



Journal Homepage: -www.journalijar.com
**INTERNATIONAL JOURNAL OF
 ADVANCED RESEARCH (IJAR)**

Article DOI:10.21474/IJAR01/6863
 DOI URL: <http://dx.doi.org/10.21474/IJAR01/6863>



RESEARCH ARTICLE

URINARY TRACT INFECTION IN CHILDREN WITH NEPHROTIC SYNDROME.

Dr Shatha Hussain Ali¹, Dr. Sarah Hussain Cooley², Jabbar Salman Hassan³ and Ali Sadiq Hassan⁴.

1. M. B. Ch. B, C.A.P.B, Professor in Pediatrics, Department of Pediatrics College of Medicine, Al - Nahrain University.
2. M.B.CH.B Imamein Kadhimein Medical City, Iraq.
3. Ph.D Medical Microbiology, Lecturer College of Medicine, Al-Nahrain University, Iraq.
4. M. B. Ch. B, F. I. C. M. S (Pediatric Nephrology)M. B. Ch. B, Imamein Kadhimein Medical City.

Manuscript Info

Manuscript History

Received: 06 February 2018
 Final Accepted: 08 March 2018
 Published: April 2018

Abstract

Background: Urinary Tract Infection (UTI) is an important cause of relapses in children with Nephrotic syndrome (NS)

Objective: Study the prevalence of UTI and clinical presentation among group of children with NS.

Study urinalysis and culture results, the causative microorganism and their sensitivity pattern to 15 types of Antibiotics

Methods: A prospective study including children with steroid sensitive NS was carried out in the Pediatric Nephrology Clinic of Al Imamain Kadhimein Medical city and Microbiology Department in Collage of medicine / AL- Nahrain University for the period from 1st Dec. 2016 – 31th Jan. 2017.

Urine samples from all patients were collected by clean catch method in sterile containers and promptly transported to the Microbiology laboratory. Culture of urine and resistance patterns of bacteria isolated to 15 various antibiotics were determined.

Result: Total number of patients was 50 patients, 30 (60%) males and 20 females (40%). Most common age group was 7 - 12 year (60%). Most common clinical presentation was abdominal pain in 21 patients (42 %). Urinalysis revealed 19 patients (38%) with more than 5 Pus cells/ HPF.

Prevalence of UTI was regarded in 17 (34%). The commonest microorganism isolated was Escherichia coli in 6 patients (35.2%).

Results revealed significant correlation of females, younger age group, pyuria > 5 pus cells/ HPF with positive urine cultures.

The highest sensitivity in 13 patients (76.06%) was to imipenem , ampicillin show no sensitivity at all and 100% resistant .

Conclusion: As UTI found in a considerable rate among children with NS, routine urine cultures should be carried out on patients with NS, especially during relapse.

Copy Right, IJAR, 2018,. All rights reserved.

Corresponding Author:- Shatha Hussain Ali.

Address:- M. B. Ch. B, C.A.P.B, Professor in Pediatrics, Department of Pediatrics College of Medicine, Al - Nahrain University.

Introduction:-

Nephrotic syndrome (NS) is a primarily a pediatric disorder and is 15 times more common in children than adults . The characteristic features are heavy proteinuria (40 mg/m²/hr in children), hypoalbuminemia (<2.5 g/dl), edema, and hyperlipidemia (cholesterol >200 mg/dL) (1, 2)

Fortunately, 80% of children with nephrotic syndrome respond to corticosteroid therapy. (2)

Seventy percent of patients with SSNS relapse at least once. Around 50 % of the latter will have frequent relapses or become steroid dependent. (3)

It is currently recognized that at least 50% of relapses are triggered by a viral upper respiratory tract infection (4, 5) other infections such as urinary tract infection (UTI), diarrhea, peritonitis and skin infections have also been implicated (4). Studies have established the role of UTI as an important cause of relapse, as well as the cause of poor response to steroid therapy (6, 7)

Aim of study:-

Study the prevalence of UTI and clinical presentation among group of children with Nephrotic syndrome. Study urinalysis findings, Urine culture results, the causative microorganism and the sensitivity pattern of the Microorganism to 15 types of Antibiotics

Patients and Methods:-

A prospective study including children with Nephrotic syndrome was carried out in the Pediatric Nephrology Clinic of Al Imamain Kadhimien Medical city and Microbiology Department in Collage of medicine / AL- Nahrain University for the period from 1st Dec. 2016 – 31th Jan. 2017. Patients are known cases of steroid sensitive NS .

