e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2023; 13(5); 275-280
Original Research Article

Major Infections in Children with Nephrotic Syndrome

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Received: 10-03-2023 / Revised: 21-04-2023 / Accepted: 15-05-2023
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Conflict of interest: Nil

Abstract

Background: The illness itself and the usage of different immunosuppressive medications put children with nephrotic syndrome at higher risk of infection. Most often, infections cause relapses that necessitate hospitalization and raise the risk of morbidity and death. Children with nephrotic syndrome (NS) have a high morbidity and mortality rate due to infections. The types of infections that are reported vary greatly, and little research has been done on how therapy or patient characteristics affect the risk of infection. In light of this context, our goal was to investigate the prevalence and pattern of infections in kids with nephrotic syndrome. Children with nephrotic syndrome continue to have significant rates of morbidity and mortality due to infections. It may also be the cause of a poor response to steroid medication and the beginning of disease or relapses.

Aim: This study was conducted to determine the frequency and type of major infections in children with nephrotic syndrome.

Material and Method: The Department of Pediatrics carried out this descriptive cross-sectional investigation. Included were all children between the ages of 2 and 12 who met the requirements of the Study of Kidney Disease in Children (ISKDC) definition for nephrotic syndrome, whether or not they had an infection. This included all relapse cases who were admitted to the hospital's pediatric ward during the study period. Children with urogenital abnormalities or acute or chronic renal insufficiency were not included. Ninety kids were eligible for the study during this time, but ten of them either ran away from the hospital or refused to agree to participate. As a result, the study comprised 80 kids in all. We began enrolling individuals in the current trial after receiving signed informed permission. Patients who wished to participate in the trial or their guardians gave written, informed consent.

Results: Among 80 study cases, 60% of cases were in the 2-5 year age group, and the rest were in the 5-12 year age group. The ratio of males and females was 0.95:1. The patients were divided into two thirds rural residents. The majority of the kids (63%) came from a middle-class socioeconomic background. Out of the 90 instances that were examined, 27% of the cases were the result of relapses, and 73% of the children were admitted because they had experienced an initial bout of nephrotic syndrome. When children with infection and non-infection cases are compared, the children with infection have lower rates of hematuria (20% vs 27%), pus cells (40% vs 60%), lymphocytes (43% vs 46%), and erythrocyte sedimentation rate (ESR) (40% vs. 51%), white blood cell (WBC) counts (51% vs. 47%), and neutrophil counts (91% vs. 29%). Only the elevated neutrophil count was Noticeably Higher, Though.

Conclusion: Children with NS frequently get infections; the most common illnesses are peritonitis, pneumonia, UTIs, and diarrhea. When compared to nephrotic children who do not have an infection, the length of hospital stay in these children is much longer when an infection occurs. We recommend broader pneumococcal vaccine coverage in such children, given the burden of pneumococcal infection in our study. In conclusion, serious infections are still a significant risk factor for children with nephrotic syndrome, particularly during relapses. Children with nephrotic syndrome who have these infections should be treated with consideration for drug-resistant organisms.

Keywords: Children, Major infections, Nephrotic syndrome, Peritonitis and Septicemia

Introduction

One of the most prevalent chronic renal illnesses in children is nephrotic syndrome (NS), which is characterized by edema, hyperlipidemia, hypoalbuminemia, and selective proteinuria. Idiopathic nephrotic syndrome (INS) is the term used to describe the majority of nephrotic syndrome cases that do not have an underlying secondary cause. These instances are further divided into steroid-sensitive (SSNS) and steroid-resistant nephrotic syndrome (SRNS) based on how well the patients respond to treatment. Over half of SSNS cases exhibit recurrent episodes or develop

steroid dependence, necessitating repeated courses of steroids and other immunosuppressive medications, including asteroid-sparing agents. [1] While this disease can strike anyone at any age, children are affected by it more often than adults. This disorder often responds to treatment in a cycle that includes a period of drug-free remission, a gradual tapering and stopping of medication, and relapse(s) that result in the body swelling again. These cycles of recovery and return in certain children can last anywhere from months to years, which causes worry for the family as well as the child. The majority of the time, the primary pathogenetic mechanism entailed is the effacing of podocyte foot processes in the absence of an inflammatory lesion or glomerular deposit. [2] Nonetheless, most children with primary nephrotic syndrome retain their glomerular function, or the capacity to filter waste materials or the glomerular filtration rate in general. [3] Infections remain an important cause of morbidity and mortality in children with nephrotic syndrome. [4,5] The most frequent invasive bacterial infections in these kids are pneumococcal infections. Recurring relapses, a poor response to steroid medication, and extended hospital stays can all be caused by infections. [6] The most common infectious drivers of relapses are urinary tract infections and acute respiratory infections. [7] In patients with nephrotic syndrome, immunosuppression may conceal the normal clinical presentation of infections, delaying appropriate treatment. In order to treat these kids appropriately and implement preventative measures, it is critical to comprehend the infection pattern. In various parts of India, the spectrum of infectious agents and the pattern of infections in these kids vary. [8]

