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Original Article

Microbiology Section

Urinary Tract Infection: Aetiology and Antimicrobial Resistance Pattern in Infants From A Tertiary Care Hospital in Northern India

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ABSTRACT

Introduction: Urinary tract infection (UTI) is one of the most common bacterial infections in childhood. Present study was undertaken to determine the occurrence of the uropathogens and their antimicrobial susceptibility pattern in infants (< 1yr) suspected with UTI.

Materials and Methods: This study was conducted in the Microbiology Department on urine samples received from infants for a period of two years from September 2011 to August 2013.

Results: Culture positivity rate was found to be 15.7%. There was an overall male preponderance in cases of UTI (70.1%). Most common bacterial isolate was *E.coli* (45.4%) followed by *Klebsiella* (16.7%) and *Enterococcus spp* (13.2%). Isolation of *candida* was 21.1%, maximum from ICU (63.1%). Maximum gram negative isolates (50%) showed high resistance to gentamicin, amikacin, cefotaxime and norfloxacin while most of the isolates (5%) were found susceptible to *nitrofurantoin* and *piperacillin-tazobactam*. 45.1% of gram negative bacilli were ESBL producer. We recommend continuous monitoring of changes in bacterial pathogens causing UTI and antibiotic sensitivity in each area for effective treatment of UTI.

Conclusion: Since antimicrobial resistance is a major problem, such study will help in formulating a strict antibiotics prescription policy in our country.

Keywords: Antibiotic sensitivity, Antibiotic prescription policy, Infant UTI

INTRODUCTION

Urinary tract infection (UTI) is one of the most common bacterial infections in childhood. During the first year of life, the male-female ratio for UTI is 2.8-5.4: 1. Beyond 1-2 yr, there is a female preponderance, with a male: female ratio of 1: 10 [1]. UTI may involve only the lower urinary tract or may involve both the upper and lower tract. Paediatric urinary tract infections (UTI) are associated with high morbidity and long term complications like renal scarring, hypertension, and chronic renal failure [2]. It has been suggested that early diagnosis, proper investigation, adequate therapy and prolonged careful follow-up in children with UTI may well decrease the number of adults who present with chronic renal failure due to pyelonephritis [3]. Gram negative enteric bacilli, especially *Escherichia coli* and *Klebsiella spp* [1] are the leading pathogens, though *Enterococcus spp*., yeasts and *Staphylococcus aureus* have emerged as prominent agents in recent years [4-6]. Therapy for these children requires urine culture and appropriate antimicrobial sensitivity testing since many of the isolates were found to be multi-drug resistant [4-6]. There are very limited studies on infant UTI especially from India. Also micro-organisms isolated, present different susceptibility patterns to antimicrobial agents, which vary according to the place where the study is performed and also over time. Hence, this study was undertaken to determine the incidence of the urinary pathogens and their antimicrobial susceptibility pattern isolated from the urine samples from suspected urinary tract infections in infants (< 1yr) in a two yr period at a tertiary care hospital in Northern India.

MATERIALS AND METHODS

This study was conducted in the Microbiology Department of Dr. Ram Manohar Lohia Hospital and PGIMER, New Delhi for a period of two yr from September 2011 to August 2013. All urine samples received from infants i.e. up to one yr age group and sent to microbiology laboratory were included in this study. Samples collected in unsterile containers as well as samples showing more than two isolates or mixtures were excluded from the study. For all cases, urine culture was done by semi-quantitative technique on 5% sheep Blood Agar and MacConkey Agar plates along with wet mount microscopy. Plates were incubated at 37°C overnight. Colony count was performed using standard technique for semi-quantitative culture of urine. Significant bacteriuria is defined as the bacterial count of 10^5 cfu/ml of a single type [7]. Various bacterial isolates were identified according to standard methods and tested against various antibiotics by Kirby Bauer's disc diffusion method & zone diameters were interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines [8]. The antibiotics tested were Ampicillin (10µg), Gentamicin (10µg), Amikacin (30µg), Ciprofloxacin (5µg), Norfloxacin, Nalidixic acid, *Nitrofurantoin*, Ceftazidime (30µg), Amoxy-clavulanic acid, Piperacillin (100µg), *Piperacillin-Tazobactam* (100/10µg), Meropenem (10µg), Cefotaxime (30µg), high dose Gentamicin (120 µg), Cotrimoxazole(1.25/23.75µg), Vancomycin (30µg) & Linezolid (30µg) (Hi-Media Pvt. Laboratories, Bombay, India). Appropriate quality control strains were used to validate the results of the antimicrobial discs. ESBL production was determined by using phenotypic confirmatory test: Antibiotic disc of ceftazidime 30µg and ceftazidime- clavulanic acid 30/10µg, also cefotaxime 30µg and cefotaxime- clavulanic acid 30/10µg (HiMedia) were placed on inoculated MHA media 30mm apart from centre to centre and incubated at 37°C for 16-18 h. The zone of inhibition were recorded and difference in zone size of 5mm or more for either antimicrobial agents tested in combination with clavulanic acid versus its zone when tested alone were considered ESBL [8]. The same laboratory protocols were followed during the whole period. Any repeat isolate from the same patient obtained on more than one occasion was not included in the study.

