Research Article

Antimicrobial resistance pattern among uropathogens isolated from paediatric patients attending a tertiary care hospital in Kalaburagi

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Abstract

Introduction: Urinary tract infection (UTI) is one of the most common bacterial diseases in children, but its diagnosis is often delayed due to obscure clinical findings. Paediatric tract UTI's are associated with high morbidity and complications like renal scarring, hypertension and chronic renal failure. In the past 20 years natural history of UTI has changed because of evolution of antibiotic resistance. **Objectives:** To study the antibiogram of UTI in children at a tertiary care hospital in Kalaburagi. **Materials and Methods:** Study was done from May 2014 to April 2015. Suspected children < 12 years were subjected for urine microscopy. Those with pus cells more than 6 / hpf were sent for culture and sensitivity. Identification of organisms was done by biochemical tests and antibiogram by disc diffusion method as per CLSI. **Results**: Of 972 cases studied, 72.7% were culture positive. The age group with maximum cases64.3%was 0 -5 yr. Most of the isolates were Gram negative 89.1%, followed by gram positive 8.9% and 2% were Candida spp. Common Uropathogenswere E. coli 53.97%, Klebsiella spp 36.98%, Proteus spp 3.17%, Citrobacterspp 2.86%, Pseudomonas aeruginosa and Non fermenters the rest 3.02%.Escherichia coli showed maximum sensitivity to Imipenem and Meropenem (97.9%), Piperacillin/Tazobactum (95%),Cefoperazone/Sulbactum (92.9%) and least sensitivity to Nitrofurantoin (26.7%), cephalosporins (5%) and Nalidixic acid (2.94%). **Conclusion**: Paediatric UTI was common in children with girls, age 0-5 yr. Spectrum of uropathogens causing UTI in our study had a preponderance of multi-drug resistant pathogens.

Keywords: Uropathogens, Escherichia coli, Klebsiella spp, UTI.

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INTRODUCTION

Urinary tract infection (UTI) is one of the most common bacterial diseases in children, but its diagnosis is often delayed due to obscure clinical findings. Diagnosis based on clinical features is difficult because of the varied non specific clinical features.[1] Paediatric urinary tract infections (UTI) are associated with high morbidity and long term complications like renal scarring, hypertension, and chronic renal failure.[3,4,5] Urinary tract infections are always treated empirically before the results of bacteriological cultures are obtained. The choice of antibiotics depends upon the causative organism and its expected local antibiotic susceptibility pattern. In the past (30-50) years natural history of pediatric UTI has changed because of evolution of antibiotic and improvement in antibiotic care.[2]

OBJECTIVES

1. Identify the bacterial isolates causing urinary tract infections in children <12 yrs attending a tertiary care hospital in Kalaburagi.
2. Study their antibiotic sensitivity pattern.

MATERIALS AND METHODS

This was a prospective study done from May 2014 to April 2015. Children aged 2 months to 12 years attending

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pediatric outpatient department with symptoms like, abdominal pain, dysuria, fever were subjected for urine routine and microscopic examination. Those with pus cells more than 6 per high power field were then sent for urine culture and sensitivity.

Sample Collection

Urine was collected by clean catch mid stream technique after cleaning the perineal area in a sterile wide mouthed container from 172 children

Procedure

For all cases of suspected UTI, urine culture was done by semi-quantitative technique on cysteine lactose electrolyte deficient medium (CLED agar) and quantitative unspun wet mount microscopy done to detect pyuria (> 6 pus cells/ high power field of centrifuged urine samples), bacteriuria, haematuria or candiduria. One µl urine was cultured using a calibrated bacteriological loop on CLED agar, and colonies were counted after overnight incubation at 37° C. Number of colonies obtained was multiplied by 1000 to obtain the colony forming units (cfu) / ml. 10^4 and 10^5 cfu/ml of bacterial growth of a single type was taken as threshold (significant bacteriuria) respectively.

