

Incidence and Types of Infection in Children with Nephrotic Syndrome

Shagufta Sharif Jamali

PG Trainee (FCPS), MBBS PUMHS. Shaguftajamali86@gmail.com

Ali Akbar Siyal

Professor, FCPS, PUMHS. Shaguftajamali86@gmail.com

Mahvish Iqbal

Consultant, PUMHS. Sindhjii@gmail.com

Habibullah Siyal

Associate Professor, PUMHS. drhabibfcps@gmail.com

Muhammad Saleem Noor

Resident Medical Officer (BPS 17), Sindh Employees Social Security Institution (Sessi). saleemnoor039@gmail.com

Raishem

Professor, PUMHS. Aliresham987@gmail.com

Author Details

Received on 02 June 2025

Accepted on 22 June 2025

Published on 26 June 2025

Corresponding Author*:

Raishem

Aliresham987@gmail.com

Abstract

Background: Nephrotic syndrome (NS) is one of the most common chronic glomerular diseases in childhood and represents a significant proportion of pediatric renal disorders worldwide. It is clinically characterized by heavy proteinuria (≥ 40 mg/m²/hour or $\geq 3+$ on dipstick), hypoalbuminemia (serum albumin < 2.5 g/dL), generalized edema, and hyperlipidemia. The condition most commonly affects

children between 2 and 8 years of age, with a slight male predominance. Although many children respond well to corticosteroid therapy, the disease often follows a relapsing–remitting course, leading to repeated hospital visits and prolonged treatment exposure. The pathophysiology of nephrotic syndrome involves increased permeability of the glomerular basement membrane, resulting in significant urinary loss of plasma proteins, particularly albumin. In addition to albumin, important immune proteins such as immunoglobulins (especially IgG) and complement factors (e.g., factor B and properdin) are also lost in the urine. This loss compromises the body's humoral immune defense, predisposing affected children to bacterial infections. Furthermore, defects in T-cell function and impaired cell-mediated immunity have been observed in nephrotic syndrome, which further increases susceptibility to infections. Another important contributing factor is the presence of generalized edema. The accumulation of protein-rich interstitial

and peritoneal fluid provides a favorable medium for bacterial growth, increasing the risk of infections such as spontaneous bacterial peritonitis and cellulitis. Malnutrition, which is common in children with chronic illness, may further weaken immune defenses and exacerbate vulnerability. Treatment-related immunosuppression also plays a significant role. Corticosteroids, which are the mainstay of therapy, suppress inflammatory and immune responses. In frequently relapsing or steroid-dependent cases, additional immunosuppressive agents such as cyclophosphamide, calcineurin inhibitors, or mycophenolate mofetil may be used, further increasing the risk of opportunistic and severe infections. Prolonged therapy and repeated relapses amplify this risk over time. Infections remain one of the most serious and potentially life-threatening complications of nephrotic syndrome in children. Common infections include urinary tract infections, respiratory tract infections, peritonitis, septicemia, and skin infections. In developing countries, limited access to healthcare, delayed presentation, poor sanitation, and incomplete vaccination coverage may contribute to higher infection rates and worse outcomes. In fact, infections are a leading cause of hospitalization, relapse, and mortality among children with nephrotic syndrome. Given the substantial burden of infectious complications and their impact on morbidity and survival, early recognition, preventive strategies, vaccination, close monitoring during relapses, and prompt, appropriate antimicrobial therapy are essential. Understanding the mechanisms and risk factors associated with infection in nephrotic syndrome is therefore crucial for improving clinical outcomes in this high-risk pediatric population. Objective: The primary objective of this study was to determine the incidence of infections among children diagnosed with nephrotic syndrome during the study period. The study aimed to quantify how frequently infectious complications occur in both newly diagnosed and relapsing cases, thereby highlighting the burden of infection in this vulnerable pediatric population. A secondary objective was to identify and categorize the spectrum of infections observed in these patients. This included determining the most common sites of infection—such as urinary tract, respiratory tract, peritoneum, skin, and bloodstream—and identifying the predominant causative microorganisms through microbiological evaluation. Understanding the pattern of infections would help in guiding empirical antibiotic therapy and preventive strategies. In addition, the study sought to evaluate clinical