Age-groups	Total	Male	Female	OPD	Ward	ICU
0-3 months	267	176	91	40	198	29
3-6 months	195	110	85	38	125	32
6-9 months	155	95	60	20	102	33
9-12 months	491	290	201	61	325	105
Total	**1108**	**671 (60.5%)**	**437 (39.4%)**	**159 (14.3%)**	**750 (67.7%)**	**199 (18%)**

[Table/Fig-1]: Age and area wise distribution of urine samples received

samples [Table/Fig-2]. 47.7% of the isolates were from ward patients followed by ICU (41.3%) and OPD (10.9%). Isolation of *candida* is maximum from patients admitted in ICU (63.1%) and wards (28.9%) [Table/Fig-2]. Maximum gram negative isolates (50%) showed high resistance to gentamicin, amikacin, cefotaxime and norfloxacin while most of the isolates (5%) were found susceptible to *nitrofurantoin* and *piperacillin-tazobactam* [Table/Fig-3]. 51 (45.1%) out of 113 gram negative bacilli were ESBL producer (Extended spectrum beta lactamase). All the gram negative bacilli were found sensitive to carbapenems. *Enterococcus* isolates were found susceptible to Vancomycin and Linezolid. [Table/Fig-3]

Isolates	Total (%)	0-1 m		1-3 m*		3-6 m		6-9 m		9-12 m		Area-wise distribution		
		M	F	M	F	M	F	M	F	M	F	OPD	Ward	ICU
E.coli	79 (45.4)	3	1	9	3	8	3	7	3	27	15	7	40	32
Klebsiella	29 (16.7)	2	1	3	1	9	1	-	1	10	1	4	17	8
Enterococcus	23 (13.2)	1	-	2	2	4	1	1	3	5	4	5	14	4
Acinetobacter	3 (1.7)	-	-	-	-	-	-	-	-	2	1	-	1	2
Pseudomonas	2 (1.1)	-	-	-	-	-	-	-	-	2	-	-	-	2
Candida	38 (21.8)	2	1	6	2	6	3	5	3	8	2	3	11	24
Total	174 (15.7)			28	11	27	8	13	10	54	23	19 (10.9)	83 (47.7)	72 (41.3)

[Table/Fig-2]: Age-wise and area-wise distribution of isolated organisms causing UTI

Antibiotic Resistance	*E.coli* n=79 (%)	*Klebsiella* n=29 (%)	*Acineto-bacter* n=3 (%)	*Pseudo-monas* n=2 (%)	*Enteroc-occus* n=23 (%)
A	64 (81)	22 (76)	3 (100)	2 (100)	13 (57)
G	42 (53)	14 (48)	3 (100)	2 (100)	-
Ak	38 (48)	12 (41)	3 (100)	2 (100)	-
Nx	60 (76)	15 (52)	3 (100)	-	18 (78)
Cf	-	-	-	2 (100)	-
Na	64 (81)	16 (55)	3 (100)	-	-
Nf	4 (5)	5 (17)	2 (67)	0	4 (17)
Ce	58 ((73)	20 (69)	3 (100)	-	-
Ca	58 (73)	20 (69)	3 (100)	1 (50)	-
Co	59 (75)	19 (69)	3 (100)	-	-
AC	56 (71)	18 (62)	3 (100)	-	-
Pc	-	-	-	0	-
PT	4 (5)	0	1 (33)	0	13 (57)
Mr	0	0	0	0	-
Gh	-	-	-	-	18 (78)
Va	-	-	-	-	0
Lz	-	-	-	-	0
ESBL	37 (47)	13 (45)	1 (33)	-	-

[Table/Fig-3]: Antimicrobial resistance among isolated bacterial isolates
*A- Ampicillin(10µg), G- Gentamicin(10µg), Ak- Amikacin(30µg), Cf-Ciprofloxacin(5µg), Nx- Norfloxacin, Na- Nalidixic acid, Nf- Nitrofurantoin, Ca-Ceftazidime(30µg), AC-Amoxy-clavulanic acid, Pc- Piperacillin(100µg), PT- Piperacillin-Tazobactam(100/10µg) , Mr- Meropenem(10µg) , Ce- Cefotaxime(30µg), Gh- high dose Gentamicin (120 µg), Co- Cotrimoxazole(1.25/23.75µg), Va- Vancomycin(30µg) & Lz- Linezolid(30µg)

