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Childhood Nephrotic Syndrome Management and Outcome in Metro Atlanta

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# Childhood Nephrotic Syndrome Management and Outcomes in Metropolitan Atlanta

By

Chia-shi Wang

M.D., Wake Forest University, 2009

Advisor: Larry Greenbaum, M.D., Ph.D.

An abstract of

A thesis submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University

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Master of Science
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Abstract

Childhood Nephrotic Syndrome Management and Outcomes in Metropolitan Atlanta

By Chia-shi Wang

There is a paucity of information on outpatient management and risk factors for hospitalization and complications in childhood nephrotic syndrome (NS). We described the management, patient adherence, inpatient and outpatient usage, and disease complications of 87 pediatric NS patients diagnosed between 2006 and 2012 in the Atlanta MSA. Multivariable analyses were performed to examine the associations between patient characteristics and disease outcome. On average, patients had 3.7 (2.0) clinic visits per year. Fifty-one percent of the patients were treated with two or more immunosuppressants. Approximately half of the patients were noted to be non-adherent with medications and urine protein monitoring. The majority (71%) of patients were hospitalized at least once, with a median rate of 0.5 hospitalizations per patient year. Mean hospital length of stay was 4.0 (3.8) days. Fourteen percent of patients experienced at least one serious disease complication. Black race, frequently-relapsing/steroid-dependent and steroid-resistant disease, and the first year following diagnosis were associated with higher hospitalization rates. The presence of co-morbidities was associated with longer hospital length of stay and increased risk of serious disease complications. Our results highlight the high morbidity and burden of NS and point to particular patient subgroups that may be at increased risk for poor outcome.

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# TABLE OF CONTENTS

# INTRODUCTION

Idiopathic nephrotic syndrome (NS) is one of the most common chronic kidney diseases in children, with a prevalence of approximately 16 cases per 100,000 (1). NS is characterized by massive proteinuria, leading to hypoalbuminemia, edema, and hyperlipidemia, and can result in serious acute complications such as infections, thromboembolic disease, and acute kidney injury (1-4). Recent research has underscored the marked burden of childhood NS on the healthcare system. A cross-sectional analysis of the Kids' Inpatient Database from the Healthcare Cost and Utilization Project (HCUP-KID) revealed that NS resulted in an estimated 48,700 inpatient days and charges totaling $259 million nationally in the years 2006 and 2009. On average, a single NS hospitalization generated charges of $26,500, compared to $9,100 for asthma, $10,691 for sickle cell vaso-occlusive disease, and $10,817 for inflammatory bowel disease. Furthermore, 16% of the discharges had at least one severe complication, including thromboembolism, septicemia, peritonitis, pneumonia, or diabetes (5). There is a great need to identify risk factors for hospitalization and potential interventions to improve outcome in childhood NS.

We performed a detailed study to assess the relationships between patient clinical and demographic characteristics and disease outcomes. A thorough review of inpatient and outpatient charts for NS patients was conducted at Children's Healthcare of Atlanta, a large academic practice that is the sole provider of pediatric care in the Atlanta MSA. We were able to capture every inpatient and outpatient nephrology encounter, and provide in-depth descriptions of outpatient management and inpatient usage, which had not previously been reported in pediatric NS. Our goal was to determine demographic and clinical factors that are associated with increased inpatient utilization and disease complications in pediatric NS. We hypothesized that patients with steroid-dependent or resistant NS have increased rates of hospitalization, longer hospital length of stay, and higher risk for severe complications, compared to those with steroid-sensitive disease. Our study added to the understanding of influences on NS morbidity.