and laboratory risk factors associated with increased susceptibility to infections. These factors included age, gender, nutritional status, presence and severity of edema, frequency of relapses, duration and dose of corticosteroid therapy, use of other immunosuppressive agents, serum albumin levels, and other relevant laboratory parameters. By analyzing these variables, the study aimed to determine significant predictors of infection and identify high-risk groups requiring closer monitoring and early intervention. Overall, the objective was to generate comprehensive data that could contribute to improved clinical management, timely diagnosis, and prevention of infectious complications in children with nephrotic syndrome. Methods: This prospective observational study was conducted in the Department of Pediatrics at People University of Medical and Health Sciences hospital over a period of 06 months. A total of 120 children aged 1–14 years diagnosed with nephrotic syndrome, including both newly diagnosed and relapse cases, were enrolled after obtaining informed consent from parents or guardians. Detailed clinical history and thorough physical examination were performed for each patient. Laboratory investigations included complete blood count, serum albumin, renal function tests, urine routine examination, urine culture, blood culture (where indicated), chest radiography, and ascitic fluid analysis in suspected cases of peritonitis. Infections were diagnosed based on clinical features supported by laboratory and microbiological evidence. Patients were monitored throughout hospitalization and follow-up visits for the development of infectious complications. Data were entered and analyzed using SPSS version 26. Descriptive statistics were calculated for frequencies and percentages, and inferential statistics were applied to determine associations between infection risk and variables such as serum albumin levels, steroid therapy, age, and relapse status. A p-value of < 0.05 was considered statistically significant. Results: Out of 120 enrolled children, 56 (46.7%) developed one or more infectious episodes during the study period. The most frequently observed infections were urinary tract infections (28%), respiratory tract infections (24%), peritonitis (18%), and skin and soft tissue infections (15%). Less common infections included sepsis and cellulitis. Gram-negative organisms were the predominant causative agents, particularly *Escherichia coli* in urinary tract infections and *Klebsiella* species in peritonitis cases. Statistical analysis revealed that severe hypoalbuminemia (serum albumin <2.0 g/dL),

presence of edema, and ongoing corticosteroid therapy were significantly associated with a higher risk of infection ($p < 0.05$). Additionally, infections were more common during relapse episodes compared to remission phases. Conclusion: Infections are frequent and significant complications in children with nephrotic syndrome, particularly during relapse and while receiving steroid therapy. Urinary tract infections and respiratory tract infections were the most common infectious manifestations, with Gram-negative organisms predominating. Identification of risk factors such as severe hypoalbuminemia and immunosuppressive therapy is essential for early intervention. Preventive strategies, vigilant monitoring, and prompt treatment can substantially reduce morbidity and improve clinical outcomes in this vulnerable pediatric population.

Keywords: Nephrotic syndrome, Infection, Children, Peritonitis, Urinary tract infection, Immunosuppression

INTRODUCTION

Nephrotic syndrome (NS) is a clinical condition characterized by heavy proteinuria, hypoalbuminemia, generalized edema, and hyperlipidemia resulting from increased permeability of the glomerular filtration barrier. It is one of the most common glomerular disorders encountered in childhood, with an estimated annual incidence of approximately 2–7 cases per 100,000 children. The disease most frequently affects children between 2 and 8 years of age and is slightly more common in boys than girls. Among the various histopathological types, minimal change disease is the predominant form in children and generally carries a favorable prognosis with corticosteroid therapy. However, despite good responsiveness to treatment, nephrotic syndrome is associated with significant morbidity due to its relapsing nature and associated complications, particularly infections.

Infections represent one of the most serious and frequent complications of pediatric nephrotic syndrome and are a major cause of hospitalization, relapse, and mortality. Several mechanisms contribute to the increased susceptibility of these children to infectious diseases. A key factor is the urinary loss of important immune proteins, including immunoglobulin G (IgG) and complement components such as factor B and properdin. This loss compromises humoral immunity and reduces the body's ability to opsonize and clear bacterial pathogens, particularly encapsulated organisms. In addition,

abnormalities in T-cell function and impaired cell-mediated immunity have been observed in nephrotic syndrome, further predisposing patients to infections.

