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PREVALENCE OF URINARY TRACT INFECTION IN PAEDIATRIC AGE GROUP AND THEIR ANTIBIOTIC SUSCEPTIBILITY

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ABSTRACT **Background:** Urinary tract infections (UTIs) are one of the major causes of morbidity in paediatric population. Sound knowledge of factors associated with UTI may allow timely intervention that can easily bring the disease under control. This study was designed to determine the prevalence of UTI in pediatric age group and their clinical profile by isolating and characterizing the different bacterial agents and evaluate their antibiotic sensitivity. **Materials and Methods:** This prospective study was conducted in Department of Microbiology, AJ Institute of Medical Science & Research Center, Mangalore from May 2021 to April 2022. A total of 113 non repetitive urine samples (clean catch midstream urine, catheter aspirated, suprapubic aspirate) were collected from paediatric patients (0-18yrs) suspected of UTI. Culture and bacterial identification was done by using standard microbiological guidelines. Antimicrobial susceptibility testing was done by Kirby-Bauer disc diffusion method following clinical and laboratory standards institute (CLSI) guidelines. **Result:** The study revealed a 27% (31/113) UTI prevalence among paediatric patients attending hospital. Fever, irritability and poor feeding were the most common symptoms in neonates while older children presented with fever and urinary symptoms. The predominant organisms isolated were E. coli 15(48%) followed by Klebsiella spp 7(23%), Enterococcus spp 4(13%), Staphylococcus aureus 3(10%), Proteus 1(3%) and Pseudomonas aeruginosa 1 (3%). All isolates of E. coli were found to be sensitive to Meropenem 15 (100%), followed by Amikacin and Gentamicin and Co-trimoxazole 11(74%). Nitrofurantoin showed 94% sensitivity and Cephalosporins showed 94% resistance. Klebsiella spp were found to be sensitive towards Amikacin 7 (100%) followed by Cefoperazone 6 (85%) and showed resistance to Ceftazidime 6 (85%). ESBL producers in gram negative bacilli accounted for 38%. Enterococcus spp were found to be sensitive to Linezolid 4 (100%) and all showed resistance to Erythromycin, Penicillin, Tetracycline, Ciprofloxacin and Norfloxacin 4 (100%). Amikacin (11% resistance) and Nitrofurantoin (5% resistance) are the most effective drugs for gram-negative bacilli (GNB) while Vancomycin and Linezolid are functional against gram-positive cocci. The positivity rate from 0-6 years, 7-12years, 13-18years were 11(35%), 3 (10%), 17 (55%) respectively. In our study, UTIs were more common in female (58%) children as compared to male (42%) children. **Conclusions** High-level antimicrobial resistance was observed in paediatric UTI with alarming incidence of superbugs like ESBL and MRSA. Regular surveillance should be carried out to determine the local prevalence of organisms and antimicrobial susceptibilities in order to guide the proper management of children.

KEYWORDS : Antimicrobial resistance; ESBL; MRSA; UTI.

INTRODUCTION:

Urinary tract infection (UTI) are one of the commonest cause of febrile illness in paediatric population with a worldwide prevalence of 2–20%[–1]. They can be associated with high morbidity and long-term complications such as renal scarring, hypertension and chronic renal failure [2]. UTI has good prognosis but pediatric UTI cases remain under-diagnosed in many instances due to absence of specific symptoms and signs, especially in infants and young children[1–3]. UTI in children can be early clinical manifestation of congenital abnormalities of the kidney and urinary tract or related bladder dysfunction[4]. It has been estimated that around 50% of UTI in children are missed [1]. Timely diagnosis and targeted treatment, decreases the risk of renal scarring and other complications [5]. For this purpose, empirical antibiotic is often prescribed even before the culture results are available. On the other hand, antibiotic resistance of urinary tract pathogens has been increasing globally[6]. Missing a febrile paediatric UTI, can prove a future catastrophe if not timely diagnosed and treated. In this perspective, the present study was designed to investigate the prevalence, clinical profile, organism spectrum and antimicrobial resistance profile in paediatric UTI in a tertiary care teaching hospital in Mangaluru.

MATERIALS AND METHODS

This is a prospective study conducted in the Department of Microbiology, A.J Institute of Health Sciences & Research Centre, Mangaluru, for a period of one year (May 2021 to April 2022). Patient's information was collected from requisition form, laboratory records and medical records.

