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Study on prevalence, clinical profile & drug use pattern of nephrotic syndrome in children aged between 1-12 years admitted in a tertiary care hospital

Abstract

Nephrotic syndrome is a common pediatric kidney disease characterized by protein leakage from the blood into urine through damaged glomeruli. It is a disease of glomerular filtration barrier failure, manifesting with severe proteinuria leading to hypoalbuminemia, hypercholesterolemia and generalized edema. The main objective of the study is to know the prevalence and clinical profile of children having nephrotic syndrome and to study the drug use pattern followed for the same. This is a retrospective cross sectional observational study. Children aged between 1-12 years and those who are steroid sensitive including both single episode and relapse is the inclusion criteria and those who are steroid resistant and congenital nephrotic syndrome are excluded in this study. This study is conducted by collecting the case sheets from the medical records department and analyzed using suitable statistical tools. This study concludes that the prevalence of nephrotic syndrome is 30% higher in males compared to females. Higher prevalence of about 41.6% of nephrotic syndrome was reported in age group of 6 to 12 years. Facial puffiness was the most common symptoms observed in nearly 94% of the cases. Prednisolone, a corticosteroid is the first choice of specific drug given for the patients with nephrotic syndrome accounting for about 73% of cases. Regimen based on body weight Mg/kg/day regimen was the mostly prescribed regimen (85.71%) compared to regimen based on body surface area mg/m^2/day of prednisolone in both single episode and relapse cases of nephrotic syndrome.

Keywords: nephrotic syndrome, glomerular filtration, proteinuria, edema, prednisolone, steroid sensitive, frequent relapse

Volume 12 Issue 3 - 2022

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Received: August 31, 2022 | **Published:** September 7, 2022

Abbreviations: NS, nephrotic syndrome; SSNS, steroid sensitive nephrotic syndrome; SDNS, steroid dependent nephrotic syndrome; FSGS, focal segmental glomerulosclerosis; MCGN, Mesangiocapillary glomerulonephritis; MG/DLN, membranous glomerulonephritis; DPGN, diffuse proliferative glomerulonephritis; MCNS, minimal change nephrotic syndrome; KDIGO, kidney disease improving global outcomes; MMF, mycophenolate mofetil

Introduction

Nephrotic syndrome is a set of signs or symptoms that may point to kidney problems. Both the adult and children can have this syndrome. Childhood nephrotic syndrome can occur at any age but is most common between the ages of 1 year 6 months and 5 years and seems to affect boys more than the girls.[1] Nephrotic syndrome is a disease of glomerular filtration barrier failure, manifesting with severe proteinuria leading to hypoalbuminemia, hypercholesterolemia, and generalized edema.[2] It is a common paediatric kidney disease characterized by protein leakage from the blood into urine through damaged glomeruli. It is classically defined by nephrotic- range proteinuria (≥ 40 mg/m^2/hour or urine protein/ creatinine ratio ≥ 200 mg/mL or 3 + protein on urine dipstick), hypoalbuminemia (< 25g/L) and oedema.[3] Thus nephrotic syndrome is a collection of symptoms that indicate kidney damage.[4]

Epidemiology

Nephrotic syndrome (NS) is the most common childhood kidney disease worldwide. It estimates on the annual incidence of nephrotic syndrome range from 2-7 per 100,000 children younger than 18 years of age, making it a relatively common major paediatric disease and prevalence from 12-16 per 100,000.

Causes of nephrotic syndrome

Nephrotic syndrome has many causes and may either be the result of a glomerular disease that can be either limited to the kidney, called primary nephrotic syndrome, or a condition that affects the kidney and other parts of the body, called secondary nephrotic syndrome. Congenital diseases- diseases that are present at birth-can also cause childhood nephrotic syndrome.

Primary nephrotic syndrome

Primary causes of nephrotic syndrome are usually described by their histology:

Minimal change disease (MCD)

It is the most common cause of nephrotic syndrome in children. It owes its name to the fact that the nephrons appear normal when viewed with an optical microscope as the lesions are only visible using an electron microscope. Another symptom is a pronounced proteinuria.

