

## Clinical Spectrum of Major Infection in Hospitalized Children with Nephrotic Syndrome at a Tertiary Care Hospital

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### Abstract

**Background :** Children with Nephrotic Syndrome (NS) are exposed to multiple infections resulting in significant morbidity and mortality. Besides being a common cause of mortality, infections may also be responsible for a poor response to steroid therapy or induce relapse in a child with Nephrotic Syndrome.

**Aims:** To assess the clinical spectrum of major infection in hospitalized children with Nephrotic Syndrome.

**Materials and Methods:** This hospital based cross-sectional study was done in the Department of Paediatrics, Sylhet M A G Osmani Medical College Hospital, Sylhet, Bangladesh. In this study, sample size was 44 diagnosed cases of Nephrotic Syndrome with infection. After taking consent, detailed history and thorough physical examination were done in each patient. All data were collected in a preformed questioner and finally collected data were expressed in tabulated form.

**Results:** In our study total 44 children with Nephrotic Syndrome were enrolled with the mean age of  $5.98 \pm 2.93$  years and most of the childhood Nephrotic Syndrome was aged between 2 to 8 years (75.0%); 23 (52.3%) patients were male, and 21 (47.7%) patients were female with a ratio of male to female of 1.1:1. The common clinical symptoms of major infection were fever (79.5%) and cough (70.5%). Other clinical presentations were throat pain (18.2%), abdominal pain (15.9%), runny nose (11.4%), burning micturition (9.1%), respiratory distress (6.8%), vomiting (4.5%) and leg pain (4.5%). Relapse of Nephrotic Syndrome was found in 33 (75.0%) cases. The most common major infection was pneumonia (50.0%), followed by urinary tract infection (20.5%), Upper respiratory tract infection (15.9%), pneumonia with UTI (6.8%), cellulitis (4.5%) and pneumonia with UTI with spontaneous bacterial peritonitis (2.3%). The most common isolated organisms in urine were *Escherichia coli* (27.3%), followed by *Klebsiella pneumoniae* (2.3%).

**Conclusion:** The common symptoms of major infection in Nephrotic Syndrome are fever and cough. The most common major infection was pneumonia and urinary tract infection.

**Key words:** Children, Nephrotic Syndrome, Infection.

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### Introduction

Nephrotic Syndrome (NS) is a common disease of childhood, characterized by massive proteinuria ( $>40\text{mg/m}^2/\text{hr}$ ), hypoalbuminaemia ( $<2.5\text{mg/dl}$ ), generalized edema and hypercholesterolemia ( $>250\text{mg/dl}$ ).<sup>1,2</sup> It is quite a common clinical condition in our country usually affecting the young children.<sup>3</sup> In children, most cases are Idiopathic Nephrotic Syndrome, without other systemic diseases.<sup>4</sup> Idiopathic (Primary) Nephrotic Syndrome (PNS) is a common renal disorder in the pediatric age group and minimal change disease (MCD) is the most common underlying histopathological lesion (80–90%). The main complication of

Nephrotic Syndrome is infection, followed by thromboembolic events. Hypertension, hyperlipidaemia, corticosteroid toxicity and behavioural disorders are less frequent.<sup>5</sup> Infection is an important cause of morbidity and mortality in nephrotic children especially in developing countries. Children with PNS have increased susceptibility to bacterial infections and various infections may result in relapses or steroid resistance or may trigger the onset of disease. Relapses in steroid sensitive Nephrotic Syndrome often follow infections of upper airway or gastrointestinal tract.<sup>6</sup>

An abnormality in the functions of the T lymphocytes and in particular the suppressor T

lymphocytes and the generation of circulating factors capable of altering the glomerular permeability to proteins seem to be involved in the pathogenesis of the disease. The episode of infection results in a group of alterations which synergically increase the patients' susceptibility to infections. These include decreased immunoglobulin (IgG) levels due to impaired synthesis and urinary loss, edema fluid acting as a culture medium, protein deficiency especially low serum albumin, hypovolemia leading to decrease perfusion of spleen, loss of complement factor B and D required for phagocytosis of encapsulated organisms, impaired T-lymphocyte function, and effects of immunosuppressive (Steroid) therapy. All these factors commonly cause children with PNS prone to infection.<sup>4</sup>

