A STUDY OF BACTERIOLOGICAL PROFILE AND ANTIBIOTIC SUSCEPTIBILITY PATTERNS AMONG CULTURE POSITIVE URINARY TRACT INFECTION IN FEBRILE CHILDREN

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ABSTRACT

BACKGROUND
Children of any age with febrile Urinary tract infection (UTI) can have acute pyelonephritis and subsequent renal scarring. UTI should be treated promptly to prevent possible progression to pyelonephritis. UTI may be suspected based on symptoms or findings on urinalysis or both. Urine culture sensitivity testing is necessary for confirmation and appropriate therapy.
Aims and Objectives- The primary aim of the study was to evaluate bacteriological profile and their antibiotic culture sensitivity pattern in culture positive UTI in febrile children.

MATERIALS AND METHODS
This cross-sectional study was conducted at outpatient clinics of our "Child Health Clinics" between May 2016 and April 2017 (One year). All children aged 0 to 12 years whose urine cultures were positive while evaluating for a febrile illness with suspected UTI were included in the study to evaluate the bacteriological profile and their culture sensitivity patterns.

RESULTS
Sixty nine (69) children with culture positive UTI were enrolled in this study in 1-year period. The most common organism isolated in our study was E. coli (Escherichia coli) 39/ 69 (56.5%) followed by Klebsiella (17.4%), Pseudomonas (13%), Proteus (8.7%) and Staphylococcus aureus (4.4%). Majority of the Gram negative isolates of our study were found sensitive (100%) to broad-spectrum antibiotics such as Imipenem, Meropenem and Tigecycline. Next to them Cefoperazone + Sulbactam was the most effective antibiotic against all four gram negative isolates of our study. The only gram positive isolate of our study, i.e. Staphylococcus aureus was found sensitive (100% - 3/3) to Cefepime, Cefotaxime, Ceftriaxone, Vancomycin, Linezolid, Azithromycin and Clarithromycin.

CONCLUSION
Urinary tract infection should be considered as one of the differential diagnosis of fever in children. Escherichia coli is the most common organism causing UTI in children. As resistance to first line antibiotics is increasing, the paediatricians should appreciate the need for urine culture and sensitivity as a part of standard evaluation of febrile children and also, they should monitor the antimicrobial culture sensitivity patterns to choose the appropriate antibiotics to treat the febrile UTI in children to prevent long-term complications.

KEY WORDS
Urinary Tract Infection (UTI), Urine Culture, Sensitivity, Resistance, Antibiotics.

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BACKGROUND

Urinary tract infection (UTI) is a common medical problem in children and an important cause of morbidity might result in renal damage, often in association with vesicoureteric reflux (VUR). If not diagnosed early and treated adequately, UTI leads to chronic ill health and long-term renal damage.[1] UTI is defined as growth of significant number of organisms of a single species in the urine in the presence of symptoms. Significant bacteriuria is a growth with colony count of >10^5/mL of a single species in a midstream clean catch urine sample. UTI may be suspected based on symptoms or findings on urinalysis or both; a urine culture is necessary for confirmation and appropriate therapy. Fever may be the only significant symptom in children with urinary tract infection and all children with otherwise unexplained fever merit evaluation for possible UTI.[2] It is essential to identify urinary tract infections in febrile children and institute prompt treatment to reduce the potential for life-long morbidity. Progressive renal damage from unrecognised pyelonephritis in childhood may lead to hypertension and chronic renal failure in later life.[3] Laboratory confirmation of diagnosis of UTI is essential and it requires the collection of uncontaminated urine sample and sending it for culture. Basing on the sensitivity and resistance pattern of uropathogens isolated, appropriate antibiotics for treating UTIs will be selected as the emergence of resistant bacteria is growing worldwide. Hence, we studied the bacteriological profile and their antibiotic susceptibility patterns among culture positive UTI in febrile children.

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MATERIALS AND METHODS

This cross-sectional study was conducted at our "Child Health Clinics" for 1 year, i.e. between May 2016 and April 2017. All children aged 0 - 12 years whose urine cultures were positive while evaluating for a febrile illness with suspected UTI at our outpatient clinics included in the study to evaluate the bacteriological profile and their culture sensitivity patterns. Children with other associated infections such as Malaria, Enteric fever, Viral haemorrhagic fevers (i.e. mixed infections) and children with proved Nephrotic Syndrome were excluded from the study. Urine specimen collection and urine cultures were done according to standard procedure in the Microbiology Department as per the Clinical Laboratory Standard Institute (CLSI) guidelines. The resultant "Antibiogram" (Culture sensitivity/ resistance) was reviewed to identify the most common pathogen causing urinary tract infection in children as well as their antibiotic susceptibility pattern.

RESULTS

The most common organism isolated out of 69 children with culture positive urinary tract infection in our study was E. coli (Escherichia coli) accounting for 56.5% (39/69) followed by Klebsiella (17.4%), Pseudomonas (13%), Proteus (8.7%) and Staphylococcus aureus (4.4%). 95.6% of isolates in our study were Gram negative bacteria and only 4.4% of the isolates were Gram positive bacteria.

