



ORIGINAL ARTICLE

Frequency of urinary tract infection in children with nephrotic syndrome.

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ABSTRACT... Objective: To Determine the Frequency of Urinary Tract Infection in Children Presenting With Nephrotic Syndrome. **Study Design:** Descriptive Cross Sectional Study. **Setting:** Department of Pediatrics, Lady Reading Hospital (LRH), Peshawar. **Period:** 16th July 2019 to 15th July 2020. **Material & Methods:** All children presenting with nephrotic syndrome were evaluated, detailed history was obtained and complete detailed examination were performed to exclude the confounders and possible bias in the results of this study. From all these children, mid-stream clean urine catch urine was obtained with strict sterile technique and the sample was to hospital laboratory to diagnose UTI. Data was analyzed by SPSS. **Results:** Of these 106 study cases, 69 (65.1%) were male patients while 37 (34.9%) were female patients. The mean age of this study population was 7.71 ± 3.11 years. Mean Duration of Illness was 5.25 ± 4.38 months and 52.8% had duration of illness up to 6 months. Of these 106 study cases, 70 (66.00%) mothers were illiterate and 36(34.00%) mothers were literate. Urinary Tract Infection (UTI) was diagnosed in 27 (25.5%). **Conclusion:** Our Study results concludes that the frequency of urinary tract infection is very high (25.5%) in children with Nephrotic syndrome.

Key words: Children, Nephrotic Syndrome, Urinary Tract Infection.

INTRODUCTION

Urinary Tract Infection (UTI) is one the most common diagnosis in outdoor patient department and common cause of hospitalization.¹ The prevalence of UTI varies with age and sex. It occurs in 3-5% of girls and 1% of boys.² In first 03 months of life, it is more common in boys with a Ratio of 5:1 and is 1: 10in later childhood.³

A UTI is a bacterial infect that affects any part of the urinary tract.⁴ For confirmation of urinary tract infection and appropriate, a urine culture is necessary. If the culture shows more than 10^5 colonies/ml of a single pathogen or the colonies are 10,000/ml and child has urinary symptoms, then he/she should be considered to have UTI.²

Nephrotic Syndrome is another common pediatric renal problem.⁵ It is characterized by proteinuria, hypoalbuminemia, hyperlipidemia and edema. The incidence of Nephrotic Syndrome is 2-3/100,000.⁷ The prevalence of UTI

in Nephrotic Syndrome is high. It is reported as 21% by McVicar et al and 13.7% by Gulati et al in his work. The increased prevalence of UTI in nephrotic syndrome is due to a number of reason; the mostly described are; immunoglobulin loss in urine, defective T-cell function, presence of ascites and relative malnutrition.⁵ The spot urine to creatinine ratio of more than 2 is diagnostic of nephrotic syndrome.⁸ The corticosteroid is the initial treatment for nephrotic syndrome.⁶

The most common cause of UTI is Escherichia coli and occurs in 75 to 90% of cases in children, however its relative frequency varies in different areas. Other organisms causing UTI are Klebsiella, Enterobacter, Pseudomonas aeruginosa, Proteus, Enterococcus and Staphylococcus aureus.¹

A study conducted in Nigeria showed that Staphylococcus aureus is the commonest organism (67.9%) causing UTI in nephrotic syndrome patients, followed by klesiella (17.9%)

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and pseudomonas (14.2%).⁵ Urinary Tract infection is a common cause of Morbidity in Children, and if not diagnosed and treated appropriately can lead to long term renal damage.³ UTI also has adverse impact on the response of nephrotic syndrome to steroids.⁵

Steroids being the mainstay of treatment of nephrotic syndrome has significant adverse influence on immunity and prone the patients to develop infectious diseases and UTI being the more common. The current study is designed to highlight the frequency of UTI and its common bacteria among our local population with nephrotic syndrome. This type of study is not done locally so far we know and there is a need to develop certain recommendations regarding best and rationale use of antibiotics which will be cleared with the results of this study. Further the frequency of UTI among patients with nephrotic syndrome in this study if found to be significantly high as compared to other studies will open further ways to research in developing the risk factors and make decisions regarding developing a mechanism for its prevention and screening procedures.