A total of 113 urine samples (clean catch midstream urine, catheter aspirated, suprapubic aspirate) of paediatric patients (0–18years age) suspected of UTI were obtained in the Microbiology laboratory. The samples were then processed by semi-quantitative streaking method using a calibrated inoculating loop (holding 0.001ml urine) onto the Cystine lactose electrolyte deficient (CLED) agar. The inoculated plates were incubated for 24hours at 37°C in aerobic atmosphere. The isolates were identified using standard microbiological methods that include colony morphology, Gram-stain, catalase, oxidase and other biochemical tests[7].

Antimicrobial susceptibility was tested by modified Kirby-Bauer disc diffusion method on Mueller Hinton agar (Hi-Media, India) following standard procedures recommended by the Clinical and Laboratory Standards Institute (CLSI) [8].

Antibiotics that were tested in our study include:
Gram negative bacilli Cefepime (50mcg), Ceftazidine (30mcg), Amikacin (10mcg), Amoxyclav (10/50mcg), Ciprofloxacin (30mcg),Gentamicin (50mcg),Co-trimoxazole (25mcg), Imipenem(10mcg), Meropenem (30mcg), Levofloxacin (10mcg), Pipericillin+Tazobactem (100mcg +10mcg), Cefoperazone (75/30mcg), Ceftriaxone(10mcg), Norfloxacin (5mcg), Nitrofurantoin (200mcg), Ticarcillin (75mcg)Gram positive cocci Cefoxitin (30mcg), clindamycin (10mcg), Erythromycin (10mcg), Linezolid(30mcg), Ciprofloxacin (30mcg), Gentamicin (50mcg), Co-trimoxazole (25mcg), Penicillin(10units), Tetracycline (10mcg), Vancomycin (30mcg), Norfloxacin (5mcg), Nitrofurantoin (200mcg),

Screening and confirmation for ESBL production

Gram-negative bacilli were screened for ESBL production by using third generation Cephalosporins discs i.e. Ceftazidime (30µg), Cefotaxime (30µg) and Cefotriaxone (30µg). If the zone of inhibition (ZOI) was ≤25mm for Ceftriaxone, ≤22mm for Ceftazidime and/or ≤27mm for Cefotaxime, the isolate was considered a potential ESBL producer and confirmed by Combination disc test (CDT) method. In this method, the organism was tested against Ceftazidime (30µg) disc

alone and Ceftazidime+ Clavulanic acid (30/10µg) combination disc. Isolate that showed increase of ≥5mm in the ZOI of the combination discs in comparison to that of the Ceftazidime disk alone was considered an ESBL producer [8].

RESULTS:

During the study period a total 113 urine samples were received from children with suspected UTI among which 31 samples (27%) yielded significant bacteriuria. Out of 113 patients 56(49.6%) were females and 57(50.4%) were males. Out of this 18(58%) samples showed growth among females and 13(42%) were culture positive among males. On the basis of age wise distribution of our patients, about 67 (57.5%) were between 0 and 6years of age, 9(8%) between 7 and 12 years of age and 39(34.5%) were between 13-18 years of age (Table1).

Table 1: Distribution based on age group

Age group	No. of samples (Total no. of samples = 113)	No. of culture positives (Total no. of samples = 31)
0-6	65 (57.5%)	11 (35%)
7-12	9(8%)	3 (10%)
13-18	39(34.5%)	17(55%)

The prevalence rates of febrile UTIs in age group 0-6 years, 7-12 years and 13 to 18 years was 19.6% (2/11), 33.8% (1/3), 12.6% (2/17) respectively. Fever was the most common clinical presentation followed by dysuria and urgency. Among neonates, fever (84%), poor feeding (76%) and irritability (70%) were the most common clinical features. Out of the 31 samples which showed growth, 15(48%) were E. coli,7(23%) were Klebsiella spp, 4(13%) were Enterococcus spp, remaining were 3(10%) Staphylococcus aureus, 1(3%) Proteus and1 (3%) Pseudomonas aeruginosa [Table2].

Table 2: Organisms isolated from the urine samples.

