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Original Research Article

Prediction of relapses in children with idiopathic steroid sensitive nephrotic syndrome: a retrospective study

Prasun B.*, Payas J., Sujaya M.

Department of Pediatrics, Sharda School of Medical Sciences and Research, Greater Noida, Uttar Pradesh, India

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***Correspondence:**
Dr. Prasun B.,
E-mail: prasun9999@gmail.com

ABSTRACT

Background: Nephrotic syndrome is a chronic recurrent disease commonly affecting children belonging to the age group 1-10 years. The purpose of the study was to identify the factors at the onset of disease responsible for relapses in nephrotic syndrome.
Methods: It was a retrospective observational study conducted in a tertiary care hospital in North India consisting of children aged 1-15 years diagnosed as nephrotic syndrome (1st episode) and followed for 12 months. Variables extracted from records (after January 2008) were age of presentation, days to remission, hematuria, and hypertension.
Results: Out of 88 cases, 23 were frequent relapsers and 65 were infrequent relapsers. It was observed that cases remitting after 2 weeks have increased chances of frequent relapses. On stratification based on presence or absence of hematuria or hypertension, it was observed that both these variables predispose the patient towards frequent relapses.
Conclusions: We concluded that variables like days to remission, haematuria and hypertension can fairly predict future relapses.

Keywords: Children, Nephrotic syndrome, Predictors, Relapse

INTRODUCTION

Nephrotic syndrome is a chronic recurrent disease commonly affecting children belonging to the age group 1-10 years.[1] The incidence of nephrotic syndrome is 2-7 cases per 100,000 children per year.[2] It is mainly characterized by massive selective proteinuria (>40 mg/m^2/hr), edema, hypoalbuminemia and hypercholesterolemia. Few patients, although uncommon may present with hypertension, hematuria along with the main clinical features. Males are more affected than females.[2-4] Various histopathological types have been defined amongst which minimal change disease is the most predominant seen in around 85% of cases and is most sensitive to the treatment. Steroid (prednisolone) is the mainstay of therapy. According to The International Study of Kidney Disease in Children (ISKDC), prednisolone is given at 60mg/m^2/day for 4 weeks followed by 40 mg/m^2/day on alternate days for 4 weeks. However, even after complete treatment about two-third of the patients suffer from relapse defined as albuminuria 3+ or more for three consecutive days. Relapses are further categorized into infrequent relapse (less than 2 relapses within initial 6 months of response or less than 4 relapses within any 12 months period) or frequent relapse (2 or more relapses within initial 6 months of response or 4 or more relapses within any 12 months period).

Frequent relapsers are at high risk of developing complications related to steroid therapy as they need repeated courses of steroid for treatment. If such relapses could be fairly predicted at the onset of disease, it would lead to a better long term management of the disease. The purpose of our study is to identify the factors at the onset

of disease responsible for relapses in nephrotic syndrome without considering histopathology.

METHODS

This was a retrospective observational study conducted in the Department of Pediatrics, Sharda School of Medical Sciences and Research, Greater Noida, Uttar Pradesh, India, a tertiary care hospital in Northern India. We analysed records of all the children aged 1-15 years who were treated and followed by us after January 2008 with first episode of idiopathic nephrotic syndrome. Before collecting the data, proper consent was obtained from the Institute's Ethics Committee and Medical Superintendant of the hospital.

Inclusion criteria

Chidren aged 1-15 years with first episode of nephrotic syndrome with generalised edema, hypoalbuminemia, proteinuria and hypercholesterolemia, for whom at least 12 months of follow up was completed.

Exclusion criteria

- Previous treatment with steroids or immunosuppressive agents
- Any systemic disease known to produce nephrotic syndrome
- Age < 1year and > 15 years
- Steroid nonresponsive patients
- At least 12 months follow up not completed

Variables

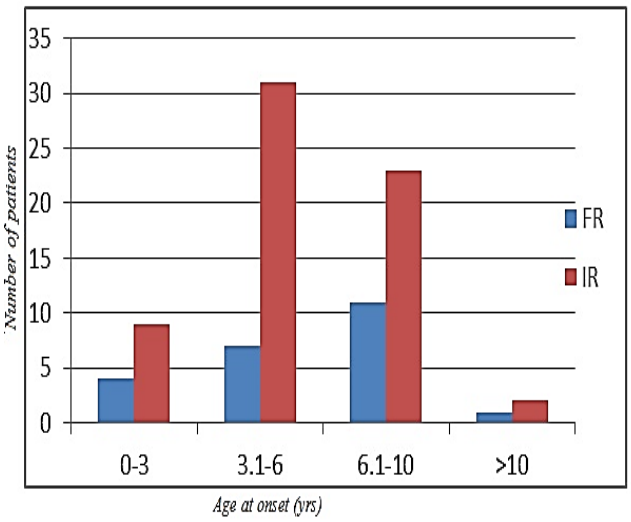
The detailed history, clinical features and physical examination of all the cases were recorded systematically from the hospital records. The variables for which the data was extracted from each patient's record were: age, gender, presence of haematuria (>5 RBC per high field in urine), hypertension (> 95th centile), time of remission (days), relapses (frequent/infrequent in next 12 months after the treatment).