# BACKGROUND

Nephrotic syndrome (NS) is caused by an alteration in the permselectivity barrier of the glomerular capillary wall, which results in the loss of protein from the bloodstream into the urine(1). Most commonly, the underlying etiology is idiopathic in children, and the condition includes patients with varied disease severity, response to treatment, and histologic findings. The two principal histologic variants of idiopathic NS in children are minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS), with MCD being more common (6). Approximately 95% of patients with MCD achieve remission (defined as urine protein to creatinine ratio (UPCR) <200 mg/g or <1+ of protein on urine dipstick for 3 consecutive days) when treated with corticosteroids, versus only 20% with FSGS (1). Children who do not achieve remission after 8 weeks of initial corticosteroid therapy are considered to have steroid-resistant NS (SRNS) (7).

By definition, all patients present with four key findings: edema, nephrotic range proteinuria (UPCR >2 mg/g), hypoalbuminemia (serum albumin<2.5mg/L), and hyperlipidemia (8). Because the majority of children are expected to have steroid-sensitive NS (SSNS), the current first-line therapy is a prolonged course of high-dose oral corticosteroids. However, 80-90% of the children will experience disease relapse (defined as UPCR ≥2000 mg/g, or ≥ 300 mg/dL or 3+ protein on urine dipstick), with half relapsing frequently or becoming dependent on corticosteroids to maintain remission. Children with two or more relapses within the first 6 months, or four or more relapses in any 12-month period, are considered to have frequently relapsing NS (FRNS). Those who have two or more relapses during tapering of corticosteroid therapy or within 14 days of cessation of therapy are defined as having steroid-dependent NS (SDNS) (8). Approximately 7.4-19.6% of children have SRNS and persist in an active disease state (6, 9, 10).

The high rates of disease relapse and resistance to corticosteroids are significant challenges to NS management. When the disease is active, the loss of protein critical for various biologic functions can result in complications such as infections, acute kidney injury, and thromboembolic events (1-4). Repeated and prolonged use of corticosteroids can have adverse effects on

metabolism, growth, and behavior (8). Second-line immunosuppressive agents, such as calcineurin inhibitors, cytotoxic agents, mycophenolate mofetil, and rituximab are used for those intolerant or resistant to corticosteroids (7, 8). These agents cause additional side effects and have expected response rates of only 20-50% (7). Patients who have treatment-refractory SRNS inevitably progress to end-stage renal disease (ESRD) (1). Most patients require long-term management of the disease and complications of therapy. Home care is a key management component and includes tasks such as urine protein and symptom monitoring, medication administration, dietary restrictions, frequent clinic appointments, and communication with providers between clinic appointments. Despite the complexity of management, few reports exist that describe management patterns. Survey studies have noted significant differences in provider preference for second-line immunosuppressants, glucocorticoid regimens, and when renal biopsies are performed (11, 12). There are no reports on outpatient clinic visit usage, urine dipstick for disease monitoring, and medication adherence.

The morbidity and financial burden of childhood NS is high. FSGS is the second-most common cause of ESRD in the North American Pediatric Renal Transplant Cooperative Study (13). Analysis of the Kids' Inpatient Database from HCUP-KID revealed charges of $259 million in 2006 and 2009 from NS hospitalizations. Sixteen percent of pediatric NS patients had at least one severe complication – thromboembolism, septicemia, peritonitis, pneumonia, or diabetes. Acute kidney injury was noted in 8% of the patients. Risk factors for increased hospitalization charges were patient age 15 years or older, black race, higher socioeconomic status, acute renal failure, thromboembolic disease, hypertension, and infections (5). As this report used a nationwide inpatient database without information on patients not hospitalized, the predictors for hospitalization itself could not be assessed. The prevalence of severe disease complications among those hospitalized is also not likely to be representative of the risk for complications among all patients. Importantly, the lack of critical clinical information, such as steroid response classification, may confound the study findings. For instance, SRNS and FSGS are more prevalent

among older, black, and Hispanic children (1), and thus may explain the association between black race and older age and increased hospitalization charges in the HCUP-KID database. Our study aims to provide an in-depth look at outpatient disease management and risk for inpatient utilization and disease complications.

