HHS Public Access

Author manuscript

Pediatr Nephrol. Author manuscript; available in PMC 2019 August 01.

Published in final edited form as:

Pediatr Nephrol. 2019 February ; 34(2): 261–267. doi:10.1007/s00467-018-4072-6.

Association of infections and venous thromboembolism in hospitalized children with nephrotic syndrome

Shannon L. Carpenter[1], **Jennifer Goldman**[1], **Ashley K. Sherman**[1], **David T. Selewski**[2], **Mahmoud Kallash**[3], **Cheryl L. Tran**[4], **Meredith Seamon**[5], **Chryso Katsoufis**[6], **Isa Ashoor**[7], **Joel Hernandez**[8], **Katarina Supe-Markovina**[9], **Cynthia D'alessandri-Silva**[10], **Nilka DeJesus-Gonzalez**[11], **Tetyana L. Vasylyeva**[12], **Cassandra Formeck**[13], **Christopher Woll**[14], **Rasheed Gbadegesin**[15], **Pavel Geier**[16], **Prasad Devarajan**[17], **William E. Smoyer**[3], **Bryce A. Kerlin**[3], and **Michelle N. Rheault**[18,19]

[1]Children's Mercy Hospital, Kansas City, MO, USA

[2]University of Michigan, Ann Arbor, MI, USA

[3]Nationwide Children's Hospital, Columbus, OH, USA

[4]Mayo Clinic, Rochester, MN, USA

[5]University of Utah, Salt Lake City, UT, USA

[6]University of Miami Miller School of Medicine, Miami, FL, USA

[7]LSU Health Sciences Center, New Orleans, LA, USA

[8]Kaiser Permanente, Los Angeles, CA, USA

[9]Stony Brook Children's Hospital, Stony Brook, NY, USA

[10]Connecticut Children's Hospital, Hartford, CT, USA

[11]University of Puerto Rico, San Juan, Puerto Rico

[12]Texas Tech University Health Sciences Center, Amarillo, TX, USA

[13]Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA, USA

[14]Yale School of Medicine, New Haven, CT, USA

[15]Duke University, Durham, NC, USA

[16]Children's Hospital of Eastern Ontario, Ottawa, Ontario, USA

[17]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, USA

[18]University of Minnesota Masonic Children's Hospital, Minneapolis, MN, USA

Michelle N. Rheault rheau002@umn.edu.

Compliance with ethical standards

The Institutional Review Board at each institution approved the study.

Conflict of interest The authors declare that they have no conflict of interest.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00467–018-4072–6) contains supplementary material, which is available to authorized users.

[19]Division of Pediatric Nephrology, University of Minnesota, 2450 Riverside Ave. MB680, Minneapolis, MN 55454, USA

Abstract

Background—Nephrotic syndrome (NS) results in hypercoagulability and increased risk of infection. Furthermore, infection increases the risk of venous thromboembolism (VTE). Our objective was to determine the prevalence of infection, VTE, and the associated outcomes among a cohort of hospitalized children with NS.

Methods—All children with NS admitted to 17 pediatric hospitals across North America from 2010 to 2012 were included. Prevalence of infection and VTE was determined. Wilcoxon rank-sum and logistic regression were performed.

Results—Seven-hundred thirty hospitalizations occurred among 370 children with NS. One-hundred forty-eight children (40%) had ≥ 1 infection (211 episodes) and 11 (3%) had VTE. Those with VTE had infection more frequently ($p = 0.046$) and were younger at NS diagnosis (3.0 vs. 4.0 years; $p = 0.008$). The most common infectious pathogen identified was *Streptococcus pneumoniae.* The median hospital length of stay for those with infection [10 vs 5 days ($p < 0.0001$)] or VTE [22 vs 6 days ($p < 0.0001$)] was longer than those without either complication. Of those with infection, 13% had an intensive care unit (ICU) stay compared with 3.3% of those without infection. Median ICU stay was 4 days in those with VTE compared to 0 days in those without ($p < 0.001$). By logistic regression, only the number of ICU days was associated with VTE (OR 1.074, 95% CI 1.013–1.138).

Conclusions—Hospitalized children with NS have high rates of infection. Presence of VTE was associated with infection. Both were associated with longer hospitalizations and ICU stays.

