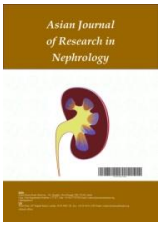

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# Review Article on Treatment of Nephrotic Syndrome in Pediatrics

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***Authors' contributions***

*This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.*

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***Review Article***

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## ABSTRACT

Nephrotic syndrome is a illness caused by idiopathic diseases like minimal change nephrotic syndrome and focal segmental glomerulosclerosis, membrane proliferative Glomerulonephritis, membranous Glomerulonephritis and is characterized by increased permeability across the glomerular filtration barrier. Nephrotic syndrome is classified as primary nephrotic syndrome secondary nephrotic syndrome, congenital nephrotic syndrome, and infantile nephrotic syndrome. Nephrotic syndrome consisting of four clinical features like nephrotic range proteinuria edema hyperlipidemia, hypoalbuminemia.

The main cause of nephrotic syndrome are diseases associated with drugs, neoplasia, and rarely genetic disorders. nephrotic syndrome is a chronic relapsing disease for most of steroid response drugs for treatment of nephrotic syndrome corticosteroids not so with immunosuppressive agents people will dependent on corticosteroid remission and some are corticosteroid resistant disease with poor renal prognosis. Using drugs to treat nephrotic syndrome, several complications are improper growth, metabolism, behaviour in patient.

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## 1. INTRODUCTION

Nephrotic syndrome is a common chronic illness caused by diseases- Minimal change nephrotic syndrome (MNCS) and focal segmental glomerulosclerosis (FSGS), Membrane proliferative glomerulonephritis, membranous glomerulonephritis and it is characterized by increased permeability across the glomerular filtrate barrier [1]. The main complications of nephrotic syndrome are infection and venous thromboembolism, septicemia, peritonitis, pneumonia with also increased risk of acute kidney injury [1,2]. Nephrotic syndrome is also caused by rare genetic disorders, diseases associated with drugs, infections and neoplasia [3,4]. Nephrotic syndrome consists of four clinical features: nephrotic proteinuria (urinary protein excretion above 50 mg/kg or 40mg/m2 per hour), hypoalbuminea (serum albumin concentration below 30 gm/L), edema and hyperlipidemia [1,4]. The pervasiveness of cases were approximately 16 cases per 100000 varying by ethnicity and region [5]. The overall incidence of childhood idiopathic syndrome was stable over the past three decades [5]. The treatment of nephrotic syndrome includes high dose oral corticosteroids [6]. But increased treatment with corticosteroids may show effect on growth, behavior and metabolism. Most of the individuals become dependent on corticosteroids to maintain remission [7] A very few proportion of children have corticosteroids – resistant disease with poor renal prognosis [8,9]. Nephrotic syndrome in pediatrics are four types. Primary nephrotic syndrome, secondary nephrotic syndrome, congenital and infantile nephrotic syndrome [1].

## 2. EPIDEMIOLOGY

Nephrotic syndrome mainly attacks 5-15 years children also from infants to adolescence [5]. The prevalence of cases were approximately 16 cases per 100000 varying by ethnicity and region. The overall incidence of childhood idiopathic syndrome was stable over the past three decades [5].

## 3. TYPES OF NEPHROTIC SYNDROME

Minimal change disease (foot process disease / lipoid nephrosis): The minimal change disease primarily effects the podocytes. Most commonly found in pediatric nephrotic syndrome is 77- 85% [10]. Effacement of the foot process can be observed on electron microscopy of a diseased person and renal biopsy sample on light microscopy shows no change. The origin of this minimal change disease are ampicillin an antibiotic and lithium an elemental antimanic agent and also by Hodgkin lymphoma.

Focal segmental glomerulosclerosis: secondclass of NS which occurs most commonly in individuals. Accumulation if IgG, C3 and C4 complement in glomeruli was observed. 15% of glomeruli are totally affected and shows tubular and interstitial damage. The etiology of FSGS includes obesity, hepatitis, sickle cell anemia [11].

Membrane proliferative glomerulonephritis. Stiffening of capillary wall is observed by intervention of mesangial matrix between normal basement membrane and endothelium and accumulation C3 component [12,13]. The cause membrane proliferative glomerulonephritis is membrane proliferative glomerulonephritis is NSAIDS like captopril, penicillamine sickle cell anemia, hepatitis B virus.

Membranous glomerulonephritis. 2-4% caused in pediatrics and most common types in adults. The presence of spikes and dome was seen on epithelial through side of capillary basement membrane through electron microscopy. Accumulation of IgG immunoglobulin and rarely C3 component was seen through immunofluorescence [14].

### 3.1 Pathophysiology

Nephrotic syndrome is caused by inflammation and damage of glomeruli [1]. This inflammation and damage isdue to immune cells antibodies, component proteins, immune complex, hypertension and sclerosis. The inflammation on podoctytic cells results in protein loss.

Podocytes are damaged with in the glomerulus and this damage of podocytic cells allows proteins to pass through into the nephron's tubule. Proteins passes through the nephrons tubules as an apart of urine [15]. Nephrotic syndrome is characterized by protein loss (proteinuria) of more than 3.5 g/34hrs. The loss of protein results in mass proteinuria with or without haematuria which is blood in urine. This haematuria essentially depends on amount of damage occurs to glomerulus. Excess loss of

antibodies in a person may have a chance of risk of infections. The mass loss of protein such as albumin from circulation results in hyperproteinemia more specifically hypoalbuminea. Hypoalbuminemia results in decreased plasma oncotic pressure. Water and electrolytes move to interstitium in which edemacan occur in hands, feet, intestinally, *etc*; The inflammation of nephrons in kidneys contribute to decreased renal blood flow (GFR) [16]. The decreased GFR actually stimulates the cell to produce renin. Renin angiotensin aldosterone system increase the blood pressure to compensate the decrease in vascular volume and decrease of GFR. Renin angiotensin aldosterone system increases the blood pressure by retaining water and sodium results in further edema because of hypoproteinurea [17].