### Materials and Methods

This was a cross sectional descriptive study, was conducted at the Department of Paediatrics of Sylhet M A G Osmani Medical College Hospital, Sylhet; over a period of 6 (six) months from October 2018 to March 2019. Sample size was 44 diagnosed cases of Nephrotic Syndrome with infection. After taking consent, detailed history and thorough physical examination were done in each patient. History included age, sex, duration of illness, number of attacks, treatment history and features of infections. Thorough physical examination was done that will include respiratory rate, heart rate, blood pressure, temperature, weight, body surface area, chest indrawing, breath sound, added sound, heat coagulation test etc. Blood samples of all the patients were obtained for full blood counts, serum albumin, A-G ratio, serum cholesterol, C<sub>3</sub> level, blood urea, serum creatinine. Urine was sent for routine examination, spot urinary protein creatinine ratio or 24 hours UTP and culture sensitivity. Chest X-ray, other fluid (pus, CSF, ascitic fluid etc.) study and culture sensitivity were done as required.

### Operational Definitions

**Major infections** were defined as disseminated, affecting deep organs, requiring hospitalization (e.g. cellulitis, disseminated varicella) or potentially life-threatening.

Specific major infections were defined as follows:

- 1) **Peritonitis:** Abdominal pain, tenderness, distension, diarrhoea, or vomiting, with ascitic fluid >100 leukocytes/mm<sup>3</sup> and minimum 50% neutrophils and/ or positive culture.<sup>7</sup>
- 2) **Pneumonia:** fast breathing and chest indrawing with chest X-ray confirmation.<sup>7</sup>
- 3) **Urinary tract infection (UTI):** Bacterial colony count of >10<sup>5</sup> organisms/mL in a clean-catch midstream urine sample with

fever (>38.5°C), dysuria or increased urination frequency.<sup>7</sup>

4) **Cellulitis:** Erythema, warmth, swelling, fever and local tenderness in any body part.<sup>7</sup>

5) **Meningitis:** Fever and one of the following: neck rigidity, altered sensorium, seizures, with confirmation by cerebrospinal fluid cytology, biochemistry and culture.<sup>7</sup>

Other operational definitions were-

1) **Severe ascites** was defined as tense ascites or ascites with dyspnea.<sup>7</sup>

2) **Generalized edema** (including scrotal edema, vulval edema or severe ascites) was considered as severe anasarca.<sup>7</sup>

3) Frequently relapsing (**FRNS**), steroid dependent (**SDNS**), steroid resistant (**SRNS**) or infrequently relapsing NS (**IFRNS**) were considered as 'more severe clinical types of NS'.<sup>7</sup>

### Results

The age of the patients at admission ranged from 1year 06 months to 12 years with the mean age of 5.98 ± 2.93 years. Most of the childhood Nephrotic Syndrome was aged between 2 to 8 years (75.0%), whereas 9 (20.5%) patients were in the age group of above 8 years and only 2 (4.5%) patients were in the age group of below 2years. In this study 23 (52.3%) patients were male and 21 (47.7%) patients were female with a ratio of male to female of 1.1:1.

In this study we found different clinical symptoms among the 44 patients. Fever was found in 35 (79.5%), cough in 31 (70.5%), throat pain in 8 (18.2%), abdominal pain in 7 (15.9%), runny nose in 5 (11.4%), burning micturition 4 (9.1%), Respiratory distress in 3 (6.8%), Vomiting in 2 (4.5%) and leg pain in 2 (4.5%) cases (Table-I)

**Table-I: Distribution of the patients by symptoms (n=44)**

Symptoms	Frequency	Percentage (%)
Fever	35	79.5
Cough	31	70.5
Respiratory distress	3	6.8
Abdominal pain	7	15.9
Vomiting	2	4.5
Runny nose	5	11.4
Burning micturition	4	9.1
Throat pain	8	18.2
Leg pain	2	4.5

Regarding severe ascites was found in 34 (77.3%) cases and not severe ascites was in 10 (22.7) cases. Serum cholesterol level above 400mg/dl was found in 24 (54.5%) cases and up to 40mg/dl was found in 20 (45.5%) cases. In this study relapse of Nephrotic Syndrome was in 33 (75.0%) and first episode of

Nephrotic Syndrome was in 11 (25.0%) cases. Types of relapses was infrequent in 22 (50.0%), frequent in 10 (22.7%) and steroid dependent in 1 (2.3%) case.