Diagnosis of NS was done according to ISKD criteria: proteinuria >40 mg/h/m² or >50 mg/kg/day or protein/creatinine ratio >0.2 g/mmol (>2 g/g) and hypoalbuminemia <25 g/l and hyperlipidemia (cholesterol >200 mg/dL) with or without edema (1, 2).

Relapse was regarded as proteinuria >40 mg/h/m² or >50 mg/kg/day or Albustix +++ for 3 consecutive days after having been in remission (1)

During relapse, all patients were sent for the following laboratory investigations; urinalysis, urine culture and sensitivity.

Urine samples from all patients were collected by clean catch method in sterile containers and promptly transported to the laboratory in the Department of Microbiology in Collage of Medicine in AL- Nahrain University .

Oral approval was taken from parents of children for taking the urine samples. All patients with no previous history of antibiotic intake. Loopful of the sample were inoculated on a blood agar and MacConkey agar aerobically for 18 – 24 hours at 37°C.

The identification of Enterobacteriaceae family was performed according to the biochemical tests indicated in the scheme of Farmer and his co-workers (8) Other bacterial species were identified by gram stain. Resistance patterns of bacterial isolated to 15 various antibiotics were determined by Kirby- Bauer's disk diffusion test (DDT).

Significant pyuria was indicated as the presence of > 5 white blood cells (pus cells)/high power field (HPF) in centrifuged urine sample (3).

The case was regarded as UTI with the detection of the pathogen by the urine culture ± presence of clinical signs and symptoms.

Results:-

Total number of patients in the present study was 50 patients; there were 30 (60%) males and females 20 (40%), with male to female ratio 1.5: 1.

Age of patients at time of presentation was ranging from 1 - 12 year (mean of 5.2 + 3.1 year), most common age group of patients was 7 - 12 year (60%).

Most common clinical presentation was abdominal pain in 21 patients (42 %), frequency in 17 patients (34 %), fever in 15 patients (30%), urinalysis revealed 19 patients (38%) with pus cell more than 5 Pus cells/ HPF, while 31 patients (62%) with pus cell less than 5 cells/ HPF.

Table (1) confirmed positive growth and isolation of bacterial organism in 17 patients (34%), no growth was observed in 33 patients (66%), accordingly prevalence of UTI was observed in 17 patients, 7 cases were males and 10 cases were females.

The commonest microorganism isolated was Escherichia coli in 6 patients (35.2%), followed by Enterococcus in 5 patients (29.4%), Klebsiella, proteus and Staphylococcus aureus in 2 patients (11.8 %) for each Table (2) Show comparison of sex, age group, clinical presentation, and presence of significant pyuria according to urine culture results. More females: 10 (58.82%) than males 7 (41.18%) were found with positive culture. P value was significant (0.0504).

Nearly all positive cultures were detected among age groups below 12 years, only 1 (5.88%) was more than 12 years. P value was significant 0.5957.

Clinical presentation had no correlation with culture result. P value 0.9403 Regarding pyuria, 11 (64.71) with > 5 Pus cells/ High power Field (PC/ HPF) had positive culture, while only 6 (35.29) patients with < 5 PC / HPF had positive culture. P value was significant 0.0124.

Table (4) Show the distribution of patients according to the sensitivity to antibiotics, which revealed that 13 patients (76.06%) were sensitive to imipenem, 9 patients (52.9%) were sensitive to amikacin, 8 patients (47.06%) sensitive to nitrofurantoin, while augmentin (amoxicillin / clavulanate), cephalexin, cefotaxim, ceftriaxone, cefixime show sensitivity in 6 patients (35.2%) for each, 5 patients (29.4%) sensitive to piperacillin, 4 patients (23.5%) were sensitive to carbencillin.

We notice a lower rate of sensitivity to commonly used antibiotics as 3 patients only (17.6%) were sensitive to trimethoprim, both gentamycin and cephalexin show sensitivity in 1 patients (5.8%), ampicillin show no sensitivity at all and 100% resistant.