### 3.2 Clinical Manifestations

Hypoalbuminea results in tiredness and also results in edema because of reduced oncotic pressure. Edema can be periorbital edema, which is fluid in eye, ascites (fluid in abdomen) and peripheral edema [1]. The hyperchloestrelemia which is called dyslipidemia and xanthelasma which is accumulation of cholesterol on eye are clinical manifestations of nephrotic syndrome. patients with nephrotic syndrome can be breathless because of pulmonary edema and pleural effusion [18].

### 3.3 Diagnosis

Nephrotic syndrome in pediatrics is confirmed by the presence of clinical manifestations like nephrotic range proteinuria, hypoalbuminea, hyperlipidemia, edema through diagnosing a patient. The diagnosis of nephrotic syndrome includes urine tests, blood test and kidney biopsy [5].

Urine analysis: Fore most test for diagnosis of any disease. Kidneys are major source for eliminating waste products. The damage of kidneys results in eliminating some important molecules.The presence of protein in theurine is asign of nephrotic syndrome The albumin in urine is determined by using a strip of paper which is chemically treated is dipped in urine. If the color change is observed the presence of albumin in urine is confirmed [1].

Urine to albumin creatinine ratio: creatinine is a waste product filtered of by kidneys and excreted in urine. Increased amount of urine albumin to creatinine ratio shows that kidneys excreting excess amount of albumin into the urine [5].

Blood test: A common sign of nephrotic syndrome is low levels of albumin and other proteins in the blood, referred to as hypoalbuminemia, which can be detected with a blood test. Hypertriglyceridemia, hypocholesterolemia. Increased number of triglycerides and cholesterol in the blood are symptoms of nephrotic syndrome [1,5].

Kidney biopsy: kidney biopsy is a method whichinvolves removing of kidney tissue by giving local anesthetic for microscopic examination. This test can help in diagnosis of childhood nephrotic syndrome [5].

### 3.4 Treatment

Nephrotic syndrome with infections and intoxications in which antigen is observed, the general treatment is given by pencillin to cure the renal disease. In Infected ventriculoatrial removal of Shunt may helps to complete the reversal of disease. In nephrotic syndrome remission should be immediately induced because nephrotic syndrome results in increased number of risk factors. In nephrotic syndrome relapse should be minimised in order to prevent new complications. Initially nephrotic syndrome is treated with steroid therapy followed by immunosuppressive drugs to prevent relapse. The first choice of corticosteroid drug is prednisolone taken at a dose of 60 mg /$m^2$ per day for 4- 6 weeks alternatively up to 6 months which minimises the number of Pediatrics relapsing by 33% [5]. The percentage of children who response to corticosteroid therapy is more. Few percentage of children experiences relapse. The relaxing children should administer prednisone dose of 1.5 mg per kg per month up to remission [19]. The children who frequently response to corticosteriods may have risk factors like obesity and improper growth and cataracts. Other than prednisone treatment the other choice of drugs used in treatment for old are Levamisole, Mycophenolate Mofetil, Cyclophosphamide, Rituximab.

Levamisole: An immunosuppressant at a dose of 5mg per kg on alternate days for about 16 weeks is used treat nephrotic syndrome. The risk factors of treating Nephrotic syndrome by levamisole is itchy skin rash abdominal pain and neutropenia [5,19].

Cyclophosphamide: A 12 weeks course of daily dose of 168 mg per kg is used for treating nephrotic.syndrome [20,21].

chlorambucil: the dose of 0.2 mg per kg for 8 to 12 weeks is generally used for treatment of nephrotic syndrome with risk factors of seizures.

Cyclopsorine: Concentration of 50- 125ng per ml with dose of 5 to 6 mg /kg to manage the disease. 85% of patients attain remission by the administration of these drugs [22,23].

Rituximab: Intravenous infusion at a dose of 375 mg per m square is administered by the effect of steroid sparing agent in Pediatrics.

Tracrolimus: The alternative drug of cyclosporine to treat nephrotic syndrome is tracrolimus. 81% of remission trait in pediatrics was observed by taking a dose of 0.1 to 0.2 mg/kgper day divided into two doses [24]. Tremor arterial hypertension, Diabetes mellitus are common side effects with tracrolimus [25,26].

Mizoribine: A dose of 3 mg per kg once daily before breakfast is administered to inhibit the DNA synthesis in cell division. Mizoribine isa effective drug in maintaining remission in nephrotic syndrome [27].

Sympathetic adrenocorticotropic analogue: Adrenocorticotropic injection is found for the treatment of nephrotic syndrome but it is replaced by another corticosteroids.30 Very little percentage of patients will respond to synthetic adrenocorticotropin [28,29].

Galactose. Galactose is a monosaccharide sugar inhibits the circulating permeability which causes nephrotic syndrome. Use of 0.2 grams per kg of two doses in a day is recommended for partial remission [30,31-35].

## 4. CONCLUSION

Nephrotic syndrome is connected with clinical features factors like proteinuria, hypoalbuminia, edema and hyperlipidemia. The very first line choice of treatment of nephrotic syndrome is with corticosteroids mainly prednisolone at a dose of 60 mg /$m^2$ per day. The risk of Side Effects was increased by regular use of these medications. The increased treatment with corticosteroids may also leads to risk factors affecting proper growth behaviour metabolism. Most of the people become dependent on corticosteroids to maintain remission and very few percentages of children are resistant to corticosteroids with renal prognosis.

## DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

## CONSENT

It is not applicable.

## ETHICAL APPROVAL

It is not applicable.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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