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Nephrotic Syndrome: Epidemiological, Clinical, Paraclinical and Therapeutic Profile

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Abstract **Original Research Article**

Background: End-stage kidney disease has several causes, including nephrotic syndrome (NS). Steroid- resistant nephrotic syndrome (SRNS) children are a difficult subset of nephrotic syndrome patients who frequently respond poorly to conventional immunosuppression. ***Objective***: The goals of our research are to analyze the different types of nephrotic syndrome, to study the epidemiological, clinical and paraclinical profile, as well as to present the difficulty in managing steroid-resistant nephrotic syndrome. ***Methods***: Our study is a cross-sectional analysis of all patients hospitalized or followed in consultation, who were diagnosed with a nephrotic syndrome at the pediatric B department of the university hospital center Mohamed VI in Marrakech, from January 2011 to January 2022. ***Results*:** We gathered 447 instances, with an annual incidence of 41 cases. The children's ages varied from 12 days to 16 years, with an average of 5 years and 9 months. Pure nephrotic syndrome was found in 302 patients and 145 patients were carriers of impure nephrotic syndrome. In our study, 81.5% of patients had nephrosis as the cause of deseas. Secondary NS was seen in 11% of the patients, infant form was found in 6% and 1.5% of cases were congenital. The treatment was mainly based on oral corticosteroid therapy. 71.4% of the patients were corticosensitive of which 45.3% became corticodependent while 28.6% of the cases were corticoresistant. Corticosteroid boluses were used in 53% of cases. Immunosuppressants were prescribed in 31.5% of patients. ***Conclusion*:** In children, nephrotic syndrome is a common and chronic illness. It is of particular interest because of the frequency of nephroses, multiple relapses, the difficulties of management and the psychological and school impact on the child.

Keywords: Nephrotic syndrome, Steroids, Immunosuppressants, Children, Nephrosis.

INTRODUCTION

NS is one of the most common glomerular nephropathies in children. Nephrotic syndrome has a wide range of underlying conditions, but they all share the same pathophysiology, which is a significant protein loss in the urine as a result of an imperfect glomerular filtration barrier. About 1-3 per 100,000 children under the age of 16 are now affected by idiopathic nephrotic syndrome (NS) each year, which is defined by significant proteinuria, hypoalbuminemia, and/or the presence of edema. Following daily oral prednisolone/prednisone (PDN) treatment at recommended doses, proteinuria completely resolves in about 85% of cases. After 4-6 weeks of therapy, those who do not experience remission are assumed to have steroid-resistant NS [1, 2].

METHODS

This is a retrospective and descriptive study which concerned 447 children followed in the pediatric department B of the University Hospital Center Mohammed VI in Marrakech for nephrotic syndrome, over a period of 11 years, between January 2011 and January 2022.

The goals of our research are to analyze the different types of nephrotic syndrome, to study the epidemiological, clinical and paraclinical profile, as well as to present the difficulty in managing steroid-resistant nephrotic syndrome. Any nephrotic child admitted to the pediatric department B was included in the data collection.

RESULTS

In a period of 11 years, a total of 447 patients with nephrotic syndrome were admitted to the Department of Pediatrics. Of these, 289 were boys and 158 were girls. The incidence of idiopathic nephrotic syndrome was 41 cases per year, with an overall

frequency of 0.91% during a period of 11 years (from 21 cases to 54 cases per year).

The average age of patients at the time of diagnosis was 5 years and 9 months, with age extremes ranging from 12 days to 16 years. The age group between 2 and 10 was the well-represented, making up 65% of the population studied. 87% of nephroses begin before the age of 12 and 29.5% begin between 1 and 4 years old. Concerning the age of revelation of the disease, 1.7% of patients had symptoms that appeared before the age of 2 months, 4.3% had symptoms that appeared between 3 months and 1 year, 64% had symptoms that appeared between 1 year and 10 years, and 28% had symptoms that appeared more than 10 years. Furthermore, the age of onset was not known for 2% of cases.

The main clinical signs were distributed as follows, the vast majority of our patients 441 cases, presented white, soft, painless edema on the face and lower limbs. Ascites affected 32% of patients, pleural effusion affected 7%, and pericardial effusion affected 2% of patients. In 32% of the patients, hydrocele was detected. 24.16 % of kids had hypertension (108 cases). 18.79% of patients had hematuria. 13% of cases had oliguria while only 2.5% of patients had anuria.