Keywords

Nephrotic syndrome; Infection; Venous thromboembolism; Focal segmental glomerulosclerosis Minimal change disease; Infection

Introduction

Nephrotic syndrome (NS) is the most common glomerular disorder of childhood and is defined by severe proteinuria leading to hypoalbuminemia, edema, and hyperlipidemia. Although it is known that children with NS are at greater risk for complications including infection, thrombosis, and acute kidney injury, the predisposing risk factors for these complications are poorly defined in the modern era [1–3]. In particular, NS has long been recognized as a hypercoagulable state partially due to the loss of hemostatic proteins, both procoagulant and anticoagulant [4, 5]. Compensatory protein synthesis in this disorder also results in an increase of factors V and VIII, fibrinogen, and von Willebrand factor, which promote coagulation. Thrombocytosis and platelet hyperreactivity have also been demonstrated in approximately 70% of patients and may be due to NS-induced pituitary adenylate cyclase-activating polypeptide (PACAP) deficiency [6–8]. Other reported risk factors for venous thromboembolism (VTE) in this population include the common use of central venous catheters (CVCs), diuretics, and intravascular volume depletion [9, 10]. The

severity of proteinuria and age ≥ 12 years have also been shown to be associated with VTE development [9].

Patients with NS also have an elevated risk for infectious complications due to loss of components of the alternative complement pathway including factors B and D into the urine [11–13]. This loss of opsonizing factors increases susceptibility to encapsulated organisms such as *Streptococcus pneumoniae, Haemophilus influenzae, and Escherichia coli,* which have traditionally been the most common infectious pathogens implicated [14]. Infection is present in 17% of hospitalizations for NS, most frequently pneumonia, peritonitis, cellulitis, urinary tract infection, and bacteremia [1]. The majority of studies evaluating the microbiological spectrum of infections in NS are from before 2000. Little is known about the epidemiology for infection in children with NS after the widespread introduction of pneumococcal vaccination in the USA in 2000 [15]. Furthermore, while the risk of VTE in those with infection has been described previously, this has not been described in children with NS [16, 17].

The current study was undertaken utilizing the Midwest Pediatric Nephrology Consortium to develop a multicenter cohort of hospitalized children with NS in order to better understand the rates of complications. The first study from this cohort showed that acute kidney injury occurs commonly and is associated with adverse outcomes [18]. The current study seeks to begin to understand the rates of infection and VTE in a cohort of hospitalized children with NS. The aims of this study are to (1) determine the type and prevalence of infection, (2) describe the epidemiology of VTE, and (3) evaluate the association of VTE with infection and with hospital outcomes.

Methods

The study design was previously reported by Rheault et al. [18]. Records of all hospitalized children ≤ 18 years with NS admitted to any of 17 participating pediatric hospitals from the Midwest Pediatric Nephrology Consortium across North America from January 1, 2010 to December 31, 2012 were included. Exclusion criteria were planned admissions for renal replacement therapy, kidney biopsy, or infusion therapy; known secondary nephrotic syndrome at time of admission (IgA nephropathy, lupus, Henoch Schönlein Purpura, malignancy, etc); hospital length of stay ≤ 1 day; or remission of nephrotic syndrome on admission (urine dipstick negative or trace or protein-to-creatinine ratio < 0.2 mg/mg). The Institutional Review Board at each institution approved the study.

Data obtained

Data including demographics, clinical pattern of NS, renal biopsy results, number of hospitalizations, nephrotoxic medication exposure, and presence of infection and VTE history were recorded. Infection and VTE were defined as positive if documented by a nephrologist in the medical record per local standards. “Infections” included peritonitis, pneumonia, bacteremia, and ear, nose, and throat (ENT) infections, gastroenteritis, cellulitis/skin infection, or urinary tract infections.

Statistical analysis

Descriptive statistics were used to determine prevalence of infection and VTE. Medians, interquartile ranges (IQR), and proportions were used to summarize the data including reporting the prevalence of infection and VTE. Chi-square, Fisher's exact, and Wilcoxon rank-sum tests were used to perform comparisons between groups. Generalized estimating equation (GEE) models were used to account for within-patient correlations when looking at hospitalization level data. Logistic regression analysis was utilized to determine variables associated with having at least one infection and also developing at least one VTE. SAS version 9.4 was used for all analyses (SAS Institute Inc., Cary, NC, USA).

