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Original Research Paper

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OUTCOME OF STEROID TREATMENT ON PEDIATRIC PATIENTS OF NEPHROTIC SYNDROME: AN OBSERVATIONAL STUDY FROM PATNA MEDICAL COLLEGE & HOSPITAL, BIHAR.

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ABSTRACT Nephrotic syndrome (NS) is a common glomerular disease in children characterized by proteinuria(≥40 mg/m^2/hr or urine protein/creatinine ratio ≥200 mg/mmol or ≥3+ protein on urine dipstick), hypoalbuminemia (<2.5gm/dl), generalized edema and hypercholesterolemia (> 200mg/dl). **Methodology:** A cross-sectional observational study was planned and executed by Department of Pediatrics, Patna Medical College & Hospital. The study sample constituted of 165 children and adolescent patients who were selected from patients attending clinic of Department of Pediatric Medicine with various spectrum of manifestation due to nephrotic syndrome, based on inclusion and exclusion criteria. The study was extended from August 2016 to January 2018 for a period of 18 months. **Results:** During the study period, a total of 165 pediatric patients treated for NS were identified of which 6 were excluded due to incomplete data on their medical records. Thus, this study included a total of 159 children treated for NS. The majority of children were boys 104 (65.4%), between the age of 4–8 years 76 (47.8%) mean age being 5.21 ± 2.66 years, and have +3 proteinuria 124 (78%) at initial diagnosis. Regarding the associated comorbidities, about half 76 (47.8%) had infections, 25 (15.7%) had reduced GFR, 68 (42.8%) had hematuria, and 32 (20.1%) patients were found with other comorbid diseases. **Conclusions:** Besides, steroid-related toxicities were higher among children with NS, the common adverse effects being hyperglycemia, elevated BP, and moon face. The independent factors predicting FR/SD NS were early age (≤6) at diagnosis, low serum albumin, presence of infection, hematuria, and acute renal failure at initial diagnosis, and lack of remission within 2 weeks.

KEYWORDS : Nephrotic Syndrome, Outcome Of Steroid Treatment

INTRODUCTION

Nephrotic syndrome (NS) is a common glomerular disease in children characterized by proteinuria(≥40 mg/m^2/hr or urine protein/creatinine ratio ≥200 mg/mmol or ≥3+ protein on urine dipstick), hypoalbuminemia (<2.5gm/dl), generalized edema and hypercholesterolemia (> 200mg/dl).[1, 2] It is one of the common childhood kidney diseases which affects up to 16 in 100,000 children.[3, 4]However, there is substantial variability in the incidence of NS with ethnic background and geographical location.[5]A study in the United States indicated that there is a higher incidence of NS in African children.[6]

The majority of the pediatrics NS patients present with idiopathic minimal change nephrotic syndrome (MCNS), which has a favorable response to treatment.[7] Over 80–90% of MCNS patients are steroid-sensitive and respond to standard prednisolone therapy with complete resolution of proteinuria. However, most patients tend to relapse, and around 50% become frequent relapsing and/or steroid-dependent (FR/SD NS). Patients developing FR/SD NS require prolonged treatment that leads to toxicity, systemic infections, and other complications. [8, 9, 10]The common complications experienced with prolonged steroid treatment were cushingoid features, hypertension, hyperlipidemia, hyperglycemia, serious infections, growth retardation, stunted growth, osteopenia, and overall poor quality of life. [9,11]

Corticosteroids remained the first-line standard treatment for NS to achieve complete remission.[10]Despite the high rate of initial remission to corticosteroids therapy, relapses are common leading to increased morbidity and cost of treatment.[7] There is a wide inter-individual variation in the clinical course, treatment response, and treatment side effects among pediatrics, which makes it difficult to predict the treatment outcome.[10] Black children respond poorly to corticosteroid and other immunosuppressive treatment and have a higher mortality rate.[12]

Studies identified different factors to be associated with FR/SD NS, which is an indicator of poor treatment outcome. The presence of hematuria, time taken to respond during initial therapy, and duration of steroid therapy were associated with higher FR/SD NS.[13, 14]Also, time to first relapse and inadequate initial therapy were reported as predictors of developing FR/SD NS disease course. [9]Patients with frequently relapsing nephrotic syndrome have treatment options that include extended dosing of glucocorticoids, cytotoxic agents, mycophenolate mofetil, or calcineurin inhibitors.[1]

METHODOLOGY

Study type & design: A cross-sectional observational study was planned and executed by Department of Pediatrics, Patna Medical College & Hospital.

