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Urinary tract infection in pediatrics patients in north India

Sumit Gupta[1], Reshma Agarwal[2], Suneel Bhooshan[3], Arti Agrawal[3], Ankur Goyal[3]

1(Microbiology Department Assam Medical College and Hospital.Dibrugarh, AssamIndia.)
2(Microbiology Department JIPMER Pondicherry India)
3(Microbiology Department S.N Medical College Agra Dr B.R. Ambedkar University Agra India)

Abstract: *Background -Urinary tract infection (UTI) is one of the most common bacterial infections seen in patient. It may lead to renal scarring, hypertension, and end-stage renal disease. Early diagnosis is important to preserve renal function of the growing kidney.*
Aim- The aim of the present study was to assess the prevalence and changing susceptibility pattern of urinary pathogensin febrile paediatrics patients.
Methods and Material- Fifty millilitres urine specimen was collected in a sterile container with sterile precaution and used for microscopic examination (pyuria detection) and for culture and sensitivity.
Results-Out of total 820 cases 170 showed significant bacteriuria of which 107(62.94%) had fever. Females showed higher positivity in UTI cases than males with ratio of 1.3:1. In our study E.coli was 27.05 % and Klebsiella 18.82% was predominant pathogen isolated. These isolates showed the highest resistance towards first line of drugs Cefadroxil, Amoxicillin and Cefuroxime, being most sensitive to Imipenem cefepime.
Conclusion-To successfully eradicate UTI by empiric treatment, knowledge of local etiologic agents and their antibiotic susceptibility is of great value.

Key Word*: Dysuria, Significant bacteriuria,UTI*

I. Introduction

Urinary tract infection (UTI) is one of the most common bacterial infections seen in patient. Neonates, girls, young women, and older men are most susceptible to UTIs. In women, bacterial cystitis is the most common bacterial infection. Around 1% of boys and 5% of girls develop UTIduring first ten years of life [1]. UTI may lead to renal scarring, hypertension, and end-stage renal disease. Early diagnosis is important to preserve renal function of the growing kidney.

Several studies have reported varying prevalence rates of UTI in children ranging from 3.3 % in USA to 37.5% in Pakistan. [2, 3]Gram negative enteric bacilli, especially Escherichia coli and Klebsiella spp. are the leading pathogens though Enterococcus spp., yeasts and Staphylococcus aureus have emerged as prominent agents in recent years, many of them resistant to multiple antibiotics [3-4].

Unfortunately, little has been published regarding Indian scenario of the range and antimicrobial susceptibility patterns in urinary tract pathogens particularly among children.The diagnosis of UTI in children possess a big challenge to the clinicians and several reasons have been responsible for the difficulties in establishing the diagnosis of UTI in children include; non-specific clinical presentation and the difficulty in getting urine sample for laboratory investigations.

We conducted an exploratory study of the prevalence of UTI describing presenting symptoms and the proportion found to have a UTI when urine samples were systematically requested from all eligible children. This study was done to establish the magnitude of UTI among febrile children.

The aim of the present study was to assess the changing susceptibility of urinary pathogens to antimicrobial agents in UTIs.

II. Materials and Methods

The present study was carried out in S.N Medical College Agra, over a period of one year from July 2012 to July 2013. Urine samples were collected from Eight hundred twentyfebrile children between 0 to 18 years of age hospitalized patient and who attended paediatric outpatient department form the study group. Detailed history (about frequency of micturation, Fever, Dysuria, Abdominal Pain, Smelly Urine, Poor Feeding and vomiting) of patients and clinical examination wasdone in all cases with special emphasis being given to UTI Symptoms.