Nephrotic syndrome affects 2 to 7 people under the age of 16 out of every 10,000 in western countries; these cases make up about 1% of hospital admissions. [9,10] Nonetheless, compared to Caucasians, Asians have a greater yearly prevalence of nephrotic syndrome. Nephrotic syndrome was 6.61 percent more common in South Asians than in Europeans in 2011. [11] Nephrotic syndrome patients have weakened immune systems, which makes them more susceptible to infection. [9,12] Numerous factors, such as tissue edema, immunoglobulin loss, urine complement, and adverse effects of corticosteroids and cytotoxic medication, might weaken the host's immune system. [13,14,15] In order to reduce morbidity and death, increased susceptibility to infection requires early identification and treatment. [9,16] It is already well documented that among children with NS, infections play a significant role in morbidity and mortality. Recurring relapses, a poor response to steroid medication, and extended hospital stays can all be caused by infections. [17] Forty percent of children with NS died before the advent of corticosteroids and antibiotics, and fifty percent of these fatalities were caused by infection, many of which could have been avoided. [18] It has been shown recently that a viral upper respiratory tract infection precedes at least 50% of instances of NS with a juvenile start. A cross-reacting antibody response or a non-specific host response to infection can both account for this. [19,20]

The purpose of this study was to examine the hematological and biochemical parameters associated with infection in hospitalized children with nephrotic syndrome and to identify the causative organisms and their sensitivity patterns for these infections. [21]

Material and Methods

The Department of Pediatrics carried out this descriptive cross-sectional investigation. Included were all children between the ages of 2 and 12 who met the requirements of the Study of Kidney Disease in Children (ISKDC) definition for nephrotic syndrome21, whether or not they had an infection. This included all relapse cases that were admitted to the hospital's pediatric ward during the study period. Children with urogenital abnormalities or acute or chronic renal insufficiency were not included. Ninety kids were eligible for the study during this time, but ten of them either ran away from the hospital or refused to agree to participate. As a result, the study comprised 80 kids in all. The lead investigator performed a thorough physical examination along with a thorough demographic and clinical history. The data was entered onto a sheet for collecting data. We began enrolling individuals in the current trial after receiving signed informed permission.

Inclusion Criteria:

In the present study, we included children between 2-12 years of age with a diagnosis of NS who were brought to either OPD or admitted to the I.P.D of the hospital.

Exclusion Criteria:

Children with congenital nephrotic syndrome, children with features of nephritis or secondary NS, as well as those admitted only for diagnostic renal biopsy or immunosuppressive drug infusion (cyclophosphamide, pulse dexamethasone), were excluded.

Specific Major Infections

Spontaneous Bacterial Peritonitis (SBP)

Abdominal pain, tenderness, distension, diarrhea, or vomiting and an ascitic fluid study showing>100 leukocytes/mm3 with at least 50% neutrophils and/or positive culture. [22,13]

Pneumonia

Fast breathing and/or chest indrawing with radiological confirmation. [1]

UTI

Bacterial colony count of > 10 5/mL in a clean-catch midstream sample with fever (≥ 38.5ºC), dysuria, or increased frequency of urination.[1]

Cellulitis

Erythema, warmth, swelling, and local tenderness with or without fever.

Septicemia

Fever with systemic symptoms like vomiting, prostration, or lethargy with or without evidence of organ failure, and a pathogenic bacterium was grown in blood culture.

Pulmonary TB

Cough with or without fever for > 2 weeks and/or contact with an open case of TB, having a positive Mantoux test and chest X-ray evidence of TB or an AFB positivity of appropriate sample.

Data pertaining to baseline attributes was gathered and recorded using an organized proforma. All of these kids underwent in-depth clinical examinations and targeted history gathering. All of these youngsters underwent routine microscopic investigations of their urine, lipid profiles, kidney and liver function tests, and complete blood counts. Children with suspected meningitis and peritonitis underwent culture, biochemistry, and ascitic fluid cytology, respectively. If the clinical condition called for it, a chest X-ray as well as a blood and urine culture were performed.

