

# Full Dose Steroid Responsiveness Within 8 Weeks in Initial Treatment of Childhood Nephrotic Syndrome

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## ABSTRACT

**Objective:** To determine the steroid responsiveness within 8 weeks of the initial treatment of childhood nephrotic syndrome.

**Patients and Methods:** This prospective study was conducted in Children Hospital, Pakistan Institute of Medical Sciences, Islamabad from January 2012 to June 2012. A total of 139 children aged 1 to 10 years of both genders diagnosed as nephrotic syndrome were included in the study. Those children who were already taking any form of therapy for Nephrotic syndrome were excluded from the study. These children were given prednisolone 60 mg/m<sup>2</sup> of body surface area, divided into 3 doses for a period of 8 weeks and then switched over to 40 mg/m<sup>2</sup> as a single morning dose on alternate days, in those children who showed a response. The primary outcome of the study was to see the response of steroid therapy at different occasions for up to 8 weeks. SPSS version 11.0 was used for data analysis. Mean and standard deviation were calculated for numerical variables and frequency and percentages were calculated for categorical variables.

**Results:** In this study 16.5% of cases responded to steroids within 2 weeks, major bulk of patients (43.5%) showed response between 3-4 weeks, (20.1%) and (2.1%) patients responded between 5-6 weeks and 7-8 weeks respectively. Steroid resistant nephrotic syndrome was seen in 16% of the study cases.

**Conclusion:** Steroids are first line treatment for the idiopathic nephrotic syndrome. The majority of the patients show a response within 8 weeks of their first presentation. Maximum number responds between 3-4 weeks.

**Keywords:** Children, Nephrotic syndrome, Steroid therapy.

### Author's Contribution

<sup>1</sup>Conception, Synthesis and Planning of the research, <sup>2,3</sup>Active participation in active methodology, Interpretation and discussion, <sup>4</sup>Data Analysis

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## Introduction

Nephrotic syndrome (NS) is characterized by heavy proteinuria (>40 mg/m<sup>2</sup>/hr), hypoalbuminemia (<2.5 gm/dL), oedema and hypercholesterolemia (>200 mg/dL). It is a very common glomerular disorder in developing countries including Pakistan and has significant morbidity and mortality due to various complications. The majority

of children with NS show a good response to steroids within 8 weeks of their first presentation. NS is a common glomerular disorder and 15 times more common in children than adults.<sup>1</sup> Estimates of annual incidence ranges from 2 to 7 new cases in children under 16 years per 100,000 population.<sup>2</sup> The general consensus for the

treatment at first presentation is daily induction therapy of prednisolone at 60 mg/m<sup>2</sup> given in 3 divided doses for 6 weeks, followed by alternate day maintenance therapy of 40 mg/m<sup>2</sup> given as single morning dose for 6 weeks.<sup>3</sup> Studies found that the longer duration of corticosteroids lasting 12-16 weeks for the initial episode results in higher remission rates, longer duration of remissions and lower rate of subsequent relapses.<sup>4-6</sup> Thus more aggressive treatment of idiopathic nephrotic syndrome with a longer initial course of corticosteroids (12-16 weeks) may improve the steroid responsiveness and consequently decrease the population of patients labeled as having a steroid-resistant nephrotic syndrome (SRNS) which is defined as failure to achieve remission on completion of 8 weeks of full dose daily steroids.

Steroid responsiveness in childhood idiopathic nephrotic syndrome (INS) have been found consistent,<sup>1,7</sup> however, in some studies variability has also been reported. Numerous reports have shown wide racial and geographical variation in the presentation of INS and response to therapy.<sup>8-10</sup> Minimal change disease (MCN) is the most common histopathological lesion (85%) and generally has a favorable response to steroids therapy in 85-90% of the patients<sup>1,7,11-13</sup> This is followed by focal segmental glomerulosclerosis (FSGS) 10% and mesangial proliferation (5%), which shows less (approx. <20%) response to steroids. Approximately 50% of patients with diffuse early membranoproliferative glomerulonephritis (MPGN) show an early response to steroid and undergo complete remission. An additional 20% have continued proteinuria and 6% progress to renal insufficiency and chronic renal failure.<sup>14</sup>

The present study was planned to estimate the efficacy of steroid responsiveness in childhood nephrotic syndrome within 8 weeks of the first presentation in order to develop strategies to reduce the complications of INS which prove to be fatal in children.

