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Urinary Tract Infection in Children with Idiopathic Nephrotic Syndrome

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Abstract

Nephrotic syndrome is a common childhood kidney disorder featured by increase protein excretion urine with low serum albumin with generalized edema and hyperlipidemia. It's mainly a disease of childhood 15 times more than an adult. The occurrence of Urinary tract infection (UTI) in these patients is increasing, this may be to immunoglobulin loss in urine, defective T cell function, immune-suppressive agents, and relative malnutrition.

Aim of the Study: It is to evaluate the occurrence of UTI, its etiological agents, antibiotics sensitivity type, and the effect of UTI on relapse and response to therapy in children with nephrotic syndrome in An Najaf Governorate.

Methods: A prospective cross-sectional study of all patients with idiopathic nephrotic syndrome from January 2018 to January 2019 visiting nephrology unit in Al Sader teaching hospital and Al Zahraa teaching hospital. The urine sample was taken by a clean catch method of midstream urine and by urine bag methods for those under 3 years old. The specimens were cultured immediately then examined under the microscope.

Results: A 101 patients were studied. The mean age and (S.D) for males was 6.3±2.35years and females with 6.5±1.9years. The age range was 1.5 year to 10 years. There were 44 patients (43.6%) had UTI, 29 patients (65.9%) of them were males and 15 patients (34.1%) females. UTI caused by E. coli. in (25) patients (58%) ,Streptococcus (8) patients(16.26%), Staphylococcus aurous (5) patients (11.36%), Proteus (3) patients(6.97%), Pseudomonas (2) patients (4.65%), Klebsiella species (1) patients (2.32%). The E.coli show very good antibiotic sensitivity to cefatriaxion, cefataxime and ciprofloxacin. Each of Proteus, Klebsiella, Pseudomonas spp. show a good sensitivity to cefatriaxion, ciprofloxacin and aminoglycoside while each of Streptococcus SPP and Staphylococcus aureus show good response to ciprofloxacin and moderate sensitivity to the augmentine (combination of amoxicillin and clavulanic acid) and to Septrin (co-trimoxazole) (combinations of Sulfamethoxazole and trimethoprim) and there was high in vitro resistance of these bacteria to ampicillin and nalidixic acid.

Conclusion: There is a high occurrence of urinary tract infection in idiopathic nephrotic syndrome children of An Najaf Al Ashraf city and its necessity to diagnose the disease early depending on clinical suspicion and doing the GUE and cultures monthly to avoid delay in diagnosis of infections and their sequels.

Keywords: Urinary Tract Infection; Nephrotic Syndrome

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Introduction

Nephrotic Syndrome (NS) is one of the kidney diseases associated with increasing the permeability across the glomerular filtration barrier. It is characterized by heavy proteinuria (>3.5 g/24 hr in adults or 40 mg/m^2 caused by hr in children), hypoalbuminemia (<2.5 g/dl), edema and hyperlipidemia [1]. The incidence of nephrotic syndrome is 2-3/100,000 children per year [2,3].

NS has been encountered as early as 6 months of age and throughout adult age. The highest incidence of minimal change nephrotic syndrome (MCNS) is find in (85–90%) of cases under 6 years of age; with the median age at diagnosis were 2.5 years for MCNS and 6 years for focal segmental glomerulosclerosis (FSGS). FSGS occurs in older children. In small children, boys are more affected than girls (ratio 2:1) [3-5].

Infection is the major complication of NS. The more common bacterial agent is streptococcus pneumonia then *Escherichia coli* [6]. In relapse patients have increased liability to bacterial infections due to:

- Losses of immune-globulins and properdin factor B in urine.
- Decrease of cell-mediated immunity.
- Immune suppression medications.
- Malnutrition.
- Tissue edema.

Bacterial peritonitis is the more frequent type of infection. Sepsis, meningitis and cellulitis are other serious infections. Although not as serious, UTI are common [7].