Study sample: The study sample constituted of 165 children and adolescent patients who were selectedfrom patients attending clinic of Department of Pediatric Medicine with various spectrum of manifestation due to nephrotic syndrome, based on inclusion and exclusion criteria.

Study period: The study was extended from August 2016 to January 2018 for a period of 18 months.

Ethical issues: An ethical clearance from the Institutional Ethics Committee, was obtained before starting the study. Written consent was obtained from parents of all patients before including them in the study.

Inclusion criteria: Patients of < 18 years who have been diagnosed and treated for NS during the study period, and with the complete data on the medical record. The pediatric patients who met diagnostic criteria of NS; proteinuria (≥40 mg/m2/hr or urine protein/creatinine ratio ≥ 200 mg/mmol or ≥3+ protein on urine dipstick), hypoalbuminemia (<2.5gm/dl), generalized edema and hypercholesterolemia (> 200mg/dl) and treated with steroid were included.

Exclusion criteria: The medical records with incomplete data (lacking proteinuria, dosage of steroid and treatment outcomes) and those who did not give consent were excluded.

Study variables: The dependent variable for this study was the treatment outcome of pediatric NS patients to steroid therapy. The treatment outcomes include achieving remission within 4 weeks of therapy, occurrence of relapse and side effects from steroid therapy. The independent variables include the demographic variables (age, sex); treatment, and disease-related variables such as duration of treatment, presence of complications, number of relapse/ hospitalizations, and length of hospital stay, time to the first relapse from remission, baseline clinical presentation, time to remission, duration of treatment, frequency of administration, and presence of baseline complications (hypertension, diabetes mellitus, thrombosis). Also, baseline laboratory findings like serum creatinine, triglyceride, total cholesterol were considered as independent variables.

Data collection: The pilot-tested structured data abstraction form was used to collect relevant data from all medical records identified. The data abstraction form included the demographic characteristics (age and gender), clinical information, the number of drugs prescribed, the duration of therapy, and the treatment outcome. The medical records were identified by swotting the patient registration book and retrieving the chart using the medical record number for NS patients admitted during the study period. Four data collectors were recruited among clinical pharmacists who are working in hospitals. The data collectors have been trained for 1 day on the objective of the study and how to properly use the data abstraction form to collect the required data from medical records. The primary investigator daily checks the completeness and correctness of collected data to ensure its quality.

Statistical analysis: All the accumulated data was analyzed by the help of Social Package for Social Sciences by IBM (Ver 20). Simple descriptive statistics such as frequencies, proportions, and percentages were used to describe the demographic and clinical characteristics of participants. Univariate logistic regression statistical tests were performed to identify the independent associations and predictors of treatment outcome. At a 95% confidence interval, $p<0.05\%$ was considered statistically significant in all tests.

RESULTS

Socio-demographic

During the study period, a total of 165 pediatric patients treated for NS were identified of which 6 were excluded due to incomplete data on their medical records. Thus, this study included a total of 159 children treated for NS. The majority of children were boys 104 (65.4%), between the age of 4–8 years 76 (47.8%) mean age being 5.21 ± 2.66 years, and have +3 proteinuria 124 (78%) at initial diagnosis. Regarding the associated comorbidities, about half 76 (47.8%) had infections, 25 (15.7%) had reduced GFR, 68 (42.8%) had hematuria, and 32 (20.1%) patients were found with other comorbid diseases. (Table 1)

Table 1: Demographic characteristics of NS pediatric patients at initial diagnosis

Characteristics	Number (%)
Gender	
Male	104 (65.4)
Female	55 (34.6)
Age at diagnosis (in years)	
1-4	68 (42.8)
4-8	76 (47.8)
8-15	15 (9.4)
Urine protein	
+3	124 (78.0)
+4	35 (22.0)
Hematuria	
Yes	68 (42.8)
No	91 (57.2)
Duration of treatment	
12 weeks	131 (82.4)
8 weeks	28 (17.6)
Frequency of drug administration	
Once daily	29 (18.2)
Twice daily	130 (81.8)
Comorbid condition	
Present	32 (20.1)
Absent	127 (79.9)
Acute renal failure	
Yes	25 (15.7)
No	134 (84.3)
Infection	
Present	79 (49.7)
Absent	80 (50.3)

Clinical characteristics

The mean baseline serum triglyceride, total cholesterol, serum creatine, and albumin were 162.92 (±44.79 SD), 252.75 (± 57.05 SD), 0.66 (±0.25SD), and 2.03 (±0.46SD), respectively. The length of hospital stay for the patients ranges from 5 to 35 days with an average of 13.37 days.