Two methods were used for collecting urine for microbiological analysis: clean catch midstream specimen method for children who were able to control urination, and sterile plastic bags method for younger children who were not able to control urination.Fifty millilitres of clean-catch midstream urine specimen was collected in a sterile universal container.[4] The semi-quantitative technique to determine significant bacteriuria

was employed by using 0.01 mL calibrated wire loop to inoculate 5% blood agar and Mac Conkey Agar with un-centrifugedurine. Culture plates were incubated at 37°C for 18–24 h, well-isolated bacterial colonies were processed for antibiotic sensitivity and biochemical tests. [4]After inoculation of media, the remaining sample was centrifuged at 2000 rpm for 5 minutes and sediment used for microscopy and gram stain.Urine samples were examined microscopically especially for pus cell to confirm urinary tract infection via quantitative unspun wet film examination.Microscopy was done to detect pyuria (> 1pus cell/7 high power fields),bacteriuria, haematuria or candidiuria of well mixed un-centrifuged urine samples. A specimen was considered positive if a single organism was isolated at a concentration of greater than 10^5 CFU/mL and associated with microscopy findings of greater than 1pus cell/7 high power fields. [4]

Bacteria were identified by Gram's stain and standard biochemical procedures.Susceptibility of isolates to antimicrobial agents of different classes was assessed by the disk diffusion technique on Mueller-Hinton agar as described by the National Committee for Clinical Laboratory Standards (presently called Clinical Laboratory Standard Institute). [5] The following antibiotics used for empiric treatment were analysed: Amoxicillin,amoxicillin- Clavulanic acid, gentamicin, amikacin,cefadroxil,cefuroxime, ceftriaxone, ciprofloxacin,nitrofurantoin, cefepime,tetracycline,chloramphenicol and cotrimoxazole andimipenem. [5]

III. Result

Out of 820 these patients, 396 were males and 424 were female children. Significant bacteriuria was found in 170 cases, 98 males and 112 females.

About 107 (62.94%) cases had temperature which was > 39.3˚C, and showed significant bacterial growth in culture. After fever, dysuria (46.47%), Burning Maturation (25.29%) and abdominal Pain (21.76%) were the common symptoms present in UTI patients. Other nonspecific symptoms like smelly urine (12.35%), the poor feeding (05.88%), and vomiting (07.64%) were also noted. [TABLE 1]

TABLE 1Correlation between Physical findingof culture positive and negative cases

Symptoms	Culture Positive Case(Total 170)		Culture Negative Case(Total 650)	
	Number	Percentage	Number	Percentage
Fever	107	62.94	266	40.92
Dysuria	79	46.47	16	2.46
Burning Maturation	43	25.29	7	1.07
Abdominal Pain	37	21.76	90	13.84
Smelly Urine	21	12.35	9	1.38
Poor Feeding	10	5.88	223	34.30
Vomiting	13	7.64	79	12.15

When the data from culture positive samples was organized as inTABLE 2 according to different age groups as well as gender wise, it appeared that the overall prevalence of UTIs in females was about 2.92% higher than males.Highest number of sample were from the age group of 16-18 years. Highest significant bacteriuria was found in patients between the age 16 year to 18 year 30.58% and lowest in 0 years to 05 years20.00%.
There was a female preponderance in the culture positive cases in all age group, with an overall male to female ratio of 1:1.33.

TABLE 2 Age and Sex Distribution of Case

				Culture Positive Cases			
Age (Months)	Male	Female	Total No of Cases	Male	Female	Total No of Cases	Percentage
0-5	70	76	146	15	19	34	20.00
06 - 10 years	84	92	176	14	21	35	20.58
11-15 years	102	106	208	21	28	49	28.82
16 - 18 years	140	150	290	23	29	52	30.58
Total	396	424	820	73(08.90%)	97(11.82%)	170(20.73%)	

Most commonly isolated pathogen was E.coli (27.05%) in both sex followed by Klebsiella (18.82%) and Proteus (11.76%) respectively. Other pathogens were isolated with lower frequency as shown in TABLE 3. E.coli was more common in females (58.69%) than males (41.30%). Same pattern was followed by Klebsiella 56.25 % prevalence among female patients and 43.75 % in male patients. While this pattern was opposite in case of S.epidermidis, Acinetobacter and Enterobacter.