Results

Seven-hundred thirty hospitalizations occurred among 370 children. Demographic and NS characteristics are included in Table 1. The median age of the cohort at diagnosis was 3 years (IQR 2, 6). The median age at first hospitalization was 6.2 year (IQR 3.3, 10.7). A total of 40.5% of children did not have a biopsy diagnosis. Otherwise, minimal change disease was the most common biopsy proven diagnosis in 30% of patients and 28% of patients were steroid resistant.

Infection

One-hundred forty-eight children (40%) had at least 1 infection with a total of 231 infections reported in 211 hospitalizations (28.9%). Eighty-three percent of infections were present at the time of admission. The most common infection was peritonitis (8.2% of hospitalizations) with bacteremia (5.2%) also frequently observed. None of the patients with peritonitis were receiving peritoneal dialysis. When an organism was identified, *S. pneumoniae* was by far the most common (Table 2). Pneumonia complicated 6.8% of hospitalizations, with viral pathogens including respiratory syncytial virus, influenza, and parainfluenza frequently identified. Urinary tract infection (1.6%), cellulitis or skin infection (2.9%), gastroenteritis (3.4%), and ear/nose/throat infections (3.8%) were less commonly observed. Seven children had *Clostridium difficile* colitis which has not been previously reported in children with nephrotic syndrome.

Those with infection were younger atNS diagnosis (3.0 vs. 4.0 years;$p = 0.008$), and steroid-resistant NS was more highly associated with infection than all other clinical phenotypes (steroid-sensitive NS, steroid-dependent NS, other) ($p = 0.003$) (Table 3). There were no differences between those with and without infection regarding sex or ethnicity.

Venous thromboembolism

Eleven (3%) children had VTE including 3 with central venous sinus thrombosis, 1 with pulmonary embolism, and 1 with bilateral renal vein thrombosis. Four of the VTEs were diagnosed on the day of admission, with the remainder developing during the hospital stay (median hospital day 4, range 1–11). Four of the 11 episodes of VTE were associated with indwelling catheters. Those with VTE had more infections ($p = 0.046$) (Table 4). Infections associated with VTE were *C. difficile* (1 subject), methicillin-sensitive *Staphylococcus aureus* (2), *S. pneumoniae* (1), and unidentified pathogens (3). For six patients with both

infection and thrombosis identified during the hospital stay who had dates of diagnosis available, 3 developed infection prior to thrombosis (range 1 −14 days) and 1 patient was simultaneously diagnosed.

Outcomes

Children with VTE, infection, or both also experienced significantly longer hospital stays. The median hospital stay for those without infection was 5 days vs. 10 in those with infection (p <0.001) (Table 3). Similarly, median hospital stay for those without VTE was 6 days as compared to 22 in those with VTE (p <0.001). Of those with infection, 13% had an ICU stay compared with 3.3% of those without. Those with VTE also had a median of 4 days in the intensive care unit (ICU) as compared to 0 days in those without VTE (p <0.001) (Table 4). There was no difference between those with VTE or infection and those without in admission serum albumin, admission protein to creatinine ratio, or percent usage of calcineurin inhibitor at admission (Supplemental Tables 1 and 2).

In a logistic regression model looking at hospitalizations, hospital days, and ICU days, only the number of ICU days was associated with the presence of VTE (OR 1.07, 95% CI 1.01–1.14). When looking at the number of hospitalizations, the number of hospital days and the number of ICU days in a logistic regression model, hospitalizations (OR 1.61,95% CI 1.21,2.14), and hospital days (OR 1.04,95% CI 1.01,1.08) were found to be significantly related to having at least one infection.

Discussion

This study provides a comprehensive description of infectious and thrombotic complications in children hospitalized with NS in a contemporary US cohort. Although previous studies have defined rates of infections and VTE among this population, little is known about the relationship between infection and VTE development. Our study confirms that hospitalized children with NS have high rates of infection (40%) and thrombosis (3%) and these complications are associated with longer length of stay and ICU care. We make the novel observation that there is an association between infection and thrombosis in children hospitalized with NS. The most common infectious pathogen identified was *S. pneumoniae,* which is unchanged from historical studies in pediatric nephrology.