## Patients and Methods

This prospective study was conducted at the Department of Pediatrics Medicine at Children's Hospital, Pakistan Institute of Medical Sciences, Islamabad from January 2012 to June 2012. A total of 139 patients, aged 1 to 10 years of both genders, with newly diagnosed Nephrotic Syndrome, including those patients who were referred

from health facilities to the Nephrology Clinic of the Children Hospital were included in the study. Children who were already taking any form of medication for NS were excluded from the study. Similarly, those patients with impaired renal function and secondary etiologies of NS like systemic lupus erythematosus, Hersch Scholien Purpura, Sickle cell anemia, malignancies, metabolic disorders, hepatitis and any form of renal malformations were excluded from the study.

Ethical approval was taken from the ethical committee of PIMS Hospital. A detailed history including history of gross haematuria, hypertension, jaundice, joint pain, rash and drug intake was recorded. Patients were evaluated for hypertension, anthropometric parameters (height, weight, body surface area) and systemic involvement. They were investigated for confirmation of nephrotic syndrome and exclusion of secondary causes. After diagnosing NS they were started on prednisolone 60 mg/m<sup>2</sup> of body surface area divided into 3 doses for a period of 8 weeks and then switched over to 40 mg/m<sup>2</sup> as a single morning dose on alternate days in those patients who showed a response, irrespective of underlying histopathology. The primary outcome of the study was to see the response of steroid therapy at different occasions up to 8 weeks. Steroid response was seen and recorded into groups i.e. within 2 weeks, 3-4 weeks, 5-6 weeks and 7-8 weeks.

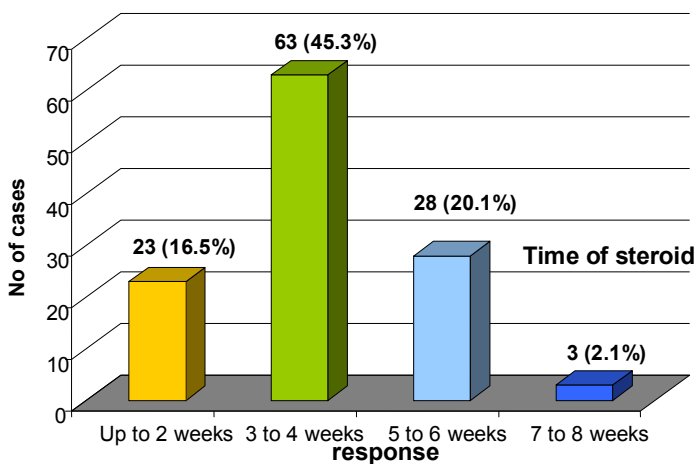
SPSS versions 11.0 was used for data analysis. The frequency and percentage were calculated for categorical data (gender, steroid response). Mean and standard deviations were calculated for numerical data (age, height, weight, body surface area).

## Results

In this study, a total of 139 patients with nephrotic syndrome were enrolled. The Mean±SD age of study patients was 48.1 months ±25.3SD, ranging from 10 to 120 months. The majority of the children 82 (58.9%) were between 24 to 59 months of age. Twenty-one (15.1%) children were up to 24 months of age while 36 (25.9%) were off 60 months or above. Male gender was found in dominance in this study, comprising of almost 75% patients. The male to female ratio was 2.9 : 1 (Table 1).