RESULTS

Total urine samples received in the laboratory in a two yr study period were 1108. Male: female ratio was found to be 3:2 with Ward: OPD: ICU ratio of 6.7:1.4:1.8 [Table/Fig-1]. 1108 urine samples were evaluated in the study, of which 174 (15.7%) children [144 male (70.1%), and 63 female (29.9%)] had culture proven UTI. There was an overall male preponderance in cases of UTI (70.1%) as shown in [Table/Fig-2]. Most common bacterial isolate was *E.coli* (45.4%) followed by *Klebsiella* (16.7%) and *Enterococcus spp*. (13.2%) out of 207 culture positive samples, *candida* was grown in 21.8%

DISCUSSION

Our study describes the distribution and antibiotic susceptibility pattern of microbial species isolated from infant population with suspected UTIs in this hospital. In this study, 15.7% of the received samples were culture positive children. There was an overall male preponderance (70.1%) which is in accordance with other studies [9,10]. Therefore, male gender is a risk factor for UTI within one yr of age. Most common bacterial isolate was *E.coli* (38.2%) followed by *Klebsiella* and *Enterococcus spp*. The results of this study are in agreement with previous studies from India and other countries [10-12] [Table/Fig-4]. *Enterobacteriacae* have several factors responsible for their attachment to the uroepithelium. These gram-negative aerobic bacteria colonise the urogenital mucosa with adhesin, pili, fimbriae and P1-blood group phenotype receptor [13]. In this study, *Pseudomonas aeruginosa* was isolated in two samples received from ICU and both the patients were catheterised. Lower UTI with *Candida* usually occurs with urinary catheters, typically after bacteriuria and antibiotic therapy. In our study, *candida* was grown in 38 (21.8%) positive samples, maximum from patients admitted in ICU (63.1%) and ward (28.9%).

Antibiotic resistance is a major clinical problem in treating infections caused by these microorganisms. The resistance to the antimicrobials has increased over the years. Resistance rates vary from country to country. Maximum gram negative isolates (50%) showed high resistance to gentamicin, amikacin, cefotaxime and norfloxacin while most of the isolates (5%) were found susceptible to *nitrofurantoin* and *piperacillin-tazobactam*, which is in accordance with other studies [11,12]. A possible cause of increased resistance might be widespread and inappropriate use of antibiotics. In this study, 51 out of 113 isolates of UTI pathogens (45.1%) were found to produce ESBL. This is consistent with other Indian studies (42%) [12]. 47 % of our *E. coli* isolates were ESBL producers, followed by 45% of *K. pneumoniae*. It might be possible that the high level of multi-drug resistance was most probably due to production of extended spectrum beta lactamases in these isolates [12,14,15]. To overcome this problem, unnecessary antibiotic therapy should be limited. It seems that the best choices for treatment of UTI in our region include *nitrofurantoin* and *Piperacillin-tazobactam*. In the present study, all the isolates were found to be sensitive to carbapenems (Meropenem). This is because carbapenem group is highly stable against β-lactamase and has an unusual property of

causing a post antibiotic effect on gram-negative bacteria [16]. Due to its small molecular size it can overcome the poor permeability of β-lactams for Pseudomonas by efficient penetration through the porin, OMP-D [17].

Features	Present study	Rasht, Iran [10]	Chandigarh, India [2]	Burdwan, India [18]
Age	< 1 yr	<2 yrs	<12 yrs	<12 yrs
Sex	Males>Females	F>M	M>F	F>M
Common isolates	*E.coli*, *Candida* and *Klebsiella*	*E.coli*, *Klebsiella*	*E.coli*, *Klebsiella* and *candida*	*E.coli*, proteus and *Klebsiella*
Multi-drug resistance	50%	66%	60-70%	67-70%
ESBL	45%	Not done	Not done	Not done

[Table-4]: Comparison of the present study with other related studies from India and neighbouring countries.

To date, there is limited literature regarding the resistance of uropathogens to antibiotics in infants with UTIs. Hence, we recommend continuous monitoring of changes in bacterial pathogens causing UTI and antibiotic sensitivity in each area for effective treatment of urinary tract infections especially in infants. The goals of treatment of UTIs in infants are to eliminate the pathogen, to prevent urosepsis, and to reduce the risk of renal scarring.

CONCLUSION

It is quite alarming to note that most of the isolates included in this study were found resistant to four or more antibiotics. Antibiotic resistance is becoming major problem which threatens the lives of hospitalized individual and add considerably to health care cost. Therefore, it is an important issue to be addressed by the policy makers to formulate a strict antibiotics prescription policy in our country.

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