Table 1:-Distribution of patients according to results of urine culture and type of organism in positive culture of 17 Patients

| Culture results | No. | % |
|-----------------------|-----|------|
| Positive | 17 | 34 |
| Negative | 33 | 66 |
| Organisms | No. | % |
| E. Coli | 6 | 35.2 |
| Enterococcus faecalis | 5 | 29.4 |
| Klebsiella | 2 | 11.8 |
| Proteus | 2 | 11.8 |
| Staph. Aurous | 2 | 11.8 |
| Total | 17 | 100 |

Table 2:-Comparison of sex, age groups, clinical presentation and Pyuria according to urine culture results

| Data | | +ve culture No. (%) | -ve culture No. (%) | P value |
|------|--------|------------------------|------------------------|---------|
| Sex | Male | 7 (41.18) | 23 (69.69) | 0.0504 |
| | Female | 10 (58.82) | 10 (30.31) | |
| Age | 1-6 | 7 (41.18) | 9 (27.27) | 0.5957 |
| | 7 - 12 | 9 (52.94) | 21 (63.64) | |
| | >12 | 1 (5.88) | 3 (9.09) | |

| Clinical presentation | | +ve culture | -ve culture | P value |
|-----------------------|--|-------------|-------------|---------|
| Abdominal pain | | 7 | 14 | 0.9403 |
| Frequency | | 8 | 9 | |
| Fever | | 6 | 9 | |
| Dysuria | | 6 | 8 | |
| Urgency | | 4 | 6 | |
| Pus cells | | +ve culture | -ve culture | P value |
| ≤5 | | 6 (35.29) | 25 (75.76) | 0.0124 |
| >5 | | 11 (64.71) | 8 (24.24) | |

Table 3:-Distribution of 17 patients according to sensitivity to antibiotics

| Antibiotics | Sensitive | | Resistant | |
|----------------|-----------|-------|-----------|--------|
| | No. | % | No. | % |
| Imipenem | 13 | 76.47 | 4 | 23.53 |
| Amikacin | 9 | 52.94 | 8 | 47.06 |
| Nitrofurantoin | 8 | 47.06 | 9 | 52.94 |
| Nalidixic | 7 | 41.18 | 10 | 58.82 |
| Augmentien | 6 | 35.29 | 11 | 64.71 |
| Cefotaxim | 6 | 35.29 | 11 | 64.71 |
| Ceftrixon | 6 | 35.29 | 11 | 64.71 |
| Cefixime | 6 | 35.29 | 11 | 64.71 |
| Norfloxa | 6 | 35.29 | 11 | 64.71 |
| piperacillin | 5 | 29.41 | 12 | 70.59 |
| Carbenicillin | 4 | 23.53 | 13 | 76.47 |
| Trimthoprim | 3 | 17.65 | 14 | 82.35 |
| Cephalex | 1 | 5.88 | 16 | 94.12 |
| Gentamycin | 1 | 5.88 | 16 | 94.12 |
| Ampicillin | 0 | 0.00 | 17 | 100.00 |

Discussion:-

Different studies (4, 9, 10, 11, 12, 13, 14, 15) agree with the findings in the present study, that the males were affected more than females, because nephritic syndrome is more common in males than females (2).

Distribution of age groups in this study was similar to the finding of an Indonesian study, in which the most common age group of patients with NS was from 9-12 year 20 patients (27%) (14). While several studies recorded younger age group below 6 year as the commonest (9, 11, 13, 16, 17). This study was conducted in tertiary center where most of the cases were referred from other centers, which explain higher age group.

This study show that UTI was present in 17 patients (10 males and 7 females) 34%, UTI was recorded in percentages ranging from 25 % - 60.7% from different studies (7, 9, 10, 11, 13, 14, 15, 16, 17).