Organisms	No. of isolates (Total no. of culture positives = 31)
E. coli	15 (48%)
Klebsiella spp.	7 (23%)
Enterococcus spp.	4 (13%)
Staphylococcus aureus	3 (10%)
Proteus spp.	1 (3%)
Pseudomonas aeruginosa	1 (3%)

Antimicrobial susceptibility test showed variable degree of resistance [Table 3-6] All isolates of E. coli (n=15) were found to be sensitive towards Imipenem 15 (100%), followed by Amikacin and Gentamicin and Co-trimoxazole i.e 11 (74%) and were 94% resistant to Cefepime. Nitrofuratoin resistance was seen in 16% of the isolates. All Klebsiella spp (n=7) were found to be sensitive towards Amikacin and Nitrofuratoin 7 (100%) followed by resistance to Cefoperazone and Ceftazidime 6 (85%). Enterococcus spp (n=4) were found to be sensitive towards Linezolid 4 (100%) and showed resistance to Erythromycin, Penicillin, Tetracycline, Ciprofloxacin and Norfloxacin 4 (100%). Twenty-five percent showed resistance to Nitrofuratoin. All Isolates of Staph.aureus (n=3) were sensitive to Linezolid, Gentamycin, Co- trimoxazole, Nitrofurantoin 3 (100%) and showed resistant to Penicillin 3 (100%). Only one Proteus vulgaris was isolated, which showed 100% sensitivity to all antibiotics. Pseudomonas aerugiosa showed 100% sensitivity to Amikacin, Gentamicin, Imipenem, Piperacillin-Tazobactam, Nitrofurantoin and Cefoperazone while showed showed resistance to Levofloxacin, Ceftazidine, Ticacillin, and Norfloxacin. Thirty-eight percentage of gram-negative bacilli were ESBL producers. Thirty-three perentage of S.aureus were methicillin resistant Staphylococcus aureus (MRSA), while none of them were resistant to Vancomycin.

Table 3: Antibiotic sensitivity of E. coli

Organisms	Antibiotics	No. of resistant strain	Percentage of resistant strain
E. coli (Total no. of isolates =15)	Ceftazidine	13	(87%)
	Amikacin	2	(13%)
	Amoxyclav	11	(74%)
	Ciprofloxacin	8	(53%)
	Gentamicin	4	(26%)
	Co-Trimoxazole	4	(26%)
	Imipenem	0	(0%)
	Meropenem	7	(47%)
	Levofloxacin	6	(40%)
	Pip+ Tazobactam	5	(34%)
	Cefoperazone	4	(27%)
	Ceftriaxone	7	(47%)
	Cefepime	14	(94%)
	Norfloxacin	6	(40%)
	Nitrofurantoin	2	(16%)

Table 4: Antibiotic Sensitivity of Klebsiella spp.

Organisms	Antibiotics	No. of resistant strain	Percentage of resistant strain
Klebsiella spp. (Total no.of isolates = 7)	Ceftazidine	6	(85%)
	Amikacin	0	(0%)
	Amoxyclav	5	(72%)
	Ciprofloxacin	5	(72%)
	Gentamicin	2	(28%)
	Co-Trimoxazole	3	(43%)
	Imipenem	1	(15%)
	Meropenem	5	(72%)
	Levofloxacin	5	(72%)
	Pip+ Tazobactam	4	(47%)
	Cefoperazone	1	(15%)
	Ceftriaxone	6	(85%)
	Cefepime	6	(85%)
	Nitrofurantoin	0	(0%)

Table 5: Antibiotic Sensitivity of Enterococcus spp

Organisms	Antibiotics	No. of resistant strain	Percentage of resistant Strain
Entercoccus spp (Total no. of isolates =4)	Gentamycin	2	(50%)
	Ampicillin	4	(100%)
	Erythromycin	4	(100%)
	Penicillin	4	(100%)
	Tetracycline	4	(100%)
	Linezolid	0	(0%)
	Vancomycin	0	(0%)
	Ciprofloxacin	4	(100%)
	Nitrofurantoin	1	(25%)
	Norfloxacin	4	(100%)

Table 6: Antibiotic sensitivity of Staphylococcus aureus

Organisms	Antibiotics	No. of resistant strain	Percentage of resistant strain
Staphylococcus aureus (Total no. of isolates =3)	Cefoxitin	1	(33%)
	Clindamycin	2	(67%)
	Erythromycin	2	(67%)
	Linezolid	0	(0%)
	Ciprofloxacin	2	(67%)
	Gentamycin	0	(0%)
	Co- trimoxazole	0	(0%)
	Pencillin	3	(100%)
	Tetracycline	1	(33%)
	Vancomycin	0	(0%)
	Norfloxacin	2	(67%)
	Nitrofurantoin	0	(0%)

DISCUSSION:

UTI is a common health problem in children and it is an important cause of morbidity and mortality, especially in the first 2 years of life [2]. In our study, 27% of total samples were positive for UTI. The finding is similar to study done by Badhan et al., [9] in India that showed 26.7% culture positivity. However, some studies showed very low rate of UTI among children i.e 9% in USA [6]. UTI is one of the common bacterial infection in children in the world[10].

