PREDICTIVE FACTORS FOR RELAPSES IDIOPATHIC NEPHROTIC SYNDROME IN CHILDREN

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Summary

As part of our study relating to the predictive factors of relapses of nephrotic syndrome, we carried out a comparison of these factors with other works, drawn up from the bibliography. This is a seven-year study, on a sample of 132 children of both sexes, multicenter and prospective, aimed at determining the diagnostic, therapeutic and progressive criteria of nephrotic syndrome, to identify the predictive factors of its relapses, in the short term and medium terms.

Keywords: Childhood nephrotic syndrome. Predictive factors of relapse. Epidemiological study. Evolution of the disease.

I. INTRODUCTION

Childhood idiopathic nephrotic syndrome (NIS), or lipoid nephrosis (NL), is the most common chronic glomerular nephropathy in young children. Its etiopathogenesis is still poorly understood, although many arguments favor immunological mediation. The precise mechanisms are not fully clarified. The duration of progression of the disease is unpredictable. Its development can last from a few months to several years, or even throughout life. Renal prognosis is linked to response to corticosteroid treatment.

II. MATERIAL AND METHODS

This is a multicenter, prospective study over a period of seven years, with a patient recruitment period of 5 years (01/01/2010 to 12/31/2014) and a minimum follow-up and evaluation period of 1 year. , on a sample of 132 children of both sexes. The objective of this study is to determine the epidemiological characteristics, clinical and progressive

aspects of children suffering from lipoid nephrosis, and to identify the predictive factors for the progression of the disease. In this study we included all children who presented with a cortico-sensitive primary nephrotic syndrome, with clinical and/or biological elements, pointing towards a pure idiopathic nephrotic syndrome, namely:

- An age between 1 year and 12 years (nephrotic syndromes exempt from renal biopsy)

- Absence of persistent hematuria.

- Absence of persistent hypertension.

- Normal supplement rate.

- Absence of persistent impairment of renal function (persistent renal insufficiency)

- A positive response to corticosteroids, with a disappearance of proteinuria with or without a bolus of methyl prednisolone (MP).

We analyzed the epidemiological, clinical, therapeutic and evolutionary data, using SPSS version 23 software. The descriptive study was carried out by calculating frequencies for qualitative variables and by calculating means with their standard deviation for quantitative variables. The analytical study was done with cross tables. The means with their standard deviation and the percentages were compared using the Student test and the Chi 2 test, according to their conditions of applicability, with a significance threshold if the "p" was less than 0 .05.

III. RESULTS

This study included a cohort of 132 children aged 12 months to 12 years, presenting with pure cortico-sensitive NIS. After analyzing the data, we noted that (Table 1):

Ninety-eight patients (74.2%) were aged less than six years, with a mean age estimated at 53.7 months. We also noted a clear male predominance (sex ratio of 1.9). After making the diagnosis of idiopathic nephrotic syndrome, the treatment instituted consisted of corticosteroid therapy based on prednisone at a rate of 2 mg per kilogram per day orally without exceeding a maximum dose of 60 mg per day. Daily monitoring of proteinuria using urine strips is carried out in order to determine the exact day on which there was disappearance of proteinuria which corresponds to the response time to corticosteroids (remission time). Note that the disappearance of proteinuria was always confirmed the same day, by analysis of 24-hour proteinuria; which allowed us to note that the majority of our patients (85.6%) responded positively to corticosteroids before the end of the second week (total disappearance of proteinuria), however, the relapse rate was high because cent- eight patients experienced relapses (reappearance of proteinuria greater than 50 mg per kilogram per day), which corresponds to 81.8% of patients. These relapses were early, occurring during the first 6 months of the disease, in seventy-six patients (57.6%), in addition to being frequent (more than two relapses per year, in 50.8% of our patients). Furthermore, this study made it possible to highlight a statistically

significant relationship (P < 0.001) between the precocity of relapses and their frequency (number of relapses per year) (Table 2).

