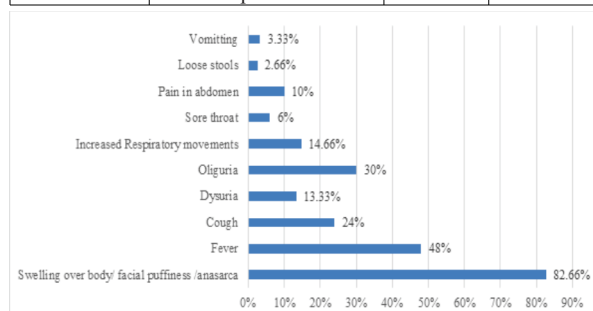


Fig 1: Distribution According to Presenting Symptoms

Table 2: Distribution According to Investigation Profile

Investigation profile		Frequency	Percentage
WBS	Normal	38	25.3
	Raised	112	74.7
Neutrophil Count	Normal	56	37.3
	Raised	94	62.7
Lymphocyte Count	Normal	114	76
	Raised	36	24
CRP	<6 mg/dl	72	48
	>6 mg/dl	78	52
ESR	<20 mm/hr	99	66
	>20 mm/hr	51	34
Sr. Albumin	<1.5 g/dl	88	58.66
	>1.5 g/dl	62	41.33
Pus cell/hpf in Urine	>10 /hpf	21	14
	<10 /hpf	129	86

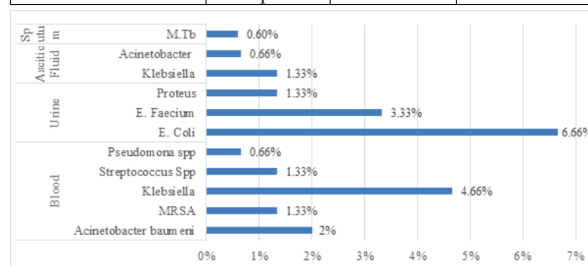


Fig 2: Distribution According to Organism Isolated

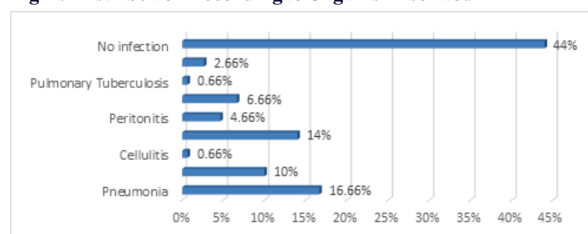


Fig 3: Distribution According to Infection in Nephrotic Syndrome Children

Table 3: Distribution According to Outcome

Outcome		Frequency	Percentage
Duration of stay	<10 days	54	36
	>10 days	96	64
Final Outcome	Discharge	149	99.33
	Death	1	0.66

Table 4 shows that, partially immunized children, raised haematocrit value, raised CRP level & Sr. albumin level had significantly higher risk of infection in children with nephrotic syndrome. The children with infection & nephrotic syndrome had significantly longer hospital stay.

Table 4: Association Between Clinic-social Parameter & Infection in Children with Nephrotic Syndrome

Clinico-social Parameter		Infection Present		Infection Absent		p value
		Fre-quency	Percen-tage	Fre-quency	Percen-tage	
Age group	1-5 Years	24	28.60	28	42.40	0.17
	6-10 Years	36	42.90	25	37.90	
	11-14 Years	24	28.60	13	19.70	
Gender	Female	38	45.23	33	50.00	0.56
	Male	46	54.80	33	50.00	
Past History	Present	45	53.57	15	22.72	0.06
	Absent	39	46.42	51	77.27	
Immunization	Completely Immunized	42	50.00	44	66.66	0.04
	Partially immunized / Un-immunized	42	50.00	22	33.33	
SES	Upper	2	2.40	6	9.10	0.47

	Upper Middle	22	26.20	14	21.20	
	Lower Middle	21	25.00	19	28.80	
	Upper Lower	18	21.40	15	22.70	
	Lower	21	25.00	12	18.20	
Type of admission	Initial Attack	30	35.71	21	32.00	0.078
	IFRNS	39	46.42	20	30.30	
	FRNS	12	14.28	24	36.35	
	Steroid dependent	3	3.57	1	1.51	
WBS	Raised	56	66.00	17	25.75	0.0001
Neutrophil Count	Raised	55	64.40	8	12.12	0.001
Lymphocyte Count	Low	25	29.76	0	0.00	0.0001
ESR	High	34	40.47	33	50.00	0.13
CRP (mg/dl)	<6	13	15.47	59	89.40	0.03
	>6	71	84.53	7	10.60	
Sr. Albumin	<1.5 g/dl	40	47.61	38	57.57	0.048
	>1.5 g/dl	44	52.38	28	42.42	
Hospital Stay	<10	11	13.10	43	65.10	0.035
	>10	73	86.90	23	34.80	

