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# PROFILE OF INFECTIONS IN NEPHROTIC SYNDROME PATIENTS OF WESTERN RURAL MAHARASHTRA.

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**ABSTRACT**

**Background**: Infection is a major complication in children with Nephrotic syndrome. Patients with relapse will have increased susceptibility to bacterial infection because of urinary losses of immunoglobulins & properdin factor B, defective cell-mediated immunity, immunosuppressive therapy, malnutrition & edema, or ascites acting as potential culture medium.

**Aims & Objectives:** To study the spectrum of infections in nephrotic syndrome of childhood.

**Material and Methods:** A longitudinal observational study was conducted including the nephrotic syndrome cases after ethical approval from the institution at a tertiary care hospital from November 2020 to October 2021.

**Results:** The sex ratio of the study was 1.44:1 with a mean age of 4.2 years. The most common presenting feature in our study was decreased urine output with generalized edema and the most common type of infection was upper respiratory tract infections. Our study found that the most common organism causing infection in NS was Escherichia coli (E. coli).

**Conclusion:** With a high index of suspicion, early institution of appropriate antibiotics, and aggressive management of infections together with use of steroids enables remission of NS and support better prognosis.

**CASE REPORT**

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## INTRODUCTION:

Nephrotic syndrome is the clinical manifestation of glomerular diseases associated with heavy (nephrotic-range) proteinuria. Nephrotic range proteinuria is defined as proteinuria >3.5 g/24 hr. or a urine protein: creatinine ratio >2. The triad of clinical findings associated with nephrotic

syndrome arising from the large urinary losses of protein are hypoalbuminemia (<2.5 g/dL), edema, and hyperlipidemia (cholesterol >200 mg/dL).[1]

Infection is a major complication in children with Nephrotic syndrome. Patients with relapse will have increased susceptibility to bacterial infection because of urinary losses of immunoglobulins & properdin factor B, defective cell mediated immunity, immunosuppressive therapy, malnutrition & edema or ascites acting as potential culture medium. [2]

Nephrotic syndrome affects 1-3 per 100,000 children <16 years of age. Without treatment, nephrotic syndrome in children is associated with a high risk of death, most commonly from infections. Fortunately, 80% of children with nephrotic syndrome respond to corticosteroid therapy. [3] The annual incidence of nephrotic syndrome in most countries in the Western Hemisphere is estimated to range from 2 to 7 new cases per 100,000 children[4-8] and the prevalence is about 16 cases per 100,000 children[4] There is a male preponderance among young children, at a ratio of 2:1 to females, although this gender disparity disappears by adolescence, making the incidence in adolescents and adults equal among males and females.[6-10]

Nephrotic syndrome may be caused by a variety of glomerular and systemic diseases, but by far the most common type in childhood is idiopathic nephrotic syndrome. Before the introduction of antibiotics, corticosteroids, and other immunosuppressive therapies, nephrotic syndrome was associated with mortality as high as 67%, usually following infections. The first significant improvement in mortality was seen in 1939 after the introduction of sulfonamides and then penicillin. The introduction of adrenocorticotropic hormone and cortisone in the 1950s contributed to an even greater decrease in mortality (to 9%), which was noted to occur in association with dramatic resolution of proteinuria. [(4)]

Intercurrent infections represent one of the most serious complications of nephrotic syndrome. Risk factors for infection include low serum IgG levels due to urinary loss of IgG, abnormal T lymphocyte function, and decreased levels of factors B (C3 proactivator) and D, each a component of the alternative complement pathway, which result in a decreased ability to opsonize encapsulated bacteria such as Streptococcus pneumoniae[11-13] In addition, use of steroids and other immunosuppressive medications during relapses further increases the risk of infection.

The most common and serious type of infection is primary bacterial peritonitis, which is estimated to have an incidence of 5% in children with nephrotic syndrome. [14] Other types of infections include cellulitis, sepsis, meningitis, and pneumonia. Most infections are due to S. pneumoniae (peritonitis) or Staphylococcus (cellulitis), although infections due to gram-negative organisms such as Escherichia coli and Haemophilus influenzae may also occur.

Our knowledge about primary NS in children is still limited & pathogenesis of the commonest form, minimal change NS, remains largely unknown. There is paucity of literature regarding spectrum of infections in childhood nephrotic syndrome from the rural areas of India. Hence the need for this study.

**MATERIALS AND METHODOLOGY:**

An observational longitudinal study was conducted, after institutional ethical approval, from November 2020 to October 2021 at pediatric department of Pravara Rural Hospital and All children in the age range 6 months to 12 years, presenting with edema both in outdoor & indoor were evaluated for proteinuria in nephrotic range & these were the subjects of our study.