Peritonitis, pneumonia, and sepsis are common infections encountered in hospitalized children with NS [2]. Despite the widespread introduction of the pneumococcal vaccine in 2000, the most common pathogen identified in this cohort remained *S. pneumoniae.* From our data, we were unable to determine vaccination status. However, PCV7 (before 2010) or PCV13 (after 2010) were recommended as part of the routine vaccine series in children starting at 2 months of age, and the polyvalent PPSV23 vaccine is recommended by the CDC for all children with NS over the age of 2 years [19]. In children with NS with a high suspicion for infection, empiric antibiotic coverage should continue to include activity against *S. pneumoniae*. Children with steroid-resistant NS were more likely to have infection than other types of NS, possibly due to severity of proteinuria or more aggressive immunosuppressive therapy [20]. The role of immunosuppression in increasing infection risk versus the infectious risk of nephrotic syndrome itself is unclear and deserves further

study. Unfortunately, however, immunosuppression history was not recorded in this database and thus could not be directly assessed for any correlation with infection risk.

This study confirms the correlation between infection and VTE in children with NS. Recently, our group identified infection as a statistically significant modifier for likelihood of thrombosis in children with chronic kidney disease (including NS) [21]. There is a complex interplay between the immune system, infectious agents, and the coagulation system which can lead to thrombosis. Exposure of tissue factor due to endothelial damage by infectious agents, microparticle formation, and the development of neutrophil extracellular traps (NETs) have all been linked to VTE [22–24]. Additionally, particular infectious agents have been shown to lead to an increased risk of thrombosis. In particular, staphylococcal infections are common among children and have a known association with thrombotic disease [16, 17]. *S. aureus* may carry virulence factors such as (Panton-Valentine leukocidin [*pvl*]) that are capable of activating the coagulation system and, thus, enhance its propensity to stimulate thromboembolic phenomena [25]. Furthermore, methicillin-resistant *S. aureus* strains are more likely to be *pvl* positive. Other *S. aureus* virulence factors including surface-associated adhesion (sdrD) and fibronectin-binding protein B (fnbB) may also be important in pediatric infection-associated thrombosis [26]. Of note, though *S. pneumoniae* was identified more commonly in the entire cohort with infection, *S. aureus* accounted for 2 of the 3 cases of VTE associated with infection where the pathogen was known, and for 2 of the 11 total patients with VTE. Thus, children with NS and infection, particularly *S. aureus* infection, are at high risk of thrombosis and a high index of suspicion for thrombosis should be maintained. Targeted VTE prophylaxis may be indicated in this subset of patients; however, further prospective studies are required given risks of anticoagulation in children.

Previous studies identified age > 12 years and severity of proteinuria as risk factors for VTE in children with nephrotic syndrome [9]. In the present study, there was no association between age, serum albumin, or urine protein-to-creatinine ratio at the time of admission and VTE (Supplemental Table 2). However, 43% of children did not have urine protein-to-creatinine ratio obtained on admission and this may have influenced the results. Additionally, prior studies included both inpatient and outpatient VTE events and were limited to a few major academic institutions and may not be comparable to the population included in the present manuscript.

Though the overall rate of VTE in this population was low (3%), this is still greater than the rate of patients without NS, and patients with VTE had significantly longer hospitalizations and were more likely to have been admitted to the ICU. We were not able to ascertain from our data whether VTE was the cause of the subjects' ICU admissions. Previous studies of hospital-acquired VTE have identified ICU admission as an independent risk factor for this complication; therefore, we are unable to determine whether the VTE occurred as a consequence of infection associated with NS or due to interventions specific to ICU care [27]. Patients admitted to ICU often have central lines placed and have higher rates of impaired mobility compared to other hospitalized patients, both of which have been shown to be risk factors for hospital-acquired VTE [9]. Central lines should be avoided in children with nephrotic syndrome if possible.