Among the 44 study patients the most common major infection was pneumonia (50.0%), followed by urinary tract infection (20.5%), Upper respiratory tract infection (15.9%), pneumonia with UTI (6.8%), cellulitis (4.5%) and pneumonia with UTI with spontaneous bacterial peritonitis (2.3%) (Table-II).

**Table-II: Distribution of the patients by major infection (n=44)**

Major infection	Frequency	Percentage (%)
Urinary tract infection	09	20.5
Pneumonia	22	50.0
Upper respiratory tract infection	07	15.9
Pneumonia with UTI	03	6.8
Pneumonia with UTI with peritonitis	01	2.3
Cellulitis	02	4.5
<b>Total</b>	<b>44</b>	<b>100.0</b>

In this study the most commonly isolated organisms were *Escherichia coli* (27.3%), followed by *Klebsella pneumoniae* (2.3%); whereas isolation of organism could not be possible in 70.5% of cases. Table-III shows the distribution of patients by isolated causative organism.

**Table III: Distribution of the patients by causative organism (n=44)**

Isolation of organism	Frequency	Percentage (%)
<i>Escherichia coli</i>	12	27.3
<i>Klebsella pneumoniae</i>	01	2.3
No isolation	31	70.5
<b>Total</b>	<b>44</b>	<b>100.0</b>

## Discussion

Infectious episodes in nephrotic patients are responsible for high morbidity and can also cause an inadequate response to corticosteroid therapy and recurrences among patients in remission. Determining the type of infection is important, not only from the therapeutic point of view, but also to establish preventive measures.<sup>8</sup> In the present study the age of the patients at admission ranged from 1 year 06 months to 12 years with the mean age of  $5.98 \pm 2.93$  years. This result correlated with the study of Ajayan et al.<sup>8</sup> where they found the mean age of the patients with Nephrotic Syndrome was  $6.8 \pm 3.5$  years. In other studies of New Zealand and Saudi Arabia showed that the mean age patients was  $5.4 \pm 3.9$  and  $4.3 \pm 3.1$  years, respectively.<sup>9,10</sup>

The present study also showed that most of the childhood Nephrotic Syndrome was aged between 2 to 8 years (75.0%),

whereas 9 (20.5%) patients were in the age group of above 8 years and only 2 (4.5%) patients were in the age group of below 2 years. In another Iranian study, 62.5% patients were in the range of 2-8 years.<sup>11</sup> Sreenivasa et al. found 74% of patients were in the age range of 2-6 years, 20% of patients were in the age range of above 6 years, whereas 6% patients were in the range of less than 2 years.<sup>12</sup>

In this study 23 (52.3%) patients were male and 21 (47.7%) patients were female with a ratio of male to female of 1.1:1. This result was consistent with the study of Ajayan et al. that 53 (52.5%) patients of childhood Nephrotic Syndrome were male.<sup>7</sup> Sreenivasa et al. found that there were 60% male and 40% female with a ratio of male to female of 1.5:1.<sup>11,12</sup>

In the current study fever was found in 35 (79.5%), cough in 31 (70.5%), throat pain in 8 (18.2%), abdominal pain in 7 (15.9%), running nose in 5 (11.4%), burning micturition 4 (9.1%), respiratory distress in 3 (6.8%), vomiting in 2 (4.5%) and leg pain in 2 (4.5%) cases. Moorani et al., found fever (86.7%), cough (46.7%), urinary symptoms (20%), vomiting (13.3%), diarrhea (11.7%), abdominal pain (6.7%) and dehydration (3.3%).<sup>6</sup> Mahvish et al., found fever (64.9%), chills/rigor (18.9%), abdominal pain (32.4%), diarrhea and/or vomiting (13.5%), urinary symptoms (dysuria, increased frequency) (24.3%), respiratory symptoms (cough and/or breathing difficulty) (32.4%), shock (8.1%) and hypotension (10.8%).<sup>13</sup>

