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ORIGINAL RESEARCH

Patterns of Antimicrobial Resistance in Urinary Tract Infections among Children Aged 1 to 5 Years

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ABSTRACT

Background: Urinary tract infections (UTI) account for a significant proportion of cases of unexplained febrile illnesses in children which are often treated with different broad-spectrum antibiotics when one with a narrow spectrum of activity may be appropriate. This study has been undertaken to know the prevalence of UTIs in febrile children (1-5 years age) and to study the antibiotic sensitivity pattern in pediatric community-acquired UTI.

Material and Methods: A Hospital-based cross-sectional descriptive study was done in children of age 1 -5 years presenting with complaints of fever without any localizing signs in tertiary care hospital over a period of 1 year. Urine samples were collected under aseptic conditions and analysed by urine culture for UTI and antibiotic sensitivity testing was done in all culture-positive cases.

Results: The overall prevalence of UTI in this study was 10.4 %. Escherichia coli was the commonest bacterial isolate from culture urine specimens accounting for 43.4%, followed by Klebsiella species at 39.1%. The frequency of isolated bacterial pathogens resistance was observed to be high against amoxicillin-clavulanic acid, ceftriaxone, and cotrimoxazole and sensitivity was high for the aminoglycoside group of drugs.

Conclusion: UTI is a significant cause of fever without focus and Urine Culture & Sensitivity is the gold standard test to confirm UTI. Escherichia coli and Klebsiella pneumonia are the most common organisms causing UTI in children in the community setting. High resistance to cotrimoxazole, amoxiclav, and cephalosporins group of drugs by all isolated pathogens was observed in this study. Amikacin was the most active agent against all isolated bacteria in this Study.

Keywords: Urinary tract infections, Antibiotic resistance, Prevalence, culture, drug sensitivity.

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INTRODUCTION

Fever may be the only significant symptom in children with urinary tract infections and all children with otherwise unexplained fever merit evaluation for possible UTI.1 Urinary tract infection is one of the most common bacterial infections and its occurrence in childhood may carry special significance.2 The risk of having a UTI before the age of 14 years is approximately 1-3% in boys and 3-10% in girls.3 Rapid evaluation and treatment of UTI is important to prevent renal parenchymal damage and renal scarring that can cause hypertension and progressive renal damage.

Urinary tract infections (UTIs) are often treated with different broad-spectrum antibiotics when one with a narrow spectrum of activity may be appropriate.4,5 Extensive use of antibiotics have resulted in development of resistance among most commonly used drugs in community acquired urinary tract infection (UTI). The resistance pattern of community acquired UTI pathogens has not been studied extensively in India.6 Studies on pediatric UTI prevalence and antibiotic sensitivity pattern are few in India and therefore this study has been undertaken to know the prevalence of UTI in febrile children (1-5 years age) and to study the antibiotic sensitivity pattern in pediatric community acquired UTI.

MATERIAL & METHODS

This hospital based cross-sectional descriptive study was conducted in Department of Pediatrics at Sri Venkateswara Ramnarain Ruia Government General Hospital, a tertiary care hospital Tirupati, Andhra Pradesh after obtaining clearance from local Ethics Committee. The study population included all children 1- 5 years of age presenting with fever without any localising signs to the hospital over a period of 1 year. Febrile children with other recognizable foci of infection, children with congenital anomalies of urinary tract, known coexisting renal diseases, known coexisting diabetes mellitus, immunosuppressed children, children with documented evidence of treatment with antibiotics for more than 48 hrs before admission are excluded from the study. All eligible participants during the 1 year study period, whose parents/guardians granted written informed consent were recruited into study. A total sample of 442 children was collected using convenient sampling by recruiting all the children who presented with fever, satisfying the inclusion and exclusion criteria during the study period.

Complete history including past history of urinary tract infections, any previously identified anatomical abnormalities of urinary tract and any neurological conditions with involvement of the bladder were collected. Necessary investigations were done to rule out other foci of infections. Clean catch mid-stream urine specimens were collected under aseptic conditions. In very young children who were not toilet trained, urine specimen was obtained by catheterization under aseptic precautions. Specimens were transported in sterile containers and were sent to the laboratory within 1 hr of urine collection or refrigerated specimens not later than 20 hours. Urine sample was centrifuged and examined under microscope for significant pyuria (>5 leukocytes per high power field). Urine culture was done by semi-quantitative technique with fresh urine specimen plated on MacConkey, Blood agar and nutrient Agar culture media and incubated overnight at 37 degrees centigrade and observed for growth of any organisms. Number of colonies obtained was multiplied by 1000 to obtain the colony forming units (cfu) / ml.

