

Original Article

Risk Factor for Relapse in Childhood Nephrotic Syndrome - A Hospital Based Retrospective Study

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Abstract

Nephrotic Syndrome (NS) is a common childhood illness characterized by massive proteinuria, hyperlipidemia, hypoalbuminemia & edema. NS is a disease of relapse and it is a major problem to manage the cases with frequent relapse. So it is very important to find out such children who are prone to develop frequent relapse. This retrospective study was conducted in the paediatric department of Dhaka Medical College Hospital (DMCH) from January to December 2005. Total 100 children with relapsed NS of them 50 had Frequent Relapse NS (FRNS) and 50 had Infrequent Relapse NS (IFRNS) were included in the study with a view to find out the risk factors for relapse. Data were collected from previous medical and hospital records. Data were analyzed by using SPSS program. Chi-squared test and Student's t-Test were used as statistical test and p value < 0.05 was taken as significant. NS was more common among 2-6 years of age (67%) with male to female ratio roughly 2:1. Most of patient with frequent relapse had age <5 years, came from rural area and belongs to poor social class compared to that of infrequent relapse. The mean age at first onset was significantly less in frequent relapse group than that of infrequent relapse group. Majority of atopic child belongs to frequent relapse cases. Low serum albumin level, low serum total protein level, culture positive Urinary Tract Infection (UTI) at initial attack were observed to be statistically significant in case of frequent relapse group.

Key words: Nephrotic Syndrome, FRNS, IFRNS, Risk Factors.

Introduction :

NS is characterized by massive proteinuria, hyperlipidemia, hypoalbuminemia & edema¹. It is 15

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times more common in children than adults². It is a quite common clinical condition in our country affecting usually the young children³. Most children (90%) with NS have a form of Idiopathic NS (INS)². Most frequent type (85%) of INS is minimal change NS (MCNS) & more than 95% MCNS well responded to steroid therapy². But INS is a chronic relapsing disease⁴. Frequency of relapses is highly variable. In a year, some patients have ≤ 3 (infrequent relapses) where as others have ≥ 4 relapses (frequent relapses)¹. International study of kidney disease in children originally reported a relapse rate of 60% but later data suggests up to 76-90% with frequently relapsing rate up to 50%⁵. Relapse is also higher in our children which is 36.4%^{6,7}.

Infection is an important cause of relapse in MCNS, prevention & treatment of which could reduce proteinuria without necessity of steroid⁸. An Upper Respiratory Tract Infection (URTI) or a febrile episode often precipitates a relapse; occasionally there is no obvious cause¹. Asymptomatic UTI might be an important and under diagnosed cause of relapse⁹. Role of Tuberculosis in inducing relapse remain controversial¹⁰.

Young age and low level of serum protein at onset are independent risk for relapse¹¹. Relapse within the first year is a powerful independent predictor of subsequent relapse and relapse within first 6 months of presentation is highly predictive of subsequent course^{12,13}. In our country poverty, inadequate health care facility and less organized referral system and lack of adequate knowledge about disease course among parents are great problem in early detection and treatment of relapse cases. Hence prediction and prevention of risk factors is the key to successful management of childhood NS. This study was carried out to find out the risk factors for relapse which will help to predict the relapse early and to reduce the risk of relapse in childhood NS.

Materials and Methods:

This retrospective study was carried out in the Paediatric department of DMCH, Dhaka from January 2005 to December 2005. A total 100 child between 1-10 years of age with relapsed NS out of them 50 having FRNS and 50 having IFRNS were taken using simple random sampling technique. Patient had features of systemic illness causing NS were excluded from the study. Several demographic, clinical and laboratory variables were studied from hospital records and discharge paper to find out the risk factors for relapse. Data were coded, edited and entered into computer and were analyzed by using SPSS program. Chi-squared test and Student's t-Test were used to analyze. Data presented on categorical scale were expressed as frequency and corresponding percentages and were compared between groups using Chi-square (χ^2) test, while data presented on continuous scale were expressed as mean and standard deviation from the mean and were compared between groups by using Student's t-Test and p value < 0.05 was taken as significant.

Result

Out of 100 patients, majority (67%) were between 2 - 6 years of age with a mean 5.3 ± 2.1 years and the lowest and highest ages were 2.3 and 10 years respectively (Table I).

Table-I: Distribution of patients by age (n = 100)

Age (yrs)	Frequency	Percentage
2 - 6	67	67.0
6 - 8	12	12.0
≥ 8	21	21.0

Sixty three of 100 subjects (63%) were male and the rest 37% was female giving a male-female ratio of roughly 2:1 (Fig I).