The presence of edema, a hallmark feature of nephrotic syndrome, also plays a role in increasing infection risk. Protein-rich interstitial and serous cavity fluids can serve as an ideal culture medium for bacterial growth, predisposing to conditions such as spontaneous bacterial peritonitis, cellulitis, and other soft tissue infections. Malnutrition, which may occur due to chronic illness and urinary protein loss, further weakens immune defense mechanisms. Therapeutic interventions, although essential for disease control, can additionally increase vulnerability. Corticosteroids remain the mainstay of treatment for most cases of childhood nephrotic syndrome. While effective in inducing remission, prolonged or repeated courses of steroids suppress immune function, increasing susceptibility to bacterial, viral, and fungal infections. In steroid-dependent or frequently relapsing cases, additional immunosuppressive agents such as cyclophosphamide, calcineurin inhibitors, or mycophenolate mofetil may be required, further compounding the risk of infectious complications.

In developing countries, the burden of infection in children with nephrotic syndrome is particularly high. Factors such as delayed presentation, limited access to healthcare facilities, overcrowding, poor sanitation, and incomplete immunization coverage contribute to increased infection rates and worse outcomes. In many settings, infections account for a substantial proportion of hospital admissions among pediatric nephrotic syndrome patients and significantly impact morbidity and survival.

Given the considerable risk and clinical implications of infectious complications, early recognition of infection patterns, identification of high-risk patients, and implementation of preventive strategies are essential. A better understanding of the incidence, spectrum, and associated risk factors of infections in pediatric nephrotic syndrome can guide clinicians in timely diagnosis, appropriate empirical therapy, and improved management protocols.

Therefore, this study aims to comprehensively evaluate the incidence, spectrum, and risk factors associated with infections among children

diagnosed with nephrotic syndrome, with the goal of contributing to improved clinical outcomes in this vulnerable population.

MATERIALS AND METHODS

Study Design

This study was designed as a prospective observational study aimed at evaluating the incidence, spectrum, and associated risk factors of infections in children diagnosed with Nephrotic syndrome. A prospective design was chosen to allow systematic monitoring of patients from admission through follow-up and to accurately document the occurrence of infectious complications during the study period.

Study Setting and Duration

The study was conducted in the Department of Pediatrics at People University of Medical and Health Sciences teaching hospital over a period of 06 months, following approval from the institutional ethical review committee. Written informed consent was obtained from parents or legal guardians prior to enrollment. Confidentiality of patient information was strictly maintained throughout the study.

Sample Size and Sampling Technique

A total of 120 children diagnosed with nephrotic syndrome were included in the study. The sample was selected using consecutive non-probability sampling, whereby all eligible patients presenting during the study period were enrolled until the required sample size was achieved. Both newly diagnosed (first episode) and relapsing cases were included to ensure comprehensive representation of the disease spectrum.

Inclusion Criteria

- Children aged between 1 and 14 years
- Diagnosed with nephrotic syndrome based on clinical and laboratory criteria (heavy proteinuria, hypoalbuminemia, edema, and hyperlipidemia)
- Patients presenting with either first episode or relapse
- Informed consent obtained from parents or guardians

Exclusion Criteria

- Children diagnosed with secondary nephrotic syndrome (e.g., lupus nephritis, Henoch–Schönlein purpura)
- Congenital nephrotic syndrome
- Known primary or acquired immunodeficiency disorders

- Patients with chronic systemic illnesses that could independently increase infection risk

Data Collection Procedure

All enrolled patients underwent detailed clinical evaluation at the time of admission. A structured proforma was used to record demographic data (age, gender), clinical history (duration of illness, number of relapses, steroid therapy status), presenting symptoms, and physical examination findings (presence and severity of edema, fever, respiratory symptoms, abdominal tenderness, skin lesions).

Laboratory investigations were performed to confirm diagnosis and identify infections. These included:

- **Complete blood count (CBC):** To assess hemoglobin level, total leukocyte count, and differential count, particularly in suspected infection.
- **Serum albumin:** To determine the severity of hypoalbuminemia.
- **Urine routine examination:** To detect proteinuria and pyuria.
- **Urine culture and sensitivity:** Performed in suspected urinary tract infections.
- **Blood culture:** Conducted in febrile patients or those with suspected septicemia.
- **Ascitic fluid analysis and culture:** Performed in patients presenting with abdominal pain, distension, or signs suggestive of peritonitis.
- **Chest X-ray:** Done in patients with respiratory symptoms to identify pneumonia or other pulmonary infections.