Proteinuria ranged from 50 to 100 mg/kg/day in 57.33% of patients, 100 to 200 mg/kg/day in 27.8% of cases, and more than 200 mg/kg/day in 9.7%. In comparison, 31.5% of patients had albuminemia levels between 10 and 20g/l, 6.3% of patients had severe hypoalbuminemia below 10g/l, and 63.2% of patients had albuminemia between 20 and 30g/l. 85% of cases had normal renal function with an average of 0.25 g/l for urea and 6 mg/l for creatinine. A complete blood count was performed in 332 patients (74.33% of cases) and revealed hypochromic microcytic anemia in 26.2% of cases and hyperleukocytosis in 53.4% of cases. Thrombocytosis was found in 27% of cases.

Chest X-ray was performed in 158 patients, it was normal in 45.8% of patients, with evidence of bilateral pleural effusion in 19 patients (12%), 2 patients in our series had pericarditis.

Renal biopsy puncture was performed in 38.25% of patients, the findings were as follows: 43.1% had Minimal Change Disease (MCD), 21.4% had Focal segmental glomerulosclerosis (FSGS), 18.2% had Membranoproliferative glomerulonephritis (MPGN), 7% GNEC and 5.3% had Extramembranous glomerulonephritis, 5% had IgA nephropathy. In our study, nephrosis accounted for 81.5% of the causes of the nephrotic syndrome. In 11% of cases, the NS was secondary. Infantile NS affected 6% of cases, and congenital NS affected 1.5% of cases.

The treatment was mainly based on oral corticosteroid therapy, when the diagnosis of nephrosis is made; corticosteroid therapy is initiated based on prednisone 2mg/kg/d without exceeding 60mg/d for 04 weeks, switching to discontinuous mode. If proteinuria persists after the first month of treatment, corticosteroid therapy in the form of a bolus of methylprednisolone is used for 3 days. 71.4% of the patients were corticosensitive of which 45.3% became corticodependent while 28.6% of the cases were corticoresistant, and just 5% were corticosteroid-resistant from the beginning. Corticosteroid boluses were used in 53% of cases. Immunosuppressive treatment was prescribed in 31.5% of patients as second intention: 36.6% of cases on cyclophosphamide, 31.7% of cases on MMF, 14.1% of cases on ciclosporin, 12.6% of cases on Tarcolimus, and 5% of cases on Rituximab. The follow-up period ranged from 3 months to 10 years. The evolution was marked by the occurrence of relapses for 71% of patients, triggered mainly by infectious episodes in 52.8% of cases.

DISCUSSION

Nephrotic syndrome in children is an anatomo-clinical entity defined by proteinuria >40 mg/h/m2 or >50mg/kg/day or urinary protein creatinine ratio (UPCR) ≥ 200 mg/mmol (2 mg/mg) or 3+ on urine dipstick plus either hypoalbuminemia (< 30 g/l) and/or edema. It's the most common pediatric glomerular illness, affecting 1-3 per 100,000 children under the age of 16 worldwide each year [1]. In our study, the overall frequency over the eleven years was 0.91% with an incidence of 41 cases per year. It is essential to research the notion of purity of the NS, to differentiate between its primitive or secondary character, as well as to define the different modalities of evolution of the NS. Idiopathic nephrotic syndrome most frequently manifests between the ages of 2 and 7 years, and there is a male predominance [2]. In our series, the age group between 2 years and 10 years was the most represented, constituting 65% of the population studied.

Although edema is typically the main symptom of nephrotic syndrome, other clinical manifestations can also arise. Nephrosis attacks cause persistently low diuresis. Acute renal failure-related oligoanuria may be initially evident, but is typically reversible. NS can be identified by hypertension, which is brought on by increased renin-angiotensin secretion, sodium and water retention, and renal failure. 25% of children with nephrotic syndrome report hypertension right before an episode [2, 3].

The hemoglobin and hematocrit levels are increased, reflecting the hypovolemia and hemoconcentration of the patients. In the long term, microcytic anemia, linked to urinary loss of siderophilin and leakage of erythropoietin, 15% of children with nephrotic syndrome had thrombocytosis. If there is chronic kidney disease or another secondary cause

(SLE or malignancy), anemia may be present, white cell or platelet depletion also increases. Functional renal failure is transient and perfectly reversible; it is more common in adults than in children [2-4]. In our series, renal function was impaired in 9.6% of cases. Rarely can a chest radiograph find malignancy-related findings. The majority of the time, little pleural effusions are present and do not need treatment [2].

In our series, renal biopsy was performed in 38.25% of patients whose main indications were mainly corticodependency, corticoresistance and nephrotic syndrome impurity.