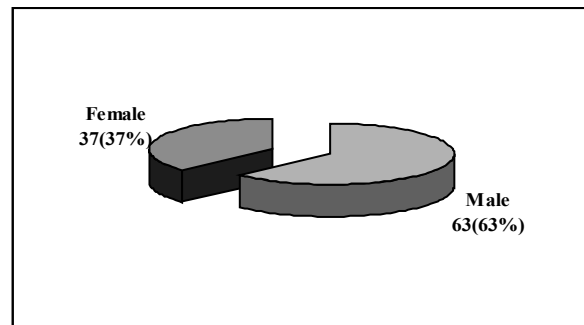


Fig. I: Distribution of patients by sex

Regarding socioeconomic condition 59% of the subjects came from poor socioeconomic class followed by 39% from middle class and only 2% from upper class (Table II).

Table II: Distribution of patients by socioeconomic condition (n = 100)

Socioeconomic condition	Frequency	Percentage
Poor	59	59.0
Middle class	39	39.0
Upper class	02	2.0

Sixty percent of the subjects came from rural, 35% from urban and remaining 5% from urban slum area (Table III).

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

Residence	Frequency	Percentage
Rural	60	60.0
Urban	35	35.0
Urban slum	05	5.0

Table IV showed that children with age < 5 years are more likely to be FRNS (68%) than those with 5 or above years of age (p = 0.019). Sex was not found to be associated with frequent relapse. Poor class children were significantly prone to develop frequent relapse than the solvent children (middle and upper class) (p < 0.001). A significantly higher incidence of FRNS was found in rural children (72%) than that in urban children (24%) (p < 0.05).

Table IV: Association of demographic features with type of relapse (n = 100)

Demographic features	Group		p-value
	Frequent relapse (n = 50)	Infrequent relapse (n = 50)	
Age			
< 5 years	34(68.0)	23(46.0)	0.019
≥ 5 years	16(32.0)	27(54.0)	
Sex			
Male	33(66.0)	30 (60.0)	0.534
Female	17(34.0)	20(40.0)	
Socioeconomic condition			
Poor	37(74.0)	22(44.0)	0.001
Middle class	11(22.0)	28(56.0)	
Upper class	2(4.0)	00	
Residence			
Rural	36(72.0)	24(48.0)	0.048
Urban	12(24.0)	23(46.0)	
Urban slum	2(4.0)	3(6.0)	

All factors suspected to be associated frequent relapse were compared between two groups. The mean age at first onset was significantly less in FRNS group than that in IFRNS group ($p < 0.001$). The mean number of relapses within 1st year was 3 in FRNS, whereas in IFRNS it was 1 ($p < 0.001$). Over half (52%) of the FRNS had a history of atopy as opposed to 22% of IFRNS ($p = 0.002$). Family history of atopy was higher in the former group (40%) than that in the latter group (26%) but difference is not significant ($p = 0.137$).

Table V: Association between disease related variables and type of relapse (n = 100)

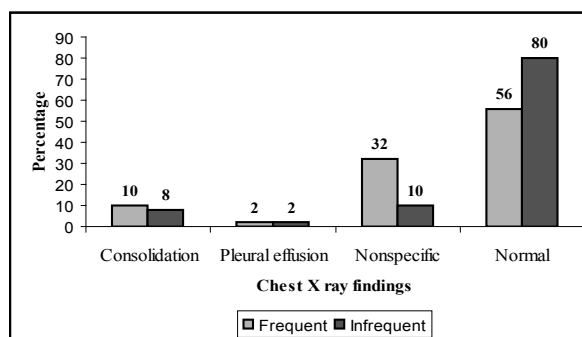
Disease related variables	Group		p-value
	Frequent relapse (n = 50)	Infrequent relapse (n = 50)	
Age at first onset (months)	21.2 ± 6.5	37.4 ± 13.1	< 0.001
Number of relapse			
within 1 st yr	3 ± 1	1 ± 1	< 0.001
Total number of relapse	5.5 ± 1.4	2.4 ± 1.2	< 0.001
History of atopy	26(52.0)	11(22.0)	0.002
Family history of atopy	20(40.0)	13(26.0)	0.137

Data on pathological and biochemical findings demonstrate that mean urine pus cell and urine RBC were significantly higher in the FRNS group than those in the IFRNS group. The frequency of culture positive urine was staggeringly higher in the former group (52%) than that in the latter group (16%). The mean serum albumin and serum total protein concentrations were significantly less in the former group than those in the latter group ($p < 0.001$). No other variables were associated with frequent relapse (**Table VI**).