MATERIAL & METHODS

This Descriptive Cross-sectional study was conducted at Department of Pediatrics, MTI/LRH (Lady Reading Hospital), Peshawar from 16/07/2019 to 15/7/2020.

OPERATIONAL DEFINITIONS

Nephrotic Syndrome

A child will be considered to have Nephrotic syndrome if he/she meets all of the following criteria;

1. Pitting edema at least at one site of the body
2. Serum albumin less than 2.5 gm/dl
3. Serum cholesterol 250mg/dl
4. Proteinuria +++ or ++++
5. Spot urine protein-creatinine ration more than 2

Urinary Tract Infection

A child will be considered to have urinary tract infection, if he/she has any one of the clinical

criteria and must have laboratory evidence;

- A. Clinical Criteria;
 1. Fever: 100°F or more body temperature and there is no other clinical focus for it
 2. Vomiting: History of expulsion of gastric contents out of the mouth at least two times within last 12 hours
 3. Dysuria: History of difficult or painful urination
 4. Poor feeding: History of refusal to take feed for 06 or more hours excluding any oral pathology
- B. Laboratory finding;

Clean catch urine culture shows $\geq 10^5$ colony forming units

Sample size was 106, using 66.7% proportion of UTI with nephrotic syndrome, 95% confidence interval and margin of error of 9%, under WHO software for sample size determination

The sampling technique adopted was Non-probability Consecutive Sampling.

SAMPLE SELECTION

Inclusion Criteria

1. All children presenting with Nephrotic Syndrome
2. Age group 1 to 15 years
3. Either gender

Exclusion Criteria

1. Children already known to have pre-existing uropathies e.g. posterior urethral valve
2. History of intake of antibiotics in last 07 days
3. Children having indwelling catheter
4. Children having an alternative site of infection detected through clinical examination

These are excluded as it will act as confounder and can introduce bias in the study if included.

Ethical Review Board

Approval reference No; 165/LRH, 2019.

DATA COLLECTION PROCEDURE

This study was approved from hospital ethical and research committee and then conducted in a tertiary care hospital. All children fulfilling the inclusion criteria [children with nephrotic

syndrome, diagnosed as per operational definition] and received from outdoor patient services or pediatric emergency department were included in this study. Parents/guardians of the diseased children were explained the purpose & benefits of the study and written informed consent were obtained.

All patients who met the criteria for inclusion, their detailed history and clinical examination were performed so that confounders and possible bias are excluded from the study. Mid-stream clean catch urine was obtained from all children under strict sterile technique and sample was sent to hospital laboratory to diagnose UTI.

All urine culture and sensitivity procedures were performed under supervision of the senior most consultant microbiologist having experience more than 5 years. All data including patient name, age and gender were recorded in the pre-designed performa.

Data Analysis

SPSS version 22 was used and all data was analyzed. Mean Standard Deviations [\pm SD] were calculated for Quantitative Variables like Age and Duration of illness. Frequency and percentage were calculated for categorical variables like gender, UTI. Stratification of UTI with age, gender and duration of disease were done to observe the Effect Modifications. Post Stratification Chi Square Test was applied and P Value of ≤ 0.05 was considered as Significant Value. All results were presented in tabulated and graphic forms.