Focal segmental glomerulosclerosis (FSGS)

It is the most common cause of nephrotic syndrome in adults. It is characterized by the appearance of tissue scarring in the glomeruli. The term focal is used as some of the glomeruli have scars, while others appear intact; the term segmental refers to the fact that only part of the glomerulus suffers the damage.

Membranous glomerulonephritis (MGN)

The inflammation of the glomerular membrane causes increased leaking in the kidney. It is not clear why this condition develops in most people, although an auto-immune mechanism is suspected.

Membranoproliferative glomerulonephritis (MPGN)

It is the inflammation of the glomeruli along with the deposit of antibodies in their membranes, which makes filtration difficult.

Rapidly progressive glomerulonephritis (RPGN)

(Usually presents as a nephritic syndrome) A patient's glomeruli are present in a crescent moon shape. It is characterized clinically by a rapid decrease in the glomerular filtration rate (GFR) by at least 50% over a short period, usually from a few days to 3 months.[3]

Secondary nephrotic syndrome

Secondary causes of nephrotic syndrome have the same histologic patterns as the primary causes, though they may exhibit some difference suggesting a secondary cause, such as inclusion bodies. They are usually described by the underlying cause.[3]

Clinical features of nephrotic syndrome include:

- Proteinuria
- Hypoalbuminemia
- Oedema

Oedema is the common symptoms, periorbital swelling and perhaps oliguria are noticed- increasing oedema- anasarca evident. The most common sign is excess fluid in the body due to the serum hypoalbuminemia. Lower serum oncotic pressure causes fluid to accumulate in the interstitial tissues. Sodium and water retention aggravates the oedema.

This may take several forms:

- Puffiness around the eyes, characteristically in the morning.
- Pitting oedema over the legs.
- Fluid in the pleural cavity causing pleural effusion. More commonly associated with excess fluid is pulmonary oedema.
- Fluid in the peritoneal cavity causing ascites.
- Generalized oedema throughout the body known as anasarca.
- Hypercoagulability
- Lipiduria or loss of lipid in the urine is indicative of glomerular pathology due to an increase in the filtration of lipoproteins
- Foamy urine, which may be caused by excess protein in your urine.
- Weight gain due to excess fluid retention.
- Symptoms of infection, such as fever, lethargy, irritability, or abdominal pain.
- Loss of appetite
- Diarrhea
- High blood pressure

Management

The first-line therapy for NS is oral corticosteroids which, in the 1960s, were found to dramatically reduce mortality (to 3%) and to induce remission in approximately 80% of children with NS.

The current KDIGO guidelines for initial corticosteroid therapy recommend a single daily dose of oral prednisone at 60 mg/m^2/day to a maximum of 60 mg/day for 4–6 weeks. This daily dose should then be followed by alternate-day dosing with 40 mg/m^2/day, continued for 2–5 months with further tapering of the dose. Total therapy should be given for at least 12 weeks.

Material and methods

Study methodology

Study place

Department of pediatrics, Rajah Muthaiah Medical College &Hospital, Annamalai University, Annamalai Nagar, Chidambaram-608002, Tamil Nadu.

Study period

3 Years [January 2017 to December 2020]

Study design:

Retrospective cross-sectional observational study.

Subject recruitment

Target population

Children with nephrotic syndrome attending Pediatrics department, RMMCH.

Study population

Children who fulfil both inclusion and exclusion criteria

Inclusion criteria

- Children with nephrotic syndrome aged between 1 – 12 years
- Children with steroid sensitive nephrotic syndrome including 1st episode and relapse.

Exclusion criteria

- Children with steroid resistant nephrotic syndrome
- Children with congenital nephrotic syndrome

Study method

- Study period will be conducted for past 3 years (from January 2017 to December 2020).
- Selection of the subjects based on the inclusion and exclusion criteria.
- The present study will be conducted by collecting the case sheets of nephrotic syndrome patients at Medical Records Department (MRD) in RMMCH.
- Demographic details, medical history, examination, lab investigations like Complete blood count(CBC), urine routine, total cholesterol, serum electrolytes, serum proteins, Renal function test , chest X ray and therapeutic management will be collected from the case sheets.
- The data will be analyzed using suitable descriptive statistical tools.
- Results generation.
- Discussion and conclusion.
- Hard copy of the project will be stored in department library for future reference in the form of project book.
- Further, the project will be set for publication.