Limitations of our study include its retrospective nature as well as the low number of VTE events recorded. Additionally, we are unable to determine from our data all of the possible risk factors for VTE or infection in this population. Identification of VTE relied on the practitioners' concern for the diagnosis. Prior publications have shown that 35% of otherwise asymptomatic adults and children with nephrotic syndrome may have computed tomography (CT) evidence of pulmonary embolism or renal vein thrombosis [28]. Therefore, some VTE may have been missed in this cohort and the rate thus underestimated. Rates of inherited thrombophilia also were not available for this population. Immunosuppressive intensity and antimicrobial therapy data were not collected, limiting our understanding of how immune status and local antibiograms may alter infection risk. In addition, comprehensive data on the past and current CVC use were not available, limiting our ability to assess the impact of CVC use on VTE risk.

Conclusions

Children with NS who are hospitalized have high rates of infection. In this cohort, the presence of VTE was associated with infection. Both infection and VTE were associated with longer hospitalizations and intensive care unit stays. *S. pneumoniae* remains the most commonly identified bacterial pathogen in children with NS despite contemporary immunization strategies. However, methicillin-sensitive *S. aureus* was identified in 2 of 11 patients with VTE. Research in pediatric nephrotic syndrome should focus not only on immunosuppressive agents to prevent or treat relapses, but also on treatment and prevention of these common complications. Further studies are needed to identify potentially modifiable risk factors that could minimize these complications in this already high-risk population, and to identify which patients may benefit most from prophylactic anticoagulation.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

References

1. Rheault MN, Wei CC, Hains DS, Wang W, Kerlin BA, Smoyer WE (2014) Increasing frequency of acute kidney injury amongst children hospitalized with nephrotic syndrome. Pediatr Nephrol 29: 139–147 [PubMed: 24037143]
2. Gipson DS, Messer KL, Tran CL, Herreshoff EG, Samuel JP, Massengill SF, Song P, Selewski DT (2013) Inpatient health care utilization in the United States among children, adolescents, and young adults with nephrotic syndrome. Am J Kidney Dis 61:910–917 [PubMed: 23434062]
3. McCaffrey J, Lennon R, Webb NJ (2016) The nonimmunosuppressive management of childhood nephrotic syndrome. Pediatr Nephrol 31:1383–1402 [PubMed: 26556028]
4. Kerlin BA, Haworth K, Smoyer WE (2014) Venous thromboembolism in pediatric nephrotic syndrome. Pediatr Nephrol 29:989–997 [PubMed: 23812352]
5. Schlegel N (1997) Thromboembolic risks and complications in nephrotic children. Semin Thromb Hemost 23:271–280 [PubMed: 9255908]
6. Eneman B, Freson K, van den Heuvel L, van Hoyweghen E, Collard L, Vande Walle J, van Geet C, Levtchenko E (2015) Pituitary adenylate cyclase-activating polypeptide deficiency associated with increased platelet count and aggregability in nephrotic syndrome. J Thromb Haemost 13:755–767 [PubMed: 25758343]