Statistical analysis

Chi square test was used to determine any difference between the groups and significant relationship if any, between different variables and the outcome. Fisher's exact test was used for n<60. A p value of <0.05 was considered significant.

RESULTS

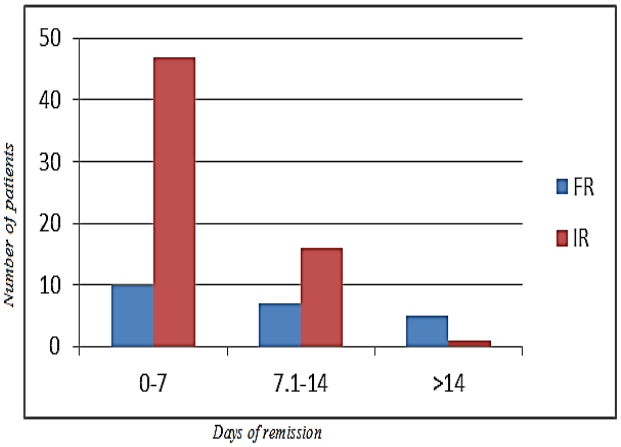
After analysing the records, 88 out of 100 cases of nephrotic syndrome were included in the study. 8 were excluded as they had no relapse in one year follow up and 4 cases were lost to follow up. There were 60 males (68%) and 28 females (32%) with M:F ratio of 2.1:1. The mean age of presentation was 5.9 years±2.2 with a range of 2-12.4 years. Mean days to remission were 6.8 +3.9days with a range of 2-22 days. At the initial presentation 22 patients (25%) had hematuria and 13 (14.7%) were hypertensive. After one year of follow up 23 (26%) patients were categorized as frequent relapser and 65 (74%) patients as infrequent relapser.



The chi-square statistic is 2.0773. The p-value is 0.55. Result is not significant at p< 0.05. No difference between the groups.

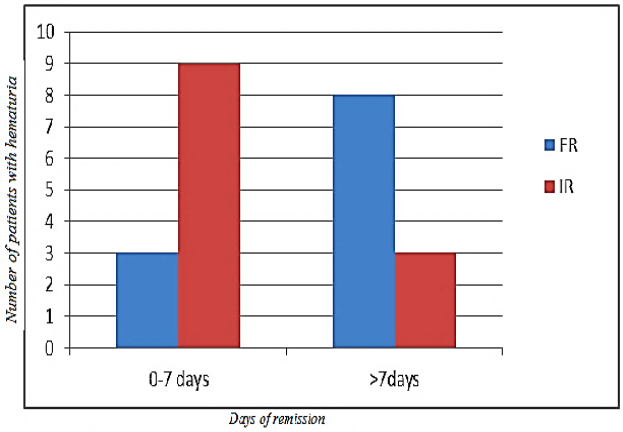
Figure 1: The chi square statistic is 2.0773. The p value is 0.55.The result is not significant at p<.05.No difference between the groups.

The age distribution and its relationship with the relapse pattern shown in Figure 1. The patients were divided into four groups depending upon the age of presentation. The patients between age 3-6 years were found to have four to five times higher number of infrequent relapsers (IR) as compared to frequent relapsers (FR) while others had twice as many infrequent relapsers compared to frequent relapsers. However, this difference was not found to be statistically significant (p-value 0.55).



The chi- square statistic is 12.73. The p-value is 0.001. The result is significant at p< 0.05.

Figure 2: The chi square statistic is 12.73. The p value is 0.001. The result is significant at p < 0.05.



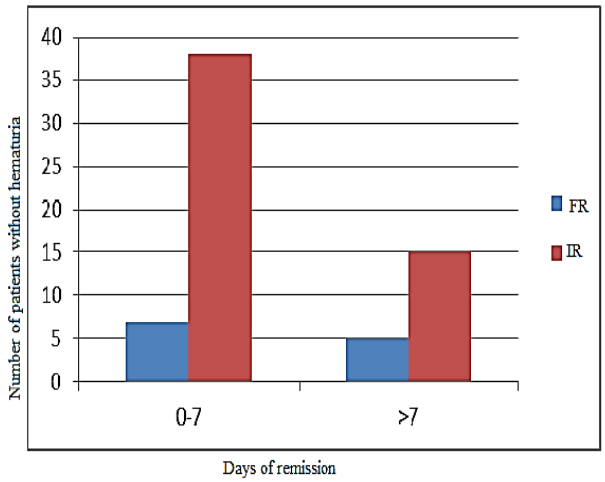
The fisher exact test statistic is 0.03. The result is significant at $p < 0.05$.