Nephrotic Syndrome and Urinary Tract Infection

UTI is a significant cause of childhood morbidity and mortality. The prevalence of UTI varies from 4% in neonatal period to 0.4% in the school and pre-school age children [8], the prevalence of UTI is high. The higher occurrence of UTI in patients with NS are due to local as well systemic causes; these include immunoglobulin excretion in urine, defective T cell function, immune suppression medications, malnutrition and others [1,9].

Locally the pressure on the collecting system by edematous pyramids causes narrowing and functional obstruction to the flow of urine predisposing them to UTI [10]. UTI has also been found to decrease the response of cases with NS to corticosteroid drugs [11]. Any how the relationship between UTI and response to steroid therapy and its effect in increasing the occurrence of relapses in NS is still not so clear [12].

Aim of the Study

Is to detect the occurrence of UTI, its etiological agents, antibiotics sensitivity and the effect of UTI on relapse and response to therapy in children with NS in An Najaf Governorate and compare with different study in the world.

Patients and Methods

A prospective cross sectional study for (101) patients with a diagnosis of primary NS visiting to the nephrology unit of AlSader and AlZahraa Teaching Hospitals in An Najaf Al Ashraf city (Iraq) from January 2018 to January, 2019. Age, Sex, urine culture results, invitro antibiotic sensitivity type of isolated bacteria were studied. Urine samples taken by clean catch method of mid-stream urine and by urine bag according to the child age following careful preparation of the urethral orifices with 70% of alcohol swabs for three time and waiting for 3 min to allow evaporation of alcohol and then mid-stream urine collected into sterile containers and as soon as possible send to the laboratory. The sample where cultured promptly and then examined microscopically.

Urine Analysis

- About urine analysis, a fresh (less than 1 hr old), urine sample of midstream urine or urine bag according to child age where collected into sterile tube immediately and if the urine analysis cannot be performed promptly we refrigerate it.
- We put 5-10 mL of well-mixed urine sample into a centrifuge tube.
- Then we examine for appearance (color, turbidity, and odor).
- Turn a capped sample at 3,000 rpm for three to five minutes.
- We use the dipstick (Nitrite) to do the dipstick evaluation on the residual sample. The test (takes usually one to two min) to avoid false results.
- We Decanting and discarding the supernatant and we mixing the remaining sediment and pipetting 1 or 2 drops onto a microscope slide and Cover it with a cover slip.
- We examine by 10 low-power fields (LPFs; 10×objectives) for epithelial cells, casts, crystals, and mucus. Casts are account as number per low-power field and we have a propensity to collect around the periphery of the cover slip.
- For detection of RBCs, WBCs, Epithelial cells, Crystals, Bacteria, and Parasites we examine multiple high-power fields (HPFs; 40×objectives).

Urine Cultures

Inoculation of a half ml of the urine specimen in a blood agar plates then incubated aerobically for eighteen to twenty four hours at 37℃ to determine

The results of cultures whether there is positive or negative growth of bacteria according to the facilities available in our center

Types of the pathogens: The bacteria identification to a species was by standard biochemical techniques and antibiotics sensitivity test were done by disc diffusion technique.

Note: unfortunately no culture media available in our country now form anaerobic microorganism.

According to the American Academy of Pediatrics (AAP) criteria for the diagnosis of UTI in children 2-24 months are the presence of pyuria and/or bacteriuria on urinalysis and of at least 50,000 colony-forming units (CFU) per mL of an uropathogen from the quantitative culture of a properly collected urine specimen [13].

Inclusion Criteria

A (101) children with idiopathic nephrotic syndrome visiting nephrology unit in Al Sader teaching hospital in An Najaf Al Ashraf city from January 2018 and January 2019. All of them live inside An Najaf Al Ashraf governorate and their age between 1.5 and 10 years diagnosed as primary nephrotic syndrome: oedema, proteinurea (3or4+), hyopoalbuminemia and hyperlipidemia.

Exclusion Criteria

a. Features suggesting a diagnosis other than idiopathic nephritic syndrome:

- Age <1.5 year
- Positive family history of renal diseases.
- Extra renal manifestations (e.g. arthritis, rash, anemia) and other chronic disease.
- Sign due to intravascular volume expansion (e.g. hypertension, pulmonary edema).
- High blood urea and serum creatinine and high serum k^+ and low C3 and C4.
- Active urine sediment (red blood cell casts).

b. Antibiotics used in the last three days prior to urine sampling.