7. Eneman B, Levtchenko E, van den Heuvel B, Van Geet C, Freson K (2016) Platelet abnormalities in nephrotic syndrome. Pediatr Nephrol 31:1267–1279 [PubMed: 26267676]
8. Loscalzo J (2013) Venous thrombosis in the nephrotic syndrome. N Engl J Med 368:956–958 [PubMed: 23465106]
9. Kerlin BA, Blatt NB, Fuh B, Zhao S, Lehman A, Blanchong C, Mahan JD, Smoyer WE (2009) Epidemiology and risk factors for thromboembolic complications of childhood nephrotic syndrome: a Midwest Pediatric Nephrology Consortium (MWPNC) study. J Pediatr 155:105–110 110 e101 [PubMed: 19394032]
10. Lilova MI, Velkovski IG, Topalov IB (2000) Thromboembolic complications in children with nephrotic syndrome in Bulgaria (1974–1996). Pediatr Nephrol 15:74–78 [PubMed: 11095017]
11. Matsell DG, Wyatt RJ (1993) The role of I and B in peritonitis associated with the nephrotic syndrome of childhood. Pediatr Res 34:84–88 [PubMed: 8356024]
12. McLean RH, Forsgren A, Bjorksten B, Kim Y, Quie PG, Michael AF (1977) Decreased serum factor B concentration associated with decreased opsonization of Escherichia coli in the idiopathic nephrotic syndrome. Pediatr Res 11:910–916 [PubMed: 407543]
13. Anderson DC, York TL, Rose G, Smith CW (1979) Assessment of serum factor B, serum opsonins, granulocyte chemotaxis, and infection in nephrotic syndrome of children. J Infect Dis 140:1–11 [PubMed: 379244]
14. Tain YL, Lin G, Cher TW (1999) Microbiological spectrum of septicemia and peritonitis in nephrotic children. Pediatr Nephrol 13:835–837 [PubMed: 10603131]
15. Haddy RI, Perry K, Chacko CE, Helton WB, Bowling MG, Looney SW, Buck GE (2005) Comparison of incidence of invasive Streptococcus pneumoniae disease among children before and after introduction of conjugated pneumococcal vaccine. Pediatr Infect Dis J 24:320–323 [PubMed: 15818291]
16. Crary SE, Buchanan GR, Drake CE, Journeycake JM (2006) Venous thrombosis and thromboembolism in children with osteomyelitis. J Pediatr 149:537–541 [PubMed: 17011328]
17. Bouchoucha S, Benghachame F, Trifa M, Saied W, Douira W, Nessib MN, Ghachem MB (2010) Deep venous thrombosis associated with acute hematogenous osteomyelitis in children. Orthop Traumatol Surg Res 96:890–893 [PubMed: 20833120]
18. Rheault MN, Zhang L, Selewski DT, Kallash M, Tran CL, Seamon M, Katsoufis C, Ashoor I, Hernandez J, Supe-Markovina K, D'Alessandri-Silva C, DeJesus-Gonzalez N, Vasylyeva TL, Formeck C, Woll C, Gbadegesin R, Geier P, Devarajan P, Carpenter SL, Kerlin BA, Smoyer WE, Midwest Pediatric Nephrology Consortium (2015) AKI in children hospitalized with nephrotic syndrome. Clin J Am Soc Nephrol 10:2110–2118 [PubMed: 26450933]
19. Robinson CL, Romero JR, Kempe A, Pellegrini C, Advisory Committee on Immunization Practices Child/Adolescent Immunization Work G (2017) Advisory committee on immunization practices recommended immunization schedule for children and adolescents aged 18 years or younger - United States, 2017. MMWR Morb Mortal Wkly Rep 66:134–135 [PubMed: 28182607]
20. Greenbaum LA, Benndorf R, Smoyer WE (2012) Childhood nephrotic syndrome-current and future therapies. Nat Rev Nephrol 8: 445–458 [PubMed: 22688744]
21. Kerlin BA, Smoyer WE, Tsai J, Boulet SL (2015) Healthcare burden of venous thromboembolism in childhood chronic renal diseases. Pediatr Nephrol 30:829–837 [PubMed: 25487668]
22. Date K, Ettelaie C, Maraveyas A (2017) Tissue factor-bearing microparticles and inflammation: a potential mechanism for the development of venous thromboembolism in cancer. J Thromb Haemost 15:2289–2299 [PubMed: 29028284]
23. Long AT, Kenne E, Jung R, Fuchs TA, Renne T (2016) Contact system revisited: an interface between inflammation, coagulation, and innate immunity. J Thromb Haemost 14:427–437 [PubMed: 26707513]
24. Kimball AS, Obi AT, Diaz JA, Henke PK (2016) The emerging role of NETs in venous thrombosis and immunothrombosis. Front Immunol 7:236 [PubMed: 27446071]
25. Martinez-Aguilar G, Avalos-Mishaan A, Hulten K, Hammerman W, Mason EO Jr, Kaplan SL (2004) Community-acquired, methicillin-resistant and methicillin-susceptible Staphylococcus aureus musculoskeletal infections in children. Pediatr Infect Dis J 23: 701–706 [PubMed: 15295218]

26. Carpenter SL, Goldman JL, Sherman AK, Bell JJ, Selvaraju S, Selvarangan R (2012) Staphylococcus aureus virulence factors surface-associated adhesion (sdrD) and fibronectin-binding protein B (fnbB) associated with deep-vein thrombosis in pediatric patients. Am J Hematol 87:S147

