

## Response to Steroid Therapy in Nephrotic Syndrome

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### ABSTRACT

Nephrotic syndrome is a common renal disorder among children. The response to corticosteroid therapy is the best prognostic marker of the disease. Steroid responsiveness, however, is not uniformly distributed globally. This is a prospective study, conducted in the Pediatric ward at Nepal Medical College Teaching Hospital, Kathmandu, Nepal from April 2013 to April 2016 to determine response to steroid therapy in nephrotic syndrome. This study included 32 children who were diagnosed to have nephrotic syndrome. There were 22 male and 10 female patients. Steroid sensitivity among the children was 93.75% (30 cases) and 6.25% (2 cases) were steroid resistant. Out of 30 steroid sensitive children, 2 (6.66%) were steroid dependent, 4 (13.33%) were frequent relapsers and 6 (20%) were infrequent relapsers. Complications were seen in 2 (6.25%) patients, who developed spontaneous bacterial peritonitis. Our study showed high steroid sensitivity among children with nephrotic syndrome.

**Keywords:** Nephrotic syndrome, Steroid sensitivity

### INTRODUCTION

Nephrotic syndrome is a common renal disorder with an incidence of 20 to 40 per million in developed countries and 90 to 100 per million in the Indian subcontinent.<sup>1</sup> The characteristic features of nephrotic syndrome are heavy proteinuria (>40mg/m<sup>2</sup>/hr), hypoalbuminemia (<2.5g/dl), edema and hyperlipidemia. The renal histology shows 85% of affected children have steroid sensitive minimal change disease, 10% have focal segmental glomerulosclerosis and 5% have mesangial proliferative glomerulonephrosis.<sup>2</sup> Investigations recommended at the initial episode includes: urine analysis, complete blood count, blood level of albumin, cholesterol, urea and creatinine. Other investigations like antistreptolysin-O, complement (C3) level and antinuclear antibodies are done if necessary.<sup>3</sup> Renal biopsy is considered among children with features that make minimal change diseases less likely (hematuria, hypertension, renal insufficiency, hypocomplementemia, age <1yr or >8yr).<sup>2</sup> The management of idiopathic nephrotic syndrome (INS) in children includes immunosuppressive and symptomatic treatment. The response to corticosteroid therapy is the best prognostic marker of the disease.<sup>4</sup> All children with presumed minimal change disease are treated with prednisone 60mg/m<sup>2</sup>/day for 4-6 weeks. After remission is achieved, prednisone is tapered to 40mg/m<sup>2</sup>/day every alternate day, which is slowly tapered and discontinued over the next 2-3 months.<sup>2</sup> Steroid responsiveness is however, not uniformly distributed globally. High steroid responsiveness has traditionally been demonstrated in

temperate regions of the world and conversely, high steroid resistance in tropical regions.<sup>5</sup> Patients who fail to show remission despite 8 weeks of daily treatment with prednisone are considered to have steroid resistance and should be considered for renal biopsy. Patients with relapse while on alternate day steroid therapy or within 28 days of stopping prednisone are termed as steroid dependent. Patient who respond well to prednisone therapy but relapse four or more times in a 12 month period are termed frequent relapsers.<sup>2</sup> As the steroid responsiveness determines the treatment, outcome and prognosis of the disease, this study is purposed to determine the prevalence of steroid responsive nephrotic syndrome in Nepal Medical College Teaching Hospital.

### MATERIALS AND METHODS

This is a prospective hospital based study conducted from April 2013 to April 2016 in Nepal Medical College. All children admitted in the pediatric ward with a diagnosis of nephrotic syndrome were included in the study. The patients were treated with the standard regime of prednisone therapy; in which, children are treated with prednisone 60mg/m<sup>2</sup>/day for 4-6 weeks, followed by tapering of prednisone to 40mg/m<sup>2</sup> day every alternate day once remission is achieved, which is slowly tapered and discontinued over the next 2-3 months. Nephrotic syndrome is diagnosed based on the following: 24-hours urine protein > 40 mg/m<sup>2</sup>/hr or spot urine protein: creatinine ratio > 2, hypoalbuminemia (serum-albumin < 2.5 g/

dl), generalized edema and hypercholesterolemia (>200mg/dl). Remission is defined as nil or trace protein in 3 consecutive early morning urine samples. Data of patients who were admitted with the diagnosis of steroid resistant nephrotic syndrome was collected in a preformed performa. Ethical clearance was obtained from NMCTH ethical committee.

**RESULTS**

This study included 32 children who were diagnosed to have nephrotic syndrome. There were 22 male and 10 female patients. The ratio of male and female is 2.2. Mean age of the patient is 8.6 years. Hematuria was present in 8 patients, hypertension in 2 and UTI in 6.

Serum albumin was decreased in 16 patient and serum cholesterol was increased in 20 of them. Mean serum albumin was 2.4gm, serum cholesterol was 325mg and serum creatinine was 0.5mg/dl in the study. Steroid sensitivity among the children was 93.75% (30 cases) and 6.25% (2 cases) were steroid resistant. Out of 30 steroid sensitive children 2 (6.66%) were steroid dependent, 4 (13.33%) were the frequent relapsers and 6 (20%) were infrequent relapsers (Table 1).

