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A CLINICO- EPIDIMIOLOGICAL PROFILE OF NEPHROTIC SYNDROME IN CHILDREN AT BENGHAZI CHILDREN HOSPITAL-2018

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ABSTRACT

Background: Nephrotic syndrome (NS) is most common chronic renal disease in children, characterized by heavy proteinuria, hypoalbuminemia (albumin <25gm/dl), oedema and hypercholesterolemia. It occurs due to alterations of permselectivity at the glomerular capillary wall, resulting in its inability to restrict the urinary loss of protein. **Aims:** This study was undertaken to explore the different patterns of nephrotic syndrome in Paediatric age group in Benghazi area (Libya) during the year 2018 and to assess clinical presentation, associated complications, investigative profile as well as evaluate the therapeutic response in the cohort. **Patients and methods:** A retrospective cross sectional study was conducted, the clinical data was retrieved from archival files of 86 children with NS who were hospitalized during the year of 2018. **Results:** Data of 86 nephrotic syndrome Libyan child were analyzed, 69.76 % male and 30.2% are female. The affected children belong mainly to the age group 1-10 years (76.7%). The dominant type of NS was steroid sensitive (SSNS) 83% of the cases, while steroid resistant type (SRNS) in 3.4%.The most repeatedly encountered pattern is infrequent relapse NS (IFRNS) 62.79 %, where the frequent relapse pattern NS (FRNS) 3.4% and the steroid dependent NS (SDNS) in 16.2% . Respiratory infection is the most common predisposing factor (32.2%) and it may be associated with Hypertension in 19.8% , peritonitis in 17 %,seizure in 15.1%, vomiting in 9.3 % , gross hematuria in 2.3% and impaired renal function 17.4%. **Conclusion:** The epidemiological criteria and classification of NS are comparable to the published data. Respiratory infection is the most common predisposing factor for relapses The relapse-specific interventions can reduce the associated morbidity and ultimately improve the management outcome as well as child's life quality.

KEYWORDS: Nephrotic syndrome, Steroid Sensitive, Resistant, Dependent, Relapse, proteinuria, Children.

INTRODUCTION

Nephrotic syndrome(NS) is a glomerular disorder, it may occur in adult population, however paediatric population is the most affected. It is characterized by high amount of protein excretion in urine and low serum albumin, abundant albuminuria, generalized edema, and hyperlipidemia.[1] No specific cause have been identified yet although there are many associated etiologic factors, and the renal pathology varies for different cases.[2,3]

Minimal change disease (MCD), is characterized as childhood NS prevalent in 77%- 85% of cases, and is idiopathic in nature. Renal biopsy samples when subjected to light microscopy the glomerulus is normal and show no change, however on electron microscopy, effacement of the epithelial cell (podocyte) foot processes is seen. Focal segmental glomerulosclerosis, prevalent in 10% -15% of cases, is characterized as adulthood NS. Light microscopy of renal biopsy sample showed sclerosis in portions of selected glomeruli, and it can progress into global glomerular sclerosis.[4]

The pathogenesis of MCD is unclear ,but there is a strong evidence of immune dysregulation, chiefly involving cell mediated immunity(CMI), as this hypothesis can be supported by he facts of the tendency of nephrotic syndrome to manifest and relapse after viral infection or an atopic episode , the association with HLA antigens and Hodgkin lymphoma , and the therapeutic response to steroids and cyclosporine A (CsA) .Most of the functional abnormalities that are described are not specific and might represent an effect (rather than a cause).[5]

The response to therapy was classified according to the international study of kidney disease (ISKDC) categories:

1. Steroid sensitive : complete resolution of proteinuria within eight weeks of prednisolone therapy
2. Steroid resistance: failure to response to eight weeks of treatment with prednisolone at 2mg\kg\day.
3. Steroid dependence :recurrence of nephrosis when the dose of corticosteroid is reduced within two months after discontinuation of therapy.
4. Frequent relapses: two or more episodes of nephrosis within six months of the initial response or more within an 12 months period (not related to change in prednisolone dos).[6]

