



## Study of Infection in Children with Nephrotic Syndrome Presenting in a Tertiary Care Centre

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### Abstract:

**Introduction:** Nephrotic syndrome (NS) in children is a disease with edema, proteinuria, hypoalbuminemia and hyperlipidemia. Due to decreased immunity, chances of infections are very high in NS and these infections may be important causes of morbidity and mortality in NS. This study was done to observe the infection pattern in NS and to identify the responsible organism. This may help in further management of the disease. **Material and methods:** This study is a hospital based, cross-sectional, descriptive study conducted between July 2022 to June 2023, in a tertiary care centre. A total of 132 nephrotic syndrome children were enrolled after applying exclusion criteria. Socio-demographic history was taken and different investigations were followed to screen for infection. The data was entered in SPSS (software version 20 and analyzed. **Results:** In this study more than half (53.3%) of the patients were male and rest were female with overall mean age of  $6.26 \pm 2.05$  years. 69.2% of children were having initial attack of nephrotic syndrome while 30.8% were relapse cases. UTI with maximum occurrence of 40% followed by pneumonia and peritonitis were found to be the most common infection in children with nephrotic syndrome and E. coli was the most common organism isolated from infected cases. **Conclusion:** Screening for infection in children with nephrotic syndrome plays an important role for early detection of any infection. Pattern of infection may vary in different geographical areas.

**Keywords:** Nephrotic syndrome, Infection, Children, UTI, Complication

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**Introduction:** Nephrotic syndrome (NS) is one of the commonest childhood kidney diseases.<sup>(1,2)</sup> Childhood nephrotic syndrome is also called nephrosis. Nephrotic syndrome happens when tiny structures in the kidneys called glomeruli stop working properly and let too much protein enter the kidneys. It is characterized by heavy proteinuria, edema, hypoalbuminemia and hyperlipidemia.<sup>(3)</sup>

The prevalence of childhood NS worldwide is approximately 16 cases per 100,000 children, with an incidence of two to seven per 100,000 children. It predominantly occurs in children between 1–6 years of age.<sup>(4)</sup>

A number of glomerular and systemic diseases are responsible for nephrotic syndrome but in children almost 90-95% is idiopathic with no any identifiable cause. While the cause remains unknown, the pathogenesis of idiopathic NS is thought to involve immune dysregulation, systemic circulating factors or inherited structural abnormalities of the podocyte.

During active disease, the loss of proteins critical for various biological functions can result in complications such as infections, thromboembolic disease and acute kidney injury.<sup>(5)</sup>

Infection is a major complication in children with nephrotic syndrome and an important cause of morbidity and mortality among them. Infections are also important cause for the relapse and poor response to treatment. This may be due to compromised immunity during the disease. Relapse is defined as urine protein >3+ (Up/Uc >2) for 3 consecutive morning samples.<sup>(6)</sup>

The pattern of infections in these children may be different in different parts of India which may vary over time. So it is important to keep clinicians updated about current infection pattern which may be helpful in better management of this condition. This study was conducted to look for infections pattern in children with nephrotic syndrome and to identify the causative organisms for the same in a Government medical college Azamgarh, Uttar Pradesh.

**Material and methods:** This hospital based, descriptive, cross sectional study was conducted in the department of paediatrics, government medical college Azamgarh. The study was done in the period between July 2022 to June 2023. After obtaining approval from institutional ethics committee, all children fulfilling the International study of kidney disease in children (ISKDC) criteria for nephrotic syndrome, attending the Department of Pediatrics, GMC Azamgarh were included in the study.

Diagnosis of nephrotic syndrome was based on the ISKDC criteria

1. Edema
2. Nephrotic range proteinuria (urinary spot protein: creatinine ratio > 2)
3. Hypoalbuminemia (Sr. Albumin < 2.5 mg/dl)
4. Hyperlipidemia (Sr. Cholesterol >200mg/dl)

After applying exclusion criteria we could enroll 120 nephrotic syndrome children in this study. Children with congenital nephrotic syndrome, steroid resistant nephrotic syndrome, any surgical procedure during hospitalization, severe acute malnutrition with edema and those not giving consent for the study were excluded. A detailed socio-demographic history was taken and clinical examination was done. Children with suspected symptoms were screened for infection by doing investigations like CBC, ESR, blood and urine culture and sensitivity, throat swab culture, abdominal ultrasonography, peritoneal cytology, Mantoux test and X-Ray chest. Details of investigation, response to treatment and complications/infections if any were noted in the pre-structured proforma.