# METHODS

## Research Goal

Our specific aims and associated hypotheses are as follows:

Aim 1. Describe inpatient and outpatient usage patterns among children with NS in a large, academic pediatric nephrology practice that is the sole provider of pediatric care in the Atlanta Metropolitan Statistical Area (MSA). *We captured the frequency of clinic visits, hospitalizations, and disease complications among children with nephrotic syndrome. We provided detailed information on the medical management of these children and their adherence to treatment.*

Aim 2. Determine demographic and clinical factors that are associated with increased inpatient utilization and disease complications in pediatric NS.

*Hypothesis: Patients with SDNS or SRNS have increased rates of hospitalization, longer hospital length of stay, and higher risk of severe complications compared to those with SSNS.*

## Study Design

A retrospective chart review was performed on pediatric NS patients diagnosed and managed by the Children's Physician Group, Children's Healthcare of Atlanta (CPG-CHOA). Outpatient and inpatient charts for up to 3 years from the time of diagnosis were reviewed. The Division of Pediatric Nephrology at CPG-CHOA includes all the pediatric nephrologists practicing in the Atlanta MSA, and the three campuses of CHOA are the only pediatric hospitals within the Atlanta MSA. We were thus able to capture all renal outpatient encounters and all inpatient encounters.

## Study Population

We screened patients followed by the Division of Pediatric Nephrology at CPG-CHOA for the diagnosis of NS by using *International Classifications of Diseases, Ninth Revision, Clinical Modification* (ICD-9 CM) diagnostic codes 581.3, 581.9, and 582.1. A single pediatric nephrologist (Chia-shi Wang, MD) reviewed each patient's demographic, clinical, laboratory, and histologic information for inclusion and exclusion.

Inclusion criteria:

a. Age >1 and <18 years of age at the onset of NS.
b. Diagnosis of NS with documented laboratory and physician exam criteria: edema, nephrotic range proteinuria (urine protein/creatinine ratio > 2mg/mg), and hypoalbuminemia (<2.5mg/L).
c. Home address within the Atlanta MSA at time of diagnosis and during the entire period of follow-up.
d. NS diagnosis made between 1/1/2006 and 1/1/2012 by the Division of Pediatric Nephrology of CPG-CHOA.

Exclusion criteria:

a. Renal biopsy findings other than MCD, FSGS, or a variant (mesangial proliferation, IgM deposits, C1q deposits).
b. Secondary causes of NS (e.g., systemic lupus erythematosus).

**Measurements**

Clinical, demographic, and outpatient care adherence characteristics were collected from outpatient records. Variables of interest included: sex, age at time of diagnosis, race, ethnicity, insurance type at time of diagnosis, renal histopathology (if biopsy performed), presence of co-morbid disease at time of diagnosis (epilepsy, congenital heart disease, inflammatory bowel disease, chronic lung disease, asthma/airway reactive disease, prematurity, or other), NS disease status (SSNS, FRNS/SDNS, or SRNS), and use of second-line immunosuppressive agents (mycophenolate, tacrolimus, etc.). NS disease status is classified based on the definitions put forth by Kidney Disease, Improving Global Outcomes (8). Patients are classified as having SRNS if they fail to achieve remission after eight weeks of corticosteroid therapy. For patients who achieve remission within 8 weeks of corticosteroid therapy—the disease is classified as FRNS if there are two or more relapses within 6 months of initial response or four or more relapses in any 12-month period; SDNS if there are two consecutive relapses during corticosteroid taper, or within 14 days

of ceasing therapy; otherwise, the disease is classified as SSNS. The classification is made based on the clinical response to corticosteroids in the first 3 years following diagnosis.

The numbers of completed and missed clinic appointments were recorded. Percent "no-show" was the number of missed appointments divided by the total number of clinic appointments. Assessment of adherence to home urine protein monitoring and medications were based on the documentation of treating physicians who subjectively noted good or poor adherence.