Identification of Isolate by

colony characteristics, Gram's staining**,** Hanging drop preparation**,** Catalase test**,** Oxidase test, OF test**,** Indole test**,** Methyl Red test**,** Voges Proskauer test**,** Citrate utilization test**,** Carbohydrate fermentation tests, Urease production, Amino acid decarboxylase test**,** Coagulase test (for Staphylococcus). Antibiotic sensitivity was put up by the Kirby Bauer method following the CLSI guidelines.[7]

Antibiotics that were used for testing

GRAM POSITIVE ORGANISMS			GRAM NEGATIVE ORGANISMS		
Sl no	**Antibiotics**	**Disk content (µg/disc)**	**Sl no**	**Antibiotics**	**Disk content (µg/disc)**
1.	Amikacin	30	1	Amikacin	30
2.	Gentamycin	10	2	Gentamycin	10
3.	Netilmicin	30	3	Netilmicin	30
4	Ofloxacin	5	4	Ofloxacin	5
5	Ciprofloxacin	5	5	Nalidixic acid	30
5	Penicillin G	10 units	6	Ceftazidime	30
6	Amoxycillin- clavulunic acid	20/10	7	Ceftriazone	30
7	Nitrofurantoin	300	8	Cefotaxime	30
8	Ceftazidime	30	9	Nitrofurantoin	300
9	Ceftriazone	30	10	Cefoperazone –sulbactum	75/10
10	Cefotaxime	30	11	Piperacillin- Tazobactum	100/10
11	Cefoperazone –sulbactum	75/10	12	Imipenem	10
12	Vancomycin	30	13	Meropenem	10
13	Clindamycin	2			
14	Linezolid	30			
15	Teicoplanin				

RESULTS

Table 1: Sex-wise Distribution of the Study Subjects

Gender	Culture positive	
	No	%
Girls	410	**58**
Boys	297	42
Total	**707**	**100**

Out of972 cases studied, 707 cases (72.7%) were culture positive. Among them girls were 410 (58%) and boys were 297 (42%).

Table 2: Age-wise Distribution of the Study Subjects

Age	Culture positive	
	No	%
< 1 yr	181	25.6
1-5 yr	274	**38.7**
5-12 yr	252	35.6
Total	**63**	**100**

Of them, 181 (25.6%) were infants, 274 (38.7%) between 1-5 yr age, and 252 (35.6%) between 5-12 yr age.The age group which had the maximum number of cases were in between 0 -5 yri-e 64.3%

Table 3: Distribution of the Study Subjects based on their Culture Positivity

Isolates	Culture positive	
	No	%
Gram Negative isolates	**630**	**89.1**
Escherichia coli	340	**53.97**
Klebsiella spp	233	36.98
Proteus vulgaris	20	3.17
Pseudomonas aeroginosa and Non fermenters	19	3.02
Citrobacter spp	18	2.86
Gram Positive isolates	**63**	**8.9**
Enterococcus spp	33	**52.4**
Staphylococcus aureus	28	44.4
Staphylococcus saprophyticus	2	3.2
Candida spp	14	2.0

Majority of the isolates 630 were Gram negative bacilli (89.1%), followed by gram positive 63 (8.9%) and rest 14 (2%) were Candida spp. Among gram negative bacilli, predominant organisms isolated were E. coli 340 (53.97%), followed by Klebsiella spp 233(36.98%), Proteus vulgaris 20 (3.17%), Citrobacterspp 18 (2.86%), Pseudomonas aeruginosa and Non fermentersforming the rest 19 (3.02%). Among gram positive cocci most predominant organism was Enterococcus spp 33 (52.4%), followed by Staphylococcus aureus 28 (44.4%) and Staphylococcus saprophyticus 2 (3.2%).

Table 4: Distribution of the Various Organisms based on their Antibiotic Sensitivity