The renal biopsy puncture enables the anatomical-clinical classification of the primary and secondary nephrotic syndromes as well as the histological investigation of the kidney. Each anatomical feature has corresponding clinical and evolutionary traits. This enables the prognosis to be predicted and a therapeutic mindset to be adopted. Minimal Change Disease (MCD) and Primary Focal Segmental Glomerulosclerosis (FSGS) account for more than 80% of instances of idiopathic nephrotic syndrome in children, Minimal change disease (MCD) is the most prevalent cause of nephrotic syndrome in children. The prevalence of FSGS rises with age; the average onset age for FSGS is six years and three years for MCD. FSGS affects 20% to 30% of adolescents with nephrotic syndrome [2, 5, 6].

More than 85% of children and adolescents (often 1 to 12 years old) with idiopathic nephrotic syndrome achieve full proteinuria remission after daily corticosteroid therapy. After four weeks of daily prednisolone therapy, patients with steroid-resistant nephrotic syndrome (SRNS) do not show signs of remission. In children, the prevalence of steroid-resistant nephrotic syndrome ranges from 35 to 92 percent [7].

The Kidney Disease Improving Global Outcomes (KDIGO) listed the key medical terms for nephrotic syndrome: Patients who relapse while reducing the steroid dose or within 14 days of stopping the steroid are considered to have steroid-dependent nephrotic syndrome (SDNS). Two or more relapses within six months of the initial response or four or more in any one year constitute frequently relapsing nephrotic syndrome (FRNS) [5].

For the first episode of nephrotic syndrome, oral prednisone is administered at a dose of 60 mg/m2/day or 2 mg/kg/day (maximum 60 mg/day) for 4–6 weeks, then 40 mg/m2/day or 1.5 mg/kg/day (maximum 40 mg/day) on alternate days for 1–2 months. Prednisone is prescribed daily for relapses and is tapered to alternate days until the urine tests negative or hardly detectable for protein for three days. Alkylating drugs, calcineurin inhibitors, mycophenolate mofetil, and rituximab are a few of the medications used to prevent relapses in individuals who experience repeated relapses, particularly if there are considerable steroid side effects. An important part of care is to monitor urine at home for relapses [2, 8. 9].

Steroid-dependent nephrotic syndrome has been treated with oral cyclophosphamide therapy administered over a 12-week period of time. There are varying opinions on the effectiveness of intravenous (IV) cyclophosphamide therapy for treating SRNS, however some healthcare practitioners have found efficacy with monthly IV cyclophosphamide therapy (500 mg/m2/dose) for a 6-month course. Calcineurin inhibitors have been employed in the treatment of SRNS for a very long time, with the majority of data supporting cyclosporine medication. According to studies, cyclosporine combined with steroids helps children with SRNS maintain remission and lower their risk of relapse. Additionally, long-term cyclosporine therapy in kids with SRNS slowed the development of CKD. Tacrolimus can be used as an alternative to cyclosporine and has slightly less undesirable side effects, such as gum hypertrophy and hypertrichosis. There have been reports of other side effects, such as tremor, hypertension, and diabetes. A full remission rate of 81% was attained. Mycophenolate mofetil (MMF) is uncertainty used to treat SRNS. Patients with SRNS who have taken calcineurin inhibitors and suffered serious side effects may occasionally use it as a substitute medication. In recent years, rituximab has gained acceptability as a first-line steroid-sparing medication in the treatment of kids with steroid-dependent nephrotic syndrome, as well as a treatment for refractory instances of pediatric nephrotic syndrome. The International Pediatric Nephrology Association (IPNA) conducted a study on the effectiveness of rituximab for SRNS and discovered that children with SRNS had a perceived response rate of 44% whereas those with steroid-dependent nephrotic syndrome had an estimated response rate of 82% [1, 10].

Within 8 weeks of starting corticosteroid therapy following their initial presentation, 95% of kids with minimal change disease (MCD) as determined by histology experienced clinical remission. It has been more challenging to treat children with steroid-resistant nephrotic syndrome (SRNS), with 36% to 50% developing to end-stage renal disease within 10 years [10].

The objectives of symptomatic treatment are to avoid and manage problems including infections and thrombosis in addition to controlling edema with a mix of albumin infusions and diuretics. To encourage growth and development, it is crucial to provide nutritional assistance and to replenish urine losses with thyroxine and cholecalciferol. Kidney transplantation for children is eventually necessary, and is frequently

followed by nephrectomies to address hypercoagulability and hyperlipidemia if the patient is still nephrotic [2, 7].

Conflict of Interest: None.

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