Original Research Article

Demographic Profile of Children with First Attack Idiopathic Nephrotic Syndrome with Relapse- A Hospital-Based Observational Study

ABSTRACT

Background: *Idiopathic nephrotic syndrome (INS) is a common childhood illness with or without relapses. So, it is very important to find out such children who are prone to develop frequent relapse and the demographic characteristics responsible for relapse. This retrospective study was conducted in the Department of Pediatric Nephrology, Bangabandhu Sheikh Mujib Medical University, from September 2016 to August 2017.*

Methods: *A total of 75 patients of idiopathic nephrotic syndrome (INS) with the initial attack, aged 1–18 years, were enrolled in this study. All patients were treated with prednisolone 60 mg/m2/day, single morning dose for 6 weeks, followed by 40 mg/m2 every alternate day for another 6 weeks and were analyzed and followed up for a minimum period of six months to identify the risk factors related to relapses.*

Result: *Among them, 50 (66.7%) were males, 25 (33.3%) were females, with a male: female ratio of 2:1. 10 (13.3%) children had no relapse, 18 (24.0%) had infrequent relapse, and 40 (53.3%) had frequent relapse. Children responding between 2 and 4 weeks after the start of treatment had a higher chance of relapse (P = 0.002) than those who responded less than 1 week. Early age at onset, male gender, rural inhabitants, low socioeconomic status and atopy, though statistically not significant, are strongly associated with frequent relapses.*

Conclusion: *Young age at diagnosis of INS, male gender, low serum albumin, and infections were predictive risk factors of multiple relapses. So, physicians should be vigilant to monitor these patients closely and counsel the families of nephrotic children regarding the prediction of subsequent relapses and outcomes.*

Keywords:*Demographic Profile, Idiopathic Nephrotic Syndrome, Syndrome, Children, INS and Relapses.*

INTRODUCTION

Idiopathic nephrotic syndrome (INS) is characterized by massive proteinuria, hypoalbuminemia, hyperlipidemia and oedema [1]. 72% to 85% of all nephrotic syndrome (NS) in children is idiopathic. About 90% of the first episodes of INS achieve remission by corticosteroid treatment. However, 70 to 80% of these children experience relapse, and 20 to 30% of them develop frequent relapse [2,3]. Multiple studies have tried to identify the demographic characteristics and risk factors associated with a relapsing pattern of illness but remains unsolved how to predict this relapse and what should be the management strategy. Some factors such as young age at diagnosis, male gender, initial time to response, decreased serum albumin level and hematuria have been reported in frequent relapsing nephrotic syndrome (FRNS) and steroid-dependent nephrotic syndrome (SDNS) with conflicting results [4]. One study in Japan showed that young age and low serum protein level at onset were independent risk factors for relapse [5]. Karim et al [6] also showed that young age and low serum level of protein at onset were associated with increased frequency of relapse. In our country, illiteracy, inadequate health care facilities and referral system, lack of knowledge about the disease and poor compliance cause the failure of early detection and prevention of disease relapse [6]. Hence, predicting and preventing risk factors is the key to successfully managing INS in children.

METHODOLOGY & MATERIALS

This observational study was conducted in the Department of Pediatric Nephrology, Bangabandhu Sheikh Mujib Medical University, from September 2016 to August 2017. Seventy-five patients of INS who fulfilled the inclusion criteria were taken. Patients with congenital nephrotic syndrome, secondary causes of nephrotic syndrome, steroid resistance, hematuria, hypertension, and incomplete medical records (demographic and laboratory data) were excluded from the study. After confirmed diagnosis and screening out of infection, all patients were treated with prednisolone 60mg/m2 /day single morning dose for 6 weeks, followed by 40 mg/m2 /day every alternate day for another 6 weeks. The following variables were recorded for all subjects: age, sex, height, body weight, social status, and inhabitance, history of infection, blood pressure, and laboratory findings such as serum protein, serum albumin, serum cholesterol, serum creatinine, complete blood count, as well as urinalysis, at the time of the INS diagnosis. The response to treatment was assessed by clinical examination, such as consecutive protein-free urine for 3 days, adequate diuresis, and no features of edema, ascites, and infections. The response was also assessed by doing spot urinary protein creatinine ratio. Parents were counselled about disease course, treatment, prognosis, and drug toxicity and trained about the interpretation and testing of urine at home by the heat precipitation method. All