RESULTS

A total of 106 patients, who met the inclusion criteria, were included in our study. Of this study group 69 (65.1%) were male patients while 37 (34.9%) were female patients. [Table-I]

Mean age of our study was 7.71 ± 3.11 years with a range from 2 to 14 years. Male patients had a mean age of 7.59 ± 3.12 years and in female patients it was 7.92 ± 3.13 , with a P value of 0.611. [Table-II]

Most of the patients in this study belonged to

rural areas i.e. 71 (67.00%) of the total 106 cases, while only 35 (33.00%) belonged to urban areas. [Table-III]. Socioeconomic status was poor in 66 (62.3%) while 40 (37.7%) patients belonged to middle income families. [Table-IV]

Maternal literacy rate in this study was 34.0% (36 mothers were literate) and 66.0% (70) mothers were illiterate. [Table-V]

Disease duration in majority of cases 56 (52.8%) was upto 03 months while the mean disease duration was 5.25 ± 4.38 months. [Table-VI] Mean body mass index of this study group was 27.58 ± 2.69 kg/m² and obesity was noted in 40 (37.7%) of patients.

Urinary Tract Infection was found in 27 (25.5%) of cases and UTI stratification was done with gender, residential status, socioeconomic status, disease duration and maternal education. [Table-VII]

Gender	Frequency (%)
Male	69 (65.1%)
Female	37 (34.9%)
Total	106 (100%)

Table-I. Gender wise distribution (total no=106).

Age Wise Group	Frequency (%)
Up to 08 Years	63 (59.4%)
More than 8 years	43 (40.6%)
Total	106 (100%)

Table-II. Age-wise distribution of study cases (total no=106).

Residential Status	Frequency (%)
Rural	71 (67.0%)
Urban	35 (33.0%)
Total	106 (100%)

Table-III. Residential based distribution of study case (total no= 106).

Socioeconomic Status	Frequency (%)
Poor	66 (62.3%)
Satisfactory Income	40 (37.7%)
Total	106 (100%)

Table-IV. Based on socio-economic status, distribution among study cases (Total No. 106)

Maternal Literacy	Frequency (%)
Illiterate	70 (66.00%)
Literate	36 (34.00%)
Total	106 (100%)

Table-V. Maternal literacy rate among study cases (Total No. 106)

Disease Duration	Frequency
≤ 3 months	56 (52.8%)
≥ 3 months	50 (47.2%)
Total	106 (100%)

Table-VI. Based on disease duration, distribution among study cases (Total No. 106)

UTI	Frequency (%)
Found	27 (25.5%)
Not found	79 (74.5%)
Total	106 (100%)

Table-VII. Distribution of Urinary Tract Infection (UTI) in study cases (Total No. 106)

DISCUSSION

Nephrotic syndrome is a clinical complex of the combination of; 1. Edema, 2. Heavy proteinuria [urine albumin +++ or ++++ called Nephrotic range proteinuria], 3. Low serum albumin [less than 2.5 g/dl] and 4, Raised cholesterol level > 200mg/dl [Hyperlipidemia].⁹ Proteinuria of Nephrotic Range in children age group is defined as excretion of protein in urine of more than 40mg/m²/hour. 24 hours urine collection in children is troublesome and can be unreliable. The alternative and preferred test in pediatrics is the quantification of spot protein loss in relation to urinary creatinine, preferably in first morning urine sample.^{10,11} Kidney Disease Improving Global Outcomes [KDIGO] group have given new management guidelines, which uses urine protein/creatinine ratio as diagnostic tool and its value ≥ 2000mg/g and it correlates with dipstick proteinuria of Nephrotic Range.¹¹

The clinical complex of nephrotic syndrome is a common presentation of glomerular disease in children.¹² Minimal change nephropathy is the most common etiology of nephrotic syndrome in children as reported by the International Study of Kidney Disease in Children {ISKDC}. This histological finding is seen in most of the children with nephrotic syndrome. Fortunately majority of patients, about more than 90% children with etiology respond well and achieve remission with oral steroids. They are called as Steroid Sensitive Nephrotic Syndrome {SSNS}.^{13,14,15} The 2nd most common cause of nephrotic syndrome after minimal change nephropathy, Focal Segmental Glomerulo-Sclerosis [FSGS] and majority of

FSGS etiology don't respond to corticosteroids. Only about 20% respond to steroids and there is high risk in children with this etiology to progress to End Stage Renal Disease.¹⁵