Inpatient records for up to 3 years from time of diagnosis were reviewed. Each hospitalization was reviewed by a single investigator (CW) for its relationship to NS. Only hospitalizations indicated for the management of NS complications or treatment side-effects were included. The number of hospitalizations, length of stay (LOS), intensive care unit (ICU) status, and serious complications were recorded. A serious complication was defined as one of the following: bacterial peritonitis (with or without culture confirmation), septicemia, shock, blood clot(s) (radiologically confirmed), acute kidney injury requiring dialysis, or seizures from hyponatremia or hypertension. Edema, asymptomatic electrolyte abnormalities, and asymptomatic hypertension were not considered serious complications. Disease complications were recorded for each patient if they were the reasons for hospitalization or if they occurred during hospitalization.

**Sample Size and Power Considerations**

There are no data on the risk of hospitalization among children with NS, the primary outcome of interest. Assuming that 50% of children with SSNS will be hospitalized, we estimated that we would need 39 patients in each disease classification (SSNS, FRNS/SDNS, SRNS) to have 80% power to detect a 60% increase in the risk of hospitalization comparing SSNS to either of the two disease groups, with a significance level of 0.05.

**Analysis**

Demographic and clinical characteristics were described by number of patients and percentages. These variables include: sex, age at diagnosis, race/ethnicity, insurance type, renal histopathology, NS disease status, presence of any co-morbid condition, NS medications, year since

diagnosis, and adherence. Demographic and clinical characteristics were described by number of patients and percentages. The number of occurrences and percentage of patients were computed for hospitalizations and serious disease complications. Mean and standard deviation or median and interquartile range, where appropriate, were computed for number of outpatient clinic visits, number of clinic appointment "no-shows," hospitalizations, and length of stay (LOS). Results of the descriptive analyses are displayed in table format.

Associations of clinical and demographic factors with the number of hospitalizations per year were assessed with Poisson regression. We applied generalized estimating equations to the Poisson distribution to account for correlated data from the same patient. Independent variables were considered for the model based on known associations to disease morbidity. The variables included were age, sex, race/ethnicity, insurance status, disease status, presence of any co-morbid condition, and year since diagnosis. Renal histopathology was not included in the model as a large number of patients did not undergo biopsy. Adherence and use of second-line immunosuppressants variables were not included in the model due to difficulty delineating the causal pathway – i.e. whether adherence/medications influences the risk of hospitalizations or whether hospitalizations influence the likelihood of adherence to therapy/medications prescribed. Parameter estimates from the model were exponentiated to produce rate ratios.

Associations of clinical and demographic factors with the development of severe disease complications in patients over 3 years of follow-up was assessed with logistic regression. Independent variables included in the model were determined a priori based on clinical significance, and included age, sex, race/ethnicity, insurance, disease status, and presence of any co-morbid condition. Model fit was assessed by the Hosmer-Lemeshow test.

Linearity of the continuous outcome variable LOS in days per hospitalization was assessed graphically and by skewness and kurtosis measures. Logarithmic transformation of LOS was carried out due to high skewness. Associations between the clinical and demographic factors with

LOS were assessed with linear regression. Parameter estimates were then back-transformed to the linear scale to produce mean proportional change in LOS associated with the exposure.

Significance level for tests of association was set at 0.05. Statistical analysis was performed using the SAS system, version 9.4 (SAS Institute, Cary, NC).

# RESULTS

## Patient Characteristics

A total of 87 patients were included. All had complete inpatient and outpatient records for 1 year following diagnosis. Eight-two patients (94%) had complete records for 2 years, and 80 patients (92%) had complete records for 3 years. Reasons for lacking year 2 and year 3 records were discharge from clinic (2 out of 87, 2%) and lost to follow-up (5 out of 87, 6%). Clinical and demographic characteristics for the total cohort and for each disease class are shown in Table 1. The majority of patients had FRNS/SDNS. Patient with SRNS tended to be older and had a more equal male to female ratio compared to those with SSNS and FRNS/SDNS. The majority of SRNS patients were also black, in contrast to patients with SSNS and FRNS/SDNS. A greater proportion of SRNS patients underwent renal biopsy.