	Number	Percentage
<b>Age (months)</b>		
Up to 24	21	15.1
24 to 59	82	58.9
60 and above	36	25.9
<b>Age (months)</b>		
Age; Mean±SD	48.1 (25.3)	
Range (min – max)	10 – 120	
<b>Gender</b>		
Male	104	74.8
Female	35	25.2
<b>Male:Female ratio</b>	2.9: 1	

The response of steroid was calculated on different occasions. In this study, 23 (16.5%) of newly diagnosed nephrotic syndrome patients responded to steroids within 2 weeks of therapy. The response rate between 3 to 4 weeks was even high as 63 (45.3%) of study patients responded in this period. Out of the total 139 patients, 28 (20.1%) patients responded between 5 to 6 weeks of therapy. Similarly, 3 (2.1%) cases responded between 7 to 8 weeks of initiation of steroid therapy. However, 22 (16.0%) of patients showed no response to steroid even in 8 weeks and were labeled as steroid resistant. (Figure 1)



**Figure 1: The trend of steroid response in the study (n = 139)**

We also analyzed the steroid response according to the gender of patients. Out of total 104 male patients, 20 (19.2%) responded within 2 weeks, 50 (48.1%) responded between 3 to 4 weeks, 19 (18.2%) responded between 5 to 6 weeks while 1 (0.9%) patient responded between 7 to 8 weeks. Fourteen (13.4%) of the male patients showed resistance. Similarly, out of total 35 female patients, 4 (11.4%) responded within 2 weeks, 13 (37.1%) responded between 3 to 4 weeks, 9 (25.7%) responded between 5 to 6 weeks and 1 (2.8%) patient responded between 7 to 8 weeks. Eight (22.8%) of the females were found resistant to steroid therapy (Table 2).

	Male (n = 104) n(%)	Female (n = 35) n(%)
<b>Up to 2 weeks</b>	20 (19.2)	4 (11.4)
<b>3 to 4 weeks</b>	50 (48.1)	13 (37.1)
<b>5 to 6 weeks</b>	19 (18.2)	9 (25.7)
<b>7 to 8 weeks</b>	1 (0.9)	1 (2.8)
<b>Resistance to steroids</b>	14 (13.4)	8 (22.8)

While analyzing steroid response according to age of the patients it was found out that of the total 22 patients of up to 24 months, 4 (18.1%) responded within 2 weeks, 11 (50.0%) responded between 3 to 4 weeks, 3 (13.6%) responded between 5 to 6 weeks while 1 (4.5%) patient responded between 7 to 8 weeks. Three (13.6%) of the under 24 months' patients showed resistance to steroid therapy. Similarly, out of total 82 patients between 24 and 59 months of age, 16 (19.5%) responded within 2 weeks, 36 (43.9%) responded between 3 to 4 weeks, 18 (21.9%) responded between 5 to 6 weeks and 0 (0.0%) patient responded between 7 to 8 weeks. Twelve (14.6%) of the patients were found to have resistance to steroid therapy. Out of 35 patients of 60 or above months of age, 4 (11.4%) responded within 2 weeks, 16 (45.7%) responded between 3 to 4 weeks, 7 (20.0%) responded between 5 to 6 weeks and 1 (2.8%) patient responded between 7 to 8 weeks. While 7 (20.0%) of the patients were found to have resistance against steroid therapy in this age group. (Table 3) Overall out of 139 patients, 22 (16.0%) had steroid-resistant nephrotic syndrome (SRNS).

**Table 3: Steroid response according to age.**

	<b>Up to 24 mon (n = 22) n(%)</b>	<b>24-59 mon (n = 82) n(%)</b>	<b>60 and above (n = 35) n(%)</b>
<b>Up to 2 weeks</b>	4 (18.2)	16 (19.5%)	4 (11.4)
<b>3 to 4 weeks</b>	11 (50.1)	36 (43.9)	16 (45.7)
<b>5 to 6 weeks</b>	3 (13.6)	18 (21.9)	7 (20.0)
<b>7 to 8 weeks</b>	1 (4.5)	0 (0.0)	1 (2.8)
<b>Resistance to steroids</b>	3 (13.6)	12 (14.6)	7 (20.0)

## Discussion

Nephrotic syndrome is the most common chronic glomerular disease in children. In 85% of children, there is minimal change disease and it generally has a favorable response to glucocorticoid therapy in 90% of patients.<sup>1</sup> In about 40% of the steroid-sensitive nephrotic syndrome (SSNS), relapse may occur and some of these patients may become steroid dependent. Response to steroids also vary geographically.<sup>15-17</sup> In few studies from the African region, the steroid response rate was as low as 20% in children with Nephrotic syndrome while some reports showed paucity of minimal change disease and also poor response to steroids.<sup>15-17</sup> In our study patients, demographic features are comparable to these reports where we found out the mean age of 4.1 years with male population in majority 75%. The dominance of male gender in our study could be due to the social norms in the developing world as parents and caretakers give priority care to boys compared to girls even for medical consultation.