Oral corticosteroids form the corner stone for management of most children with nephrotic syndrome.[7] Levamozole, an anthelminthic drug with immuno-stimulatory properties has been reported to be effective as a steroid sparing agent.[8]

ACEIs and ARBs are increasingly being used for nonspecific reduction of nephrotic range Proteinuria.[9] Currently all patients with SRNS should receive enalapril, A number of novel approaches are being tried for patient with SRNS, plasmapheresis or immuno-adsorption has been employed to remove the" putative vascular permeability factor" with variable results.[10] The present study was designed to investigate the different patterns of nephrotic syndrome, assess the clinical presentation, associated complications, investigative profile and evaluate the therapeutic response in children with nephrotic syndrome.

PATIENTS AND METHODS

Study design: A retrospective cross sectional descriptive study.

Study setting: The clinical data related to children diagnosed with NS was retrieved from archival files, the patients who were under the care of Paediatric Nephrology clinic at Benghazi Children Hospital, the parents of all cases consented in advance for the use of data of their children for any scientific purpose. All medical records were subjected to comprehensive data collection, with focus on criteria required to diagnose NS, including edema massive proteinuria (more than 40mg\m2\hr), proteinuria in 24 hours urine analysis, hematuria, total serum protein, blood, serum creatinine (protein \creatinine ratio more than 0.2mg\mg) and hypoalbuminemia (less than 2.5 mg\dl).

Statistical data and analysis Data was uploaded and analyzed using SPSS version 19 for windows, Standard descriptive statistical tests were performed as indicated with displaying summarizing graphs and table as appropriate. The numerical data were shown as percent. Chi-squire test was used to find the significance of observed difference between the studied variable, P value <0.0 5 was taken as level of significance.

Ethical considerations

The data was accessed after obtaining an official permission letter to be presented to the authorized personnel, the privacy of the patients was assured by expressing the results anonymously.

RESULTS

This study analyzed data of 86 paediatric nephrotic syndrome cases all of them were Libyans, 69.76 % male and 30.2% were female (figure1). Age distribution of the cohort was as the following, 12 case (13.9%) were less than one year, 66 case (76.7%) were between 1 and 10 years, and 8 cases (9.3%) were more than 10 years and all of the later age group were males (table 1).

The dominant type of NS among this study sample was steroid sensitive nephrotic syndrome (SSNS) which accounted for 83% of the cases, followed by congenital NS in 14% and the least for steroid resistant nephrotic syndrome (SRNS) in 3% and frequent relapse NS (FRNS) occurred in only 3 cases (figure 2). According to relapse pattern, the most frequent pattern is infrequent relapse NS (IFRNS) as it affected 54 (62.78%) (table 2). Regarding the clinical feature of the sample, all of the cases (100%) presented with generalized edema, 19.8% (17 case) had high blood pressure, peritonitis occurred in 17.4% (15 case), upper respiratory tract infection (URTI) in 15.1% (13 case) and seizure in 15.1% (13 case), vomiting in 9.3 % (8 cases), diarrhea and gross Hematuria in 6.9% (six cases) and2.3% (two cases) respectively. Besides that, 58.6% of the sample had normal renal function while 17.4% their renal function was impaired (figure 3& 4). NS can be classified according to therapeutic response of the disease where steroid dependent NS (SDNS) in 14 (16.2%) and 50% of cases were treated with cyclosporine (figure 5).

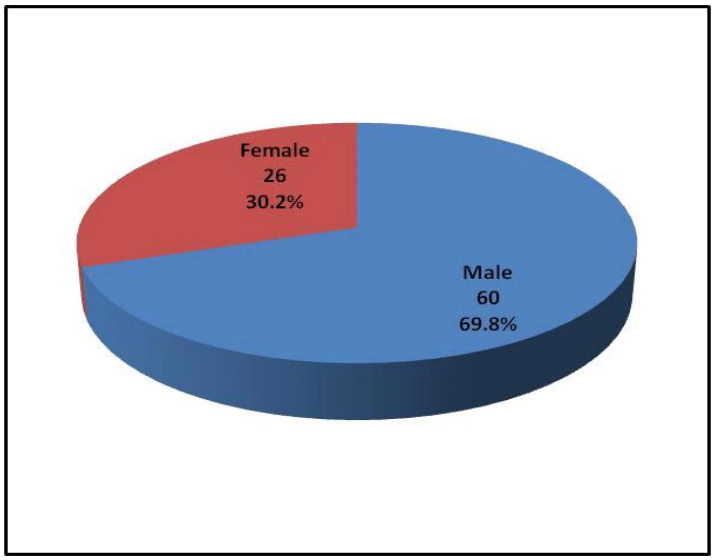

Figure (1): Gender distribution of the cohort.

