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Research Article

**ANALYSIS OF RECENT ADVANCES AND TREATMENTS OF  
CHILDHOOD NEPHROTIC SYNDROME IN PAKISTAN**Dr. Numan Javed<sup>1</sup>, Dr. Kainat Usman<sup>2</sup>, Dr. Khula Sidra<sup>3</sup>

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**Abstract:**

**Introduction:** Nephrotic syndrome is characterized by gross proteinuria, hypo albuminemia, hyperlipidemia, and peripheral edema. The etiology of nephrotic syndrome in adults is complex and ranges from primary glomerulonephritis to secondary forms. **Objectives of the study:** The main objectives of the study is to find the recent advances and treatments of childhood nephrotic syndrome in Pakistan. **Methodology of the study:** This study was done at Sialkot hospital with the collaboration of DHQ hospital Bahawalpur during May 2018. This study was done according to the rules and regulations of hospital ethical authority. The data was collected from 100 patients of both genders which was suffering from nephrotic syndrome. The basic purpose of this data is to find and investigate the recent advances and treatments of nephrotic syndrome in Pakistani hospitals. **Results:** The study group comprised of 100 patients 72 (93.5%) were initial steroid resistant and 28 were late non-responders. Gender distribution showed 49 (63.6%) males and 28 (36.4%) females with a ratio of 1.75. Age range of patients was 1-15 years with a mean of  $8.11 \pm 3.58$  years. Sixty nine (89.6%) patients underwent renal biopsy. Patients with focal segmental glomerulo sclerosis (FSGS) were least likely to respond to treatment followed by mesangio proliferative glomerulonephritis and minimal change disease. **Conclusion:** Nephrotic syndrome can increase your child's risk of infection and blood clots. It always affects both kidneys and usually appears in the early years of your child's life. Most children with this disorder outgrow it by young adulthood. We conclude that NS in children is a difficult disease with significant morbidity.

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**INTRODUCTION:**

Nephrotic syndrome is characterized by gross proteinuria, hypo albuminemia, hyperlipidemia, and peripheral edema. The etiology of nephrotic syndrome in adults is complex and ranges from primary glomerulonephritis to secondary forms. Primary forms of nephrotic syndrome in adults are comprised of three histological disease entities: idiopathic membranous nephropathy (iMN), minimal change disease (MCD), and focal segmental glomerulo sclerosis (FSGS) [1]. The basis for therapy of primary nephrotic syndrome is mostly of supportive nature. Supportive strategies include antihypertensive and anti-proteinuric therapy and dietary recommendations. Patients with nephrotic syndrome are also at increased risk to develop thromboembolism. In patients with membranous nephropathy, the adjusted hazard ratio for thromboembolism was 10.8 compared to patients with IgA nephropathy [3]. In contrast, for patients with FSGS the hazard ratio was 5.9. Hence, anticoagulant therapy is recommended in patients with a primary nephrotic syndrome, especially in iMN and serum albumin < 2.5 mg/dl. In 2014, Lee et al. proposed a practical approach to prophylactic anticoagulation therapy in patients with iMN. The presented model takes into account the serum albumin concentration; the individual patient's bleeding risk, and the risk tolerance as reflected by the selected benefit-to risk ratio [3].

Idiopathic, or primary, nephrotic syndrome is often used to describe the group of patients for whom no specific cause has been identified, and the histology is relatively non-specific [4]. These patients will usually receive immunosuppression without knowledge of the mechanism and be categorized according to response. So the challenge is to understand and categorize the underlying injury at a molecular level and therefore adapt treatments according to the likely mechanism<sup>5</sup>.

**Objectives of the study**

The main objective of the study is to find the recent advances and treatments of childhood nephrotic syndrome in Pakistan.

**METHODOLOGY OF THE STUDY:**

This study was done at Sialkot hospital with the collaboration of DHQ hospital Bahawalpur during May 2018. This study was done according to the rules and regulations of hospital ethical authority. The data was collected from 100 patients of both genders which were suffering from nephrotic syndrome. The basic purpose of this data is to find

and investigate the recent advances and treatments of nephrotic syndrome in Pakistani hospitals. The main objectives in management of nephrotic syndrome are to induce quick remission to ensure freedom from edema and consequences of persistent nephrotic state such as hyperlipidemia, protein malnutrition, thromboembolic episodes, severe infections, etc. Demographic data of the patients, treatment received, and outcome of treatment and complications were recorded.

**Statistical analysis**

Student's t-test was performed to evaluate the differences in roughness between group P and S. Two-way ANOVA was performed to study the contributions. A chi-square test was used to examine the difference in the distribution of the fracture modes (SPSS 19.0 for Windows, SPSS Inc., USA).