Citation: Siyamala G R S,Dhanalakshmi P,Kaviya V, et al. Study on prevalence, clinical profile & drug use pattern of nephrotic syndrome in children aged between 1-12 years admitted in a tertiary care hospital. *J Pediatr Neonatal Care*. 2022;12(3):136–141. DOI: 10.15406/jpnc.2022.12.00470

Discussion and results

Nephrotic syndrome is the most common kidney disease among the world and is a chronic kidney disease in paediatric age group, having prevalence of 12-16 per 100,000 people. Epidemiological studies showed that incidence of nephrotic syndrome in children are higher in the region of South Asia (Figure 1).

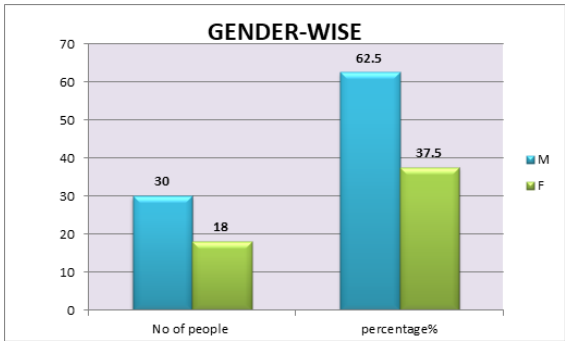

Figure 1 Shows gender wise distribution of nephrotic syndrome patients.

In this study, totally 48 patients were included. There were 30 male patients and 18 female patients.

From this graph, males were more prevalent to nephrotic syndrome than female patients.

A total number of 48 patients with nephrotic syndrome were included in this study. The patient demographic details showed that among these patients, more number of male patients (62.5%) were enrolled than the female patients (37.5%) which was in concordance with the study done by Jeetendra Kumar et al., which showed male dominance (66%) (Figure 2).[7]

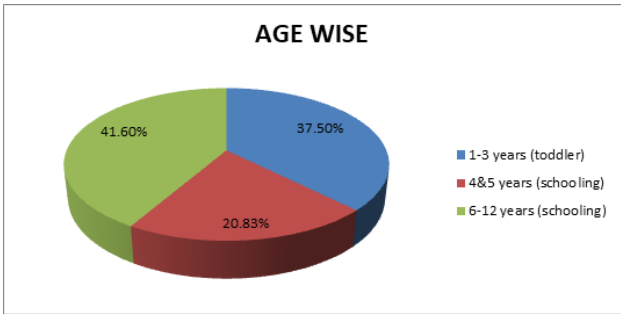

Figure 2 Indicates age wise distributions of nephrotic syndrome patients.

Patients aged between 1 to 12 years were included in this study. In that, patients aged between 6 to 12 years consisted of more number of patients (41.6%) followed by age group of 4 to 5 years having (20.83%) and 1-3 years (37.5%) of patients. Sahana KS et al., concluded similar result with age group 6 to 12 years having more number of patients (Figure 3).[6]

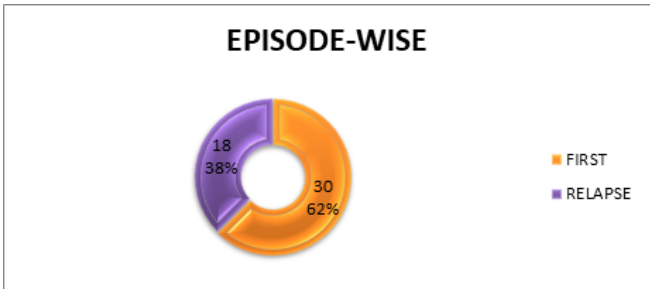

Figure 3 Indicates episode wise distributions of nephrotic syndrome patients.