DISCUSSION

In the present study, the majority of children with nephrotic syndrome were aged 6-10 years (40.7%), with a mean age of 7.25 years. In a study by Mahmud et al[6] in Dhaka, the mean age was reported as 4.5 years, with a higher prevalence in children aged 2-6 years (63.49%). Similarly, in a study by Ahmed et al[7], found the mean age to be 5.98 years, with 75% of their cohort falling within the 2-8 years range. Meanwhile, Pandey et al[8] observed a slightly older age distribution, with a mean age of 6.26 years and the majority (62.5%) in the 1-5 year group. In the present study, males represented 52.7% of the cohort, slightly outnumbering females Sethi et al[9] observed a slightly higher male proportion (52%) in their sample. Hassan et al[10] found that 68.5% of nephrotic syndrome patients with infections were boys, with a male-to-female ratio of 2.2:1. In the present study, 60 percent children were admitted without past history of infection and 40% were with past history of infections. In Ajay Sethi et al[11] study it was found that 66% of children were admitted without past history of infection and 33% were with past history of infections. In the present study, 57.33% children are completely immunized as per NIS while 42.7% are unimmunized. This shows a large group of children are unimmunized. In the present study, the largest group of participants belonged to the lower middle class (26.7%). Mohammed Y et al[12] found that 66.7% of nephrotic syndrome patients belonged to the lower socioeconomic classes, highlighting the association between lower socioeconomic status and the prevalence of nephrotic syndrome. Similarly, other studies, such as Hassan et al[10], reported a significant concentration of patients in lower socioeconomic brackets.

In the present study, the majority of the children were admitted due to a relapse (66%), while the remaining 34% were experiencing an initial attack. This distribution is consistent with findings from Mohammed Y et al[12], who observed that 66.6% of admissions were due to relapse. Hassan et al[112] reported that a significant proportion of their patients were also admitted during relapse episodes (59%). In the present study, oedema was the most prevalent symptom, affecting 82.66% of the participants, followed by fever (48%). Sethi et al[11] reported anasarca (90%) as the most common symptom, followed by fever (88%), abdominal pain (35%) and cough (30%). Additionally, the frequency of burning micturition indicates a significant incidence of urinary tract infections among the patients, further complicating their clinical presentation. In the present study, 74.7% of the participants had elevated white blood cell (WBC) counts, and 62.7% had raised neutrophil counts, suggesting an active infectious process in a significant portion of the cohort.

The mean serum albumin was 1.7 ± 0.9 which was relatable with Manish Kumar et al[13] which had mean serum albumin 1.5 ± 0.5 . The high prevalence of abnormal lab findings in the present study underscores the importance of routine laboratory investigations to

monitor for infections in nephrotic syndrome patients, particularly during relapses or periods of active disease. The presence of raised WBC and neutrophil counts highlights the ongoing inflammatory response in these patients, which requires prompt medical intervention to prevent further complications. In the present study, 56% of the children had an active infection, which is comparable to the 66.6% infection rate reported by Mohammed Y et al[12]. Hassan et al[10] observed a lower infection rate of 50%, primarily driven by spontaneous bacterial peritonitis and pneumonia.

In the present study, *E. coli* was the most frequently isolated organism (12%), followed by *klebsiella*, *Proteus* and *Streptococcus*. This is consistent with the findings of Mohammed Y et al[12], who reported that *E. coli* was the most common pathogen (25%), followed by *Shigella* and *Klebsiella*. Hassan et al[10] also identified *E. coli* as a common causative organism in urinary tract infections, though Gram positive bacteria were more prevalent in their cohort. The predominance of *E. coli* in the present study aligns with the broader trends in nephrotic syndrome-related infections, particularly UTIs, and underscores the need for targeted antimicrobial therapy to address these infections effectively. 36% (54) patients has stay <10 10 days. This shows that more patients having stay more than 10 days. This mirrors the study done by Manish Kumar et al[13], average stay was more in patients with infection (12±8) compared to patients without infection.

In the present study one patient died due to sepsis with multi organ failure (0.66%) of all patients and rest 149 (99.33%) patients discharged. Manish Kumar et al[14] noted 2.5% death rate which was due to sepsis with multi-organ failure. The International Study of Kidney Disease in Children (ISKDC) followed almost 389 children with minimal change disease for 5-10 years and reported 10 deaths, of which six were due to infection. The low mortality rate in our study can be explained by early presentation, high index of suspicion for infections and prompt institution of treatment.

CONCLUSION

This study confirms that infections are a major complication in children with nephrotic syndrome, contributing significantly to morbidity. The data underscore the need for proactive infection prevention strategies, including regular laboratory monitoring and early intervention to manage infections effectively. The high prevalence of infections across different socioeconomic and age groups suggests that nephrotic syndrome patients remain vulnerable throughout the disease course, whether during initial attacks or relapses. Tailored infection control measures, alongside continuous patient and caregiver education, are essential to improve outcomes in this population. By comparing with reference studies, this study highlights the importance of considering local epidemiological factors in the management of nephrotic syndrome and its complications.

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