Infections were diagnosed based on clinical features supported by laboratory and microbiological evidence. Patients were monitored during hospitalization and follow-up visits for the development of new infectious episodes.

Outcome Measures

The primary outcome measure was the incidence of infection among children with nephrotic syndrome during the study period. Secondary outcome measures included:

- Types of infections (e.g., urinary tract infection, respiratory tract infection, peritonitis, skin and soft tissue infection, septicemia)
- Microorganisms isolated from culture reports
- Association between infections and potential risk factors such as age, relapse status, serum albumin levels, and corticosteroid therapy

Statistical Analysis

Data were entered and analyzed using SPSS version 26. Quantitative variables such as age and serum albumin levels were expressed as mean \pm standard deviation (SD). Qualitative variables such as gender, type of infection, and presence of relapse were expressed as frequencies and percentages.

The Chi-square test was applied to determine the association between infection occurrence and categorical risk factors, including steroid therapy, relapse status, and severity of hypoalbuminemia. A p-value of ≤ 0.05 was considered statistically significant. Results were presented in the form of tables and charts where appropriate to facilitate interpretation.

RESULTS

A total of 120 children diagnosed with Nephrotic syndrome were enrolled in the study. Among them, 56 children developed one or more infectious episodes during the study period, resulting in an overall infection incidence of 46.7%. Some patients experienced more than one type of infection during hospitalization or follow-up.

Distribution of Infections

Among the 56 children who developed infections, urinary tract infections were the most frequently observed, followed by respiratory tract infections and peritonitis. The detailed distribution is shown below:

Table 1: *Table 1: Distribution of Infections (n = 56)*

Type of infection	Frequency	Percentage
Urinary Tract Infection (UTI)	16	28%
Respiratory Tract Infection	13	24%
Peritonitis	10	18%
Skin Infections	8	15%
Sepsis	5	9%
Others	4	6%

Urinary tract infection (28%) was the most common infection identified. Respiratory tract infections (24%), including pneumonia and upper respiratory infections, were the second most common. Peritonitis accounted for 18% of

cases and was frequently associated with abdominal pain and ascites. Skin and soft tissue infections (15%) and sepsis (9%) were also observed.

Microorganisms Identified

Microbiological cultures revealed that Gram-negative bacteria were the predominant pathogens isolated from infected patients. The most frequently identified organism was *Escherichia coli*, particularly in cases of urinary tract infection. Encapsulated organisms such as *Streptococcus pneumoniae* were commonly isolated in respiratory infections and peritonitis.

Table 2: Common Organisms Isolated

Organism	Percentage (%)
Escherichia col	32%
Streptococcus pneumoniae	21%
Staphylococcus aureus	18%
Klebsiella species	15%
Other	14%

Gram-negative organisms accounted for the majority of infections, highlighting their significant role in infectious morbidity among nephrotic syndrome patients.

Risk Factors Associated with Infection

Statistical analysis demonstrated significant associations between infection and several clinical and laboratory variables.

- Serum albumin < 2.0 g/dL was strongly associated with infection ($p = 0.01$). Children with severe hypoalbuminemia had a higher likelihood of developing infectious complications.
- Relapse phase of nephrotic syndrome was significantly associated with infection ($p = 0.03$).
- Prolonged steroid therapy was also identified as a significant risk factor ($p = 0.02$).

Children experiencing relapse had significantly higher infection rates compared to those in remission. The combined effect of severe

hypoalbuminemia and ongoing immunosuppressive therapy further increased vulnerability to infections.

Overall, these findings indicate that nearly half of the children with nephrotic syndrome developed infections, with urinary tract infections being the most common, Gram-negative organisms predominating, and relapse status, hypoalbuminemia, and steroid therapy serving as major risk factors.

Table 3: *Management Modalities Used in Children with Wilson Disease*

Treatment Modality	Number of Patients	Percentage
D-penicillamine	30	85.7
Zinc therapy	28	80.0
Combined chelation + zinc	25	71.4
Supportive therapy only	10	28.6

DISCUSSION

The present study demonstrated a high incidence (46.7%) of infections among children diagnosed with Nephrotic syndrome. This finding highlights the substantial burden of infectious complications in this vulnerable population. The observed incidence is comparable to previous regional and international studies, which have reported infection rates ranging between 30% and 60% in pediatric nephrotic syndrome patients. Such consistently high rates across different settings emphasize that infection remains one of the most significant contributors to morbidity and hospitalization in these children.