The data was entered in SPSS (Statistical Package for Social Science, IBM Corp.) software version 20 and analyzed. Modified BG Prasad classification was used for socio-economic classification.<sup>(7)</sup> Chi-square test was applied to see the association between different variables. A p-value <0.05 was considered to be statistically significant.

## Results:

A total of 120 children were enrolled for the study. Table 1 shows that 64 (53.3%) patients were male and 56 (46.7%) were female. Age range was 1 to 12 years with mean age of  $6.26 \pm 2.05$  years. Nephrotic syndrome was more common (61.7%) in younger children (1-5 years of age) as compared to older one. Of the total patients, 73.3% were Hindus and rest

were muslims. As far as socio-economic status was concerned, almost 2/3<sup>rd</sup> of the patients belonged to class IV and V of BG Prasad scale and association of socio-economic scale with nephrotic syndrome was not significant.

Almost 69.2% of children were having initial attack of nephrotic syndrome while 30.8% were relapse cases. Our study found relapse to be significantly more common in males than in females (p-value<0.5).

**Table 1: Socio-demographic profile of children**

Characteristics		Male (64) n (%)	Female (56) n (%)	Chi square	p-value
Age	1-5 years	40 (62.5%)	34 (60.7%)	0.129	0.719
	6-12 years	24 (37.5%)	22 (39.3%)		
Religion	Hindu	48 (75.0%)	40 (71.4%)	0.195	0.658
	Muslim	16 (25.0%)	16 (28.6%)		
Socioeconomic status*	Class II	9 (14.1%)	12 (21.4%)	1.134	0.768
	Class III	12 (18.7%)	10 (17.8%)		
	Class IV	19 (29.7%)	15 (26.8%)		
	Class V	24 (37.5%)	19 (33.9%)		
Admission	Initial attack	39 (60.9%)	44 (78.6%)	4.355	<b>0.036</b>
	Relapse	25 (39.1%)	12 (21.4%)		

\*modified BG Prasad classification

Table 2 illustrates the types of infection in nephrotic children. As can be seen, out of 120 children, 55 (45.8%) were showing major infection. 7 among them showed multiple infections, so the total count of infection was found to be 62. Among all the infection UTI cases was maximum with 40% occurrence followed by pneumonia (30.9%) and peritonitis (18.2%). Pharyngo-tonsillitis and Septicemia were found in 10.9% and 9.1% cases respectively. We could also found 1 case each of cellulitis and pulmonary tuberculosis.

**Table 2: Pattern of infection in Nephrotic syndrome children (n=55)**

Infection status	Total	Male	Female
UTI	22 (40.0%)	10 (34.5%)	12 (46.1%)
Pneumonia	17 (30.9%)	10 (34.5%)	7 (26.9%)
Peritonitis	10 (18.2%)	5 (17.2%)	5 (19.2%)
Pharyngo-tonsillitis	6 (10.9%)	4 (13.7%)	2 (7.7%)
Septicemia	5 (9.1%)	3 (10.3)	2 (7.7%)
Cellulitis	1 (1.8%)	0	1 (3.8%)
Pulmonary tuberculosis	1 (1.8%)	1 (3.4%)	0
<b>Total infection</b>	<b>55</b>	<b>29</b>	<b>26</b>
<b>No infection</b>	<b>65</b>	<b>35</b>	<b>30</b>

Lab investigation reports can be seen in table 3. WBC and neutrophil counts are significantly increased among patients with one or other infection as compared with those without infection. Similarly hematuria was significantly more common in nephrotic syndrome with any infection. More patients with infection showed pus cell and low lymphocyte than patients without infection. ESR is not significantly associated with infection in nephrotic syndrome.

**Table 3: Lab investigation in nephrotic syndrome children**

Parameters	With infection (N=55)	Without infection (N=65)	Chi square	p-value
Raised WBC (n=62)	42 (76.4%)	20 (30.8%)	24.801	<0.001
Raised neutrophil (n=62)	48 (87.3%)	14 (21.5%)	42.728	<0.001
Pus cells (n=60)	38 (69.1%)	22 (33.8%)	14.803	<0.001
Low lymphocyte (n=28)	18 (32.7%)	10 (15.4%)	5.009	0.0252
High ESR (n=50)	25 (45.4%)	25 (38.5%)	0.599	0.438
Hematuria (n=20)	14 (25.4%)	6 (9.2%)	5.646	0.0174

As depicted in table 4, out of total 55 infected cases, causative organism for infection could be isolated from 35 cases (63.6%). Most common bacteria isolated from infected patients was E. coli (31.4%) followed by Proteus (22.8%), Klebsiella (17.1%) and Streptococcus species (17.1%). 2 cases were positive for MRSA. H. influenzae and M. tuberculosis was also found in one case each.