Figure 3: The Fisher exact test statistic is 0.03. The result is significant at p< 0.05.

The distribution according to days to remission and its relationship with the relapse pattern is shown in Figure 2. The number of days to remission has a significant relationship with the pattern of relapse (p value 0.001). There are more number of cases as infrequent relapsers if they remit early (<14 days) whereas cases remitting after 2 weeks have an increased tendency for frequent relapses.

Stratification

We did a stratified analysis for two variables, hematuria and hypertension to find the impact of their presence or absence on the relapse pattern.

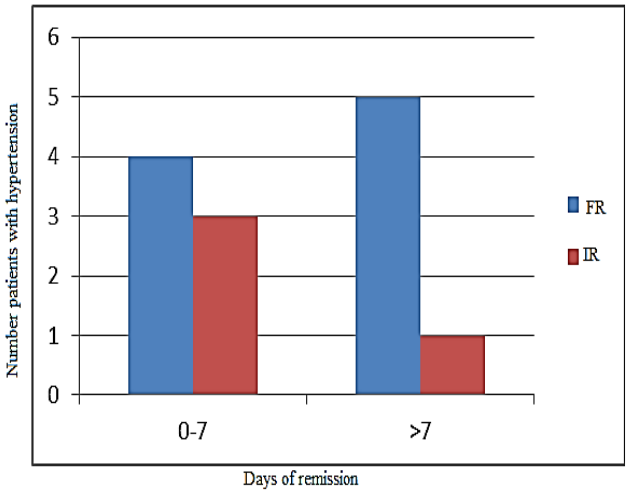


Chi-square statistic is 0.82. The p-value is 0.36. The result is not significant at $p < 0.05$.

Figure 4: The chi square statistic is 0.82. The p value is 0.36. The result is not significant at p < 0.05.

Hematuria

Figure 3 shows the distribution according to days to remission for patients with hematuria. It shows a significant relationship (Fishers exact, p-value 0.033) showing that there are about three times higher number of infrequent relapsers when they remit in less than 7 days and three times higher number of frequent relapsers when they remit after 7 days suggesting that for chidren with hematuria at onset there are higher chances of relapse if they remit after 1 week. The results were not significant for patients without hematuria (Figure 4).

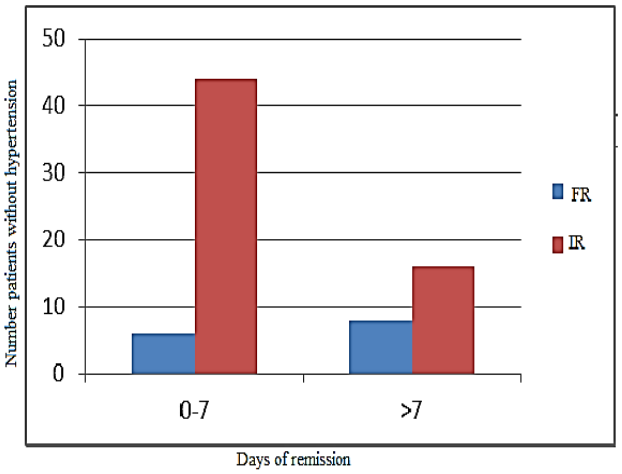


Fisher exact test statistic is 0.55. The result is not significant at p< 0.05.

Figure 5: The Fisher exact test statistic is 0.055. The result is not significant at p<0.05.

Hypertension

Patients with hypertension had more chances of frequent relapses irrespective of days to remission but the results were not significant (Figure 5). Patients without hypertension have decreased chances of frequent relapses with statistically significant results (p-value 0.02) as shown in Figure 6.



The chi-square statistic is 4.81. The p-value is 0.02. The result is significant at $p < 0.05$.

Figure 6: The chi square statistic is 4.81. The p value is 0.02. The result is significant at p<0.05.

DISCUSSION

Nephrotic syndrome is a chronic condition of childhood with around 80-90% chances of relapse.[5] This study population showed a similar percentage of relapses (88%). The relapse pattern is thought to be dependent on numerous factors by various investigators i.e. age at onset, time to remission, albuminuria, hypertension, hematuria. The results of our study suggested that days to remission, presence of hematuria, and hypertension are the risk factors that can predict the relapse pattern. The patient who remitted after 2 weeks showed an increased tendency of frequent relapses, suggesting days of remission as an independent factor that can predict relapses.