Table 1: General and progressive parameters of nephritic syndrome

General parameters of nephrotic syndrome		Workforce (n=132)	Percentage (%)
Age at first push (years)			
	≤ 2	25	18,9
	3 - 4	50	37,9
	5 – 6	23	17,4
	7 – 8	14	10,6
	9 - 10	15	11,4
	≥ 11	5	3,8
Sex			
	Female	45	34,1
	Male	87	65,9
Inbreeding			
	Present	36	27,3
	Absent	96	72,7
Response time			
	Before15 days	113	85,6
	After 15 days	09	6,8
	After 3 boluses of MP	10	7,6
Occurrence or no relapses			
	No relapse	24	18,2
	Presence of relapse	108	81,8
Number of relapses			
	No relapse	24	18,2
	Relapse during first 6 months	76	57,6
	Relapse after 6 months of treatment	32	24,3

With regard to the analysis of predictive factors for the development of nephrotic syndrome in children, namely age, sex and time to remission during the first attack; and, research of a possible relationship between these 3 factors and the progressive profile of the nephrotic syndrome, with the aim of identifying the parameter(s) which can allow us to predict the evolution in our nephrotic children. We noted that:

The results obtained made it possible to objectify the presence of a statistically significant relationship (P < 0.001 for the risk of early relapse and P < 0.001 for the risk of frequent relapses) between the sex of the patient and the risk of occurrence of relapses and their frequency per year. In addition, this study demonstrated that boys are more often subject to relapses particularly during the first 6 months of the disease compared to girls (early relapse). Regarding age and remission time; this study did not show any relationship between these two parameters and the evolution of the disease in our population, with P: 0.697 and 0.593 for age and 0.256 and 0.268 for the response time (remission time) (Table 2).

Table 2: The risk of relapses and their frequency according to age, sex and time to response to corticosteroid therapy

	NO relapses	Relapses		P	Relapses / year		P
		< 6 months	≥ 6months		< 2 relapses	≥ 2 relapses	
Age ≤ 3 years >3 years	8 (33,3%) 16 (66,7%)	32 (42,1%) 44 (57,9)	14(43,8%) 18 (56,3%)	0,697	16 (29,6%) 25 (32,1%)	30 (55,6%) 37 (47,4%)	0,593
Sex Male Feminine	8 (9,2%) 16 (35,6%)	60 (69%) 44 (36,6%)	19 (21,8%) 18 (28,8%)	**<0,001**	28 (32,3%) 16 (35,6%)	51 (58,6%) 13 (28,8%)	**<0,001**
Response time Medium (days) Median (days)	17,95 8	9,94 7	11,65 8	0,256	10,40 7	10,47 8	0,268
relapses/year <2 relapses > 2 relapses	/ /	17 (17,1%) 63 (82,9%)	28 (87,5%) 4 (12,5%)	**<0,001**	/ /	/ /	/

IV. DISCUSSION

1. Epidemiological characteristics of our study

Numerous epidemiological studies of childhood NIS have shown that the average age of onset varies between 4.6 and 5.4 years [1-2] and that the age group most affected is between 2 and 6 years [1, 3, 4, 5]. These data therefore agree with the results of our study where the average age is estimated at 4.5 years (53.7 months), with an age less than 6 years in 74.2% of patients. The sex ratio in our study is 1.9, in accordance with literature data [6] (Table 3).

Table 3: Average age and sex ratio according to literature data

Studies	Average age (years)	Sex-ratio
EL ZOUKI (Benghazi. Libye 1984) [7]	5,7	1,3
BOURQUIA (Casablanca. Maroc 1994) [8]	6	1,4
NURAY (Ankara. Turquie 2004) [9]	4,6	1,4
AIT SAB (Marrakech. Maroc 2010) [10]	6,3	1,4
ERNOULD (la Gironde. France 2011) [11]	3,6	2
KADDAH (Caire. Egypte 2012) [12]	4,4	2,8
Notre étude	4,5	1,9

Concerning the rate of inbreeding, the results obtained in our study correspond to the results found in the two national surveys on inbreeding, carried out in Algeria, in 1970 and 1979 respectively: 22.6 p. hundred and 32 p. cent, compared to 27 p. hundred in our study. [13] (Table 4).