**Table 4: Organisms isolated in infected children of Nephrotic syndrome**

Bacteria isolated	Total number of patients n (%)
E. coli	11 (31.4%)
Proteus	8 (22.8%)
Klebsiella	6 (17.1%)
Streptococcus species	6 (17.1%)
H. influenzae	1 (2.8%)
MRSA	2 (5.7%)
M. tuberculosis	1 (2.8%)
<b>Total</b>	<b>35 (100%)</b>

**Discussion:** Immuno-compromised status in children of nephrotic syndrome puts them at risk of several infection.<sup>(8)</sup> These infection may contribute significantly to the morbidity and mortality in nephrotic syndrome. In the current study 53.3% patients were male and 46.7% were female with male:female ratio of 1.14 :1. This is in consistent with the study by Ajayan et al. and Begum et al.<sup>(9,10)</sup> In our study 69.2% of children were having initial attack of nephrotic syndrome while 30.8% had a relapse. This is comparable to the result by Anisur Rahman et al. in 2022 in Dhaka where they found initial attack to be 73% and relapse 27%.<sup>(11)</sup> Tippiarthy S also found first episode of nephrotic syndrome to be 75% and relapse in 25% cases.<sup>(12)</sup>

Our study found that nearly half (45.8%) of the nephrotic syndrome children showed one or the other infection. Other studies reported a lower rate of infection in nephrotic syndrome. Ajeyan et al reported 36.6 % incidence of major infections. Although Raichandani H in his study found that out of 44 patients of nephrotic syndrome, 35(79.5%) had evidence of infection and 9 (20.5%) had no evidence of infection.<sup>(13)</sup> This variation of proportion may be due to different geographical and socio-economic profile in different area. Most common infection found in the current study was UTI as 2/3<sup>rd</sup> of those suffering from infection had

UTI. This is followed by pneumonia which was prevalent in 30.9% of infected patients. This was comparable to Afroz et al.<sup>(14)</sup> Salarzaei M and Narain U also found in their study that most common infection in children with nephrotic syndrome was UTI.<sup>(15,16)</sup> Other study showed lower (nearly 25%) rate of UTI in children with nephrotic syndrome.<sup>(17,18)</sup> This higher percentage of urinary tract infection seen in the present study could most probably be due to the low socioeconomic background of the child, lack of hygiene and lack of proper sanitation. In other studies, most common infection in children with nephrotic syndrome was upper respiratory tract infection.<sup>(16,19)</sup> Whereas in Taiwan, pneumonia was found to be most common.<sup>(20)</sup> Peritonitis may be a cause of mortality in nephrotic syndrome children. In our study, it was 3<sup>rd</sup> most common infection present in almost 1/5<sup>th</sup> of infected case. In the study by Ajayan et al., it was found to be the most common infection.<sup>(9)</sup> We also found just 1 child to be diagnosed with pulmonary tuberculosis and cellulitis. Study by Senguttuvan P also showed similar result.<sup>(21)</sup>

Lab investigation reports in the current study revealed that children with infection had significantly raised WBC and neutrophil and lower lymphocyte count. This was in accordance to the finding by Anisur Rahman et al.<sup>(11)</sup> Pus cells were mainly present in children with UTI while level ESR was not associated with present of infection in nephrotic syndrome.

Out of all infected cases, causative organisms could be isolated from nearly 2/3rd cases. The most common bacteria isolated was E. coli followed by Proteus, Klebsiella and Streptococcus. Similar results were found by Anisur Rahman et al.<sup>(11)</sup> In India, however, Senguttuvan P identified higher incidences (28%) of Klebsiella spp. Infections.<sup>(21)</sup>

**Conclusion:** Infection is very common in nephrotic syndrome. So screening plays an important role for early detection of any infection. In our study, UTI was the commonest infection in children with nephrotic syndrome and E. coli being the most common bacteria identified. Since immunity of patients is deranged, separate room or cubicle for these children may reduce the chance of hospital acquired infection. The counseling of parent/guardian regarding sanitation and hygiene is an important task. Communicating with them regarding its nature of relapsing also helps in better management of the disease.

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