Colony count of $>10^5$ per mL of a single species in a midstream clean catch sample or >5 × 104 /mL for specimen obtained by urethral catheterization was considered significant and taken as an evidence of presence of urinary tract infection[7]. However, when there was mixed growth of two or more pathogens or growth of organisms that normally constitute the periurethral flora (lactobacilli in healthy girls; enterococci in toddlers), urine culture was repeated to rule out contamination of urine specimen. Isolates were identified by Gram stain, motility test and routine biochemical reactions.

Antibiotic sensitivity was put up by the Kirby Bauer method- disc diffusion method following the clinical laboratory standards institute (CLSI) guidelines[8]. All Enterobacteriaceae species were tested against first-line agents -Gentamicin (10µg) , Amikacin (30µg) , Trimethoprim sulphmethoxazole (1.25-23.75µg) , Ciprofloxacin (5µg), Ceftazidime(30µg) Ceftriaxone(30µg) , Amoxiclav (30µg). Pseudomonas aeruginosa against Amikacin (30µg) Gentamicin (10µg) Ceftazidime(30µg) and

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Ciprofloxacin (5µg). Second line antibiotics were tested only for organisms in those isolates resistant to all 1st line antimicrobials or specifically requested for by the attending physician. These included Imipenem (10µg) and levofloxacin(5µg) for all Enterobacteriaceae spp. and Pseudomonas isolates. E. coli ATCC 25922, E. coli ATCC 35218 and P. Aeruginosa ATCC 27853, Staphylococcus aureus ATCC 25923 were used as controls. Based on the culture report antimicrobial susceptibility pattern was analysed. The data was entered into MS Excel software and analysed using Epi-info 7.1.4.0 version software and chi-square test was applied for testing statistical significance of difference between proportions.

RESULTS

Overall during the study period 442 children with fever satisfying inclusion and exclusion criteria were recruited in the study. Out of those recruited, 244 (55.2%) were males and 198 (44.7%) were females. Among 442 children, 46 children had urine culture positive and were diagnosed UTI, 396 children had urine culture negative and were declared to have no UTI. The prevalence of UTI is 10.4% in the present study.

UTI was more prevalent in the 13-24 months category 11 % (9/82) and was least prevalent in 37-48 months category 9.4% (9/95) ,the difference in UTI prevalence observed in the age categories was not statistically significant (p=0.988). It was observed that UTI occurred in children belonging to all age groups and there was no specific predilection for particular age group. In the present study, 46 (10.4%) of 442 children had confirmed UTI, females had a higher prevalence of UTI 11.6% (23/198) as compared to males 9.4% (23/244) ,however the difference of prevalence of UTI based on gender was not statistically significant (p=0.259) (Table 1).

Table 1: Distribution of UTI in children based on age and gender

Age Group (months)	No. of cases with fever N (%)	Culture positive cases N (%)	
13-24	82(18.5)	9(11)	Chi square – 0.129 df – 3 p value – 0.998
25-36	171(38.6)	18(10.5)	
37-48	95(21.4)	9(9.4)	
48-50	94(21.2)	10(10.6)	
Gender			
Male	244(55.2)	23(9.4)	Chi square – 1.27 df- 1 p value – 0.259
Female	198(44.7)	23(11.6)	

The most common organisms isolated on urine culture were Escherichia coli isolated in 20(43.3%) of children with UTI followed by Klebsiella pneumoniae 18(39.1%) other isolates included staphylococcus aureus (8.6%), Pseudomonas aeruginosa (8.6%). (Table 2).

Table 2: Distribution of various organisms isolated in urine specimens of urine culture-positive cases

Organisms isolated	No. of cases	Percentage
Gram positive organisms		
Staphylococcus aureus	4	8.6
Gram negative organisms		
Escherichia coli	20	43.4
Klebsiella pneumonia	18	39.1
Pseudomonas aeruginosa	4	8.6
Total	46	100

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Escherichia Coli has good sensitivity amikacin (84.8%), levofloxacin (93.7%), imipenem (100%). But it has resistance to commonly used cephalosporins group (ceftazidime – 94.4% resistant, ceftriaxone – 86.2% resistant), cotrimoxazole (72.4%) resistant, amoxiclav (100%) resistant. Klebsiella species was sensitive to levofloxacin (83%), ciprofloxacin (72%), imipenem (89%). It showed resistance to amikacin (78.7%), cephalosporins, cotrimoxazole (89%). (Table 3) Staphylococcus aureus was sensitive to Fluoroquinolones, Imipenem, Cotrimoxazole but resistant to Cephalosporins. Pseudomonas showed good sensitivity to all antibiotics except to amoxiclav and cotrimoxazole for which it was resistant. Resistance of organisms was found mainly to commonly used antibiotics – cephalosporins group (ceftriaxone, ceftazidime), amoxiclav, cotrimoxazole. (Table 3).