27. Mahajerin A, Branchford BR, Amankwah EK, Raffmi L, Chalmers E, van Ommen CH, Goldenberg NA (2015) Hospital-associated venous thromboembolism in pediatrics: a systematic review and meta-analysis of risk factors and risk-assessment models. Haematologica 100:1045–1050 [PubMed: 26001789]

28. Zhang LJ, Zhang Z, Li SJ, Meinel FG, Nance JW Jr, Zhou CS, Zhao YE, Schoepf UJ, Lu GM (2014) Pulmonary embolism and renal vein thrombosis in patients with nephrotic syndrome: prospective evaluation of prevalence and risk factors with CT. Radiology 273: 897–906 [PubMed: 25072187]

Table 1

Demographic and clinical characteristics

	Participants *N* (%)
Sex (*N* = 370)	
Male	227 (61.4%)
Race/ethnicity (*N* =311)	
White	145 (46.6%)
Hispanic	62 (19.9%)
Black	70 (22.5%)
Other	34 (10.9%)
Clinical pattern of NS (*N* = 354)	
Steroid sensitive-infrequently relapsing	104 (29.4%)
Steroid sensitive-frequently relapsing or	146 (41.2%)
steroid dependent	99 (28.0%)
Steroid-resistant	5 (1.4%)
Congenital or infantile	
Biopsy diagnosis (*N* = 370)	
Minimal change disease (± mild mesangial	111 (30.0%)
hypercellularity)	85 (23.0%)
FSGS or FGGS	24 (6.5%)
Membranous, MPGN, others	150 (40.5%)
No biopsy	

FGGS focal global glomerulosclerosis, *FSGS* focal segmental glomerulosclerosis, *MPGN* membranoproliferative glomerulonephritis, *NS* nephrotic syndrome

Table 2

Organisms responsible for infection in children hospitalized with nephrotic syndrome

Infection type	*N* (% of total hospitalizations)
Peritonitis	60 (8.2%)
S. pneumoniae (*N*=11)	
Other[a] (*N*=4)	
No organism identified (*N*=45)	
Pneumonia	50 (6.8%)
Respiratory syncytial virus (*N*= 5)	
Influenza (*N*= 4)	
Human metapneumovirus (*N*= 3)	
Parainfluenza (*N*= 3)	
Mycoplasma pneumoniae (*N*= 2)	
No organism identified (*N*=33)	
Bacteremia/bloodstream	38 (5.2%)
S. pneumoniae (*N*= 22)	
Coagulase negative *Staph* (*N*= 3)	
E. coli (*N*= 3)	
S. aureus (*N*= 2)	
Klebsiella pneumonia (*N*= 2)	
Other[b] (*N*= 6)	
Ear/nose/throat (sinusitis, tonsillitis, etc)	28 (3.8%)
Group A *Strep* (*N*= 2)	
Other[c] (*N*=2)	
No organism identified (*N*= 24)	
GI/gastroenteritis	25 (3.4%)
C. difficile (*N*= 7)	
Other[d] (*N*=2)	
No organism identified (*N*=16)	
Cellulitis/skin infection	21 (2.9%)
Varicella (*N*=2)	
Other[e] (*N*=4)	
No organism identified (*N*=15)	
Urinary tract infection	12 (1.6%)
E. coli (*N*= 6)	
Other[f] (*N*=5)	
No organism identified (*N*=1)	

[a] One each Streptococcus parasanguinis, Staphylococcus epidermidis, Citrobacter freundii, and K. pneumoniae

[b] One each S. parasanguinis, C. freundii, Enterococcus sp., Salmonella type D, Candida parapsilosis, and cytomegalovirus

[c] One each Herpes simplex virus, Candida albicans

[d] One each Campylobacter sp., C. albicans

[e] One each S. aureus, K. pneumoniae, Herpes simplex virus, Acinetobacter sp.