In a study by Safaei A and Maleknejad S on the spectrum of childhood Nephrotic syndrome, the mean age of patients was 4.8 years and the male population was dominant with 66% proportion.<sup>18</sup> In another study the mean age of patients was 5.8 years and gender distribution was equal with 50% in each strata.<sup>12</sup> In this study conducted for evaluation of steroid response in children with NS, 17% of cases responded to steroids within 2 weeks, 46% responded between 3 to 4 weeks while 22% and 9% patients responded to steroid between 5 to 6 weeks and 7 to 8 weeks respectively. It was proven again that NS responds well to steroids in the pediatric

population as more than 60% of our patients responded within 4 weeks of start of therapy. Steroid resistance was found in 16.0% of our cases. In a local study by Azam M and colleagues on nephrotic syndrome, the steroid response was reported to be 76% within 4 weeks of therapy, 16% responded within 8 weeks of steroid therapy while 6% did not responded even after 8 weeks.<sup>8</sup>

In another study by Anochie I and colleagues on the pattern of steroid response in children with NS after 1 month of therapy, more than 70% had responded well and 57% got complete remission while 14.3% had resistance against steroids. Another 14.3% had frequent relapsing nephrotic syndrome and became steroid dependent.<sup>12</sup> In a study from Iran it was reported that 66% children with Nephrotic syndrome were steroid sensitive, 20% were steroid resistant while 14% were steroid dependent.<sup>18</sup> The above-mentioned steroid response rate is comparable to our study findings, we found out that more than 60% of the children responded to steroid within 4 weeks of therapy, 22% responded between 5 to 6 weeks while 10% responded between 7 to 8 weeks after start of steroid therapy. In our study, more than 53% of the responders were between 2 to 6 years of age. These findings are almost similar to Anochie I's study, where they noted that about 50% of cases who responded to steroid therapy were between 1 to 4 years.<sup>12</sup> The steroid response according to the gender of patients was quite similar. Out of total 104 males, 18.2% responded within 2 weeks, 48.1% responded between 3 to 4 weeks, 18.2% responded between 5 to 6 weeks while 0.9% responded between 7 to 8 weeks. Similarly, of total 35 female patients, 11.4% responded within 2 weeks, 37.1% responded between 3 to 4 weeks, 25.7% responded between 5 to 6 weeks and 2.8% responded between 7 to 8 weeks.

Overall out of 139 study patients, 22 (16.0%) had steroid-resistant nephrotic syndrome (SRNS). In a study by Iyengar A and colleagues, steroid resistance was found in 36% of under 24 months' patients while in 46.2% patients above 24 months of age.<sup>19</sup> Overall 58.3% of their study patients had steroid resistance, which was quite high compared to our study as we found steroid resistance in 16% cases. Another study from Iran reported a similar (20.0%) resistance to steroids which is close to our study findings.<sup>18</sup> The current study was one of the very few



prospective trials done in the local settings on children with nephrotic syndrome. The sample size was adequate for a reasonable study population comprising of 139 children. One of the benefits of the study is that steroid response has been evaluated in almost all pediatric age groups from 1 year to 10 years.

There were few limitations of the current study, as there was no collection of information regarding patients presenting complaints and etiology of the disease. A more dynamic approach of collection study information would have provided some details regarding etiology of study patients and understanding the pattern of steroid response better.

### Conclusion

Our study approves the scientific evidence in favor of steroids for children with nephrotic syndrome. Idiopathic nephrotic syndrome is a constant presentation in our setting and steroids can be a sensitive drug for its treatment. The majority of the patients showed a response within 8 weeks of their first presentation. Most of these patients respond to steroid therapy during 4 weeks of initiation of treatment. There is also a need to study different doses of steroids for the different duration in these patients to check efficacy.

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