When combined with hematuria, there was an increased tendency of being a frequent relapser for those patients who remitted after 7 days. This suggests that presence or absence of hematuria can be the predictor of relapse.

Similar to hematuria, we did a stratified analysis for patients with hypertension. There was a tendency for hypertensive patients to be frequent relapsers irrespective of days to remission. However, this result came out to be insignificant. But patients without hypertension showed an increased tendency to be infrequent relapsers with significant results. This suggested that the presence or absence of hypertension has an impact over relapse pattern and thus it can be the predictor of future relapses.

The male:female ratio in our study was 2.1:1 that was consistent with many other study population.[6] The mean age of presentation was 6 years which was almost similar to aretrospective analysis of 54 patients by Anderson et al where mean age of patients was 5.5 years.[7] The relapse rate in our study was 88 % which was consistent with the literature. Seventy four percent of the relapses were infrequent while rests were frequent. Noer et al analysed 63 children with 79 % infrequent relapsers and 21 % as frequent relapsers.[7]

A case control study by Jahan et al, demonstrated that age at onset at the time of initial attackis an independent risk factor for frequent relapsing idiopathic nephrotic syndrome. Similar to this our study demonstrated a significant difference when age at onset was compared with the relapse pattern.[8]

This study similar to Mishra et al, demonstrated that delayed response to the therapy i.e more number of days to remission is a significant predictor of frequent relapses.[9]

Constantinescu et al in their retrospective study showed that early initial response to steroids with hematuria is a predictor of relapse.[10] In their study this was indirect evidence as the results were significant only with the patients without hematuria and those with hematuria had similar chances of being infrequent or frequent relapse which was explained by them in their study. However, our study showed a significant difference with hematuria suggesting a definite role of hematuria in predicting a relapse.

Apart from that, our study was also different as we were able to show a role of another variable i.e. hypertension in predicting relapse pattern. Patients with hypertension showed a tendency to be frequent relapsers irrespective of number of days to remission. The results of this analysis were not significant meaning the patients with hypertension had similar chances of either frequent or infrequent relapse. However, the patients without hypertension showed a significant increase in infrequent relapses suggesting the role of hypertension as a predictor of future relapses.

CONCLUSION

In variables like early or late remission, presence or absence of hematuria and hypertension can fairly predict the future relapses and thus these variables should be kept in mind and should be well documented at the time of initial presentation of nephrotic syndrome.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. International study of kidney disease in children. Nephrotic syndrome in children: prediction of histopathology from clinical and laboratory characteristics at time of diagnosis. Kidney International. 1978;13(2):159-65.
2. Swartz SJ, Eldin KW, Hicks MJ, Feig DI. Minimal change disease with IgM+ immunofluorescence: a subtype of nephrotic syndrome. Pediatr Nephrol. 2009;24(6):1187-92.
3. Andolino TP, Adam RJ. Nephrotic syndrome. Pediatrics Review. 2015;36(3):117-26.
4. Sureshkumar P, Hodson EM, Willis NS, Barzi F, Craig JC. Predictors of remission and relapse in idiopathic nephrotic syndrome: a prospective cohort study. Pediatr Nephrol. 2014;29(6):1039-46.
5. Sivaraj P, Das L, Swain A, Pradhan S. Spectrum of clinico-pathological profile and treatment response in children with nephrotic immunoglobulin a nephropathy. Saudi J Kidney Dis Transplant. 2015;26(4):708.
6. Andersen RF, Thrane N, Noergaard K, Rytter L, Jespersen B, Rittig S. Early age at debut is a predictor of steroid-dependent and frequent relapsing nephrotic syndrome. Pediatr Nephrol. 2010;25(7):1299-304.
7. Noer MS. Predictors of relapse in steroid-sensitive nephrotic syndrome. Southeast Asian J Trop Med Public Health. 2005;36(5):1313-20.

8. Jahan I, Hanif M, Ali MA, Hoque MM. Prediction of risk factors of frequent relapse idiopathic nephrotic syndrome. Mymen Med J. 2015;24(4):735-42.
9. Mishra OP, Abhinay A, Mishra RN, Prasad R, Pohl M. Can we predict relapses in children with idiopathic steroid-sensitive nephrotic syndrome? J Trop Pediatr. 2013;59(5):343-9.
10. Constantinescu AR, Shah HB, Foote EF, Weiss LS. Predicting first-year relapses in children with nephrotic syndrome. Pediatrics. 2000;105(3):492-5.

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