Statistical Analysis

It was made by using SPSS (statistical package for social sciences) version 20. In which we use independent sample T-test for measurement data and chi square for categorical data. We set P value <0.05 as significant. Written consent was taken from all families. Written consent was taken from all families.

Results

There were 101 patients with nephrotic syndrome studied. There were 68(67.3%) males and 33(32.7%) females with a mean age±standard deviation for males was 6.39±2.35 years while for females 6.5 ± 1.9 years. The age range was 1.5 to 10 years. The present study shows that

44 (43.6%) patients of (101) patients with primary NS had UTI. The sex and age distribution is occur in table 1.

Discussion

NS as an important cause of referral to pediatric nephrologists because of the chronic pattern of the disorder and the complex aspect of its evaluation [14,15]. As N.S male: female ratio we find a male predominance among the study samples, M: F ratio (2:1), it was similar to Holliday MA, et al. (1986) in USA [16] and Frankul FM et al. (2003) Iraqi study [17] also similar to Coovadia HM, et al. (1979) Southern Nigeria study [18] were they showed a 2:1 ratio but differ to that found in other studies like Tej K Matto et al. (1990) in Saudi Arabia [19] (1.5:1) and slightly higher than Muhammed TF, et al. (2008) Baghdad study that show (1.8:1) [20] and Abdulrahman MB, et al. (1984) study in Africa [21] study that show same ratio.

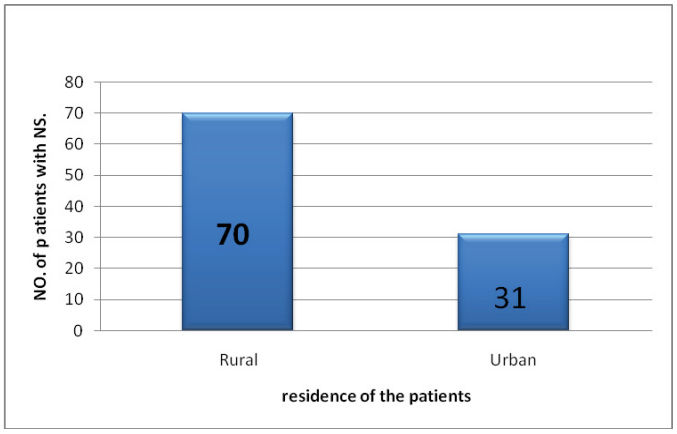

Figure 1: Residence of the patients.

Table 1: Age and sex distribution of studied patients.

		Sex		Total
Age distribution/years	**Years**	**Male**	**Female**	
	1.5-5	35(34.7%)	15(14.8%)	50(49.5%)
	>5-10	33(32.7%)	18(17.8%)	51(50.5%)
Total		68(65.9%)	33(34.1%)	101(100%)

The present study shows that 44 patients (43.6%) of 101 patients with primary NS had UTI, this watching of less occurrence of UTI among NS patients have been encountered by other studies. Adeleke SI, et al. (2005) in Kano Nigeria reported occurrence of (66.7%) [22]. Ibadin MO, et al. (1998) in Southern Nigeria [23] reported occurrence of (44.8%) and this is similar to our study. However, Gulati S, et.al. (1995) in India [24], encountered (13.8%) and McVicar M, et al. (1973) in Newyork, USA [25] reported a prevalence of 21%.

Most of our patient in this study are from rural area as shown in figure 1 of low social class and educations more prone to infections in addition to the similarity our environment and that of southern Nigeria making similarity to the result of study done by Ibadin MO, et al. (1998) in Southern Nigeria [23] while high occurrence rate of U.T.I reported by Adeleke SI, et al. (2005) in Kano Nigeria [22], because he include other ages and types of nephrotic syndrome like secondary NS which is common in the tropical areas due to malaria infections [24]. Unlike our study where all our patients were aged 1.5 year to 10 years were diagnosed as primary nephrotic syndrome. The low rate of UTI reported by McVicar M, et al. (1973) in Newyork, USA [25] may be due to their developed health systems and availability of health facilities like investigations and drugs etc. About sex influence in the development of U.T.I.