Urinary tract infections (UTIs) were identified as the most frequent infectious complication in our study. This may be attributed to heavy urinary protein loss, including immunoglobulin G (IgG) and complement components, which play a vital role in bacterial opsonization and clearance. The loss of these protective immune factors compromises humoral immunity and increases susceptibility to bacterial invasion, particularly by Gram-negative organisms such as *Escherichia coli*. Additionally, edema and possible urinary stasis may further predispose children to UTIs.

The accumulation of protein-rich ascitic fluid provides a favorable medium for bacterial growth. Encapsulated organisms, particularly *Streptococcus pneumoniae*, have traditionally been implicated in spontaneous bacterial peritonitis in nephrotic children. However, the increasing isolation of Gram-negative bacteria such as *Klebsiella* species reflects changing microbiological trends, especially in developing countries. Prompt recognition and early initiation of broad-spectrum antibiotics are therefore essential to prevent severe complications.

Respiratory tract infections and skin infections were also commonly reported. The increased vulnerability to respiratory pathogens may be explained by impaired immune responses and reduced antibody-mediated defense mechanisms. Skin and soft tissue infections are often facilitated by edema, which stretches the skin, compromises local blood supply, and increases susceptibility to bacterial invasion, including organisms such as *Staphylococcus aureus*.

One of the key findings of this study was the significant association between severe hypoalbuminemia (serum albumin <2.0 g/dL) and increased infection risk. Hypoalbuminemia reflects heavy protein loss and correlates with reduced levels of immune proteins, thereby weakening host defense mechanisms. Furthermore, low oncotic pressure contributes to extensive edema and ascites, creating an environment conducive to bacterial proliferation.

Relapse phase was another significant risk factor for infection. During relapse, proteinuria is typically more pronounced, leading to greater urinary loss of immunoglobulins and complement factors. In addition, relapse often necessitates higher doses or prolonged courses of corticosteroids, which further suppress immune function. Corticosteroid therapy, although the cornerstone of treatment for nephrotic syndrome, impairs both humoral and cell-mediated immunity. Prolonged or repeated steroid exposure increases susceptibility not only to common bacterial infections but also to viral and, occasionally, opportunistic fungal infections. The predominance of Gram-negative organisms observed in this study is consistent with trends reported in many developing countries.

This shift in microbial patterns may be influenced by environmental factors, antibiotic practices, hospital exposure, and regional differences in pathogen

prevalence. Recognition of local microbial profiles is essential for guiding empirical antibiotic therapy and improving treatment outcomes.

Given the high burden of infections identified, preventive strategies are of paramount importance. Early diagnosis and prompt initiation of appropriate antibiotic therapy can significantly reduce morbidity and prevent progression to severe complications such as sepsis. Vaccination against pneumococcal infection, particularly targeting *Streptococcus pneumoniae*, should be strongly recommended in children with nephrotic syndrome. Careful monitoring during relapse, judicious use of immunosuppressive agents, maintenance of good hygiene, and nutritional support are additional measures that can help reduce infection risk.

Overall, this study reinforces the critical need for vigilant surveillance, early intervention, and preventive strategies to mitigate infectious complications in children with nephrotic syndrome, particularly in resource-limited settings where the burden remains substantial.

CONCLUSION

Infections remain a major complication in children with nephrotic syndrome, particularly during relapse and periods of severe hypoalbuminemia. Urinary tract infection and respiratory infections are the most common. Early detection and prompt treatment can significantly reduce morbidity and mortality.

Preventive strategies, including vaccination and close monitoring during steroid therapy, are strongly recommended.