Table 1: Age distribution of the sample.

Total (%)	Male	Female	Age
12 (100.0%)	8 (67.7%)	4 (33.3%)	< 1Y
66 (100.0%)	44 (67.7%)	22 (33.3%)	1-10Y
8 (100.0%)	8 (100.0%)	0 (0.0%)	>10Y
86 (100.0%)	60 (69.8%)	26 (30.2%)	Total

Chi square = 3.8, *P* = 0.148 (NON SIGNIFICANT)

Table (2): Gender distribution of study population among types of nephrioc syndrome.

Total	Gender		Type of NS
	Female	Male	
54 (100.0%)	16 (29.6%)	38 (70.4%)	IFRNS
3 (100.0%)	1 (33.3%)	2 (66.7%)	FRNS
14 (100.0%)	4 (28.6%)	10 (71.4%)	SDNS
3 (100.0%)	1 (33.3%)	2 (66.7%)	SRNS
12 (100.0%)	4 (33.3%)	8 (66.7%)	Congenital
86 (100.0%)	26 (30.2%)	60 (69.8%)	Total

Chi square = 0.05, P = 0.997 (No significant difference)

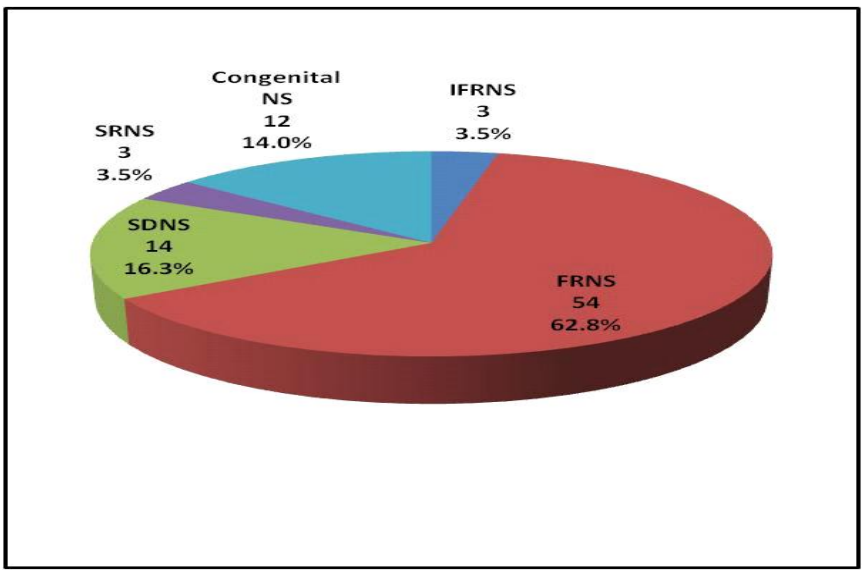

Figure (2): Types of Nephrotic syndrome.