Every kid who met the requirements for inclusion underwent a comprehensive clinical assessment. In every patient, investigations were conducted, including CBC, ESR, urine albumin and microscopy, blood urea, serum creatinine, and albumin. When necessary, the following tests were performed: serum cholesterol, blood, urine, chest radiography, abdominal ultrasonography, peritoneal fluid cytology and culture, Mantoux test, and stomach aspirate for AFB. Age, gender, clinical characteristics, test results, and infection type were among the data that were computed. To represent each variable, percentages, frequencies, and descriptive statistics were computed.

Statistical Analysis

After collection, data were checked meticulously, then entered and analyzed using SPSS (Statistical Package for Social Science, IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Proportions were compared with the Chi-square test or Fisher's Exact test where appropriate. When comparing baseline patient characteristics, a p-value <0.05 was considered significant. Descriptive statistics were presented with frequency and percentages.

Result: -

Table 1: Socio-demographic and clinical characteristics of the study population

Characteristics	Number	Percentage (%)
Age group		
2-5 year	52	60
>5-12 year	28	40
Sex		
Male	38	49
Female	42	51
Residence		
Rural	50	67
Semi-urban/ Urban	30	23
Socio-economic status		
Low	24	27
Middle	56	63
No. of family members		
≤4	61	79
≥5	19	21
Admission		
Initial attack	56	73
Relapse	24	27

A total of 80 children were included in this study. Table 1 shows the socio-demographic and clinical characteristics of the study population (N=80). Among 80 study cases, 60% of cases were in the 2–5-year age group, and the rest were in the 5–12-year age group. The ratio of males and females was 0.95:1. Two-thirds of the patients came from rural areas. Most of the children (63%) were from middle socio-economic status. Among 90 studied cases, 73% of children were admitted due to an

initial attack of nephrotic syndrome, and in the rest of the cases, 27% were due to relapse.

Table 2: Distribution of studied children according to laboratory investigations with or without infection

Characteristics	With Infection (n=25) n(%)or, Mean±SD	Without Infection (n=55) n(%) or, Mean±SD
High ESR (n=38)	12 (40%)	26 (51%)
High WBC (n=43)	15 (51%)	28 (47%)
High neutrophil (n=43)	29(91%)	14(29%)
Hematuria (n=20)	6 (20%)	14 (27%)
Presence of pus cells (n=44)	13 (40%)	31 (60%)
Low lymphocyte	15 (43%)	28 (46%)
Serum albumin (gm/dl)	1.5 ± 0.1	1.5 ± 0.1
Serum cholesterol (mg/dl)	355 ± 78	395 ±78
Serum total Protein (gm/dl)	3.1 ± 0.4	3 ± 0.5
Serum creatinine (mg/dl)	0.5 ± 0.1	0.6 ± 0.1

Table 2 shows the distribution of various laboratory values among children with nephrotic syndrome, with and without infections. Comparing infection and non-infection cases, children with infection have higher Erythrocyte Sedimentation Rate (ESR) (40% vs. 51%), white blood cell (WBC) counts (51% vs. 47%), and neutrophil count (91% vs 29%), but lower rate of haematuria (20% vs 27%), pus cells (40% vs 60%) and lymphocytes (43% vs 46%). However, only the high neutrophil count was significantly higher.

Table 3: Pattern of infections in nephrotic syndrome

Major infections	Total n (%)	Initial episode n (%)	Relapses n (%)
Pneumonia	21 (41.7%)	6 (10.4%)	15 (31.3%)
Urinary tract infections	13 (25%)	2 (4.2%)	11(20,8%)
Septicemia	9 (16.7%)	2 (4.2%)	7(12.5%)
SBP	4 (8.3%)	0	4 (8.3%)
Cellulitis	2 (4.2%)	2 (4.2%)	0
Perinephric abscess	1 (2.1%)	1 (2.2%)	0
Pulmonary tuberculosis	1 (2.1%)	1 (2.2%)	0
Total infections	**51 (19.6%)**	**14 (27%)**	**37 (73%)**

There were 51 (19.6%) episodes of major infections in 48 children with nephrotic syndrome. Three children had multiple infections. Thirty-Seven (73%) episodes of major infections occurred during relapses and 14 (27%) during the initial episode of nephrotic syndrome.