**Table 1:** Steroid sensitivity pattern of the patients

S. No.	Pattern	Number (percentage)
I	Steroid sensitive:	30 (93.75%)
	Cured	18 (60.00%)
	Steroid dependent	2 (6.66%)
	Frequent relapse	4 (13.33%)
II	Infrequent relapse	6 (20.05%)
	Steroid resistant	2 (6.25%)

Most of the children improved after treatment with the standard regime of steroid therapy with prednisone except 2(6.25%) patients, who were referred to the other center for renal biopsy (Table 2). Complication was seen in 2 (6.25%) patient who developed spontaneous bacterial peritonitis. Both of them improved after being treated with appropriate antibiotics.

**Table 2:** Patient outcome

S. No.	Outcome	Number (percentage)
1	Improved	26 (81.25%)
2	LAMA <sup>#</sup>	2 (6.25%)
3	DOR <sup>§</sup>	2 (6.25%)
4	Referred for renal biopsy	2 (6.25%)

<sup>#</sup> Left Against Medical Advice; <sup>§</sup>Discharged On Request

**DISCUSSION**

The result of our study showed 30(93.75%) children to have steroid sensitive nephrotic syndrome and only 2 (6.66%) were steroid resistant. A study done in India showed majority of cases (97%) were responders to steroid therapy, whereas reports from Nigeria showed the steroid sensitivity between 71% to 83%.<sup>5-7</sup> In a study done in Turkey, out of the 114 patients, 30 children had an initial response, 25 children had infrequent relapse, 19 had frequent relapse, 25 had steroid dependence and 15 children had steroid resistance.<sup>8</sup> Up to 80% of children with idiopathic nephrotic syndrome respond to corticosteroids. Approximately, one third of these patients have only one attack and are definitely cured after the course of corticosteroids. Ten to 20% of patients experience relapses several months after stopping the treatment and a cure takes place after three or four episodes. The remaining 40 to 50% of patients experience frequent relapses. These steroid-dependent patients may have a prolonged course. In the long term, the risk for relapse and the adverse effects of the treatments remain the main concerns.<sup>9</sup> In a study done in United Kingdom to determine the incidence of steroid sensitivity among the children of Asia, Europe and Afro-Caribbean showed steroid sensitivity was six times high in Asian children.<sup>10</sup> Both the steroid resistant patients were referred to other center for renal biopsy as the facility is not available in our center for the children. In a study done in another center of Nepal showed nephrotic syndrome was the most common indication for renal biopsy (31.02%) in children, among them steroid resistant nephrotic syndrome and steroid dependent nephrotic syndrome was 24.13% and 6.89% respectively. It also showed focal segmental glomerulosclerosis (27.58%) and lupus nephritis (27.58%) were the most common glomerular disease in children.<sup>11</sup> In a study conducted in North America, Europe, and Asia, the distribution of patients among histopathological categories revealed that 76.6% had minimal change nephrotic syndrome, 7.5% had membranoproliferative glomerulonephritis and 6.9% had focal segmental glomerulosclerosis.<sup>12</sup> As the facility to do renal biopsy in children is not available in our center we could not categorized the patient according to histopathology. Steroid resistant nephrotic syndrome presents mainly as focal segmental

glomerulosclerosis which has a very bad prognosis with the majority of cases evolving to terminal renal insufficiency within several years.<sup>13</sup> Age of the onset of the disease is one of the important factors that predict the outcome of disease. Though the most common age for presentation of nephrotic syndrome is between 1 to 10 years, most of the children in our study were between the age of 10 -14 years with male predominance. Another study done in Nepal also showed most of the patient were between the age of 10 -14 year with 62% male and 38% female.<sup>14</sup> In another study common age of presentation was between 2-15 years with male to female ratio of 3.27:1.36.<sup>6</sup> Edema is one of the most important clinical features of nephrotic syndrome. It was present in all the patient and pleural effusion was present in 25% in our study. Similar result was seen in another study with puffiness of face and swelling of limbs were present in all the patient and pleural effusion in 15% of cases.<sup>6</sup> In our study, 40.60% of cases have infection with UTI in 18.75%, acute gastroenteritis in 18.75% and acute respiratory tract infection in 12.50%. Acute respiratory infections and urinary tract infections are the most frequent infectious triggers of relapse, which was seen in our study also where 4 cases of frequent relapsers were precipitated by acute gastroenteritis and 2 cases of infrequent relapsers by acute respiratory tract infection.<sup>15</sup> In one of the study also Infections were seen in 31% of cases with UTI being the commonest infection (25% of infections).<sup>6</sup> In our study, hematuria and hypertension was present in all patients with steroid resistant nephrotic syndrome. Our finding is supported by a study done in Indian children which showed the factors predicting a poor response to standard prednisolone therapy were age of onset more than eight years, male sex, hypertension, microscopic hematuria and presence of non-minimal change nephrotic syndrome lesions on histopathology.<sup>16</sup> Our study reports high steroid sensitivity in children with nephrotic syndrome. As the study was conducted in limited number of

patient and in a single center, further multicenter studies should be conducted in larger population to determine the actual scenario in our country.

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