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KEY WORDS: Nephrotic syndrome; urinary tract infection; E.coli; Meropenem; Colistin.

STUDY OF ANTIBIOTIC SENSITIVITY PATTERN IN CHILDREN WITH NEPHROTIC SYNDROME PRESENTING WITH UTI

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ABSTRACT

BACKGROUND: Nephrotic syndrome (NS) results in proteinuria of more than 3.5 g protein per day and is characterized by edema, hyperlipidemia, hypoproteinemia and other metabolic disorders. Prevalence of UTI in nephrotic syndrome is high. It precipitates relapse and delays remission.

AIMS AND OBJECTIVES: The aim of this retrospective study is to analyze the incidence of UTI, its Predisposing factors along with its bacterial and fungal etiologies in patients with NS and antibiotic sensitivity pattern in nephrotic children with UTI.

METHODS: This retrospective study was carried out in a tertiary care, CIVIL HOSPITAL,AHMEDABAD between July 2018 and July 2019 among the admitted cases of nephrotic children under 12 years of age.

Examinations for microscopy and cultures of urine, sputum, throat swab, blood and fluid were also carried out in the children, along with routine examination, if found necessary.

Urinary specimens were collected by clean catch method following careful preparation of urethral orifices. The specimens were immediately inoculated on culture media. Identification of organisms and antibiotic sensitivity susceptibility testing was performed according to CLSI guidelines 2010 by Kirby –Bauer disc diffusion method.[1]

RESULTS: Total 41 nephrotic children were enrolled. Incidence of UTI was fairly high in nephrotic syndrome, especially in frequent relapse (48.48%). Kleibsella pneumonia (45.5%) was the most common organism, followed by E.coli (24.24%), responsible for UTI in both first episode and frequent relapse of nephrotic syndrome in the following study.

CONCLUSION: As per the study, common isolates of UTI in nephrotic syndrome have developed resistance to commonly used oral or parenteral drugs. In my study, it is observed that colistin was the most sensitive parenteral drug for all isolates followed by Meropenem and aminoglycoside.

INTRODUCTION:

Nephrotic syndrome (NS) results in proteinuria of more than 3.5 gm protein per day(more than 40 mg/m2/hr; 1gm/m2/24hr) and is characterized by oedema, hyperlipidemia, hypoproteinemia and other metabolic disorders.[2]

The course of NS is often complicated by frequent relapses, steroid resistance, thrombosis and infections. The common infections seen in NS are pneumonia, urinary tract infection (UTI), bacteraemia, peritonitis and cellulites. Of these, UTI is often under diagnosed in NS and may also be responsible for poor response to steroid therapy.

These children were treated using standard protocol. The initial episode was treated with prednisolone in doses of 2 mg/kg daily for 6 weeks followed by 1.5 mg/kg on alternate days for 6 weeks.[2]

Any form of relapse was treated with prednisolone in doses of 2 mg/kg/d until remission for 3 days followed by 1.5 mg/kg on alternate days for 4 weeks. An adjunctive therapy (cyclophosphamide, mycophenolate, tacrolimus or cyclosporine) was administered in standard regimens to frequent relapses, steroid dependent and steroid resistant NS. according to guidelines whenever indicated.[2]

Some studies have shown that UTI is the most common infectious complication of NS. However some others suggest that the incidence of UTI is low in the first episode and higher following the relapses in NS.

The aim of this retrospective study is to analyze the incidence of UTI, its predisposing factors along with its bacterial and fungal etiologies in patients with NS.

AIMS AND OBJECTIVES:

The aim of this retrospective study is to analyze the incidence of UTI, its Predisposing factors along with its bacterial and fungal etiologies in patients with NS and antibiotic sensitivity pattern in nephrotic children with UTI.

Materials And Methods

Between July 2018 and November 2019, we retrospectively analyzed the data of 41 children of Nephrotic Syndrome, under 12 years of age, fulfilling the criteria required as per the International Study of Kidney Disease in Children suffering from NS.

These children were treated using standard protocol.

Urine routine & microscopic examination was done in all cases. All nephrotic syndrome patients were subjected for culture examination before starting empirical antibiotics. A positive urine culture was defined as follows: midstream clean-voided specimens in symptomatic patients with isolation of $\geq 10^5$ CFUs/ mL of a single organism. Isolated organism had been subjected further for antibiotic sensitivity analysis.[3]

Urine was cultured in the following circumstances:

(1) For a screening investigation before the initiation of steroid therapy;
(2) When the response to a standard 4-week course of steroids was null
(3) When remission suggested symptoms of UTI such as fever, dysuria or hematuria.