## Outpatient Management

Patients had an overall mean (SD) of 3.7 (2.0) clinic visits per year, with a mean of 5.0 (2.0) visits in the first year, 3.0 (1.6) visits in the second year, and 2.8 (1.6) visits in the third year. Forty-four patients (51%) were treated with at least one immunosuppressive agent in addition to corticosteroids. The most common treatment prescribed was mycophenolate mofetil (30 out of 87 patients, 34%), followed by cyclophosphamide (9 patients, 10%), tacrolimus (8 patients, 9%), and cyclosporine (8 patients, 9%).

Only 39 out of 71 patients (55%) who were prescribed urine dipsticks for home monitoring were adherent. The rest were subjectively noted by their treating physicians to be nonadherent with urine protein monitoring. Thirty-seven out of 87 (43%) patients were subjectively noted by their treating physicians to be poorly adherent to prescribed NS medications. Mean percentage of “no-shows” was 14% (22), with a mean of 11% (16) in the first year, 15% (24) in the second year, and 19% (25) in the third year.

## Inpatient Care Utilization

A total of 184 hospitalizations relating to the management of NS complications or treatment side-effects were recorded for the 87 patients. Median hospitalization rate was 0.5 hospitalization per patient year (interquartile range = 0.0 to 1.0). Sixty-two patients (71%) had at least one hospitalization, and 13 patients (15%) had 5 or more hospitalizations in the first 3 years following diagnosis. The mean (SD) LOS per hospitalization was 4.0 (3.8) days.

**Complications**

Four out of 184 hospitalizations (2%) resulted in an ICU stay. Twelve of the 87 (14%) patients experienced serious complications in the first 3 years of disease. Eight patients (9%) experienced bacterial peritonitis, 4 patients (4.6%) experienced septicemia or shock, 2 (2%) experienced blood clots, 1 patient (1%) required renal replacement therapy for acute kidney injury, and 1 patient (1%) developed seizures from hypertension.

**Predictors for NS Morbidity**

HOSPITALIZATION

Our multivariable analysis showed that FRNS/SDNS and SRNS were associated with >4-times higher rates of hospitalization (rate ratio (RR) = 4.43, 95% confidence interval (CI) = 2.74 to 7.15; and RR = 4.14, CI = 1.64 to 10.44; respectively), relative to SSNS. Black race was also significantly associated with increased hospitalization rates (RR =1.84, CI = 1.04 to 3.25), compared to white race. The hospitalization rates were lower in the second and third year of disease, compared to the first year (RR = 0.35, CI = 0.25 to 0.51; and RR = 0.26, CI = 0.16 to 0.41; respectively). Age at diagnosis, sex, insurance status, and presence of co-morbidities were not significantly associated with the hospitalization rate in this analysis. The results of the analysis are presented in Table 2.

LENGTH OF STAY

Multivariable analysis of LOS results is presented in Table 3. The presence of co-morbidities and severe disease complications were associated with higher LOS (mean increase of 42% (CI = 5% to 93%) and 43% (CI = 6% to 92%), respectively). On average, hospital LOS for black patients

was 28% shorter than for white patients (CI = 0.52 to 1.00). Age at diagnosis, sex, insurance status, and disease status were not significantly associated with LOS in this analysis.

SERIOUS COMPLICATIONS

Only the presence of co-morbidities was found to be associated with the risk of serious complications (OR = 5.36, CI = 1.26 to 22.87). Age at diagnosis, sex, race and ethnicity, insurance status, and disease status were not found to be significantly associated with serious complications. The results of the regression analysis are presented in Table 4.