Regarding the pathogens and their sensitivity to antibiotics we find that *E. coli* was the most common organism comprising (58.1%) of isolates, followed by Streptococcus (16.26%) and Staphylococcus (9.3%). This finding is similar to, Tsau YK, et al. (1991) [26] who reported that *E. coli* comprising (51%) of isolates microorganisms causing UTI, in patients with nephrotic syndrome but differ from the study by Ibadin MO, et al. (1998) [23] who found (54.3%) of isolates were that of Streptococcus, in which E. coli responsible for (12%) only.

The sensitivities of most common pathogen (*E. coli*) to ciprofloxacin, ceftriaxone and cefataxime were high but their liability to usually used drugs like ampicillin and nalidixic acid were lower.

There is an growing pattern of resistance by most common bacteria to regular antibiotics (nalidixic acid and ampicillin) this had been distinguished in other studies like McEnery MD, et al. (1976) in United States [27] and Conway PH, et al. (2007) in United States [28]. The usual practice of self use of medications also use of substandard regime could explain this unfortunate condition [29].

Table 2: Frequency of Bacteria type.

Type of bacteria	Ceftriaxone	Cefotaxime	Ciprofoxacine	Augmentin	Amikacin	Nitrofurantoin	Gentamycine	Ampicilline	co-trimoxazole	Nalidaxic acid
E.Coli	100%	100%	100%	24%	75%	8%	64%	25%	50%	12%
Streptococcus	75%	64%	100%	50%	0%	50%	50%	50%	44%	16%
Proteus	100%	100%	100%	50%	75%	25%	75%	24%	8%	32%
Klebsiela	100%	100%	50%	0%	75%	8%	75%	7%	25%	60%
Pseudomonus	100%	25%	100%	50%	75%	50%	75%	20%	8%	25%
Staph.Aureus	25%	50%	100%	75%	52%	80%	50%	50%	51%	48%

Table 3: Antibiotics sensitivity pattern of bacteria isolated from NS children with UTI.

Type of Bacteria	Frequency
E.Coli	25(58.1%)
Streptococcus	8(16.26%)
Staph.Aureus	5(11.36%)
Proteus	3(6.97%)
Pseudomonus	2(4.65%)
Klebsiela	1(2.32%)
Total	44 (100 %)

Table 4: Relation between relapse and UTI.

Relapse	UTI		Total
	Yes	No	
Yes	31	27	58
	53.40%	46.60%	100.00%
No	13	30	43
	30.20%	69.80%	100.00%
Total	44	57	101
	43.60%	56.40%	100.00%
P value	0.02*		

Where: p value is significant*

Table 5: Comparison in different characteristics in relation to presence or absence of UTI.

Characteristic	UTI		P value
	Yes (mean±SD)	No (mean±SD)	
Age(years)	6.477±2.17	6.395±2.2653	0.854
Body Weight(Kg)	24.4884±8.53668	24.5789±9.75585	0.961
Age of Onset (years)	4.937±1.9199	5.533±2.3459	0.181
Albumin(+)	2.70±1.286	1.37±1.085	<0.001*

Where: p value is significant*

We find that there is correlation between the occurrence of relapse and presence of urinary tract infections and these result similar to that obtained by Gulati S, et.al. (1995) in India [24] and by Iqbal SMJ, et al. (2002) study in Pakistan [30]. In our study there is 53.4% of those with history of relapse had UTI which is significantly differ from those without history of relapse.

Conclusion

- We believe that UTI is an important but often under diagnosed infection in children with nephrotic syndrome.
- UTI may be the cause of delay response to immune suppressive agents.
- UTI may be the cause for relapse in patients with nephrotic syndromes.

Recommendations

- Follow up of nephrotic patients by GUE and early urine cultures to allow early recognition and managements of UTI, because UTI often under diagnosed infection.
- Any patient with drug resistance or frequent relapse should exclude UTI.

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