Both single episode patients and relapse patients were included in this study. In this, single episode patients were more (62%) when compared to relapse patients (38%) which were contrast to the study of Sahana KS et al. (Figure 4).[6]

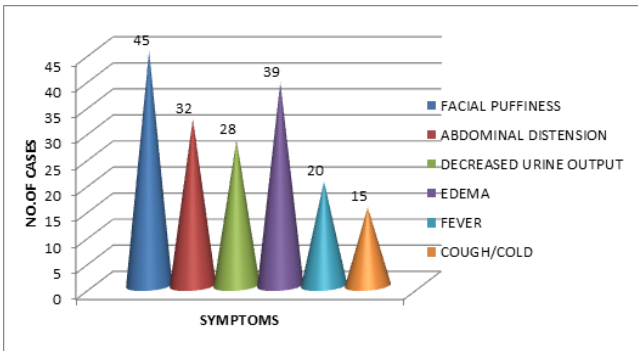

Figure 4 Indicates the presenting symptoms in nephrotic syndrome patients.

From the above graph, facial puffiness (93.7%), edema (81.25%) were considered as chief presenting symptoms followed by abdominal distension, decreased urine output and others.

Patients having symptoms of nephrotic syndrome were included. Symptoms like facial puffiness, abdominal distension, decreased urine output, edema, fever, cough, cold and other minor symptoms were observed. In that, nearly 93.7% of people were having facial puffiness followed by 81.25% of people with edema, 66.6 % with abdominal distension, 58.3% with decreased urine output, 41.6% with fever and 31.25% with cough and cold. This was in accordance with jeetendra Kumar et al., showing edema as a common symptom followed by abdominal distension and others (Figure 5).[7]

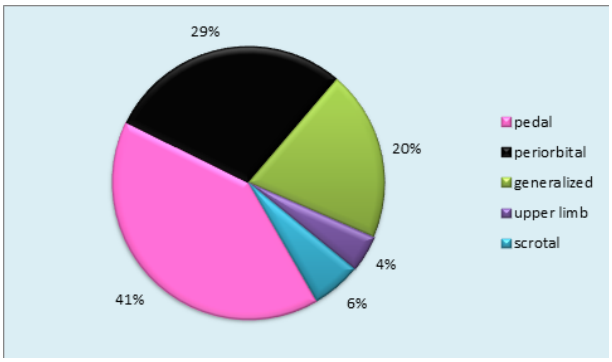

Figure 5 Indicates the location of edema in the body of nephrotic syndrome patients.

Edema is one of the chief symptoms in nephrotic syndrome patients. Edema which is present in various parts of the body like pedal edema(foot), periorbital edema(eyes), generalised edema, edema in upper limbs and edema in genitals(scrotal and vulvar) were observed. In that, pedal edema is the most common accounting for about 41% followed by periorbital of about 29%, generalised edema of about 20%, edema in upper limbs 4% and scrotal edema of 6% is seen (Figure 6).

Laboratory findings consisting of serum cholesterol, serum albumin, urine protein and other investigations were also observed. Hypercholesterolemia (>200 mg/dl), hypoalbuminemia (< 3 g/dl), heavy proteinuria indicates the presence of nephrotic syndrome. In that hypoalbuminemia is the chief laboratory sign accounting for about 85.4% of patients followed by hypercholesterolemia in 83.3% of patients and proteinuria in 79.1% of patients. Protein in urine was

detected by urine spot pcr analysis, 24 hours urine protein and urine albumin by SSA (sulfosalicylic acid) method.

Hypertension is also observed in 48% of patients (Figure 7).

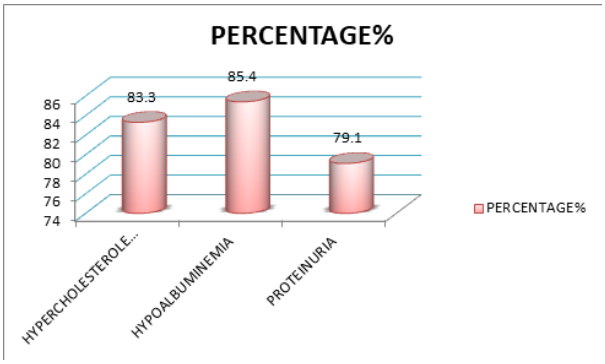

Figure 6 Indicates the laboratory finding that occurs in nephrotic syndrome patients.