## DISCUSSION

Our findings support previous published reports that childhood NS is a disease of high morbidity and results in significant healthcare burden. The average NS-related hospitalization rate of our cohort was high, at 0.74 hospitalizations per patient year, and the majority of patients were hospitalized at least once (71%). Serious complications occurred in 14% of the patients in the first 3 years of follow-up. These results suggest that each NS patient has the potential to contribute significant burden to the healthcare system.

Outpatient management of our patient cohort was also resource-intensive. Clinic visits averaged 3.7 per year in the first 3 years of diagnosis. More than half of the patients were treated with second-line immunosuppressants in addition to corticosteroids, carrying additional monitoring needs. Significantly, providers noted nonadherence to urine monitoring and medications in nearly half of the patients. Furthermore, the rates of "no-shows" to appointments were high at an average of 14%. This is a serious concern as nonadherence is a major cause of treatment failure in pediatric chronic diseases (14).

We hypothesized that disease classification based on steroid response and frequency of relapse would be a predictor of increased hospitalizations, length of stay, and complications, as it is an important determinant of disease prognosis (1). This was substantiated in our analysis on hospitalizations. FRNS/SDNS and SRNS were associated with increased hospitalization rates compared to children with SSNS. Patients were hospitalized more frequently in the first year of diagnosis. Black race was also found to be associated with increased hospitalization rates despite controlling for disease status and other clinical and demographic factors. This suggests that there are other social, economic, or provider/patient factors not captured by our analysis. Disease classification was not associated with increased risk of serious complications as we had hypothesized. It may be possible that our sample size and the number of serious complications were too small to detect a significant difference. Similar to analyses of the HCUP-KID data (5, 15), serious NS complications were associated with longer hospitalizations. In our analysis, black

patients had shorter hospitalizations compared to white patients. This again suggests the need to explore determinants of health and disease management that result in racial differences. The presence of any co-morbid condition, not surprisingly, was significantly associated with increased LOS and development of serious complications. Interestingly, patients with FRNS/SDND and SRNS did not have longer hospitalizations compared to those with SSNS in our analysis, though they were hospitalized more frequently.

Our study provided a detailed description of inpatient and outpatient care usage in children with NS. The strengths of our single center analysis include the ability to accurately define a cohort of incident patients with idiopathic NS and capture all instances of disease complications without relying on ICD-9 CM diagnostic codes. We were able to report for the first time hospitalization rates, outpatient clinic visit rates, frequency of various immunosuppressant usage, and adherence in children with NS. We were also able to study the influence of NS disease classification on outcomes.

As a single center report, our findings on management patterns may have limited generalizability to other regions. Due to the restrictive inclusion and exclusion criteria with respect to patient address, our sample size is small. This may have affected the validity of our multivariable analyses and reduced our ability to detect significant associations. In addition, as a retrospective study, we were unable to obtain objective measures for medication and urine monitoring adherence or delineate the causal pathway between adherence and NS disease outcome, a variable we suspect to be crucial in chronic disease outcome. Lastly, the duration of follow-up for our cohort is relatively short. Thus, we did not assess rates of important complications such as end-stage renal disease.

In conclusion, our study examined NS disease management and inpatient and outpatient usage, and described the associations between clinical and demographic characteristics and disease outcome. Our results suggest that patients with FRNS/SDNS and SSN with other co-morbidities

are a vulnerable group. Multicenter, prospective studies would enhance our understanding of how outpatient management and adherence patterns of NS patients influence outcome.

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TABLES/FIGURES

Table 1. Characteristics of Patients with Childhood Nephrotic Syndrome Diagnosed between 2006 and 2012 in the Atlanta MSA