The diagnosis of nephrotic syndrome was based on the standard ISKDC criteria [(15)]-

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)
And the patients of NS who underwent surgical procedures during the hospitalization, severe acute malnutrition with edema and cases of angioneurotic edema were excluded from the study.

After the patient fulfilled the inclusion criteria, informed consent was obtained, and the data was collected with a detailed history and physical examination followed by through laboratory evaluation. The collected data was then tabulated and was analyzed using appropriate statistical tools.

**Observations & Results:**

**Table 1**: The spectrum of infections (multiple response) in NS in the study population.

| Sr.no. | Signs | Frequency (%) |
|---|---|---|
| 1 | URINARY TRACT INFECTION | 14(31.81) |
| 2 | SEPTICAEMIA | 8(18.18) |
| 4 | UPPER RESPIRATORY TRACT INFECTION | 16(36.36) |
| 5 | PERITONITIS | 4(9) |
| 6 | AGE | 3(6.81) |
| 7 | SCABIES | 1(2.27) |
| 8 | TUBERCULOSIS | 1(2.27) |
| 9 | ABSCESS | 1(2.27) |

**Table 2:** Age wise distribution of the spectrum of infection in NS (multiple response)

| Sr. no. | Age group (Yrs.) | UTI | Peritonitis | Abscess | Scabies | AGE | URTI | Septicemia | TB |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 1-5 | 7 | 1 | 00 | 00 | 01 | 08 | 04 | 00 |
| 02 | 5-10 | 6 | 02 | 01 | 01 | 01 | 05 | 02 | 01 |
| 03 | >10 | 1 | 00 | 00 | 00 | 01 | 03 | 02 | 00 |
| | Total | 14 | 4 | 01 | 01 | 03 | 16 | 08 | 01 |

**Table 3:** Distribution of Nephrotic patients with and without infection (n=44)

| Sr. No. | Infection | Age Group (years) | Male | Female | Total | Grand Total |
|---|---|---|---|---|---|---|
| | | 1-5 | 10 | 6 | 16 | |
| 1 | PRESENT | 5-10 | 8 | 6 | 14 | 35 |
| | | >10 | 3 | 2 | 5 | |
| | | 1-5 | 2 | 2 | 4 | |
| 2 | ABSENT | 5-10 | 2 | 1 | 3 | 9 |
| | | >10 | 1 | 1 | 2 | |
| | TOTAL | | 26 | 18 | 44 | |

**Table 4:** Distribution of UTI patients according to organism isolated in urine culture

| Sr.no. | Organism Isolated from culture | No of cases (%) |
|---|---|---|
| 1 | Klebsiella | 03 (23.07) |
| 2 | E. coli | 04(30.07) |
| 3 | Staph aureus | 03(23.07) |
| 4 | Pseudomonas | 02(15.38) |
| 5 | Proteus | 1(7.69) |
| | Total | 13 (100) |

**Table No. 5:** Days to remission after starting full dose of steroids with and without infection.

| Days required | No. of patients(n=44) (%) |
|---|---|
| Days required for remission with infection | |
| 5-10 | 3(6.81) |
| 11-15 | 20(45.45) |
| 16-20 | 12(27.27) |
| Days required for remission without infection | |
| 5-10 | 7(15.9) |
| 11-15 | 2(4.54) |
| 16-20 | 0 |

In our study, the mean age of all NS patients in our study was 4.2 years with standard deviation of 2.62. The Mean age of boys 4.87 ± 2.94 years whereas the mean age of girls 5.58 ± 3.10 years with a male predominance of 1.44:1.

In our study, decreased urine output with generalized edema (80%) was commonest presentation of all cases of NS followed by fever (62%), cough & cold (60%), breathing difficulty (26%), abdominal pain (20%), loose stools & vomiting (8%). Whereas the commonest sign of infection in NS patients in our study was facial puffiness with fever (72%) followed by throat congestion (56%), wheeze & crepitation (49%), abdominal tenderness (23%), and skin lesions (3%).

The spectrum of infections encountered in our study was, Urinary Tract Infection14(31.81%), Upper Respiratory Tract Infection 16(36.36%), septicaemia 8(18.18%), peritonitis 4(9%), acute gastroenteritis 3(6.81%), scabies 1(2.27%), tuberculosis 1(2.27%) & abscess 1(2.27%). In our study, acute respiratory illness was most commonly seen in 1-5 years' age group along with septicemia, peritonitis, Acute gastroenteritis whereas scabies and tuberculosis were seen more commonly in 5-10 years age group. Female predominance was seen in Acute respiratory illness and UTI, whereas male predominance was seen in Acute gastroenteritis, septicemia, however due to smaller sample size gender predominance for illnesses such as scabies, abscess or tuberculosis was not significant statistically.