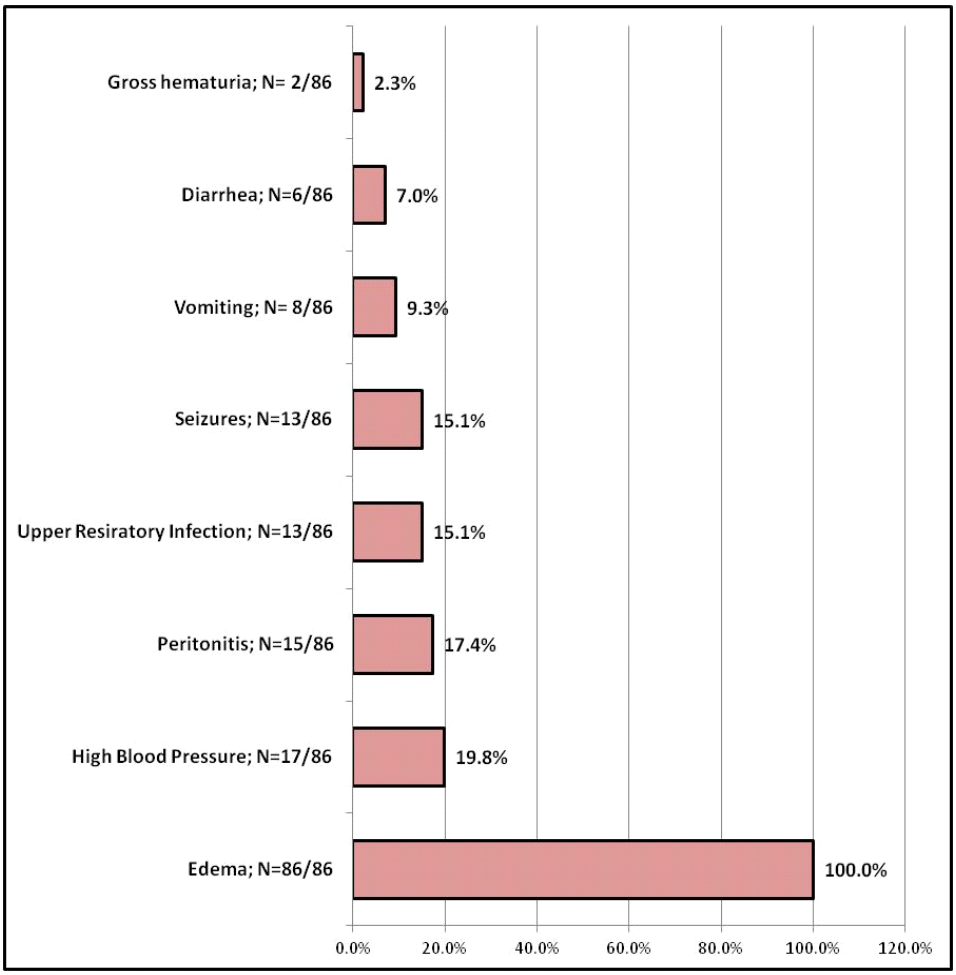

Figure (3): Clinical presentations of the study sample.