| Characteristic | SSNS (n=23) | FRNS/SDNS (n=48) | SRNS (n=16) | Total (n=87) |
|---|---|---|---|---|
| Sex | | | | |
| Male | 17 (74) | 32 (67) | 9 (56) | 58 (67) |
| Female | 6 (26) | 16 (33) | 7 (44) | 29 (33) |
| Age at diagnosis | | | | |
| 1 - 5 years | 17 (74) | 27 (56) | 3 (19) | 47 (54) |
| 6 - 12 years | 6 (26) | 15 (31) | 5 (31) | 26 (30) |
| 13 - 18 years | 0 (0) | 6 (13) | 8 (50) | 14 (16) |
| Race and ethnicity | | | | |
| White, non-Hispanic | 6 (26) | 15 (31) | 2 (13) | 23 (26) |
| Black | 7 (30) | 19 (40) | 13 (81) | 39 (45) |
| White, Hispanic | 4 (17) | 9 (19) | 1 (6) | 14 (16) |
| Other | 6 (26) | 5 (10) | 0 (0) | 11 (13) |
| Insurance | | | | |
| Private | 11 (48) | 22 (46) | 6 (38) | 39 (45) |
| Medicaid | 11 (48) | 23 (48) | 8 (50) | 42 (48) |
| None | 1 (4) | 3 (6) | 2 (13) | 6 (7) |
| Histopathology | | | | |
| No biopsy | 22 (96) | 27 (56) | 2 (13) | 51 (59) |
| MCD | 0 (0) | 17 (35) | 5 (31) | 22 (25) |
| FSGS | 1 (4) | 1 (2) | 6 (38) | 8 (9) |
| Other | 0 (0) | 3 6) | 3 (19) | 6 (8) |
| Co-morbidity | | | | |
| None | 19 (83) | 40 (83) | 11 (69) | 70 (80) |
| Asthma | 3 (13) | 7 (15) | 1 (6) | 11 (13) |
| Epilepsy | 1 (4) | 0 (0) | 2 (13) | 3 (3) |
| Inflammatory Bowel Disease | 0 (0) | 1 (2) | 1 (6) | 2 (2) |
| Prematurity | 0 (0) | 2 (4) | 0 (0) | 2 (2) |
| Other | 1 (4) | 1 (2) | 1 (6) | 3 (3) |

Data are presented as the number of patients with the percentage in parenthesis.

Abbreviations: FRNS, frequently relapsing nephrotic syndrome; IV, intravenous; MCD, minimal change disease; FSGS, focal segmental glomerulosclerosis; SDNS, steroid-dependent nephrotic syndrome; SRNS, steroid-resistant nephrotic syndrome; SSNS, steroid-sensitive nephrotic syndrome.

Table 2. Association between Patient Characteristics and Hospitalization Rate

| Variables | | Adjusted RR (95% CI) | *P value* |
|---|---|---|---|
| Age | 1 - 5 years | 1.00 (referent) | |
| | 6 - 12 years | 1.10 (0.63 to 1.91) | 0.74 |
| | 13 - 18 years | 1.11 (0.52 to 2.36) | 0.79 |
| Sex | Male | 1.00 (referent) | |
| | Female | 0.82 (0.55 to 1.23) | 0.34 |
| Race and Ethnicity | White, non-Hispanic | 1.00 (referent) | |
| | Black | 1.84 (1.04 to 3.25) | 0.04* |
| | White, Hispanic | 1.41 (0.65 to 3.07) | 0.38 |
| | Other | 1.11 (0.56 to 2.21) | 0.76 |
| Insurance | None | 1.0 (referent) | |
| | Medicaid | 1.15 (0.59 to 2.23) | 0.67 |
| | Private | 0.74 (0.36 to 1.57) | 0.45 |
| Disease Status | SSNS | 1.00 (referent) | |
| | FRNS/SDNS | 4.43 (2.74 to 7.15) | <0.001* |
| | SRNS | 4.14 (1.64 to 10.44) | 0.003* |
| Presence of Any Co-morbid Condition | No | 1.00 (referent) | |
| | Yes | 1.33 (0.75 to 2.37) | 0.33 |
| Year Since Diagnosis | 1 | 1.00 (referent) | |
| | 2 | 0.35 (0.24 to 0.51) | <0.001* |
| | 3 | 0.26 (0.16 to 0.41) | <0.001* |

