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Childhood Idiopathic Nephrotic Syndrome: A Single-Center Hospital Study

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Abstract

Introduction: Idiopathic nephrotic syndrome (INS) is one of the leading causes of childhood morbidity worldwide. This study was undertaken to complete the epidemiological, clinical, therapeutic and evolutionary aspects of NIS in hospitalized patients. **Methodology:** We conducted a retrospective study of patients with childhood NIS who had been admitted to our department from January 2017 to December 2018. Diagnosis, remission and relapse of idiopathic NS were defined according to the recommendations of the French Society of Pediatric Nephrology. We included all patients aged 2 to 14 years presenting a NIS picture. **Results:** During the study period, 35 patients with idiopathic NS had been hospitalized, representing a frequency of 1% of patients hospitalized in the department. The sex ratio was 2.22. The average age of the patients was 7.5 ± 3.5 years. Generalized edema was observed in all our patients. Arterial hypertension (36%) and abdominal pain (24%), hematuria (9%) were the main associated signs. Malnutrition was present in 66%, urinary tract infection in 20% and malaria in 24%. Cortico-sensitivity was obtained in 86% of patients, 14% were cortico-resistant and 11% were cortico-dependent. Relapses (6%) had been observed among cortico-sensitive patients. The mortality rate was 11%. **Conclusion:** This study calls for more trials to better elucidate prognostic indicators and develop better therapeutic approaches adapted to epidemio-clinical contexts.

Keywords

INS, Children, Corticosteroids

1. Introduction

Idiopathic nephrotic syndrome (INS) is one of the most common chronic kidney diseases in children [1] [2]. It accounts for 90% of nephrotic syndromes in children before the age of 10 and 50% after this age [3]. NIS is characterized by massive albuminuria responsible for hypoalbuminemia, edema, hyperlipidemia and various complications including infectious and thromboembolic [4]. It is a universal disease that affects all races and all continents [2]. Several researchers believe that there are geographic and ethnic disparities [1] [2] [4].

In the United States and Europe, the annual incidence of nephrotic syndromes in children was estimated to be between 1 and 7 per 100,000 children [2] [4]. In the United Kingdom, a study had shown that NIS was 6 times more common in children of Asian origin than in European children [5]. In sub-Saharan Africa, nephrotic syndrome is the main cause of chronic renal failure and end-stage renal disease in children [6]. In multiracial countries, people of African descent have been shown to be at higher risk of developing steroid-resistant nephrotic syndrome [6] [7].

Nephrotic syndrome in children can be classified into 3 three groups: secondary, congenital and infantile or idiopathic [4]. The etiology of most childhood nephrotic syndromes remains unknown, although immunological, systemic or genetic implications have been reported by several studies [5]. Nephrotic syndromes can occur at any age, but begins most often (in 90% of cases) in children under 10 years of age, often after an infectious or allergic trigger [5]. Kidney biopsy is indicated in cases of atypia: child under 1 year or over 12 years old, macroscopic hematuria, severe arterial hypertension, extrarenal signs, hypocomplementemia, renal failure, positive hepatitis serology [6] [8] [9]. Pathologically, minimal glomerular lesions present the most common appearance.

Lack of equipment and personnel for the processing and interpretation of kidney biopsies is a major barrier across Africa and needs to be addressed [6]. The treatment of the first attack is based on corticosteroid therapy (prednisone) for several weeks [2] [3]. Nephrotic syndromes treatment guidelines developed in Western countries are not always applicable in low-resource settings [5] [6] [8]. Rational management is then based on knowledge of relevant epidemiological data [6] [9].

In this study, we sought to describe the epidemiological, diagnostic and evolutionary aspects of NIS in children hospitalized in a pediatric department.

2. Methodology

This was a retrospective, single-center descriptive study conducted from January 1, 2017 to December 31, 2018 in the general pediatrics department of the Gabriel Touré University Hospital Center (Bamako, Mali). The general pediatrics department includes 4 units and 72 hospital beds. It receives an average of 2162 patients per year, 55% of whom are referred by peripheral health structures.

We included the medical records of all children hospitalized for idiopathic

nephrotic syndrome during the study period. Patients with incomplete records and those with no or poor follow-up were excluded. Congenital and secondary nephrotic syndromes cases were also excluded.

The idiopathic character of the nephrotic syndromes was retained in front of a negative etiological assessment comprising a search for sickle cell anemia, lupus, diabetes, human immunodeficiency virus (HIV) and hepatitis B virus (HBV) [3].

Data collection was done on a survey form from medical records, the follow-up notebook and department registers. The parameters studied were age, sex, clinical signs, urinalysis results, estimated 24-hour urinary protein, serum creatinine, serum protein, response to corticosteroid therapy, occurrence of relapse, follow-up, progress under treatment and duration of treatment.

All the patients had been treated with corticosteroids by referring to the national care protocol (PNDS) "idiopathic nephrotic syndrome in children" established by the French Society of Pediatric Nephrology and the rare disease reference center INS of the child and adult [2] [8].

