Original Research Article

Five-year trends in antimicrobial susceptibility of uropathogens isolated from paediatric patients attending a tertiary care teaching hospital

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ABSTRACT

Background: Urinary tract infection (UTI) is a common bacterial infection encountered by paediatrician in their routine clinical practice, globally. To avoid complications, accurate diagnosis and initiation of appropriate antimicrobial therapy is very important. To reduce the treatment failure, the change in antimicrobial resistance (AMR) pattern is very essential. Aim was to study the trend of antimicrobial susceptibility of uropathogen in paediatric patients attending the tertiary care hospital.
Methods: It was a retrospective study conducted in the department of microbiology, paediatrics and quality control, the records of paediatric patients i.e., between 1-16 years age, diagnosed with UTI between January 2017-December 2021 were collected. The age, gender, uropathogens and their antimicrobial susceptibility were noted. The data was analysed by frequency and percentage.
Results: A total of 276 paediatric patients were diagnosed with UTI during the study period. The highest number of patients i.e., 109/276 (39.5%) belonged between 1-5 years of age with female predominance. *E. coli* (148/ 276, 53.62%) was the most common uropathogen isolated followed by *Klebsiella spp.* (57/276, 20.7%). *Staphylococcus spp.* and *Enterococcus spp.* were the common Gram-positive pathogens. Highest resistance was observed to ampicillin followed by 3rd generation cephalosporin (3GC), folate inhibitors among the *E. coli* and similarly in *Klebsiella* isolates. There was increasing rate of resistance seen in ampicillin, 3GC, nitrofurantoin, beta lactum-beta lactamase inhibitor combination.
Conclusions: *E. coli* is the most common cause of UTI with changing resistance pattern over five years. So, the antibiogram needs to be closely monitored and the AMA for empirical therapy needs modified annually.

Keywords: Paediatric, UTI, *E. coli*, Antimicrobials, Trend, Five years

INTRODUCTION

Antimicrobial resistance (AMR), a global threat to health, is associated with increased healthcare cost and higher morbidity and mortality. The first line of drugs become ineffective in treatment of these multi-drug resistant organisms (MDRO), leading to use of high end or restricted antimicrobial agents, which are expensive and toxic at higher dose. In-appropriate use, over use and misuse of antimicrobial agents in community and health

care setting, contributes to this global threat as a vicious cycle.

Children are vulnerable to receive higher number of AMA in the primary care due to non-specific signs and symptoms like fever, lethargy, poor feeding, failure to thrive, irritability and vomiting, especially preverbal children. Older children, who are toilet trained, may present with frequency, urgency, dysuria, incontinence, suprapubic pain. Around six to eight percentages of children below nineteen years with non-specific signs and symptoms with or without fever may have urinary tract infection.[1]

UTI, a bacterial infection, is also a leading cause for illness encountered by paediatricians in developing countries. It is more common in female children due to shorter urethra. Any cause leading to stasis of urine like structural anomalies or neurogenic bladder, allows the bacteria grow well in the urine and cause infection. If not treated promptly, it causes recurrent infection leading to complications like renal scarring, hypertension and renal failure.[2] The most common bacterial cause for UTI is *E. coli*, accounting for 80% of all the cases. Other common pathogens causing UTI in paediatric age are *Klebsiella spp, Pseudomonas, Enterococcus spp.*[3] In paediatric patients suspected with urinary tract infection, anti-microbial agents are prescribed empirically due to delay in availability of antimicrobial susceptibility test results. If the empirical therapy is inappropriate, this leads to complications like bacteremia, sepsis and the death. To start an appropriate anti-microbial agent, the paediatrician needs to know the bacterial profile as well as their AMR pattern.

Therefore, this study was undertaken with the aim to know the trend of anti-microbial susceptibility of uropathogen in paediatric patients attending the tertiary care hospital over five years i.e., from 2017 to 2021.

METHODS

Type of study and study setting

It was a retrospective record-based study conducted in the department of microbiology, paediatrics and quality control of the MES medical college hospital, Perinthalmanna, Kerala after obtaining clearance from the institutional ethics committee (IEC/MES/26/2017).

Inclusion criteria

Paediatric patients i.e., between 1-16 years age, diagnosed as UTI clinically and confirmed bacteriologically as significant bacteriuria (more than 10^5 Colony forming unit/ ml of urine with single bacterial pathogen) between January 2017-December 2021 were included in the study.

Exclusion criteria

Patients with other infections like pneumonia, Skin and soft tissue infection, meningitis were excluded from the study.