Antibiotics	Organisms											
	E coli			Klebsiella spp			Proteus spp			Pseudomanas aeroginosa		
	S	I	R	S	I	R	S	I	R	S	I	R
Amikacin	75	10	15	38.1	0	61.9	65	0	35	89.4	0	10.6
Gentamycin	80	05	15	38.9	10	51.1	75	0	25	68.9	10	21.1
Netilmicin	85	0	15	28.9	20	51.1	75	0	25	58.4	10.5	21.1
Ofloxacin	71.1	8.1	20.8	70.8	6	29.2	70	0	30	53.5	20.1	26.4
Ciprofloxacin	62.9	10	27.1	49.9	20	30.1	70	0	30	63.1	0	36.9
Ceftazidime	0	5	95	0	3.43	96.6	10	0	90	36.8	0	63.2
Ceftriazone	5	0	95	3.43	0	96.6	50	0	50	63.6	10	26.4
Cefotaxime	5	0	95	0	3.43	96.6	40	0	60	36.8	0	63.2
Ceftizoxime	0	5	95	0	3.43	96.6	10	0	90	36.8	0	63.2
Nitrofurantoin	21.7	5	73.3	12.4	0	87.6	0	0	100	0	0	100
Nalidixic acid	2.94	0	97.06	8.58	0	91.42	40	0	60	50	0	50
Cefoperazone/Sulbactum	92.9	0	7.1	90.5	0	9.5	95	0	5	73.6	0	26.4
Piperacillin/Tazobactum	80	15	5	74.9	10	15.1	95	0	5	94.7	0	5.3
Imipenem	97.9	0	2.1	94.8	0	5.2	100	0	0	100	0	0
Meropenem	97.9	0	2.1	94.8	0	5.2	100	0	0	100	0	0

Escherichia coli isolates showed 97.9% sensitivity to Imipenem and Meropenem, followed by Piperacillin/Tazobactum (95%),Cefoperazone/Sulbactum (92.9%) Gentamycin and Netilmicin (85% each), Ofloxacin (79.2%), Amikacin (75%), Ciprofloxacin (72.9%). E coli isolates showed least sensitivity to Nitrofurantoin (26.7%) followed by third generation cephalosporins (5% each), Nalidixic acid (2.94%).Maximum sensitivity for Klebsiellaspp was seen with Imipenem and Meropenem (94.8%) followed by Cefoperazone/Sulbactum (90.5%), Piperacillin/Tazobactum(84.97%). Ofloxacin (70.8%), Ciprofloxacin (69.9%), Gentamycin (48.9%),. Least sensitivity of Klebsiellaspp was noted with Amikacin (38.1%), Nitrofurantoin(12.4%), followed by Nalidixic acid (8.58%).Most of the isolates were found to be resistant to third generation cephalosporins.(3.43% sensitive). Pseudomonas aeroginosa was found to be 100% sensitive to Imipenem and Meropenem, Piperacillin/Tazobactum (94.7%), Amikacin (89.4%) and Gentamycin and Netilmicin (78.9% each), Ofloxacin (73.6%), Cefoperazone/Sulbactum (73.6%), Ceftriazone (73.6%), Ceftotaxime (63.1%), Ciprofloxacin (63.1%) and lowered sensitivity to other third generation cephalosporins (36.8%).Proteus isolates was found to be100% sensitive to Imipenem and Meropenem, Piperacillin/Tazobactum (95%), Cefoperazone/Sulbactum (95%), Gentamycin and Netilmicin (75% each), Ciprofloxacin (70%) Ofloxacin (70%), Amikacin (65%), Ceftriazone (50%), Cefotaxime (40%), and lowered sensitivity to other third generation cephalosporins (10%) and 100% resistant to Nitrofurantoin Staphylococcus aureus was found to be 100 % sensitive to Vancomycin, Clindamycin, Linezolid, Teicoplanin. All the Enterococcus isolates were found to be 100 % sensitive to Linezolid and Teicoplanin, 90.9% sensitive to Vancomycin and 72.7 % sensitive to Amoxicillin-Clavulunate.

DISCUSSION

The appropriate choice of antibiotic for the treatment of UTI requires an adequate understanding of microbiological profiles of local antimicrobial resistance of associated uropathogen. Antibiotic sensitivity change over a period of time.[2] Pediatricians therefore should be aware of the rising resistance of urinary pathogens to commonly prescribed antibiotics as well as the profile of antibiotic resistance within their community[8]. Therefore, periodic evaluation of sensitivity pattern is essential for rational and appropriate use of antibiotics.[10] Majority of growth positive cases were in the age group of 0- 5 yrs (64.3%). This could be because younger children are not well toilet trained and likelihood of ascending infection with fecal flora is more common in this age group.[1,11] This is in accordance with various studies[9]. UTI occurs in about one percent of boys and three to five percent of