The initial treatment of the idiopathic nephrotic syndrome included prednisolone at a dose of 60 mg/m^2/day (2 mg/kg/d) in 2 oral doses without exceeding 60 mg/d for 4 weeks.

Corticosensitivity was defined by the disappearance of proteinuria after four weeks of oral treatment with prednisone at a dose of 2 mg/kg/day or after 3 boluses of methylprednisolone at a dose of 1 g/1.73m^2 of body surface area per bolus [3].

In the event of corticosteroid sensitivity, continue with the same doses every other day for 2 months then reduction by quarter of the dose (0.5 mg/kg) every 15 days (*i.e.* approximately 4 and a half months of treatment).

In case of cortico-resistance or cortico-dependence, add Cyclophosphamide (2 - 3 milligrams/kilogram/day for 2 - 3 months). Corticoresistance was defined by the absence of remission eight days after methylprednisolone infusions. Corticodependency was defined as a relapse during the tapering of corticosteroid therapy or less than three months after stopping it [3].

Patients were seen every 2 to 4 weeks depending on their place of residence and the evolution of symptoms. Clinical and biological constants were assessed at each follow-up visit.

Data were analyzed using Statistical Software for the Social Sciences (SPSS), version 20.0.

3. Results

3.1. Epidemiological Aspects

During the study period, 3744 children had been hospitalized in the general pediatrics department, 35 had an INS. The frequency of idiopathic nephrotic syndrome was 1%. **Table 1** shows the distribution of patients by age, gender and clinical outcomes of children at the time of admission to the service. The mean age of the patients was 7.5 ± 3.5 years. The age range was 2 to 14 years old.

Table 1. Distribution of patients by age, sex and clinical results.

Variables		Workforce	Percentage
Age	2 to 5 years	12	34
	6 to 10 years old	9	26
	10 to 14 years old	14	40
Sex	Male	24	69
	Feminine	11	31
Consultation period	[3, 6 weeks]	13	37
	[6, 9 weeks]	10	29
	[9, 12 weeks]	1	3
	[12, 15 weeks]	2	6
	>at 15 weeks	5	14
Clinical signs	Edema	35	100
	Malnutrition	23	66
	hypertension	12	36
	Abdominal pain	8	24
	Respiratory distress	8	24
	Cloudy urine	8	24
	Hematuria	3	9
	Fever	3	9
	Oliguria	2	6
	Altered Consciousness	1	3

Children under 10 accounted for 60% of the workforce. The sex ratio was 2.22. Patients resided in rural areas in 54% of cases. The average consultation time was 52 days with extremes of 6 days and 188 days. Before their admission to our service, 24 children (67%) had been treated by traditional healers with medicinal plants.

3.2. Clinical Aspects

Clinically, edema was the only reason for consultation. It was a generalized edema in 91% of cases. The main clinical signs associated with edema were hypertension (36%), abdominal pain (24%) and respiratory distress (24%). The urine dipstick had objectified hematuria in 9%, leukocyturia in 23% and bacteriuria in 23% of cases.

3.3. Paraclinical aspects

Mean proteinuria was 132.8 ± 53 mg/kg/24h. It exceeded 100 mg/kg/24h in 77% of patients. Mean serum albumin was 13.25 ± 5 g/L. Serum creatinine was above 100 µmol/l in 20% of cases. Creatinine was normal in all our patients. The com-

plement C3 fraction measured in 15 patients was normal in all cases. C-reactive protein (CRP) was elevated in 69% of cases. Hyperleukocytosis (over 10,000 leukocytes/mm^3) was observed in 43% of cases. The mean hemoglobin level was 9.8 ± 2.4 g/dl. The hemoglobin level was below 8 g/dl in 25% of patients. The mean globular volume (MCV) was less than 70 fl in 31% of cases. Thrombocytopenia was observed in 14% of patients.

A urinary tract infection had been objectified in 7 patients (20%). Thick film was positive in 24% of patients.

3.4. Therapeutic and Evolutionary Aspects

All our patients had received corticosteroid therapy; diuretics were prescribed in 94% of patients and antibiotics in 87%. Deworming and calcium supplementation were systematic. The mean hospital stay was 24 ± 13.7 days.

Corticosensitivity was retained in 86% (n = 30) (Table 2). Cyclophosphamide was combined with corticosteroid therapy in one corticosteroid-dependent patient (3%). The complete remission rate was 67%. The evolution was marked by 4 deaths (11 patients).

4. Comments and Discussion

Despite the methodological limits of our study, in particular the retrospective

Table 2. Therapeutic and evolutionary aspects of idiopathic nephrotic syndrome.

Variables		Workforce	Percentage
Treatments	Corticosteroid therapy	35	100
	Diuretic	33	94
	Antibiotic therapy	30	87
	calcium channel blocker	7	20
	IEC	3	9
	Methylprednisolone Boulus	2	6
	Cyclophosphamide	1	3
Duration of hospitalization	[1 to 2 weeks]	10	29
	[3 to 4 weeks]	16	46
	[5 to 6 weeks]	6	17
	>at 6 weeks	3	8
Become	Steroid sensitive	30	86
	Complete remission	24	67
	Steroid-dependent	4	11
	Relapse	2	6
	Steroid-resistant	5	14
	deceased	4	11

and monocentric nature, we were able to appreciate the epidemiological, clinical, paraclinical and therapeutic aspects of the idiopathic nephrotic syndrome in the general pediatrics department of the CHU-GT.