Table 4: The rate of inbreeding according to the different surveys

Investigations	Inbreeding rate
National Consanguinity Survey 1970	22,6%
National Inbreeding Survey 1979	32%
Our study	27%

1. Evolutionary data from our patients

In our study, 92.4 percent of patients responded to oral corticosteroid treatment; only ten patients, or 7 percent, required boluses of methyl prednisolone (MP). The average response time was estimated at 12 days, with a median duration of 7 days (from 4 to 66 days). Note that 85.6 percent of patients responded to corticosteroid treatment before the end of the second week (Table2). These results are not different from those of other studies where the average time to remission is evaluated between 08 and 15 days [14] and the median time is evaluated between 07 and 11days [11-15]. The same is true for the remission rate at the end of the fourth week: 92.4 percent in our study versus 95 to 97 percent according to literature data [14, 16,17]. Concerning the rate of relapses and their frequency, in our study, 108 children (81.8%) experienced relapses (Table 1). Among these children, 70.4% relapsed within six months following the date of the first attack (Table 2); 32 children (29.6%) relapsed after 6 months. Furthermore, 67children (50.8%) had frequent relapses (two or more relapses per year) and 41children (31.1%) had in frequent relapses (less than two relapses per year) (Table2). 24 children, o ronly 18.2%, had a single flare-up. Here too, the results obtained are not different from the data in the literature [11, 15, 17, 18,19] (Table5).

Table 5: The evolutionary aspect according to literature data. Dmr: median duration of remission, TR (28d): response rate on the 28th day, Sr: single relapse, R: relapse, ifR: infrequent relapses, fR: frequent relapses

Studies	Mdr(d)	TR(28d)	Sr	R	ifR	fR
KOSKIMIES 1982 [17]	/	95%	24,4%	75,6%	22,3%	53,2%
VIVARELLI 2009 [15]	7	97%	8,7%	91,3%	24,3%	/
ERNOULD 2011[11]	11	/	17%	83%	/	/
DOSSIER 2014 [19]	/	/	21%	79%	/	23,3%
Our STUDY	7	92	18,2%	81,8%	31,1%	50,8%

2. Analysis of the predictive factors of our patients:

The predictive factors for the evolution of SNI described in the literature [11], namely age, sex and time to remission, were analyzed in this study. An age of less than 3 years at the time of diagnosis of SNI is considered one of the predictive factors of progression [11,20]. Indeed, contrary to what has been described in the literature, in our study, there was no difference in terms of evolution between the group of children aged less than 3years old, and the group of children aged more than 3 years. These two groups had practically the same risk of relapse in terms of time and number (p: 0.697).

On the other hand, this study showed that the sex of the patient played an important role in the evolution of SNI, because 90.5 percent of the boys in this study presented relapses, 69 percent presented early relapses and 58 percent presented frequent relapses, while lower rates were found in girls, thus confirming the relationship between sex of the patient and progressive aspect of the NIS (Table 2). The results obtained regarding this parameter are consistent with the results of other studies where male sex is considered a poor prognosis factor [11,20]. Indeed, in our study, there is a significant difference in the evolutionary profile of SNI between the group of boys and the group of girls: 90.8 percent of boys presented relapses with a rate during the first 6 months, estimated at 35.5 percent and a rate of frequent relapses at 58.6 percent, while these rates are much lower in the group of girls: respectively 64.44 percent (p: 0. 0003), 35.6 percent (p:0.0001) and 35.6 percent (Table 2). The time to remission is currently considered an important prognostic marker in the evolution of SNI [15]. Moreover, many studies have demonstrated the relevance of recording the time of remission at the beginning of the disease in order to predict the evolution and prognosis of SNI [21,22], because a time of remission greater than fifteen days [11,15],nine days for some authors [23], is currently considered a risk factor for relapse and/or corticosteroid dependence. From these data, this "remission time – evolution" relationship, analyzed in our study, did not show any difference in evolution, between the group of patients with are mission timeless than or equal to15 days and the group of patients with a longer delay, especially since there is no difference in remission time between the group of patients with frequent relapses and infrequent relapses (p: 0.263)

V. CONCLUSION

After comparing the analyzed data, with those of the bibliography consulted, concerning the same parameters, it emerges from our study, that in terms of evolution, there is no difference between the groups of children under and more than three years, contrary to the results of the literature. Furthermore, we have found that boys are more often subject to relapses than girls, and this, without any relation to the composition of our sample which contains a sex ratio of 1.9%. Concerning the other parameters studied, our results agree with those of the literature, with perfect congruence.

Declaration of Relationship of Interest: No Relationship of Interest.

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