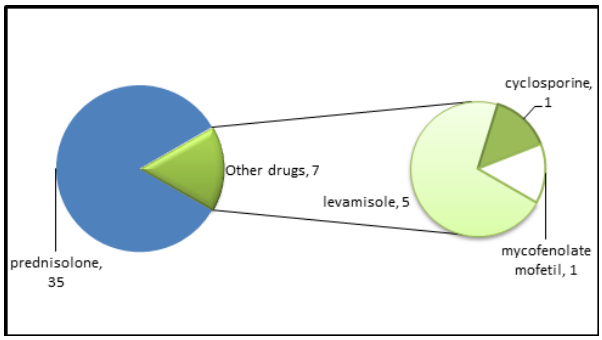

Figure 7 Indicates the specific drug treatment in nephrotic syndrome patients.

From the above graph, it is clearly known that prednisolone is the most common drug being given as specific treatment for nephrotic syndrome patients. Here, in this study, prednisolone has been given for only 21 patients as the remaining patients had spontaneous remission. From this Figure l evamisole is most commonly used among the given steroid sparing drugs in frequent relapsing cases.

Prednisolone and steroid sparing drugs like levamisole, mycophenolate mofetil, cyclosporine, and tacrolimus are the specific drugs being given for nephrotic syndrome. In that, prednisolone is the most common drug accounting for about 73% is given as first line choice in specific treatment for nephrotic syndrome patients followed by other steroid sparing drugs as second line choice of drugs. This was in accordance with study done by Priya Nair et al., (Figure 8).[8]

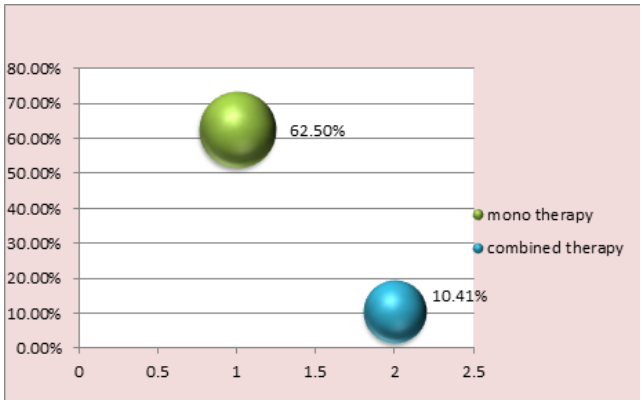

Figure 8 Indicates distributions of patients based on drug use of specific therapy.

The above graph shows that mono therapy by using one specific drug (prednisolone) is most common compared to combined therapy.

62.5 % of patients are on mono therapy taking only prednisolone whereas, 10.41% of patients are on combined therapy with second line drugs. Mostly frequently relapse patients are given with combined therapy which correlates with study done by Priya Nair et al., which showed most of the patients used mono therapy with prednisolone (Figure 9).[8]

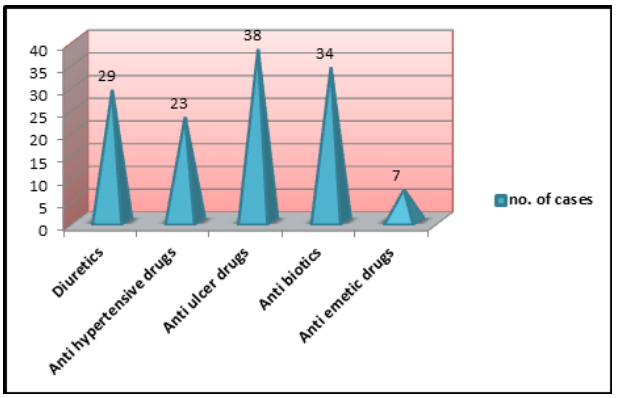

Figure 9 Indicates the use of supportive drugs by nephrotic syndrome patients.