Out 44 patients, 35(79.5%) had evidence of infection and 9 (20.5%) had no evidence of infection. The incidence of UTI was more below 10 years if age with male preponderance in 1-5 years and girl's preponderance in 5-10 years of age group. The

most common organism in culture proven infection was E. coli followed by Klebsiella, staph. Aureus, pseudomonas and proteus.

The incidence of acute respiratory illness was commonest in 1-5 years age group with boy's preponderance and least common in >10 years age group. It was observed that majority of patients of NS with infection required approximately 2 wks. for remission with range from 1 to 3 wks. whereas majority i.e., 7 (77.8%) patients of NS without infection achieve remission within 10 days after starting full dose of steroids. Patients of NS with major infections like peritonitis, septicaemia and abscess required 3wks for induction of remission after starting full dose of steroids whereas URTI, AGE showed remission within first wk. and TB, pneumonia, scabies and UTI within 2nd wk.

**DISCUSSION:**

In present study of 44 cases of NS, with male to female ratio of1.44:1 which was similar to various other studies such as, Gulati et al[13], P Senguttuvam et al[14](1.6:1), Sarker et al[15] (1.7:1), Moorani et al[16] (1.3:1), Ajayan et al[17] (1.1:1), Barua et al[18] (1.08:1), Noushadali et al[19] (3.1:1).

Of the 35 patients of NS with infection, 31.81% patients had Urinary Tract Infection. This compares well with the studies of P Senguttuvam et al[14] i.e. 46%, Sarker et al[15] i.e. 56%, Barua et al[18] i.e.30.8%, Noushadali et al[19] i.e. 22% but at variance with Gulati et al[13] i.e. 13.7%, Ajayan et al[17] i.e. 8 1%. Our study showed female predominance in UTI which was consistent with senguttuvam et al[14], & Barua et al[18] whereas Noushadali et al[19] showed male predominance.

The commonest etiology of UTI in our study was E. coli followed by Klebsiella and Staph aureus> Pseudomonas >Proteus similar to Moorani et al[16], Senguttuvam et al[14], Ajayan et al[17], noushadali et al[19] and Barua et al[18]. The incidence of Acute respiratory illness was more below 10 years of age in our study which was found consistent with Senguttuvam et al[14], and Sarkar et al[15] whereas much higher incidence was seen in Paul et al[20]. This can be attributed to underdeveloped respiratory function along with lower socioeconomic status and presence of industry near the residence.

The spectrum of infections in NS in this study, showed that septicaemia is the third commonest infection (18.18 %). Of the 35 NS patients with infection, 8 (18.18%) patients had septicaemia. This was in contrast with Moorani et al[16] i.e. only 1(1.7%) case of septicaemia.

Maximum patients of septicaemia were a combination of Peritonitis with UTI (2), peritonitis with URTI with UTI (1), peritonitis with URTI (1), peritonitis with AGE with pneumonia with UTI(l), UTI with URTI (1), UTI with URTI with scabies with AGE (1), and UTI with URTI with AGE (1); with no mortality in any category in contrast to Senguttuvam et al[14,21] who reported all deaths due to sepsis.

The commonest organisms isolated in our study from blood in cases of peritonitis were S. aureus (2), Klebsiella (1) & E. coli (1) similar to Uncu et al[21]. whereas Ajayan et al[17] had only 1 of 14(7.14%) cases peritoneal fluid culture positive i.e. Streptococcus pneumoniae Most studies have shown similar poor yield of peritoneal fluid culture and hence rely on surrogate cultures.

In our study, 3 cases of acute gastroenteritis were noted similar to Moorani et al[16] and Naushadali et al[19] whereas higher incidence was seen by Paul et al.[20] (34.8%) which can be attributed to the poor hygiene and lower socioeconomic status.

Several infections other than seen in our study have been reported by other workers like P Senguttuvam et al[14] reported measles , vulval candidiasis, chickenpox, enteric fever &hepatitis, Naushadali et al[19] reported skin infections & pyomeningitis, Moorani et al[16] reported enteric fever , meningitis& chicken pox, Paul et al[23] reported philariasis &

chickenpox, Sarker et al[15] reported helminthiasis & chickenpox, Ajayan et al[17] reported osteomyelitis , disseminated varicella, herpes zoster & meningitis & also Gulati et al[15] reported pyomeningitis & skin infections.

**CONCLUSION:**

The need for hospitalization to confirm the diagnosis of NS and assess the presence of infection as well as other complications is essential. Provision for furnished & self-contained separate cubicle/ ward for NS will likely reduce the risk of nosocomial infections since they are already immunocompromised. The communication with parents & patients as well as other caretakers about chronicity of disease with its relapsing & remitting nature is of utmost important to plan a successful strategy for management

**CONFLICT OF INTEREST**: NIL

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