Most of pediatric nephrotic syndromes are Steroids Sensitive Nephrotic Syndrome and respond well to steroids and goes into remission. However often get relapse following infection of respiratory tract or gastro-intestinal tract.^{16,17} The exact mechanism how the infection induces relapse in SSNS is not clear, however some evidence has suggested that the perturbed cell-mediated immunity, its association with atopy and elevated levels of IgE and up-regulated expression of gene associated with Interleukin-4 {IL-4} and Interleukin-3 {IL-3} causing T-helper 2 {Th2} cytokine bias. Some studies have found low zinc level in blood in patients with SSNS. It is not known whether zinc deficiency has role in it or not, there is some evidence that Zinc Deficiency may lead to down-regulation of Th 1 cytokines and relative bias in Th 2 and so there increased risk for infections. Looking into data from meta-analysis on zinc role in pediatric infections, it is shown that zinc administration to children decreases the incidence of diarrheal diseases and respiratory infections. And as infection induces relapses in pediatric nephrotic syndrome patients, it is likely that zinc will reduce relapses in nephrotic syndrome by decreasing risk of infections.¹⁸

Our study group consisted of 106 pediatric patients who meet our inclusion criteria of this study. 69 [65.1%] of them were male and 37 [34.9%] were female patients. Various studies performed in children with nephrotic syndrome have shown male predominance as is the case of our study. Arun et al¹⁸ in his study found 67.5% patients were male. Similarly Sherali et al¹⁹ found 72% of patients being from male gender in his study and comparable result was reported by Abeyagunawardena et al.²⁰ Similar result was also reported by Vidianty et al²¹ in his study conducted in Indonesia and found 65% patients were male. So our study results are comparable to other national and international studies in gender distribution.

Our study group has mean age of patients of 7.71 ± 3.11 years with a range of 2 to 14 years. The mean age was 7.59 ± 3.12 years in male patients and 7.92 ± 3.13 years was noted in female patients with a P value of 0.611. Majority of patients 63 [59.4%] in our study are upto age 8 years. Arun et al¹⁸ reported $88.4\% \pm 38.3$ months in children with nephrotic syndrome. Sherali et al¹⁹ has mentioned mean age of 7.65 ± 3.20 years of his study group patients. Similar results, mean age of 07 years, are seen in the Indonesian study performed by Vidianty et al.²¹ These results of other studies are consistent with findings in our study.

The residential distribution of our study group was 71 patients out of 106 [67.0%] belonged to rural areas and 35 [33.0%] to urban areas. Socioeconomic status was poor in 66 patients [62.3%] while 40 [37.7%] belonged to middle income families. Our study group patients had mean body mass index of 27.58 ± 2.69 kg/m² and obesity was noted in 40 [37.7%] cases. Vidianty et al²¹ found in his study in Indonesia obesity of 23% in children with nephrotic syndrome. This is similar to the findings of our study.

We found in our study group Urinary Tract Infection in 27 out of 106 patients [25.5%]. Adeleke et al⁵ has reported very high UTI prevalence in nephrotic syndrome of 66.7% in his study. Narain et al²² found UTI in 15% of nephrotic syndrome patients, a result similar to our study results. Similar report was made by Gulati et al²³ of 40% of UTI in children nephrotic syndrome, a finding close to our results.

CONSLUION

Urinary tract infection of high frequency was found in children suffering from nephrotic syndrome. UTIs weresignificantly associated with female gender, rural residential status, increasing age and long disease duration. Physician treating such patients should anticipate UTI for early diagnosis which will lead timely and appropriately management. This will decrease morbidities, improve prognosis and also improve quality of life of these patients.






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No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
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2	Furqan Ahmad	Data collection and following ethical committee, Proceedings.	
3	Masroor Bibi	Study design and review.	
4	Inayatullah Khan	Corresponding author, data collection.	
5	Ayesha	Literature Search.	
6	Salman Said	Literature review and data collection.	