Use of supportive drugs like diuretics, anti-hypertensive drugs, anti-ulcer drugs, antibiotics and anti-emetic drugs were also observed in the study. In that anti-ulcer drug (79%) category were the most commonly used supportive drugs followed by antibiotics (70.8%), diuretics (60.4%), anti-hypertensive drugs (48%) and anti-emetic drugs (14.5%) (Figure 10).

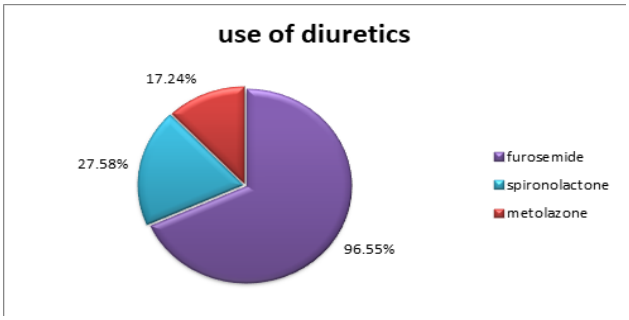

Figure 10 Indicates the use of diuretics in nephrotic syndrome patients.

Amongst the diuretics given, furosemide is the most commonly used diuretic accounting for (96.55%) followed by spironolactone (27.58%) and metalazone (17.24%) which correlates with the study done by Priya Nair et al., (Figure 11).[8]

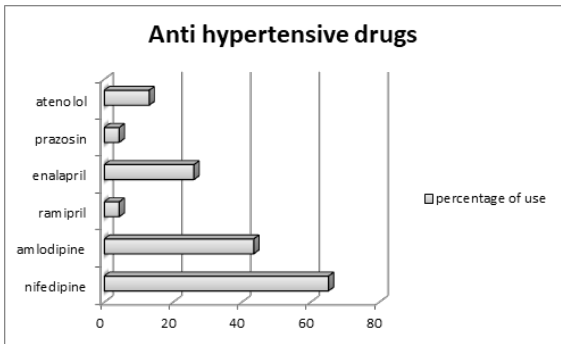

Figure 11 Indicates the use of anti-hypertensive drugs in nephrotic syndrome patients.

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Amongst the anti-hypertensive drugs given, nifedipine (65.21%) is the most commonly used anti-hypertensive drug followed by amlodipine (43.47%) , enalapril (26.08%), atenolol(13%), prazosin and Ramipril both accounting for (4.34%) is seen (Figure 12).

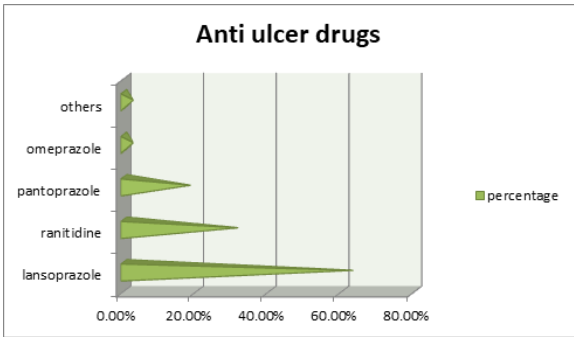

Figure 12 Indicates the use of anti-ulcer drugs in nephrotic syndrome patients.

Use of anti-ulcer drugs like lansoprazole, ranitidine, omeprazole, pantoprazole and others were observed in this study. In that lansoprazole 63.15% is the most commonly used anti-ulcer drug. Ranitidine 31.57% is the second commonly used drug followed by other anti-ulcer drugs like pantoprazole 18.42%, omeprazole and others 2.63%.

Use of antibiotics

Some of the antibiotics given to the patients in this study are given here: (Table 1)

Table 1 Antibiotics given to patients with nephrotic syndrome in this study

Anti-biotics category		No of cases	Percentage
Beta Lactam Antibiotics	• Penicillin	23	67.6%
• Cephalosporins		26	76.4%
Aminoglycosides		5	14.70%
Nitroimidazole		3	8.80%
Tetracycline		1	2.90%
Sulphonamides		2	5.80%
Urinay antiseptic		1	2.90%

Antibiotics have also been given in this study with penicillin and cephalosporin being the most commonly prescribed antibiotic in the patients which was in accordance with study by Priya Nair et al.,.[8]

Supplements like calcium, zinc and drugs like paracetamol and other symptomatic drugs were given to the patients.