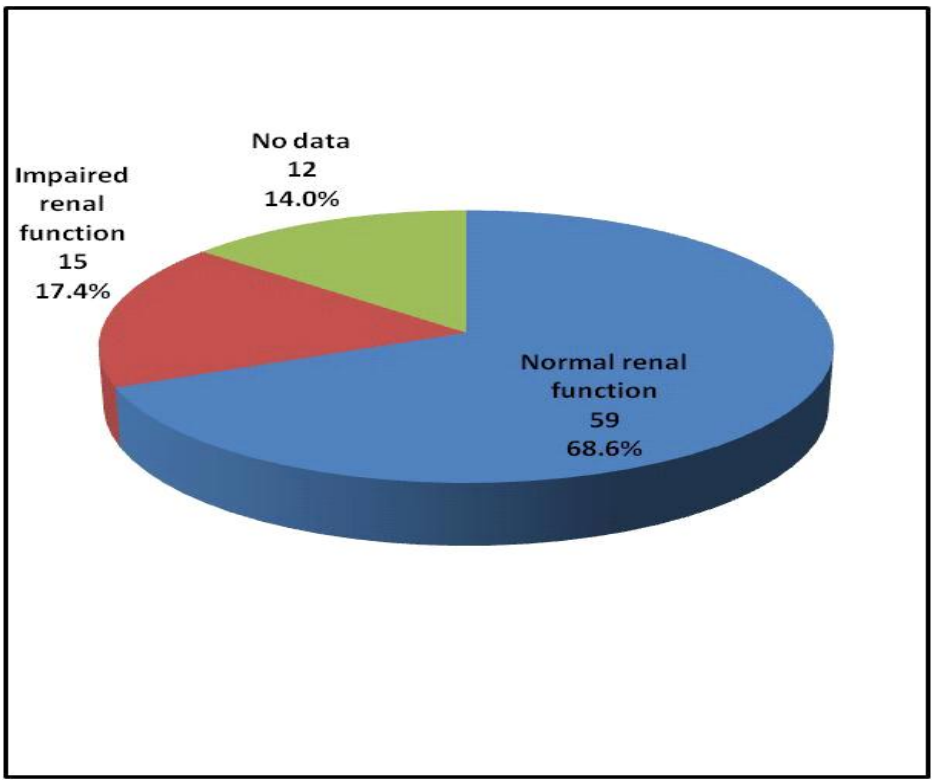

Figure (4): Distribution of study population according to renal function.

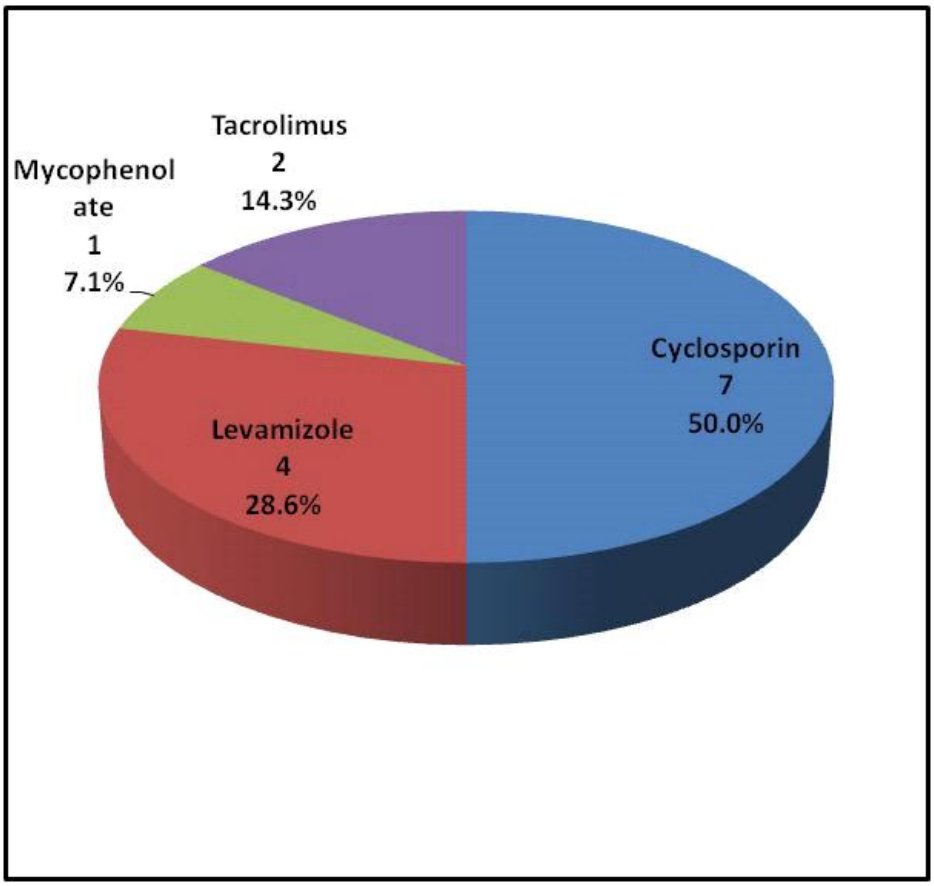

Figure (5): Distribution of the cases of SDNS according to treatment used

DISCUSSION

This study was conducted to describe nephrotic syndrome cases among children. Male represented more than two thirds of the study sample as they were 69.76% compared to female 30.2%, this result is in agreement with many studies addressing the same issue. Since it is well documented that NS is more prevalent in male young children than female of the same age group. However, this gender difference diminishes by adolescence, when the incidence in adolescents and adults equally among males and female.[11]