Children with UTI usually present with non-classical clinical features and these are difficult to diagnose[11]. In our study, fever, poor feeding and irritability were the common clinical features in neonates while the

older children presented with fever and dysuria. Our data agree with other reports, where fever, abdominal pain, vomiting, dysuria, poor feeding, and irritability are reported as frequent signs and symptoms of UTIs [12, 13]. Diagnosis of UTI is really challenging due to its vague presenting symptoms, especially in young children. Thus, a high index of suspicion is needed when a young child presents with fever [11].

In our study, incidence of UTI was higher in female (58%) children as compared to male (42%) children in the age group of 13-18years.This is because of shorter length of urethra in females. With the increase in age, female children show considerable increase in UTI compared to male children. The similar result was also seen in the study conducted by Rabina ganesh et al [14,15].

The most common organism isolated in our study was *E. coli* (48%) This was followed by *Klebsiella spp (23%), Enterococcus spp (13%), Staphylococcus aureus (10%), Proteus vulgaris (3%) and Pseudomonas aeruginosa (3%).* This data is consistent with study conducted by Mahmut Abuhandan et al., where the predominant uropathogen was *E. coli* followed by *Klebsiella spp*[4] and in a study by Jules et al., the most prevalent was *E. coli* followed by *Staph.aureus*[15]. *E. coli* is the most common etiological agent responsible for UTI irrespective of age, sex, community or country and accounts for 50–90% of cases. Uropathogenic *E. coli* (UPEC) originate from the faecal flora, spread across the perineum, and invade the bladder through the urethral opening [9 11]. Although gram-negative bacteria are responsible for majority of UTI, gram-positive organisms have become important cause of UTI in recent years [16].

The most striking finding of our study is the prevalence of antibiotic resistance among the organisms isolated form suspected paediatric UTI. Among gram-negative bacilli, 38% were ESBL producers. Similar results were reported by Parajuli et al., (38.9%) [17] and Fatima et al. (33.5%) [18]. Higher rates of ESBL producers have been reported in other studies [19]. However, Wu et al., [20] reported very low prevalence of ESBL producer (14%) in pediatric UTI. Pediatric UTIs due to ESBL-producing bacteria are an important part of the problem as they limit therapeutic choices and increases morbidity of infection [20]. All isolates of *E. coli* were sensitive to Imipenem 15 (100%). Most of the strains were sensitive to Amikacin and Gentamicin i.e 11 (74%) and 94% of strains were resistant to Cefepime and Ceftriaxone. Similar antibacterial sensitivity pattern was exhibited by *E. coli* in a study done by Mohmed motamedifer et al [21]. Nitofurantoin resistance was seen in 16%. Our study shows that Nitrofurantoin is still the most effective antimicrobial agent for the treatment of UTI. The finding is in agreement with studies done elsewhere [22]. Nitrofurantoin remains a reliable first-line agent for the empirical treatment of acute uncomplicated cystitis [23].

Among gram-positive bacteria, all isolates of *Enterococcus spp* and *Staphylococcus aureus* showed 100% sensitivity towards Vancomycin and Linezolid. The finding is similar to study done by Kaur et al., [24] in India. Enterococcus (n=4) showed 25% resistance to Nitrofurantoin but all strains (n=3) of *Staphylococcus aureus* were sensitive to Nitrofurantoin and 33.3% *Staphylococcus aureus* were Methicillin Resistant Staphylococcus aureus (MRSA). A similar result was seen in a study conducted by Lok Bahadur Shrestha et al., that showed 38% of *Staphylococcus aureus* were MRSA [2]. Recent studies have reported the increasing prevalence of multi drug resistant *Staphylococcus aureus especially MRSA* in UTIs [25].

CONCLUSION

High-level antimicrobial resistance was observed in paediatric UTI with alarming incidence of superbugs like ESBL and MRSA. Regular surveillance should be carried out to determine the local prevalence of organisms and antimicrobial susceptibilities in order to guide the proper management of children

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