Abbreviations: CI, confidence interval; FRNS, frequently relapsing nephrotic syndrome; RR, rate ratio; SDNS, steroid-dependent nephrotic syndrome; SRNS, steroid-resistant nephrotic syndrome; SSNS, steroid-sensitive nephrotic syndrome.
*$p < 0.05$

Table 3. Association between Patient Characteristics and Length of Stay among Hospitalized Patients

| Variables | | Adjusted e^β estimate (95% CI) | *P value* |
|---|---|---|---|
| Age | 1 - 5 years | 1.00 (referent) | |
| | 6 - 12 years | 1.21 (0.89 to 1.65) | 0.21 |
| | 13 - 18 years | 1.24 (0.88 to 1.75) | 0.21 |
| Sex | Male | 1.00 (referent) | |
| | Female | 1.11 (0.86 to 1.43) | 0.41 |
| Race and Ethnicity | White, non-Hispanic | 1.00 (referent) | |
| | Black | 0.72 (0.52 to 1.00) | 0.05* |
| | White, Hispanic | 0.76 (0.51 to 1.14) | 0.18 |
| | Other | 0.61 (0.37 to 1.01) | 0.06 |
| Insurance | None | 1.00 (referent) | |
| | Medicaid | 0.83 (0.53 to 1.30) | 0.41 |
| | Commercial | 0.74 (0.46 to 1.19) | 0.21 |
| Disease Status | SSNS | 1.00 (referent) | |
| | FRNS/SDNS | 0.81 (0.59 to 1.12) | 0.20 |
| | SRNS | 0.87 (0.58 to 1.29) | 0.47 |
| Co-morbidity | No | 1.00 (referent) | |
| | Yes | 1.42 (1.05 to 1.93) | 0.03* |
| Complications | No | 1.00 (referent) | |
| | Yes | 1.43 (1.06 to 1.92) | 0.02* |

Abbreviations: CI, confidence interval; FRNS, frequently relapsing nephrotic syndrome; SDNS, steroid-dependent nephrotic syndrome; SRNS, steroid-resistant nephrotic syndrome; SSNS, steroid-sensitive nephrotic syndrome.

*$p < 0.05$

Table 4. Association between Patient Characteristics and Serious Complications in the First 3 Years Following Diagnosis

| Variables | | Adjusted OR (95% CI) | *P value* |
|---|---|---|---|
| Age | 1 - 5 years | 1.00 (referent) | |
| | 6 - 12 years | 0.64 (0.11 to 3.75) | 0.62 |
| | 13 - 18 years | 1.42 (0.19 to 10.65) | 0.74 |
| Sex | Male | 1.00 (referent) | |
| | Female | 0.83 (0.18 to 3.86) | 0.81 |
| Race and Ethnicity | White, non-Hispanic | 1.00 (referent) | |
| | Black | 1.90 (0.30 to 12.19) | 0.50 |
| | White, Hispanic | 0.97 (0.06 to 14.89) | 0.98 |
| | Other | 1.36 (0.09 to 21.12) | 0.83 |
| Insurance | None | 1.00 (referent) | |
| | Medicaid | 0.31 (0.03 to 2.99) | 0.31 |
| | Commercial | 0.29 (0.03 to 3.01) | 0.30 |
| Disease Status | SSNS | 1.00 (referent) | |
| | FRNS/SDNS | 1.81 (0.30 to 10.87) | 0.52 |
| | SRNS | 1.17 (0.10 to 13.89) | 0.90 |
| Co-morbidity | No | 1.00 (referent) | |
| | Yes | 5.36 (1.26 to 22.87) | 0.02* |

Abbreviations: CI, confidence interval; FRNS, frequently relapsing nephrotic syndrome; SDNS, steroid-dependent nephrotic syndrome; SRNS, steroid-resistant nephrotic syndrome; SSNS, steroid-sensitive nephrotic syndrome.
*$p < 0.05$