[f] One eachK.pneumoniae, Enterococcus sp., Enterobacter sp., coagulase negative Staph, Chlamydia trachomatis

Table 3

Patients with ≥ 1 infection vs. no infection

	Infection (*N* = 148)	**No infection (*N* = 222)**	***p* value**
Age (years) at first hospitalization (median, IQR)	5.9 years (3.1, 10.5)	6.6 years (3.5, 11.3)	0.008
Sex (*n*, %)			0.486
Male	94 (63.5)	133 (59.9)	
Race/ethnicity (*n*, %)			0.185
White	59 (47.2)	86 (46.2)	
Hispanic	29 (23.2)	33 (17.7)	
Black	21 (16.8)	49 (26.3)	
Other	16(12.8)	18(9.7)	
Clinical pattern of NS (*n*, %)			0.002
Steroid sensitive-infrequently relapsing	29 (19.6)	75 (33.8)	
Steroid sensitive-frequently relapsing	26 (17.6)	32 (14.4)	
Steroid sensitive-steroid dependent	31 (21.0)	57 (25.7)	
Steroid-resistant	53 (35.8)	46 (20.7)	
Congenital or infantile	4 (2.7)	1 (0.5)	
Biopsy diagnosis (*n*, %)			0.441
Minimal change disease (± mild mesangial hypercellularity)	48 (32.4)	63 (28.4)	
FSGS or FGGS	38 (25.7)	47 (21.2)	
Membranous, MPGN, others	9 (6.1)	15 (6.8)	
No biopsy	53 (35.8)	97 (43.7)	
Baseline eGFR ml/min/1.73m^2 (median, IQR)	129.5 (99.0, 173.1)	128.9 (95.0, 166.4)	0.633
Number of hospitalizations (median, IQR)	2 (1,3.5)	1 (1,2)	<0.001
Overall hospital days (median, IQR)	10(6,22)	5 (3,8)	<0.001
ICU days (median, IQR)	0 (0, 0)	0 (0, 0)	<0.001

NS nephrotic syndrome, *eGFR* estimated glomerular filtration rate, *ICU* Intensive Care Unit, *FGGS* focal global glomerulosclerosis, *FSGS* focal segmental glomerulosclerosis, *MPGN* membranoproliferative glomerulonephritis

Table 4

Patients with VTE vs. no VTE

	VTE (*N* =11)	No VTE (*N* = 359)	*p* value
Age in years at first hospitalization (median, IQR)	6.8 (2.6, 10.7)	6.2 (3.4, 10.7)	0.869
Sex (*n*, %)			0.348
Male	5 (45.5)	222 (61.8)	
Race/ethnicity (*n*, %)			0.369
White	6(75)	139 (45.9)	
Hispanic	0 (0)	62 (20.5)	
Black	1 (12.5)	69 (22.8)	
Other	1 (12.5)	33 (10.9)	
Clinical pattern ofNS (*n*, %)			0.842
Steroid sensitive-infrequently relapsing	3 (27.3)	101 (28.1)	
Steroid sensitive-frequently relapsing	2 (18.2)	56(15.6)	
Steroid sensitive-steroid dependent	2 (18.2)	86 (24.0)	
Steroid-resistant	3 (27.3)	96 (26.7)	
Congenital or infantile	0(0)	5 (1.4)	
Biopsy diagnosis (*n*, %)			0.438
Minimal change disease (± mild mesangial hypercellularity)	6 (54.6)	105 (29.3)	
FSGS or FGGS	2 (18.2)	83 (23.1)	
Membranous, MPGN, others	0 (0)	24 (6.7)	
No biopsy	3 (27.3)	137 (41.0)	
Baseline eGFR ml/min/1.73m^2 (median, IQR)	119.2(77.4, 131.5)	129.1 (97.1, 171.9)	0.086
Number of hospitalizations (median, IQR)	2 (1,3)	1 (1,2)	0.412
Overall hospital days	22 (16, 26)	6 (3, 11)	<0.001
ICU days	4 (0, 15)	0 (0, 0)	<0.001
Number of infections	1 (0, 2)	0 (0, 1)	0.046

VTE venous thromboembolism, *NS* nephrotic syndrome, *eGFR* estimated glomerular filtration rate, *ICU* intensive care unit, *FGGS* focal global glomerulosclerosis, *FSGS* focal segmental glomerulosclerosis, *MPGN* membranoproliferative glomerulonephritis