Table VI: Comparison of type of relapse with investigation findings (n = 100)

Investigations findings at initial attack	Group		p-value
	Frequent relapse (n = 50)	Infrequent relapse (n = 50)	
Total WBC count (./c mm)	10954 ± 3242	9941 ± 2573	0.087
Neutrophil count (%)	64 ± 7	61.0 ± 9.4	0.068
Lymphocyte count (%)	32 ± 7	33 ± 5	0.309
Urine pus cell (./hpf)	7 ± 6	4 ± 3	0.001
Urine RBC (./hpf)	2 ± 2	1 ± 1	0.002
Urine culture (+ve)	26(52.0)	8(16.0)	< 0.001
Serum albumin (gm/dl)	1.5 ± 0.2	1.9 ± 0.3	< 0.001
Serum total protein (gm/dl)	3.9 ± 0.3	4.7 ± 0.4	< 0.001
Serum cholesterol (mg/dl)	407.4 ± 81.6	391.8 ± 77.7	0.329
24 hour UTP (gm/m ² /24 hr)	1.7 ± 0.4	1.6 ± 0.3	0.395
Blood urea (mg/dl)	13.6 ± 18.7	12.0 ± 3.1	0.546
Serum creatinine (mg/dl)	0.7 ± 0.1	0.7 ± 0.1	0.725

Chest X-ray revealed that 80% of the IFRNS and over half (56%) of the FRNS had normal finding. Ten percent of the frequent relapsers exhibited consolidation, 2% pleural effusion and 32% non-specific pulmonary lesions. Among infrequent relapse group, 8% had consolidation, 2% had pleural effusion and 10% non-specific lesions (**Figure II**).

**Figure II:** Distribution of subjects by chest X-ray

Data show that the FRNS group had a significantly higher incidence of UTI and RTI compared to the IFRNS. The total frequency of infection was observed to be almost double in the former group (72%) than that in the latter group (38%). The distribution of Chronic Suppurative Otitis Media (CSOM) and helminthiasis were almost identical between groups (Table VII).

Table VII: Association between infection/infestation and type of relapse (n = 100)

Infection/infestation in the Initial attack	Group		p-value
	Frequent relapse (n = 50)	Infrequent relapse (n = 50)	
UTI	22(44.0)	12(24.0)	0.035
RTI	17(34.0)	8(16.0)	0.038
CSOM	3(6.0)	2(4.0)	0.500
Helminthiasis	4(8.0)	2(4.0)	0.339
Presence of infection	36(72.0)	19(38.0)	0.001

Discussion:

To identify the risk factor for relapse, total 100 cases of relapsing NS of which 50 with FRNS and 50 with IFRNS were studied. Out of 100 children, majority (67%) were between the age of 2-6 years, this findings is consistent with the finding of Hossain et al³ and Vogt et al². Among the studied cases male to female ratio roughly 2:1 which is comparable with the finding of Karim MA¹⁴, Gulati et al¹⁵ and Mendoza et al¹⁶. In this study, majority of patients (59%) came from poor class family and they were significantly prone to develop FRNS than the children belongs to middle and upper class (p = 0.001). This is comparable with the finding of Biswas et al⁸.

Significantly higher incidence of FRNS was found in rural children than that in urban children (p < 0.05). There are no available comparable data but this factor may be responsible for delay in the initiation of specific treatment in rural area and further study should be done to conclude it. Children with FRNS had early age of onset (21.2 ± 6.5 months) than that with IFRNS (37.4 ± 13.1 months), this comparison is statistically significant (P < 0.001). This is comparable with the finding of Atshushi Takeda et al¹⁷ and Mendoza et al¹⁶.

Number of relapse within first year was significantly higher among FRNS group (3 ± 1 vs 1 ± 1 with a p value < 0.001). This was also described by Takeda et al¹² and International study of kidney disease in children¹³. Statistically significant number of children with FRNS had history of atopy. There is no comparable data but Meadow et al¹⁸ described that children with steroid sensitive NS had a higher incidence of atopic disorder.

Mean serum albumin level in FRNS group was significantly lower than that of IFRNS group

(P < 0.001). Same difference was true for serum total protein also, with a p value < 0.001. This finding is consistent with that of Takeda et al¹¹. UTI was found in 34 children at initial episode. Out of them 22 ultimately develop frequent relapse and 12 has got infrequent relapse, this comparison is statistically significant (P < 0.05). Biswas BK⁸ described that infection is an important cause of relapse and Gulati et al⁹ stated that asymptomatic UTI might be an important and under diagnosed cause of relapse.

Out of 55 infected cases most frequent type of infection was UTI in 34 cases followed by RTI in 25 cases, CSOM was in 5 cases and another 6 patients had Helminthiasis out of which 3 was infected with *Ascaris Lumbricoides* and rest 3 were infected with both *Ancylostoma Deodenale* and *Ascaris Lumbricoides*. This finding is comparable with the finding of Karim MA¹⁴ and Mahmood¹⁹. Similar result with higher incidence of UTI also had been reported by Gulati et al¹⁵.

Conclusion:

In this study, it was found that poor socioeconomic condition, rural residency, early age of onset, history of atopy, low serum albumin and total protein level at the time of initial attack and infection were significantly associated with frequent relapse and can be concluded that these are the risk factors for relapse of childhood NS. This study may not reflect total community as it was conducted in single hospital and over a limited number of populations. Further study should be carried out at different centre for universal acceptability of the result.

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