patients were followed for at least 6 months after completion of the treatment of the first episode. Search for infection was done at every visit in both relapse and no-relapse groups. Patient characteristics (age, sex) and clinical parameters (presenting complaints, treatment history, time to remission, number of relapses within 6 months) were obtained and recorded in the data collection sheet. Relapse was detected by using bedside urine for albumin 3+ or more for 3 consecutive days. Relapse was treated by the daily dose of prednisolone 60mg/m2 /day up to protein-free for 3 consecutive days. Then, 40mg/m2 every alternate day for 4 weeks in infrequent relapse (IFRNS), and gradually, the dose was tapered by 5mg every 2 weeks in frequent relapse (FRNS). Patients were categorized during follow-up into the following groups, depending on their response to therapy: Remission: bedside urine albumin nil for 3 consecutive days. Relapse: urine albumin 3+ or more for 3 consecutive days, previously in remission. IFRNS: <2 relapses within 6 months of initial response. FRNS: ≥2 relapses within 6 months of initial response or 4 or more relapses within 1 year. All the investigations were done at the pathology and biochemistry laboratory, BSMMU, Shahbag, Dhaka. After collection, all the data were checked and edited. Several demographic, clinical and laboratory variables were studied from hospital records and discharge papers to determine relapse risk factors. Data were coded, edited, entered into a computer, and analyzed using the SPSS program. Data presented on a categorical scale were expressed as frequency and corresponding percentages. They were compared between groups using the Chi-square ($\chi 2$) test. In contrast, data presented on a continuous scale were expressed as mean and standard deviation from the mean. They were compared between groups using Student's t-test and further analyzed by multivariate regression analysis to determine relapse risk factors where p-value < 0.05 was taken as significant.

RESULT

Out of 75 patients, the majority (61.3%) were between 1-5 years of age, with a mean of 5.3±3.3 years. Fifty of 75 subjects (66.7%) were male, and the rest (33.3%) were female, giving a male-female ratio of roughly 2:1 (Figure 1). Regarding socioeconomic condition, 66.7% of the subjects came from poor socioeconomic class, followed by 29.3% from the middle class and only 4% from the upper class (Table II). Sixty percent of the subjects came from rural, 35% from urban areas, and 5% from urban slum areas (Table III). Among the study subjects, atopy, family history of kidney disease, hypertension and hematuria were presented at 56%, 10.7%, 20% and 16%, respectively. Table IV shows the baseline characteristics of study subjects at presentation. The parameters such as gender, infections, and serum albumin level did not differ significantly among the three age groups except serum cholesterol level and UTP, which were significantly (p=0.03) lower (≤500mg/dl) in the 1-5 years age group and UTP is higher (5.90±3.54 mg/dl, p=0.003) in children >10 years of age. Bar diagram showing the association of age of onset with relapse in study subjects. The mean age of children with relapse was 5.48 ± 3.39, and without relapse was 4.38 ± 1.90 years, but there was no statistically significant difference between these two groups (Figure 2).

Table I: Distribution of patients by age (N=75).

Age in years	Frequency (n)	Percentage (%)
1-5	46	61.3
6–10	24	32
>10	5	6.7
Mean±SD	5.3±3.3	

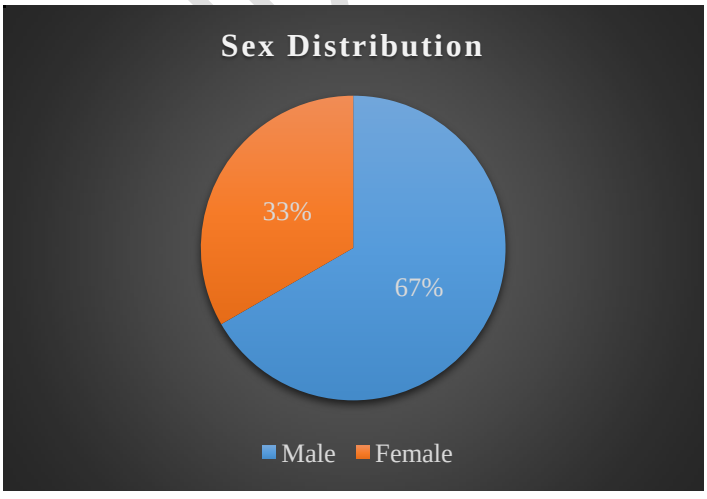

Figure 1: Sex distribution of the study population (N=57).

Table II: Distribution of patients by socioeconomic condition (N=75).

socioeconomic condition	Frequency (n)	Percentage (%)
Poor	50	66.7
Middle class	22	29.3
Upper class	3	4

Table III: Distribution of patients by residence (n = 100)

Residence	Frequency (n)	Percentage (%)
Rural	42	56
Urban	27	36
Urban slum	6	8

Table IV: Risk factors distribution of the study patients (n = 75)

Parameters	Age (years)						P-value
	1-5 (n=46)		6-10 (n=24)		>10 (n=5)		
	n	%	n	%	n	%	
Gender							
Male	29	63.04	17	70.83	4	80.00	0.65^{ns}
Female	17	36.96	7	29.17	1	20.00	
UTI	12	26.09	10	41.67	3	60.00	0.18^{ns}
RTI	12	26.09	8	33.33	1	20.00	0.75^{ns}
Peritonitis	4	8.70	0	0.00	0	0.00	0.26^{ns}
Serum Albumin (g/dl)							
Mean±SD	1.39±0.25		1.35±0.26		1.26±0.31		0.47^{ns}
Serum Cholesterol (mg/dl)							
≤500	40	86.96	18	75.00	2	40.00	0.03^{s}
>500	6	13.04	6	25.00	3	60.00	
Urinary total protein (mg/dl)	3.96±1.56		5.18±1.14		5.90±3.54		0.003^{s}

Ns=Notsignificant(p>0.05),s=Significant(p<0.05)
P value was reached from the Chi-Square test for qualitative data and the ANOVA test for quantitative data.