TABLE 3 Gender wise patterns of Isolates

Isolates	Female (%)	Male (%)	TotalIsolates (%)
E.coli	27(15.88)	19(11.17)	46 (27.05%)
Klebsiella	18(10.58)	14(8.23)	32 (18.82%)
Pseudomonas	10(5.88)	4(2.35)	14 (8.23%)
Proteus	12(7.05)	8(4.70)	20 (11.76%)
Acinetobacter	1(0.58)	2(1.17)	3 (1.76%)
Enterobacter	1(0.58)	3(1.76)	4 (2.35%)
Streptococcus	6(3.50)	2(1.17)	8 (4.70%)
S.pyogenes	2(1.17)	0(0)	2 (1.17%)
Staphylococcus aureus	3(1.76)	4(2.35)	7 (4.11%)
Enterococcus	9(5.29)	6(3.50)	15 (8.82%)
CoNS	5(2.94)	9(5.29)	14 (8.23%)
Yeast	3(1.76)	2(1.17)	5 (2.94%)
	97 (57.05)	73(42.94)	170

The antimicrobial spectrum of 14 antibiotics against uropathogens is summarized inTABLE 4.
UTI isolates showed High resistance towards most commonly used antibacterial agents such as cefadroxil varying from 80-96%, Cefuroxime 75-83%, amoxicillin 66-80%, gentamicin 50-66%. The most effective antibiotic was carbapenems having the least resistance followed by cefepime, amikacin and nitrofurantoin among the gram negative isolates. Most predominant isolates (E.coli & klebsiella) were more susceptible to cefepime, amikacin and nitrofurantoin. Resistance pattern of different gram negative isolatesshowed in TABLE 4.

TABLE 4 Drug resistance patterns of Gram Negative Bacilli

Antibiotics	E.coli	Klebsiella	Pseudomonas	Proteus	Acinetobacter	Enterobacter
Amoxicillin	76(35)	72(23)	71(10)	80(16)	66(2)	75(3)
Amoxicillin- Clavulanic Acid	52(24)	47(15)	43(6)	45(9)	66(2)	50(2)
Cefadroxil	96(44)	97(31)	79(11)	75(15)	100(3)	100(4)
Cefuroxime	83(38)	78(25)	79(11)	75(15)	66(2)	75(3)
Cefotaxime	65(30)	59(19)	86(12)	75(15)	66(2)	75(3)
Cefepime	15(7)	13(4)	14(2)	10(2)	33(1)	25(1)
Amikacin	28(13)	31(10)	43(6)	25(5)	33(1)	25(1)
Gentamicin	59(27)	56(18)	64(9)	70(14)	66(2)	50(2)
Nitrofurantoin	28(13)	38(12)	71(10)	ND()	33(1)	25(1)
Chloramphenicol	50(23)	47(15)	43(6)	50(10)	66(2)	50(2)
Ciprofloxacin	70(32)	59(19)	64(9)	50(10)	66(2)	75(3)
Tetracycline	41(19)	59(19)	57(8)	55(11)	66(2)	50(2)
Cotrimoxazole	54(25)	50(32)	64(9)	70(14)	33(1)	50(2)
Imipenem	04(2)	06(2)	07(1)	05(1)	00(0)	00(0)

IV. Discussion

Out of 820 febrile patients, 170 had UTI an overall prevalence of 20.73%.The reason behind the high prevalence of UTI among paediatrics patients in over study was probable inclusion of outpatient and inpatient in our study. This prevalence was comparable to many other study conducted worldwide. [2, 3]
Our study showed UTI was more common in females than male patients. The ratio of female: males in over study were 1.3:1. Similar to other study 2.3:1 [6,7]Several studies in peadritics reported female predominance, with a variable ratio ranging from 6:1 to 1.33:1, depending upon the different sample size, and difference in age groups being studied. [8-13]Reason behind low percentage of UTI among males was longer course of urethra and bacteriostatic secretion by prostate gland [7, 14, 15], which was also supported by our study.
Fever was the most common consistent symptom present in 107 (62.94%) patients with UTI. Other study also reported fever as most common symptoms in 54.9% UTI cases.[16]Other physical findings in our study which were predominant after fever were dysuria (46.47%), Burning Mituration (25.29%) and abdominal Pain (21.76%) [7]well correlated to study conducted byMalla KK 2008.