Table 3: Antibiotic sensitivity pattern of all isolated organisms in the study

Antibiotic	Escherichia coli		Klebsiella spp		Staphylococcus aureus		Pseudomonas aeruginosa	
	Sensitive N(%)	Resistance N(%)	Sensitive N (%)	Resistance N(%)	Sensitive N(%)	Resistance N(%)	Sensitive N(%)	Resistance N(%)
Aminoglycosides								
Amikacin	16(84.8)	3(15.1)	4(21.2)	14(78.7)	2(50)	2(50)	4(100)	0
Gentamycin	9(48.3)	11(51.6)	5(28)	13(70.8)	2(50)	2(50)	4(100)	0
Cephalosporins								
Ceftazidime	1(5.5)	17(94.4)	0	18(100)	0	3(100)	0	3(100)
Ceftriaxone	4(13.7)	16(86.2)	1(5.5)	17(94)	0	4(100)	3(75)	1(15)
Fluoroquinolones								
Ciprofloxacin	5(26.3)	14(73.6)	15(83)	3(20)	3(100)	0	4(100)	0
Levofloxacin	15(93.7)	1(6.25)	13(72)	5(27)	1(25)	3(75)	4(100)	0
Sulphonamides								
Cotrimoxazole	6(27.5)	14(72.4)	2(11)	16(89)	2(66)	1(33)	1(25)	3(75)
Penicillin								
Imipenem	18(100)	0	16(89)	2(11)	1(100)	0	1(50)	1(50)
Amoxiclav	0	10(100)	0	15(100)	-	-	1(33)	2(66)

DISCUSSION

Urinary tract infection is one of the most common bacterial infections in children. In young children making the diagnosis is difficult as the clinical presentation of UTI is often with non-specific clinical signs such as fever, irritability, and vomiting that are also commonly seen in many acute self-limiting childhood viral illnesses and localizing symptoms are minimal. The overall prevalence of UTI in this study was 10.4% which was almost similar to a study by Saravanan et al [9], who showed a prevalence of 10.9%. Few studies showed lower prevalence rates at round 4-6%, where most of the pediatric patients were not malnourished.[10-11]

We found that in the age group of 1-5 , UTI was common in all ages and occurred with similar incidence in all age groups without any specific predilection for certain age group. Our findings are similar to those of many other studies which reported a high prevalence of UTI in children and uniform distribution across all ages excluding infants. Taneja et al.[12] in their study found that among 558 culture proven cases of UTI, 25% were infants, 38% were in the age group of 1-5 years and 37% belonged to the 6-12 year age group. Research has established that in infancy, UTI is more common in boys and after 1 year of age it becomes common in girls than boys. Even though statistically not significant, in present study also, the prevalence of UTI in girls was 11.6% higher than males (11.6% to 9.4%) and the reasons adduced for this are variable and include causes like short urethra in females which facilitates the ascent of bacteria in the urinary tract.

Escherichia coli was the commonest bacterial isolate from culture urine specimens accounting for 43.4% of all. This was followed closely by Klebsiella species which accounted for 39.1% (18 of 46 positives). This finding is in accordance with other findings, where E.coli was substantially reported more than any other organism.[13-15] The current study observed isolated bacterial pathogens resistance to be high against amoxicillin-clavulanic acid, ceftriaxone, cotrimoxazole and sensitivity was high for aminoglycoside group of drugs. It has been reported recently that there was high resistance to

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ampicillin, cotrimoxazole which are WHO recommended first line drugs for treatment of UTI. This high resistance to commonly used antibiotics was accounted due to inadequate dosage of these antibiotics used during self-medication and these are highly prescribed drugs over the counter. [16]
E.Coli showed good sensitivity to aminoglycoside group – amikacin (84.8% sensitive). E.Coli was 100% sensitive and no invitro resistance to Imipenem was observed. But high degree of resistance was observed to cephalosporin group (94% resistant to ceftazidime, 86% resistant to ceftriaxone) and to cotrimoxazole (72.4% resistant), similar to other studies. Klebsiella isolates in this study showed more resistance than E.coli isolates. The major difference was observed for gentamicin and amikacin, E.coli isolates showed low resistance to amikacin and gentamicin, while Klebsiella isolates showed high resistance to these agents despite being sensitive for many years. [17-18].

CONCLUSION

Children of age less than 5 years presenting with fever and suspected of having UTI who are not very sick, should first have their urine specimen submitted for culture and sensitivity testing before starting presumptive antimicrobial therapy. Ongoing surveillance for antimicrobial susceptibility pattern for isolated uro-pathogens should be established to provide basis for the presumptive treatment of UTI.

Limitations of study

Our prevalence rates are based on small sample size and one sample of children presenting to an urban, tertiary care children's hospitals and since this is a highly selected hospital based study, it may not be generalized to all patient populations in the community and clinical practice. Children less than 1 year of age were not included in the study.

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