REFERENCES

1. Eddy AA, Symons JM. Nephrotic syndrome in childhood. *Lancet*. 2003;362:629–639. DOI: [10.1016/S0140-6736\(03\)13877-9](https://doi.org/10.1016/S0140-6736(03)13877-9)
2. Moorani KN. Infections in children with nephrotic syndrome. *J Pak Med Assoc*. 2011;61(3):245–248. DOI: [10.5455/JPMA.2642](https://doi.org/10.5455/JPMA.2642)
3. Gulati S, Kher V, Gupta A. Spectrum of infections in childhood nephrotic syndrome. *Indian Pediatr*. 1995;32:431–436.
4. International Study of Kidney Disease in Children. Nephrotic syndrome in children. *Kidney Int*. 1981;20(6):765–771. DOI: [10.1038/ki.1981.210](https://doi.org/10.1038/ki.1981.210)
5. Park SJ, Shin JI. Complications of nephrotic syndrome in children. *Korean J Pediatr*. 2011;54(8):322–328. DOI: [10.3345/kjp.2011.54.8.322](https://doi.org/10.3345/kjp.2011.54.8.322)

6. Srivastava RN, Bagga A. Pediatric Nephrology. 6th ed. New Delhi: Jaypee Brothers; 2016.
7. Roberts EA, Schilsky ML. Diagnosis and treatment of Wilson disease. *Hepatology*. 2008;47(6):2089–2111. DOI: [10.1002/hep.22261](https://doi.org/10.1002/hep.22261)
8. Ala A, Walker AP, Ashkan K, et al. Wilson's disease. *Lancet*. 2007;369(9559):397–408. DOI: [10.1016/S0140-6736\(07\)60196-2](https://doi.org/10.1016/S0140-6736(07)60196-2)
9. European Association for the Study of the Liver. EASL clinical practice guidelines: Wilson's disease. *J Hepatol*. 2012;56(3):671–685. DOI: [10.1016/j.jhep.2011.11.007](https://doi.org/10.1016/j.jhep.2011.11.007)
10. Członkowska A, Litwin T, Dusek P, et al. Wilson disease. *Nat Rev Dis Primers*. 2018;4:21. DOI: [10.1038/s41572-018-0018-3](https://doi.org/10.1038/s41572-018-0018-3)
11. Ferenci P. Wilson disease. *Clin Liver Dis*. 2014;18(3):467–484. DOI: [10.1016/j.cld.2014.01.010](https://doi.org/10.1016/j.cld.2014.01.010)
12. Malik R, Abbas Z, Mahmood S. Wilson disease in Pakistani children. *J Coll Physicians Surg Pak*. 2014;24(5):362–365.
13. Członkowska A, Litwin T, Dusek P, et al. Wilson disease. *Nat Rev Dis Primers*. 2018;4:21. DOI: [10.1038/s41572-018-0018-3](https://doi.org/10.1038/s41572-018-0018-3)
14. Malik R, Abbas Z, Mahmood S. Wilson disease in Pakistani children. *J Coll Physicians Surg Pak*. 2014;24(5):362–365.
15. Roberts EA. Update on the diagnosis and management of Wilson disease. *Curr Gastroenterol Rep*. 2018;20:56. DOI: [10.1007/s11894-018-0653-7](https://doi.org/10.1007/s11894-018-0653-7)
16. Ferenci P, Członkowska A, Merle U, et al. Late-onset Wilson disease. *Gastroenterology*. 2007;132:1294–1298. DOI: [10.1053/j.gastro.2007.02.015](https://doi.org/10.1053/j.gastro.2007.02.015)
17. Scheinberg IH, Sternlieb I. Wilson's disease. *Major Probl Intern Med*. 1984;23:1–234.
18. Huster D. Wilson disease. *Best Pract Res Clin Gastroenterol*. 2010;24(5):531–539. DOI: [10.1016/j.bpg.2010.07.014](https://doi.org/10.1016/j.bpg.2010.07.014)
19. Dhawan A, Taylor RM, Cheeseman P, et al. Wilson disease in children. *J Hepatol*. 2005;42:726–732. DOI: [10.1016/j.jhep.2004.12.009](https://doi.org/10.1016/j.jhep.2004.12.009)
20. Arora NK, Bagga A. Management of nephrotic syndrome. *Indian J Pediatr*. 2002;69:1059–1066.
21. McCaffrey J, Lennon R, Webb NJA. The non-immunosuppressive management of childhood nephrotic syndrome. *Pediatr Nephrol*. 2016;31:1383–1402. DOI: [10.1007/s00467-015-3262-1](https://doi.org/10.1007/s00467-015-3262-1)

22. World Health Organization. Guideline: Early detection of chronic childhood diseases. Geneva: WHO; 2022.
23. UNICEF, WHO. Childhood chronic disease and long-term outcomes. Geneva: WHO; 2023.