A positive urine culture was defined as follows:

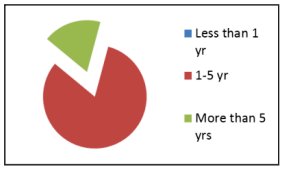
(1) Suprapubic aspirate
(a) isolation of ≥100 colony-forming units (CFUs)/mL or a single Gram negative bacillus or
(b) isolation of ≥1000 CFUs/mL of single Gram-positive cocci;
(2) Midstream clean-voided specimens in symptomatic patients with isolation of ≥100000 CFUs/ mL of a single organism.[3]

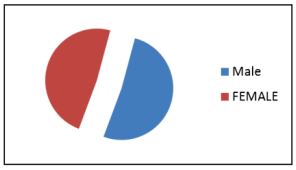
RESULTS :

Total 41 children were admitted with nephrotic syndrome out of which 33 had UTI during study period accounting for 84.48 %.

Table 1 & Chart 1: Age wise distribution of Nephrotic syndrome.

	Male	Female	Total (%)
Less than 1 yr	0	0	0
1-5 yr	16	11	27 (81.8)
More than 5 yrs	1	5	6 (18.2)
Total	**17**	**16**	**33**





81.78% patients were in the age group of 1-5 years and there was no patient in less than 1 year age group which is suggestive of the typical age of presentation for nephrotic syndrome.

In present study male to female ratio was 1.06:1, which shows that there is no significant sex difference.

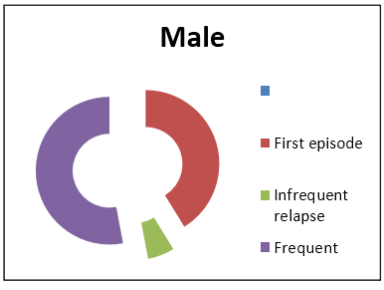
Table 2: Categorization of nephrotic syndrome:

Category	Male	Female	Total(%)
First episode	7	5	12 (36.37%)
Infrequent relapse	1	4	5 (15.15%)
Frequent	9	7	16 (48.48%)
Total	**17**	**16**	**33 (100%)**

36.37% patients presented for the first time as nephrotic syndrome whereas 63.63% patients had relapse. Overall frequent relapse cases were maximum (48.48%).

Recurrent infections are common amongst the frequent relapse due to prolonged immunosuppressive therapy. UTI is one of the frequent bacterial infections amongst nephrotic syndrome.

Chart 2- categorization of nephrotic syndrome in male and female



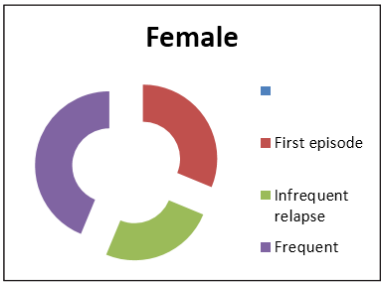
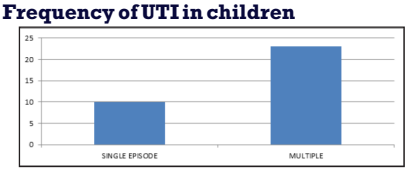


Table 3: Frequency of UTI amongst nephrotic syndrome.

Number of episodes	Number of patients	Percentage (%)
Single	10	30.3
Multiple	23	69.69

Chart 3: Frequency of UTI in children



Out of 33 patients,10 had single episode of UTI ,whereas remaining 23 had multiple episodes in the past.

The majority of patients with multiple episodes (21/23) were of relapse group suggesting that they are more prone for recurrent infections. It is also possible that UTI could be precipitant cause for relapse in this group.

Table 4(a): Organism isolated in First episode Nephrotic syndrome:

ORGANISM	NUMBER	Percentage (%)
KLEBSIELLA	5	41.7
E.COLI	4	33.3
CANDIDA	1	8.3
ENTEROBACTER	1	8.3
PROTEUS	1	8.3
ACENETOBACTER	0	0
	12	**100**

The Kleibsella was the most common isolated organism (41.7%) followed by E.coli (33.3). Candida ,Enterobacter and Proteus were also isolated. There was no organism from gram positive bacteria group.