In comparison to culture negative case, fever, dysuria and burning micturition was far more common in culture confirmed UTI cases which highly suggest Routine urine culture may be beneficial in the patient with fever and dysuria as they showed good co-relation with positivity.Routine culture in the patient with poor feeding and vomiting is not justified.

Data acquired after Distribution of isolates according to age and sex was satisfying and similar to the various studies [17] (TABLE 3). There was a slight predominance (30.58 %) of culture positivity in the group age of 15 year to 18 years. This may be because of sexual activity increase during this age.

E.coli (27.05%) was the commonest organism isolated in both sex (male) from UTI cases in this study. Second most common isolates was klebsiella which was well correlating to other study [18-20]

Prevalence of E.coli and Klebsiella was high in girls; similar result was reported by study conducted bySpahiuL in 2010[19]

Although E. coli, Klebsiella were the principal uropathogens in our study, there were other pathogens of our interest due to their resistance pattern like, Pseudomonas, Proteus, Staphylococcus, Acinetobacter and Enterobacter. Resistance in these pathogen was as high as E.coli and klebsiella.

Proteus was the third most common isolates in our study occupying 11.67% of all isolates. Which was well justified by other study. [15, 19, 21]

Pseudomonas was isolated in 14% of UTI cases. This high prevalence of pseudomonas in comparison to may be due to inclusion of inpatient (Hospitalized). Pseudomonas is more common in nosocomial infection. [21]The percentages of resistance of all isolates to different antimicrobial agents were varying from 00% to 100% in over study. Higher resistance was noted among first line of drugs (cephalosporins) and Gentamycin, Amoxicillin classes of drugs this limits there utility in UTI treatment. While most of the organism being sensitive to Imipenem, cefepime, nitrofurantoin, amikacin at the rate of over 93%.E.coli was resistant to Imipenem 04%, cefepime 15% nitrofurantoin 28% and amikacin 28%. In case of E.coli sensitivity pattern finding of our study was similar to conducted by Tada Dharmishtha[23].E.coli showed highest resistance to Amoxicillin 76% Cefadroxil 96% Cefuroxime 86%. Various studies around the world suggest higher resistance prevalence to these antibiotics. Klebsiella showed least resistant towards imipenem 6%, to cefepime 13% to amikacin 31% and nitrofurantoin 38%. Resistance in klebsiella against other classes of antibiotic was similarly higher as seen in E.coli, which was well correlating to studyMohammed Akram[14]

Resistance was higher among Proteus and pseudomonas against Amoxicillin (80% & 71%), Cefadroxil (75% & 79%), and Cefotaxime (75% & 86%). [24]As these drugs were the first line drugs given to hospitalized patient.

From the result of this study it can be concluded that the drugs such as Cefadroxil, Amoxicillin and Cefuroxime were of less use respectively to all isolates. And drug Imipenem, Cefepime, Amikacin & nitrofurantoin can be used in empirical therapy in serious cases before drug sensitivity is performed.

In gram positive pathogen S. pyogens was solely isolated from females Even though the prevalence of these isolates was low, we suggest regular monitoring on their prevalence and resistance pattern to implicate an empiric treatment policy in this locality.Predominant pathogen in gram positive isolates was Staphylococcus species respectively S. aureus 7 and CoNS (S. epidermidisand*Staphylococcus saprophyticus)* 14 isolates.[25]Discussing about drug resistance and prevalence of gram positive isolates will be way too early due to less numbers of these isolates. Five specimens showed significant growth of yeast for which drug susceptibility was not performed.

V. Conclusion

The antibiotic sensitivity pattern of organisms changes rapidly over a short period. Studies have demonstrated geographic variation in etiologic characteristics of UTI and their resistance patterns to antibiotics. Therefore to successfully eradicate UTI by empiric treatment, knowledge of local etiologic agents and their antibiotic susceptibility is of great value. This study reports the percentage of etiologic agents of UTI, most common symptoms in UTI patient and their antibiotic susceptibility in Northern India.It is important for clinician in order to facilitate the empiric treatment of patients and management of patients with symptoms of UTIs. Moreover, the data would also help to formulate antibiotic prescription policies

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