This wide variation is related to adoption of different definitions for UTI. High rate of 60.52% in Dillip Kumar study may be because of inclusion of urine culture negative with signs and symptoms as UTI cases (16). On the other hand lower rate of UTI in Sawai study (26.32 %) may be related to restricted definition for UTI with urine culture positive plus pyuria of > 5/ HPF (15). Moorani in his study depend on presence of signs and symptoms in addition to positive urine culture for diagnosis of UTI in a rate of 25% . (10)

All these studies proved that UTI is a common infection associated with NS. Significant pyuria with > 5 PC/ HPF was found in (38%) of cases in this study. Study from India reported slightly less figure of 26.32% (15)

Another 2 studies, regarded pyuria as presence of > 10 PC /HPF in non centrifuged urine sample, reported higher figures of 64% and 57.89% respectively (13, 16)

The presence of >5 PC/HPF in a centrifuged sample and 10 PC/HPF in an uncentrifuged sample of urine is seen in the majority of patients with UTI (3)

Although pain was the commonest symptom among our study population, 2 studies reported lower rates of pain with 6% and 10% respectively (11, 13)

Two studies from Pakistan reported fever as high as 86.6% and 86% respectively (10, 11), while another study from India reported low rate of 18% for fever. (13)

Differences in clinical presentation varies between population and different age groups and is often nonspecific. Different studies show that the commonest organism isolated was *Escherichia coli*, which was agreed upon in this study (9, 10, 13, 14, 15, 16, 18)

Enterococcus faecalis ranked second in this study with 29.4%. Compared with 2 other studies, lower rates of 5% and 21.1% was found respectively (15,18)

Striking finding came from Adeleke study with *Staphylococcus aureus* as the commonest organism with 67.9% (17). The differences in the types of NS in different regions compared to those seen in Caucasians of this study may account for the varying causative microorganisms for UTI in patients with NS

As seen in Table 2; data revealed significantly more females (58.82%) than males (41.18%) with proven positive urine culture among children with NS. This is similar to Indonesia study who found that UTI was more common in Females (67.6%) compared to males (32.4%) (14). It is well established that overall prevalence of UTI occurred more frequently in females (2)

Two studies found no significant correlation between sex and UTI in children with NS (6, 15), while another 2 studies found male predominance (13, 16)

This study found significant involvement of 52.94% of age group 7 – 12 Yr and 41.18% of 1 – 6 Yr group with UTI compared with older ages among children with NS. Similarly a recent Indian study found 70% of 2 – 6 Yr age group compared to 30% in > 6 years group. (13). other studies found no such correlation (6, 15, 16)

This study found that clinical presentation had no correlation with culture result. No physical sign is pathognomonic for UTI.

Among children with positive urine culture; Significant Pyuria with > 5 PC/HPF was detected in 64.71% compared to 35.29% of pyuria < 5 PC/HPF.).

Sreenivasa and Dilip also detected similar finding that Pyuria with > 10PC/HPF were found more than pyuria < 10PC/HPF among NS children with UTI. (13, 16)

Pyuria suggests infection, but infection can occur in the absence of pyuria; this finding is more confirmatory than diagnostic. Conversely, pyuria can be present without UTI. Sensitivity 73%, specificity: 81% (2)

Table 3 shows in-vitro sensitivity pattern of isolated organisms to 15 various antibiotics; Imipenem, amikacin, nitrofurantoin and Nalidixic acid showed the best sensitivity pattern. While sensitivity of the same organism to commonly used antibiotics including Augmentin (amoxicillin /clavulanate), cephalexin, cefotaxim, ceftriaxone, cefixime, was 35.29%.

On the lower scale of the table we see resistant to common routine antibiotics; Trimethoprim, Cephalexin and Gentamycin and striking finding that Ampicillin had 100% resistance.

Similarly, 2 recent studies from Indonesia and China found the most common antibiotics to which bacteria were sensitive were imipenem and amikacin (14, 18)

Dillip; found all *E.coli* species were 100 % sensitive to amikacin and ceftriaxone. Also much better sensitivity patterns to other antibiotics. (16)

Sawai found 50% sensitivity to amikacin, while 90% for gentamycin , 100% for Cefixime , which much higher than us.(15)

Also Adeleke from Nigeria reported invitro sensitivity to commonly used antibiotics including trimethoprim sulphamethoxazole ampicillin, and nitrofurantoin was 35 percent or less (17)

These observations pointing that there is an increasing resistance of bacteria mainly to common antibiotics. The malpractice and drug abuse could explain this unfortunate trend.

Conclusion:-

As UTI found in a considerable rate among children with NS, routine urine cultures should be carried out on patients with NS, especially during relapse.