Sampling technique

Convenient sampling technique, all paediatric patients who were diagnosed with UTI during the study period were included in the study.

Data collection and analysis

The medical records of all patients included in the study were collected from medical record department and the age, gender, uropathogen and their antimicrobial susceptibility were noted in the proforma.

All the collected data was entered in Microsoft excel and analysed as frequency and percentage.

RESULTS

A total of 276 patients of age between 1-16 years were diagnosed with UTI with single bacteria from 2017 to 2021. Among them, 46 were diagnosed in 2017, 47 each in 2018 and 2019, 53 in 2020 and 83 in 2021. The male: female ratio was 1.09 i.e., 144: 132. There was around 40%, 28% and 32% of patients of the age group of 1-5, 6-10 and 11-16 years (Table 1).

The gram-negative pathogens accounted 93.12% of the 257 isolates. Among the gram-negative pathogens, *Escherichia coli (53.63%)* was the most common followed by *Klebsiella spp* (20.65%). Non-fermenters like *Acinetobacter* spp and *P. aeruginosa* accounted for 3.99% and 2.9%, respectively. The gram-positive pathogens were very less accounting for 6.88% of the total isolates, *Staphylococcus spp* and *Enterococcus spp* were only isolated. *Candida* species was isolated only in 3 patients.

We studied the AMR pattern over 5 years in *E. coli* and *Klebsiella spp* which accounted for nearly three fourth of the total isolates. The *E. coli* showed increase in resistance for orally administered drugs like ampicillin, norfloxacin, folate inhibitors and paternal drugs like beta lactam-beta lactamase inhibitor combination. Meanwhile, there was emergence of drug resistance to amikacin, nitrofurantoin and meropenem (Table 2).

In *Klebsiella spp,* there was rise in resistance rate to 3rd generation cephalosporins, folate inhibitors and fluoroquinolones. There was emergence of resistance to amikacin, nitrofurantoin, piperacillin-tazobactum and meropenem over five years (Table 3).

Table 1: The demographic and common pathogens isolated from paediatric patients diagnosed with UTI.

Variables	Year	2017	2018	2019	2020	2021	Total	Percentages (%)
	Total no. of isolates	46	47	47	53	83	276	
Age (in years)	1-5	14	25	13	24	33	109	39.49
	6-10	17	8	18	17	16	76	27.54
	11-16	15	14	16	12	34	91	32.97
Gender	Female	25	20	21	28	50	144	52.17
	Male	21	27	26	25	33	132	47.83
Uropathogens	**Gram negative**						257	93.12
	E. coli	20	27	30	27	44	148	53.62
	Klebsiella spp.	8	14	8	13	14	57	20.65
	Citrobacter spp.	11	2	2	6	4	25	9.06
	Pseudomonas aeruginosa	0	2	1	2	6	11	3.99
	Acinetobacter spp.	1	0	1	0	6	8	2.90
	Proteus spp.	3	0	1	2	2	8	2.90
	Gram positive						19	6.88
	Staphylococcus spp.	3	0	1	0	4	8	2.90
	Enterococcus spp.	0	2	2	2	2	8	2.90
	Candida spp.	0	0	1	1	1	3	1.09

Table 2: The antibiotic resistance pattern of *Escherichia coli* isolated from paediatric patients UTI over 5 years.

Year	2017	2018	2019	2020	2021	Total
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
No. of isolates	20	27	30	27	44	148
Ampicillin	19 (95)	27 (100)	28 (93.33)	27 (100)	44 (100)	145 (97.97)
Ceftriaxone	3 (15)	23 (85.19)	27 (90.00)	25 (92.59)	25 (56.82)	103 (69.59)
Cotrimoxazole	3 (15)	18 (66.67)	17 (56.67)	13 (48.15)	20 (45.45)	71 (47.97)
Gentamicin	4 (20)	14 (51.85)	13 (43.33)	10 (37.04)	5 (11.36)	46 (31.08)
Amikacin	0	4 (14.81)	2 (6.67)	1 (3.70)	0	7 (4.73)
Norfloxacin	3 (15)	19 (70.37)	16 (53.33)	18 (66.67)	12 (27.27)	68 (45.95)
Piperacillin tazobactum	0	3 (11.11)	4 (13.33)	8 (29.63)	14 (31.82)	29 (19.59)
Meropenem	0	0	0	0	5 (11.4)	5 (3.38)
Nitrofurantoin	0	2 (7.41)	6 (20)	5 (18.52)	0	13 (8.78)

Table 3: The antibiotic resistance pattern of *Klebsiella spp.* isolated from paediatric patients UTI over 5 years.