Chart 4(a): Frequency of organism isolated (First episode)

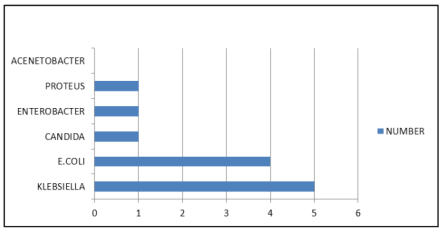


Table 4(b): Organism isolated in relapsed cases of Nephrotic syndrome:

ORGANISM	NUMBER	PERCENTAGE (%)
KLEBSIELLA	10	47.6
E.COLI	4	19.1
CANDIDA	3	14.3
ENTEROBACTER	2	9.6
PROTEUS	1	4.7
ACINATOBACTER	1	4.7
TOTAL	**21**	**100**

Maximum no of uti noted in a particular children during study period was 3 times , maximum no of time isolated organism was Klebsiella(47.6%) followed by E coli(19.1).

Candida Sp. also found to be causative for recurrent UTI in 3 patients(14.3).

In 4 (19.1%) patients there was more than single isolates during the same episode of UTI.

Chart 4(b): Organism isolated in relapsed cases of Nephrotic syndrome:

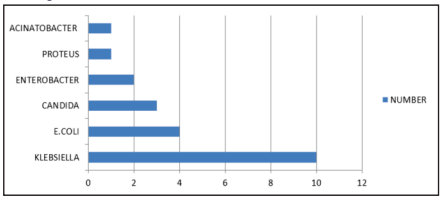
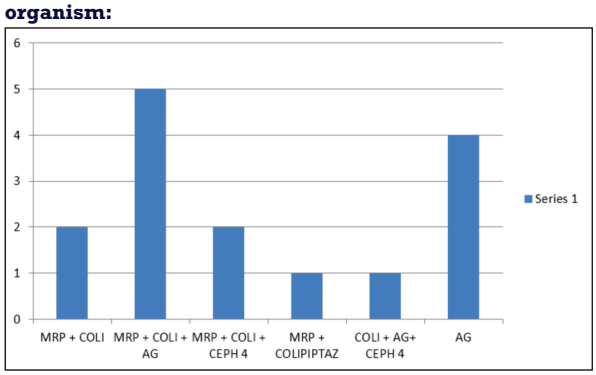


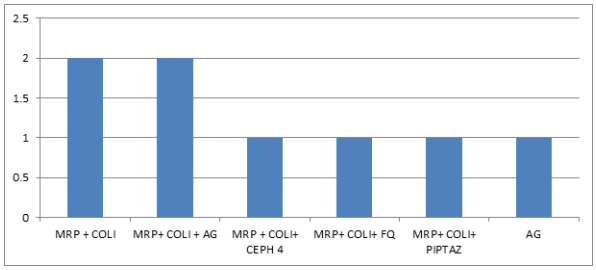
Chart 5 : Sensitivity to antimicrobial to Klebsiella organism:



Culture study shows maximum no of isolates of Klebsiella is sensitive to Meropenam, Colistin and Aminoglycoside . Meropenam and Colistin was found uniformly sensitive to isolates although two isolates (N=28) were resistant to Meropenam.

7 isolates were uniformly sensitive to above mentioned all group of antibiotics which commonly used for treatment.

Chart 6 : Sensitivity of antimicrobial to E coli :



Isolates of E coli was maximally sensitive to Meropenam, Colistin and Aminoglycoside , no resistence to either Colistin or Meropenam noted

Isolates of Candida Sp. were sensitive to Fluconazole, Itraconzoleand, Amphotericin B.

DISCUSSION :

Total 41 nephrotic children were enrolled. In present study Incidence of UTI was 80.48%, fairly high in nephrotic syndrome , especially in frequent relapse (48.48%) as compare with Tanuka et al study incidence is only 30.8% done in chhittagong medical college admitted children. But attack of UTI in male and female was equal as 1.06:1 which similar to comparative study of Tanuka et al.[4]

In our study, the most common organism isolated was Klebsiella pneumonia (45.5%) followed by E.coli (24.24%) as compared with Tanuka et al study in which most common organism was E coli (50%) followed by Klebsiella (25%).[4]

As compare to Adeleke et al study done in Kano,Nigeria suggest most common organism cause UTI was Staphylococcus areus in 67.9% followed by Klebsiella (17.9%) and Pseudomonas (14.2%) and there was high resistance to Nalidixic acid and Ampicillin in vitro. In present study some species of Klebsiella was resistance to Meropenem in vitro with sensitive to Collistin and Aminoglycoside.[5]

CONCLUSION :

As per the study, common isolates of UTI in nephrotic syndrome have developed resistance to commonly used oral or parenteral drugs. In my study, it is observed that Colistin was the most sensitive parenteral drug for all isolates followed by Meropenem and Aminoglycoside.

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