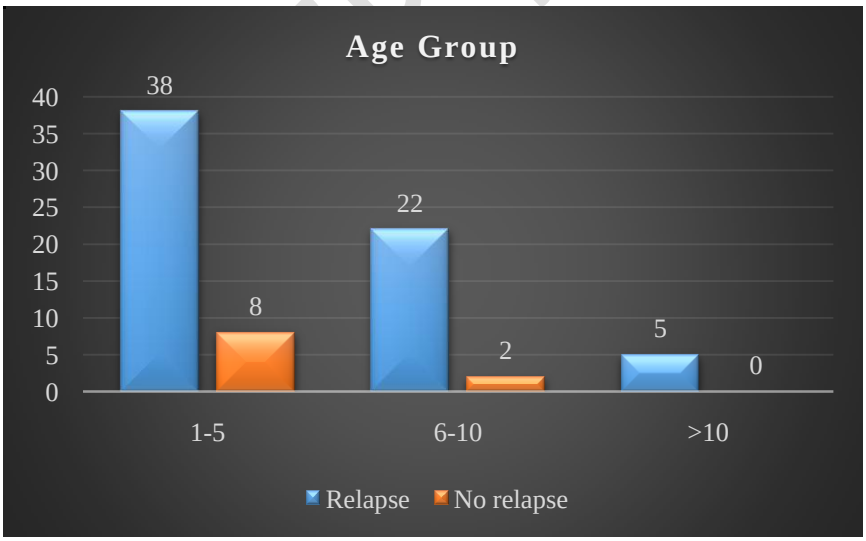

Figure 2: Patient characteristics at presentation according to age groups (n=75).

DISCUSSION

A total of 75 patients with an initial episode of INS were analyzed and followed for at least 6 months after the completion of treatment of the initial attack. Most 40 (53.3%) children had two or more than two relapses, 18(24%) had less than two relapses, 10(13.3%) children had no relapse, 5(6.7%) had steroid resistance, and 2(2.7%) had steroid dependence within 6 months of follow- up period. This finding is comparable with Chwat et al., where frequently relapsing nephrotic syndrome is the commonest sub-group [11]. The mean age of the patient ranges from 5.48±3.39 years in the relapse group and 4.38±1.90 years in the relapse group. Constaninescu et al.and Takeda et al. found no correlations between age at presentation and future relapses among patients with NS [3,5]. On the other hand, Andersen et al. and Sarker et al. found a significant correlation between age at presentation <4 and <5 years, respectively and an increased incidence of relapses in the future [4,12]. Sinha et al. found that patients with FR were younger at the onset of the disease, and the frequency of relapses declined with age [13]. Out of 75 patients, 50(66.7%) were male, and 25(33.3%) were female, with a male-to-female ratio of 2:1. Male predominance was observed in patients with relapse. Andersen et al. reported that the male gender was associated with a higher risk of steroid dependency and FRNS despite the prolongation of the steroid course [12]. Noer et al. also found that male gender is a predictive factor for FR [14]. In this study, the majority of patients (66.7%) came from poor-class families, and they were significantly more prone to develop FRNS than the children belonging to the middle and upper classes. This is comparable with the findings of Biswas et al. [7]. A Significantly higher incidence of FRNS was found in rural children than in urban children, which was also found in a similar study done in our country [4]. A statistically significant number of children with FRNS had a history of atopy. There is no comparable data, but Meadow et al. described those children with steroid-sensitive NS as having a higher incidence of the atopic disorder [15]. Takeda et al. showed that low serum protein or albumin is a significant predictor for frequent relapses in future [5]. Our study also showed that out of 75 patients, albumin levels did not differ significantly among the three age groups except serum cholesterol level and UTP, which were significantly ($p=0.03$) lower (≤500mg/dl) in 1-5 years age group and UTP (5.90±3.54 mg/dl, $p=0.003$) in >10 years age groups. This finding is comparable with that of Ali et al. [16]. However, Respiratory tract infection was the most common (26.1%) in the relapse group, followed by urinary tract infections (26.1%) and peritonitis (8.7%). Biswas BK [7] described that infection is an important cause of relapse, and Gulati et al. stated that asymptomatic UTI might be an important and underdiagnosed cause of relapse [8].

Limitations of the study: Every hospital-based study has some limitations and the present study undertaken is no exception. The limitations of the present study are mentioned. Therefore, the results of the present study may not be representative of the whole of the country or the world at large. The number of patients included in the present study was less in comparison to other studies. Because the trial was short, it was difficult to remark on complications and mortality.

CONCLUSION AND RECOMMENDATIONS

Early age at diagnosis of INS, male gender, low socioeconomic condition, rural inhabitants, atopy, infections and increased serum cholesterol level were predictive risk factors of multiple relapses. So, physicians should keep those factors in their mind closely which might help them regarding the prediction of subsequent relapses.

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