Acknowledgments:-

No conflicts of interest for the authors

References:-

1. P. Niaudet and O. Boyer, Idiopathic nephrotic syndrome in children: clinical aspects. In : Pediatric Nephrology, E. D. Avner,W. E. Harmon, P. Niaudet, N. Yoshikawa, F. Emma, and L. S. Goldstein, Eds., Lippincott Williams & amp; Wilkins, Philadelphia, Pa, USA, 7th edition, 2016. pp. 839–869
2. P Priya , Avner E. Nephrotic Syndrome. In: Kliegman RM, Stanton BF, St Geme JW, Schor NF, Behrman RE (Eds). Nelson textbook of Pediatrics. 20th edition 2015 , Elsevier, Philadelphia Ch. 527, P. 2521-2523.
3. Bitzan M, Glomerular Diseases .In : Manual of Pediatric Nephrology, K. Phadke, P. Goodyer, andM. Bitzan, Eds. Springer, London, UK, 2014. pp. 141–229.
4. Moorani KN. Infections are common a cause of relapse in children with Nephrotic syndrome. Pak Paed J. 2011; 35(4) :213–219.
5. Takahashi S, Wada N, et al. Triggers of relapse in steroid-dependent and frequently relapsing nephrotic syndrome. Pediatr Nephrol. 2007; 22:232–236.
6. Gulati S, Kher V,et al. Spectrum of infections in Indian children with nephrotic syndrome. August 1995, Volume 9, Issue 4, pp 431-434 .
7. Afroz S, Hossain Khan MA, et al . Urinary Tract Infection (UTI) is associated with higher rate of relapse in children with nephrotic syndrome. DS (Child) H J 2010; 26 (2) : 82-86.
8. Farmer JJ, Davis RB, hickman brenner fw. biochemical identification of new species and biotypes of Enterobacteriaceae isolated from clinical specimens .J Clin. Microbiol. 1985; 21 : 46 – 76 .
9. Senguttuvan P, Ravanan K, et al . Infections encountered in childhood nephrotics in a pediatric renal unit. Indian J Nephrol 2004;14: 85-88.
10. Moorani KN, Raj M. Spectrum of Infections in Children with Newly Diagnosed Primary Nephrotic Syndrome. Pak J Med Res Vol. 51, No. 1, 2012. Pg: 10 – 14.
11. Jamro B, Lal S,et al . Types of Infection in Primary Nephrotic Syndrome. Pak Paed J 2012; 36(2): 87-91
12. Adedoyin OT, Ojuawo IA,et al . Urinary Tract Infections in Children with Primary Nephrotic Syndrome and Acute Glomerulonephritis. West African Journal of Medicine . July – August 2010. Vol. 29, No. 4 . 235 – 238.
13. Sreenivasal B, C L Murthy1 S, et al . Urinary tract infection at presentation of nephrotic syndrome: A clinical evaluation. Indian J Child Health . Jan - Mar 2015. Vol 2 , Issue 1. Pg: 1 - 4
14. Gunawan PY , Umboh A. The risk of urinary tract infection in children with nephrotic syndrome. • Paediatr Indones, July 2016. Vol. 56, No. 4, 238 – 241.
15. Lora SS, Goyal VK, et al . Prevalence and bacterial spectrum of urinary tract infection in nephrotic syndrome: a cross sectional study from a tertiary care centre. International Journal of Contemporary Pediatrics | October-December 2016 , Vol 3 , Issue 4, Page 1344 - 1347
16. Dash DK, Bisoi SK,et al . To study the frequency, etiology and predisposing factors of urinary tract infection in children with nephrotic syndrome in Eastern Odisha Region: a hospital based study. International Journal of Contemporary Pediatrics | January-February 2017 , Vol 4 , Issue 1 Pg: 140 – 144.
17. Adeleke SI and Asani MO. Urinary tract infection in children with nephrotic syndrome in kano, Nigeria. Annals of African Medicine, 2009, Vol. 8, No. 1: 38 – 41
18. Shao Na S, Bi – Li Z,et al . Spectrum and drug sensitivity of pathogenic bacteria in children with nephritic syndrome complicated by Urinary tract infection : an analysis of 97 cases. Chin J Contemp Pediatr. , 2012 , 14 (9) : 657 – 660.