1) Epidemiology

NIS is a common universal disease in pediatric hospitals [10]. The frequency of NIS is highly variable in studies around the world. In our study, it was estimated at 1%. This rate was statistically close to that obtained in Congo Brazzaville by Moyen *et al.* (0.8%) [11] but slightly lower than the rate obtained by Keita *et al.* in Senegal (1.56%) [3].

2) Age

On admission, the average age of our patients was 7 years 5 months. Our results were similar to those of Kari *et al.* in Saudi Arabia but below the average reported by Moyen *et al.* who found 10 years and 8 months [11] [12]. According to the literature, NIS can occur at any age, but most often begins between 2 and 7 years of age, often after an infectious or allergic trigger [8]. The age of patients seems to be older in African countries, probably because it is rare to diagnose congenital and infantile nephrotic syndromes in sub-Saharan Africa [13]

3) Sex

Boys were more affected than girls in our study (sex-ratio = 2.22). This male preponderance had been reported in previous studies in Africa [9] [13] [14]. No reason had been advanced in the literature to explain this male predominance. The sex ratio was in most studies and depending on the geographical location between 1 (absence of male preponderance) and 3.8 (overwhelming majority of boys) [9] [13] [14]. The male preponderance tends to vanish as adolescence approaches [9] [14]. The majority of our patients lived in rural areas (54%), so it would be interesting to look for an interaction between SN and climatic factors and the use of pesticides or other products used in field work. The consultation delay was particularly long in our study because of cultural beliefs, poverty and ignorance [13].

4) Clinical data

In our study, edema was present in all patients; it was generalized in 91%. This state would be mainly due to the long delay of medical consultation. Arterial hypertension (HTA) due to stimulation of the renin-angiotensin-aldosterone (RAA) system was very common in our series (36%). Our results were similar to those noted in African studies [6] [15]. A Chinese study had shown a link between an age greater than 8 years at the onset of nephrotic syndromes and a high risk of hypertension and hematuria [16]. In our context, the complications would be mainly linked to the delay in diagnosis and adequate management [13] [10] [17].

5) Biological data

In our series, the average proteinuria was particularly massive (greater than 100 mg/kg/24h) and the excessive hypoalbuminuria (albuminemia < 20 g/l). These two phenomena were associated with severe malnutrition constituting a factor of poor prognosis on the evolution of the nephrotic syndromes towards

corticodependency or corticoresistance [3] [18]. Parasitic (malaria) and bacterial (respiratory and urinary) infections were very frequent. During the NS, the urinary leakage of immunoglobulins (useful in the defense against microbes) leads to an immune deficiency with a significant increase in the risk of infections responsible for recurrences in patients in remission and an inadequate response to corticosteroid therapy [19] [20]. Anemia and malnutrition were frequently observed in our patients. Their origin could be multifactorial, linked to significant urinary losses of EPO and transferrin but also to a deficiency in vitamins and trace elements which requires supplementation (vitamin D, zinc, iron) and an adapted diet [21] [22].

No kidney biopsy was performed in our patients. Renal biopsy (RPB) allows the precise identification of renal lesions and their nosological classification, the assessment of signs of severity, and the evaluation of the importance of chronic lesions [23].

6) Therapeutic and evolutionary aspects

The pathophysiological consequences of the nephrotic syndrome such as hypovolemia, acute renal failure, edema, hypercoagulation and infections were treated symptomatically according to the recommendations of the literature [3] [8]. In our study, the symptomatic treatments combined sodium restriction, a diet low in fast sugars, vitamin-calcium supplementation, anticoagulation in the event of a proven risk and, exceptionally, albumin infusions. Diuretics were prescribed with caution in patients with signs of intolerance or for the treatment of hypertension.

Corticosteroid therapy was the cornerstone of the management of our patients. It had achieved complete remission in 67% of patients. Relapses were observed in 6% of steroid-sensitive patients. These rates were lower than those reported by most African authors [13]. According to several authors, corticosteroid resistance is the main factor in the poor prognosis of NIS [10] [19] [24]. In our context marked by the poverty of the populations and the technical platform, non-compliance and delay in treatment had also been cited as one of the major causes of therapeutic failure in the event of idiopathic nephrotic syndrome [1] [25]. Despite several advances in pathophysiology, NIS remains a complex disease that requires new therapeutic approaches adapted to local contexts.

5. Conclusions

NIS is a common condition in pediatrics. The majority of cases occur in school-aged children. Edema was the main clinical manifestation. It was generally associated with hypertension and hematuria. The course under corticosteroid therapy was marked by complete remission in the majority of cases. Relapses were not uncommon (11%). Cyclophosphamide had been used in a patient with corticosteroid-resistant nephrotic syndromes.

For optimum management, the treatment must be adapted according to the clinical presentation, the histopathology and the socio-economic conditions of

the children.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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