The greater bulk of the sample of this study were of age ranged between 1-10years who represented more than three quarter of the sample, those who were less than one year represented 13.9%, despite that there was no data about age of disease onset or age at first presentation. NS is commonly seen in pre-school children and it was confirmed that age at initial presentation has an important impact on the disease relapse frequency, as early presentation age is associated with more frequent relapses 70% of MCNS patients are younger than 5 years; 20–30% of adolescent nephrotic patients have MCNS and FSGS develops in children at a median age of 6 years.[12]

The current study presented all patients presented with generalized edema, which is one of the prominent feature of nephrotic syndrome. In the literature generalized edema is one of the most important complications in NS patients which could sometimes cause critical conditions like pulmonary oedema, heart failure, ascites and hypertension.

Etiology of the oedema includes possible decrease in glomerular filtration rate, inadequate excretion of sodium in distal tubules and hypoalbuminemia.[13]

Another supporting evidence for the presenting symptoms came from an Indian study in which they found that bilateral pitting pedal edema with facial puffiness was present in 100 % of cases [(14)]. In addition to Ascites which was positive in 63% of cases, pleural effusion was detected in 15% of cases.

Nephrotic syndrome related ascites is reported to be more common in paediatric age group than in adults (52% vs 23%).[15] however we have to take in account that, the clinical signs as ascites are not specific for nephrotic syndrome.[16,17]

In NS there is an increased predisposition to infections due to loss of complement immunoglobulins, properdin deficiency, altered T cell functions, immunosuppressive therapy and presence of oedema. Of the severe infections, peritonitis has an incidence of 2-6%. Other common infections have been reported as cellulitis, pneumonias and upper respiratory tract viral infections.[18]

Immunosuppressants such as cyclophosphamide and cyclosporine have been increasingly used in patients with refractory (steroid-dependent and -resistant) nephrotic syndrome. There are no published data directly targeting patients with nephrotic syndrome under treatment with immunosuppressants and thus the prevalence of infection due to use of immunosuppressants in patients with nephrotic syndrome has not yet been determined.[19] Hypertension was noticed in 19.8% in the current study, this is than the figures presented in an Indian study which showed that, hypertension was noted in 12 % o f cases.[18] In a review of ISKDS study hypertension was found to be present in 20.7% of cases with MCNS and in 25.7% of cases with other histological types. According to Nelson, hypertension can be present in about 10% of MCNS while as nephrotic syndrome due to significant glomerular lesion, the incidence of HTN varies from 20-35%.[20]

CONCLUSION

Nephrotic syndrome is a challenging kidney disease of childhood. This study depicted features for NS in concordance with typical nephrotic syndrome in children. Pattern of nephrotic syndrome and response to treatment, the results did not differ significantly from other reviewed studies. The main finding are male predominance who represented more than two thirds of the study sample. The majority of the sample of this study were of age ranged of 1-10 years who represented more than three quarter of the sample. The whole sample presented with generalized edema, which is one of the prominent feature of NS. In addition to other clinical features such as high blood pressure, peritonitis, URTI, seizure, vomiting, diarrhea and gross hematuria. additionally, The present study sample showed normal renal function test in 58.6% of the sample.

Recommendations

Assessment of renal function and monitoring of vital signs such as blood pressure should be done for each patients especially those with high risk for complication to avoid unnecessary complications.

Prescribing daily prednisolone during episodes of upper respiratory infections remains a relevant intervention aimed to reduce the risk of relapse, also zinc supplements which reduces both the frequency of respiratory tract infections and relapse rates as recommended by KDIGO.

The number of patients included in this study is small which doesn't permit confirmation of the results reported by other international studies about factors affecting the types of relapse in children with newly diagnosed NS. A larger cohort and a longer duration study are required for a better understanding of these factors. Long-term studies as well as the exchange of multi-center data should be encouraged for continuous update of published recommendations and guidelines.

LIMITATION

- Difficulty in data collection from the files because of poor archiving system and poor system of none computerized file saving.
- Failure of case follow up system for the hospital in general and OPD nephrotic syndrome cases specifically which is a consequence of for poor system and unorganized work.
- Retrospective study design which is one of the basic types of study designs.

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