Table 2: Laboratory findings of pediatric NS patients included in the study

Lab variables	Minimum	Maximum	Mean, SD
Random blood glucose	56	158	85.6, 16.9
Total cholesterol	138	472	252.7, 57.1
Serum Triglycerides	103	659	162.9, 44.8
Serum albumin	1.2	3.2	2.1, 0.5
Serum creatinine	0.2	1.5	0.7, 0.3

Outcome of patients to standard course of steroid therapy

Among the study participants, a total of 150 (94.3%) NS pediatric patients achieved remission in 4 weeks of therapy and 9 (5.7%) did not respond at all. More than half 80 (53.3%) the remission occurred within 2 weeks of steroid therapy. However, only 33 (20.8%) patients remained steroid-sensitive throughout the follow-up period. About three-fourths (117 [73.6%]) of patients relapse after achieving remission; 52 (32.7%) patients develop infrequent relapse and 65 (40.9%) patients had FR/SD NS. (Figure 1)

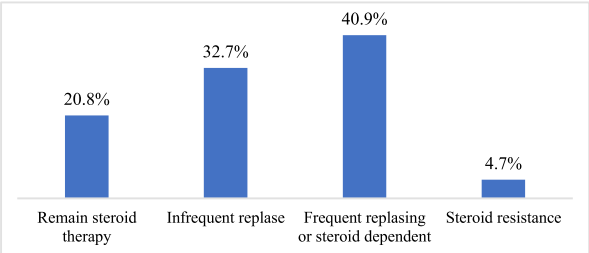

Figure 1: Bar diagram showing the response of steroid treatment response among children treated for NS

Factors influencing prognosis

On running the test of association of outcome variables with various independent factors, age (p 0.06), presence of hematuria (p <0.00), infection (<0.00), acute renal failure (0.01), time for initial remission (<0.00), and low serum albumin (0.01) were found to be significantly altering the outcome of steroid therapy.

DISCUSSION

This study has determined the treatment outcome of the pediatric nephrotic syndrome patients with steroids in two hospitals located in Tigray, Ethiopia. Accordingly, 94.3% of the participants achieved remission within 4 weeks of steroid therapy, among which 50.3% achieved remission within 2 weeks of treatment. This finding is similar to the 90–95% rate of response to steroid therapy in minimal change NS children. [7, 15, 16] Achieving remissions with steroid therapy in 8 weeks is

predictive of MCNS3 suggesting most of our participants had MCNS. The possible reason for this variation could be the difference among the study participants, age at diagnosis, ethnicity, or presence of complication at diagnosis. For instance, the mean age of our study participants was 5.21 years whereas the mean ages of participants were 5.3 and 7.9 years in studies by Bakhiet et al [17] and Asinobi et al [18] respectively.

Despite a good response rate with initial steroid therapy, our study found 73.6% relapse among the initial responders. Patients that encounter frequent relapses and/or steroid dependence indicate unfavorable features suggesting poor prognosis.1 Among our study participants, 40.9% of patients had FR/SD NS disease course.Steroid-resistant NS is difficult to treat with 36–50% of the patients progress to end-stage renal disease. In this study, 5.7% of the patients were resistant to steroid therapy throughout the follow-up period.Our study revealed that the predictors for FR/SD NS with steroid therapy were younger age (≤6 years) at initial diagnosis (p=0.00), presence of hematuria (p=0.00), infection (p=0.01), acute renal failure (p=0.01), serum albumin below 1.5g/dl (p=0.01) at diagnosis and lack of remission within 2 weeks (p=0.0) of therapy.

CONCLUSIONS:

Most of the pediatric NS patients treated have achieved remission with initial to steroid therapy. However, there was a higher relapse rate among pediatric NS patients who achieved remission. Besides, steroid-related toxicities were higher among children with NS, the common adverse effects being hyperglycemia, elevated BP, and moon face. The independent factors predicting FR/SD NS were early age (≤6) at diagnosis, low serum albumin, presence of infection, hematuria, and acute renal failure at initial diagnosis, and lack of remission within 2 weeks.

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Conflict of interest: None declared by any of the authors

Ethical issues: All the aspects were duly considered and taken care of

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