Year	2017	2018	2019	2020	2021	Total
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
No. of isolates	8	14	8	13	14	57
Ceftriaxone	6 (75)	11 (78.57)	7 (87.5)	11 (84.62)	12 (85.71)	47 (82.46)
Cotrimoxazole	2 (25)	7 (50.00)	3 (37.5)	8 (61.54)	6 (42.86)	26 (45.61)
Gentamicin	3 (37.5)	9 (64.29)	2 (25)	5 (38.46)	5 (35.71)	24 (42.11)
Amikacin	0	3 (21.43)	2 (25)	0	0	5 (8.77)
Norfloxacin	1 (12.5)	10 (71.43)	0	11 (84.62)	10 (71.43)	32 (56.14)
Piperacillin tazobactum	0	2 (14.29)	0	3 (23.08)	4 (28.57)	9 (15.79)
Meropenem	0	0	0	0	3 (21.43)	3 (5.26)
Nitrofurantoin	1 (12.5)	13 (92.86)	1 (12.5)	1 (7.69)	3 (21.43)	19 (33.33)

DISCUSSION

This is a unique study conducted on UTIs in paediatric age, where bacterial profile and its AMR pattern were studied over five years. In our study, we have observed that the female out-number the male patients. This gender difference in occurrence of UTI may vary in the different population.[3-5] The shorter urethra in female is main predisposing factor for the UTI, as the colonised enteric flora from perineum can easily migrate into urinary bladder causing cystitis. Increased adherence of these enteric organisms to vaginal epithelium and raised vaginal pH help pathogens to the colonise in in female perineum.[6]

In our study, the children of less than 5 years constituted 39% of the study population. The incidence of UTI varies with age of the children. The common cause for UTI in first year of life is mainly attributed to the congenital anomalies of genito-urinary system.[7] The incidence of UTI is peak in first year of life and between 2-4 years, i.e. toilet training age.[8] The UTI in paediatric age group may be categorised as asymptomatic bacteriuria, acute cystitis, acute pyelonephritis.[1,9] The severity of UTI depends on risk factors, symptoms, site, episode and age of patients.

E. coli, a member of *Enterobacterales* family, is the most common uropathogen isolated in our study, which is in consistent with studies conducted at various geographical locations, globally.[3-5,10,11] Various serotypes of uropathogenic *E. coli* (UPEC) have been associated with UTI, common being O1, O2, O4, O6, O7, O75, O83.[12] Other virulence factors (VF) in *E.coli* attributing for its uropathogenicity are antigens like H (flagellar), K (capsular); toxins like CNF-1 (Cytotoxic necrotizing factor-1), SAT (Secreted Autotransporter toxin), bacterial cell surface virulence factors like type 1 fimbriae and P fimbriae; secretory VF like haemolysin and siderophores; and heamaggultinin (Mannose sensitive and Mannose Resistant).[13] *Klebsiella spp*, *Citrobacter* spp, *Proteus spp,* were among the other members of *Enterobacterales*; non-fermenters like *P. aeruginosa* and *Acinetobacter spp.* were isolated in our population, similar to bacterial profile of patients found in our geographical areas.[1,3,9,13]

E. coli and *Klebsiella spp* isolated were resistant to commonly prescribed AMA like ampicillin, norfloxacin, nitrofurantoin, 3rd generations cephalosporins (ceftriaxone). Such a resistance pattern is also observed in other Indian population.[3,13,14] There was increasing rate of resistance to ampicillin, ceftriaxone, Cotrimoxazole, norfloxacin and nitrofurantoin; decreasing rate in gentamicin and amikacin over five years, which is similar to change in resistance pattern in Ethiopian adult population over a decade.[15] Rising resistance to reserve antimicrobial agents like piperacillin tazobactum and meropenem among emerging MDR uropathogen is of great concern as the morbidity and mortality in paediatric population.

This was a single centric retrospective study; we were unable to analyse the association of laboratory and clinical data with response and outcome of the antimicrobial therapy. A multicentre prospective study needs to be conducted to know the changing trend of AMR and implementation of AMSP.

CONCLUSION

The gram negative *Enterobacterales* are the leading causing of UTI in paediatric patients. The emergence of resistance to the commonly prescribed AMA for UTI warrants the need of AST for the patients with urinary symptoms and treat with targeted AMA rather than use ineffective empirical therapy. Regular monitoring of antibiogram for the change in trend of the AMR pattern is also very much essential to implement antimicrobial steward ship programme in the hospital efficiently.

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