Discussion

Nephrotic syndrome in children is associated with a large death and morbidity rate due to major infections. Major infections in children with nephrotic syndrome are the subject of very few research conducted in India. In a study in which children with life-threatening complications were the inclusion criteria, Ajeyan et al 2013 [17] reported a 36.6 % incidence of major infections. The incidence of major infections in nephrotic children brought to our institute was 35.9%. This is quite comparable to the findings of Manish et al2019 [23] who in their Indian study found the incidence of major infection in hospitalized nephrotic children to be 43.8%. Referral bias and a high level of clinical suspicion for infections in these children can potentially account for the comparatively higher frequency of infection in our study cohort, even though the majority of Indian studies have shown major infection incidences in the range of 20–35%. Infections with UTIs, pneumonia, diarrhea, and peritonitis were the most prevalent in our study.

Senguttuvan et al 2004 [24] observed E. coli and Klebsiella as predominant organisms in peritonitis. Similar to our finding that UTI was the commonest infection in such children, one of the largest retrospective analyses in children with NS to determine the incidence of UTI found that 15% of children had UTI, with more than 50% being asymptomatic and diagnosed as a part of screening investigations for relapse and non-response. [25] This emphasizes how crucial it is to screen for UTI in all children with NS who relapse or do not respond to corticosteroids because the anti-inflammatory properties of drugs may disguise symptoms. The death rate in our research was 3 (2.9%). All of the deaths were attributable to sepsis-induced multiorgan failure and happened in nephrotic youngsters with severe illnesses. However, Srivastava et al1987 [26] reported a

higher death rate (13% of children died of infection) and mortality were highest within the first 24 hours of admission which indicates a fulminant nature of infections associated with NS. Nevertheless, the lower mortality rate in our study can be explained by early presentation, a high index of suspicion for infections, and prompt institution of treatment.

One potentially fatal side effect of nephrotic syndrome is peritonitis. [22] Based on the presence of ascites, vomiting, fever, and abdominal pain; we believe that 16 (18%) of our patients had peritonitis. In nine of these cases, the diagnosis has been confirmed by the culture sensitivity test. In our study, peritonitis was the second most prevalent infection, although, in a study by Ajayan et al. 2013 [17], it was the most common infection. However, their culture-positive rate was lower, most likely because the majority of individuals were given antibiotics by their general practitioners prior to the ascitic fluid sample collection.

Spontaneous bacterial peritonitis is a serious complication of nephrotic syndrome with an incidence of 2-6%, and overwhelming infection carries a mortality risk of 1·5%. [27] It usually occurs within the first 2 years of diagnosis of nephrotic syndrome. [28] Low serum albumin, ascites, and an impaired immune system predispose to peritonitis and most often it is multifactorial in origin. [29] Majority of peritonitis is caused by encapsulated gram-positive organisms, particularly streptococcus pneumonia, but may also be caused by gram-negative organisms. [30]

Both children with multiple infections presented with pneumonia and UTI was detected incidentally. Gulati et al1995 [5] also reported multiple infections. In our study, there was no fatality. From 40% in the pre-antibiotic era to 16% with the widespread use of antibiotics, death rates decreased. [13] The zero-mortality seen in this study may have been caused by early treatment commencement made possible by early health-seeking behavior as a result of the high literacy rate in this region of the country and improved awareness about the condition. Klebsiella sp. was found in 17.1% of the isolates in the urine sample of the patient with UTI, and in the blood sample of the children with septicemia, which is comparable to the study conducted by Adeleke et al 2009 [31], in Nigeria. In contrast, Eddy et al. 2003 [10], reported that pneumonia was more prevalent in children younger than 10 years of age, while UTI was most prevalent in children older than 10 years of age.

In our investigation, there was a high culture yield. This might be because the majority of the kids with follow-up nephrotic syndrome came straight to our facility with severe symptoms and no history of antibiotic use.

Different bacterial species are becoming more concurrently resistant to antimicrobials of different structural classes, which can make treating infections therapeutically more difficult. [32] The isolates in this investigation, particularly the uropathogens, exhibited a significant level of multidrug resistance. The main causes of the emergence of MDR microorganisms are empirical antibiotic therapy, misuse, and inadequate antibiotic courses. [33]

Conclusion

Children with NS frequently get infections; the most common illnesses are peritonitis, pneumonia, UTIs, and diarrhea. When compared to nephrotic children who do not have an infection, the length of hospital stay in these children is much longer when an infection occurs. We recommend broader pneumococcal vaccine coverage in such children, given the burden of pneumococcal infection in our study. In conclusion, serious infections are still a significant risk factor for children with nephrotic syndrome, particularly during relapses. Children with nephrotic syndrome who have these infections should be treated with consideration for drug-resistant organisms. Parental counseling is crucial to the timely care of these kids.

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