girls[11]. In our study the prevalence in girls was 58%.In the present study culture positivity rate was 72.7%, which differs from that of Shrestha *et al*[19] 35.7%and Rai *et al* [12]28.6%, which can be explained, as our study included only those cases which were urine microscopy screening test positive i-e > 6 pus cells/hpf. E. coli and Klebsiella form the bulk of the organism isolated and constitute 81.04 % of all cases. This was less than what Rai *et al*[12] reported (93%) and similar finding reported by Rimal *et al*[16] (89.2%).E. coli constituted 59.4% of the nosocomial UTI in hospitalized patients as reported by Das *et al*.[14] Another study done by Al Abraham *et al*[15] in children observed E coli in the urine isolates even higher (96.4%) than our study. Five bacterial genera that dominated the bacteriological profile were E. coli, Klebsiella sp., Citrobacter sp., Proteus sp., and Enterococcus sppwhich is similar to what Marzouk *et al*[13] reported. UTI caused by Gram positive cocci was 8.9% which is higher as compared to0.7% observed by RaiGK *et al*[12] Jitendranath *et al*[6] reported a 11.5% incidence of gram positive UTI in their study. Enterococcus spp (52.4%) was the predominant gram positive cocci isolated in our study. Whereas Staphylococcus saprophyticus 50 % was the major gram positive isolate in a study conducted by Jitendranath *et al*[6] and S.aureus was the only isolate observed by Rai GK *et al*[12] In our study, Escherichia coliand Klebsiella isolates showed most sensitivity to Imipenem and Meropenem, followed by Piperacillin/Tazobactum, Cefoperazone/Sulbactum, and least sensitivity to Nitrofurantoin, Nalidixic acid and third generation Cepahalosporins. In contrast Rajbhandari *et al*[17] earlier have reported Nitrofurantoin as most sensitive antibiotic (68.8%) followed by Gentamycin, Norfloxacin and Ciprofloxacin.[17] However, there may be non-compliance to Nitrofurantoin due to its bitterness. Rajbhandari*et al*[17] also found cephalexin to be least effective followed by Ampicillin, Nalidixic acid and Cotrimoxazole. In a study conducted by Kumari*et al*[18] E. coli was found to be resistant to Ampicillin and Ciprofloxacin. Another study done by Das *et al*[14] found E. coli to be most sensitive to Amikacin (98.0%) followed by Gentamycin (87.9%), Ceftazidime (80.8%), Norfloxacin (78.4%) and Cotrimoxazole (77.9%). In our study Pseudomonas aeroginosa was found to be 100% sensitive to Imipenem and Meropenem, Piperacillin/Tazobactum (94.7%), Amikacin (89.4%) and Gentamycin and Netilmicin (78.9% each), Ofloxacin (73.6%), Cefoperazone/Sulbactum (73.6%), Ceftriazone (73.6%), Ceftotaxime (63.1%), Ciprofloxacin (63.1%) and lowered sensitivity to other third generation cephalosporins (36.8%). Proteus spp was identified as a causative agent for UTI only in a small number of cases (3.17%) in this study. This was in agreement with the finding by Shrestha *et al*[19] (2.4%) but is much lower than the finding by Moderres *et al*[20] (male children: 24.8%). However, the finding in female children was similar (2.8%). One study in Nepal found Proteus sp only in 1.6% of the positive isolates.[12] Proteus isolates was found to be 100% sensitive to Imipenem and Meropenem, Piperacillin/Tazobactum (95%), Cefoperazone/Sulbactum (95%), Gentamycin and Netilmicin (75% each),Ciprofloxacin (70%) Ofloxacin (70%), Amikacin (65%), Ceftriazone (50%), Ceftotaxime (40%), and lowered sensitivity to other third generation cephalosporins (10%) and 100% resistant to Nitrofurantoin in our study. A study conducted by Rai GK *et al*[12] showed Proteus sp. to be most sensitive to ceftriaxone, cefotaxime, ofloxacin and ciprofloxacin and was resistant to cephalexin, gentamycin and nitrofurantoin as observed in our study.

CONCLUSION

Extensive use of antibiotics have resulted in development of resistance among most commonly used drugs in urinary tract infection (UTI).Restricted use of antibiotics and combination therapy may limit the increasing pattern of antibiotic resistance.

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