High protein diet, salt restricted diet and fluid restriction were followed for the patients as non-pharmacological therapy (Figure 13).

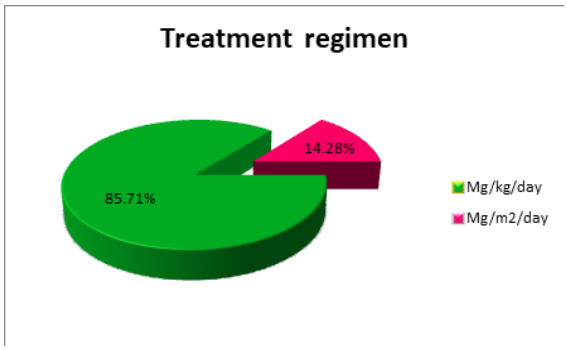

Figure 13 Shows treatment regimen followed for prednisolone.

In this study, two different dosage regimens of prednisolone were given to the patients. Dosage regimen based on Body Surface Area (BSA) mg/m^2/ day and dosage regimen based on body weight mg/kg/day was followed. In that, dosing regimen based on mg/kg/day (85.71%) is the most commonly prescribed regimen of prednisolone when compared to the regimen mg/m^2/day (14.28%) which is less commonly prescribed.

Conclusion

In the present study entitled "Study on prevalence, clinical profile and drug use pattern of nephrotic syndrome in children aged between 1 to 12 years admitted in a tertiary care hospital" we have made an attempt to know the prevalence, clinical profile, treatment pattern and the drug regimen followed in children with steroid sensitive nephrotic syndrome.

- This study concludes that the prevalence of nephrotic syndrome is 30% higher in males compared to females. Higher prevalence of about 41.6% of nephrotic syndrome was reported in age group of 6 to 12 years.
- Steroid sensitive nephrotic syndrome is more prevalent compared to all other types of nephrotic syndrome.
- Facial puffiness was the most common symptoms observed in nearly 94% of the cases. Hypoalbuminaeia, hypercholesterolemia, proteinuria were the main laboratory signs indicating nephrotic syndrome. The signs and symptoms observed in this study correlates with the standard clinical manifestations of nephrotic syndrome.
- Prednisolone, a corticosteroid is the first choice of specific drug given for the patients with nephrotic syndrome accounting for about 73% of cases. Levamisole, an antihelmintic drug and an immunomodulatory agent is the most commonly used steroid sparing drug which is mostly being given for frequent relapse conditions.
- Regimen based on body weight Mg/kg/day regimen was the mostly prescribed regimen (85.71%) compared to regimen based on body surface area mg/m^2/day of prednisolone in both single episode and relapse cases of nephrotic syndrome. The dosing regimen used in the study place was based on ISPN (Indian Society of Paediatric Nephrology) guidelines.
- Supportive treatment drugs like

o Furosemide was commonly used (96.55%) among the given diuretics;

o Nifedipine (65.21%) among the given antihypertensive drugs;

o Lansoprazole (63.15%) among the given anti-ulcer drugs;

o Penicillins and cephalosporins among the given antibiotics were used.

- In this study, no mortality is involved.
- This study provided a baseline data regarding clinical profile, drug use pattern and treatment regimen followed in nephrotic syndrome.

Acknowledgments

We express our profound & sincere gratitude to our Institutional Guide, Mr. P. Mahendravarman, Assistant Professor, and Department of Pharmacy; and to our Hospital Guide, Dr. M. sucindar, Assistant Professor, Department of Paediatrics, RMMC, Annamalai University, Annamalai Nagar, for their valuable guidance and support. We also thank our beloved family for completing the study.

Financial support and sponsorship

None.

Conflicts of interest

The author declares that there are no conflicts of interest.

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