**RESULTS:**

The study group comprised of 100 patients 72 (93.5%) were initial steroid resistant and 28 were late non-responders. Gender distribution showed 49 (63.6%) males and 28 (36.4%) females with a ratio of 1.75. Age range of patients was 1-15 years with a mean of 8.11 ± 3.58 years. Sixty nine (89.6%) patients underwent renal biopsy. Patients with focal segmental glomerulosclerosis (FSGS) were least likely to respond to treatment followed by mesangio proliferative glomerulonephritis and minimal change disease.

**Table 01:** Demography of 100 selected patients

Category	Number (% age)
<b>Biopsied</b>	69(89.6%)
<b>Un biopsied</b>	08(10.4%)
<b>Initial SR</b>	72(93.5%)
<b>Late SR</b>	05(6.5%)
<b>Males</b>	49(63.6%)
<b>Females</b>	28(36.4%)
<b>Age(Years)</b>	
<b>&lt;4</b>	22(28.6%)
<b>4-10</b>	31(40.2%)
<b>&gt;10</b>	24(31.2%)

The patients in group 1 received CsA plus PDN, MMF plus PDN, combined CsA and MMF plus PDN, and intravenous MP pulses ± oral PDN and CPM as S1, S2, S3, and S4 treatment respectively. Following S1, 31/61 patients (50.8%) achieved complete remission, 5/61 (8.2%) were partial responders, and 25/61 (41%) were non-responders. Three patients (4.9%), who were resistant to both steroids and CsA, went into remission with MMF plus steroids (S2). Six patients (9.8%) got remission

with S3. After three steps of treatment, 40/61 (65.6%) children went into remission. Mendoza protocol<sup>28</sup> (Table 2) (S4) was effective in inducing remission in further 4/61 (06.6%) patients who did not respond to S1- S3. In group1, 02/61 (3.3%)

patients were partial responders and 15/61 (24.6%) were non-responders to any immunosuppressive treatment (Table 3). These 17 (27.9%) patients in group1 went on to develop CKD.

**Table 02: Treatment of nephrotic syndrome**

Sequential Treatment Step	Drugs	Number of Patients	Complete Remission	Partial Remission	No Remission
Step 1	CsA + PDN	61 (79.2%)	31 (50.8%)	05 (8.2%)	25 (41%)
Step 2	MMF + PDN	30 (49.2%)	03 (4.9%)	07 (11.5%)	20 (32.8%)
Step 3	CsA + MMF +PDN	27 (44.3%)	06 (9.8%)	09 (14.8%)	12 (19.7%)
Step 4	IVMP + PDN ± CPM	21 (34.4%)	04 (6.6%)	02 (3.3%)	15 (24.6%)
Total: Steps 1-4		61 (100%)	44 (72%)	02 (3.3%)	15 (24.6%)

### DISCUSSION:

There have been no consistent clinical cues to either whether a patient with nephrotic syndrome has the risk of becoming steroid-resistant in the future or whether they will suffer recurrence post-transplant<sup>6</sup>. There are weak clinical associations with recurrence (for example, age at onset of disease, race, and serum albumin at diagnosis or time to first dialysis/transplant. Interestingly, the last two features may point to the possibility that CFD has a more aggressive presentation and natural course, compared with the monogenic or 'other' groups [6]. To address the question of whether there are clinical features that pertain to CFD, we hypothesized that patients with the archetypal CFD, those with post-transplant recurrence, would have distinct early clinical features regarding their initial response to immunosuppression [7]. If a patient has initial steroid sensitivity (otherwise described as secondary steroid resistance), they are likely to have an immune-mediated circulating factor causing their underlying disease and therefore high risk of recurrence [8].

Treatment of SRNS in children continues to pose a therapeutic challenge to the pediatric nephrologists. The lack of large-scale randomized controlled trials leads to a paucity of strong evidence to inform treatment decisions. The treatment strategies are heterogeneous with variable efficacy and side effects' profile. Optimal strategies with least toxicity remain to be determined [9]. Without effective treatment, progression to the end-stage kidney disease is very likely [10]. We have been treating our SRNS children employing a sequential stepwise approach using different immunosuppressive therapies. Failure to respond to any step of treatment or intolerance/toxicity to any drug was the criterion to use the next treatment step [11].

Nephrotic syndrome (NS) is not a disease in itself; rather, it is a group of kidney-related findings in your child's body that indicate damaged glomeruli (kidney's filter) resulting in too much release of protein from the blood into the urine [12]. This leads to edema (swelling), high cholesterol levels, high levels of protein in urine (proteinuria) and low levels of protein in blood (hypoalbuminemia). Nephrotic syndrome can be categorized into two subtypes, which further divide into various diseases and circumstances that damage the glomeruli [13].

### CONCLUSION:

Nephrotic syndrome can increase your child's risk of infection and blood clots. It always affects both kidneys and usually appears in the early years of your child's life. Most children with this disorder outgrow it by young adulthood. We conclude that NS in children is a difficult disease with significant morbidity. However, remission is achievable in majority of patients with cyclosporine and other immunosuppressive agents.

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