In our study severe ascites was found in 34 (77.3%) cases and not severe ascites was in 10 (22.7%) cases. This result was correlated with the study of Ajayan et al., found that severe ascites was found in 61.4% of cases of Nephrotic Syndrome.<sup>7</sup>

In the present study serum cholesterol level above 400 mg/dl was found in 24 (54.5%) cases and up to 400 mg/dl was found in 20 (45.5%) cases. This result was correlated with the study of Ajayan et al., found serum cholesterol (>400 mg/dl) in 12 patient (86 %) out of 14 patients with peritonitis.<sup>7</sup>

In our study relapse of Nephrotic Syndrome was in 33 (75.0%) and first episode of Nephrotic Syndrome was in 11 (25.0%) cases. Ajayan et al., found that relapse of Nephrotic Syndrome was in 55.4% cases and first episode of Nephrotic Syndrome was in 44.6% cases.<sup>7</sup>

In the present study types of relapse was infrequent was in 22 (50.0%), frequent in 10 (22.7%) and steroid dependent in 1 (2.3%) cases. Whereas first attack Nephrotic Syndrome was found in 11 (25.0%) cases. Ajayan et al., found that IFRNS was in 20.8% cases, FRNS was in 8.9% cases, SRNS was in 18.8%

cases and SDNS was in 6.9% cases.<sup>7</sup> Safaei et al., found that 29 (66%) patients were Steroid Sensitive Nephrotic Syndrome, 9 (20.5 %) were Steroid Resistant Nephrotic Syndrome, and 6 (13.5%) Steroid Dependent Nephrotic Syndrome. Of patients with Steroid-Sensitive Nephrotic Syndrome, 37% were non relapses, 38.8% Frequent Relapse of Nephrotic Syndrome (FRNS), and 26.4% infrequent relapses.<sup>14</sup>

The most common major infection in this study was pneumonia (50.0%), followed by urinary tract infection (20.5%), Upper respiratory tract infection (15.9%), pneumonia plus UTI (6.8%), cellulitis (4.5%) and pneumonia plus UTI plus spontaneous bacterial peritonitis (2.3%). Paul et al., found that acute respiratory infection (ARI), acute watery diarrhea and urinary tract infection (UTI) were the most common infections on admission (53.57%, 34.82%, and 7.14% respectively).<sup>8</sup> A recent study in Pakistan showed that ARI was the commonest infection in children with newly diagnosed primary Nephrotic Syndrome.<sup>6</sup> Three studies from Iran, Taiwan and Brazil also found similar result.<sup>14,15,16</sup> Gulati et al., found urinary tract infection as the commonest one and one study from India found it as the 3<sup>rd</sup> most common infection.<sup>17</sup>

The most commonly isolated organisms were *Escherichia coli* (27.3%), followed by *Klebsiella pneumoniae* (2.3%); whereas isolation of organism could not be possible in 70.5% of cases. This result correlated with the study of Ajayan et al., that *Escherichia coli* (2 cases; 20.0%) and *Klebsiella* (1 case; 10.0%) in UTI.<sup>7</sup> Soeiro et al., also reported that *Escherichia coli* was the most common organism isolated in 10 (50%) cases followed by *Klebsiella pneumoniae* species cultured in 4 (8%) of cases.<sup>15</sup> In another study Sreenivasa et al., found that the commonest organism isolated was *E. coli* followed by *K. pneumoniae*; while *Citrobacter* and *Enterobacter* were isolated occasionally.<sup>12</sup>

## Conclusion

In this study the common symptoms of major infection in Nephrotic Syndrome were fever and cough. Severe ascites, serum cholesterol level above 400 mg/dl was common finding in Nephritic Syndrome with infection. The most common major infection was pneumonia, followed by urinary tract infection, Upper respiratory tract infection, pneumonia with UTI, cellulitis and pneumonia with UTI with spontaneous bacterial peritonitis. The most commonly isolated organisms in urine were *Escherichia coli*, followed by *Klebsella pneumoniae*.

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