Sex	Total Number	%
Male	33	47.8
Female	36	52.2
Total	**69**	**100**

Table 1. Distribution of Culture Positive UTI Cases in the Present Study

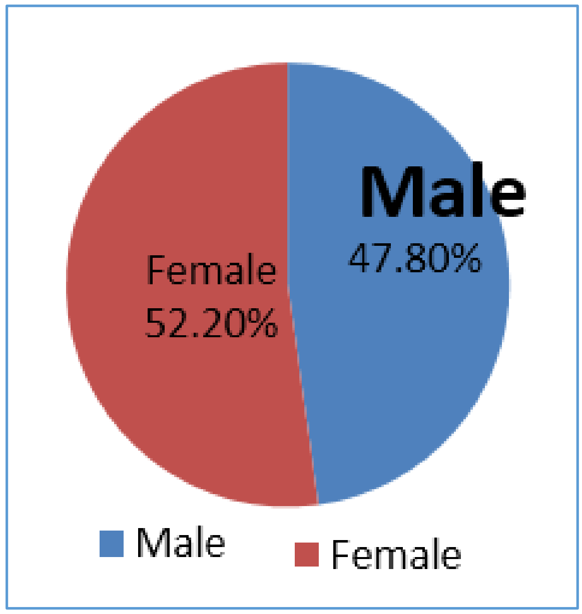

Figure 1. Sex Distribution of Culture Positive UTI Cases in the Present Study

Organism	Number	%
E. coli	39	56.5
Klebsiella	12	17.4
Pseudomonas	9	13
Proteus	6	8.7
Staphylococcus aureus	3	4.4
Total	**69**	**100**

Table 2. Bacteriological Profile of Culture Positive UTI Cases in the Present Study

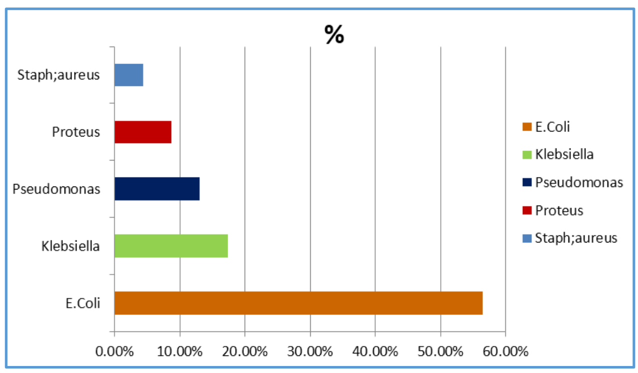

Figure 2. Bacteriological Profile of Culture Positive UTI Cases in the Present Study

Study	E. coli n (%)	Klebsiella n (%)	Pseudomonas n (%)	Proteus n (%)	Staph. aureus n (%)	CONS (Coagulase -ve Staphylococci) n (%)
Ravikiran CH et al (n= 38)	25 (65.7)	06 (15.8)	01 (2.6)	04 (10.5)	02 (5.3)	--
Ashoka C et al (n= 20)	16 (80)	3 (15)	--	1 (5)	--	--
Amatya P et al (n= 48)	32 (67)	10 (21)	--	1 (2)	--	1 (2)
Hussain M et al (n= 117)	67 (57.2)	22 (18.8)	6 (5.1)	4 (3.4)	16 (13.6)	--
Present study (n= 69)	39 (56.5)	12 (17.4)	9 (13)	6 (8.7)	3 (4.4)	--

Table 3. Comparison of Bacteriological Profile of Culture Positive UTI in Children among Different Studies

Antibiotic	E. coli S/R n= 39	Klebsiella S/R n= 12	Pseudomonas S/R n= 9	Proteus S/R n= 6
Ampicillin	0/39	0/12	0/9	0/6
Gentamycin	30/9	2/10	0/9	0/6
Amikacin	33/6	8/4	6/3	1/5
Amoxyclav	5/34	0/12	0/9	0/6
Amp. + Sulbactam	2/37	1/11	3/6	0/6
Pipzo (Piperacillin + Tazobactam)	37/2	4/8	0/9	1/5
Cefuroxime	6/33	2/10	0/9	0/6
Cefepime	30/9	8/4	6/3	3/3
Cefotaxime	33/6	6/6	1/8	1/5
Ceftriaxone	34/5	7/5	2/7	1/5
Ciprofloxacin	33/6	0/12	4/5	0/6
Levofloxacin	38/1	8/4	2/7	3/3
Imipenem	39/0	12/0	9/0	6/0
Meropenem	39/0	12/0	9/0	6/0
TMP + SMZ (Trimethoprim + Sulfamethoxazole)	12/27	2/10	0/9	0/6
Norfloxacin	4/35	1/11	7/2	0/6
Cefoperazone + Sulbactam	39/0	9/3	8/1	5/1
Nitrofurantoin	37/2	9/3	8/1	5/1
Tigecycline	39/0	12/0	9/0	6/0
Ceftazidime	4/35	7/5	8/1	5/1

Table 4. Antibiogram (Sensitivity/ Resistance Pattern of Culture Positive UTI in Febrile Children) of Gram Negative Isolates in the Present Study

S- Sensitivity, R- Resistance.

Antibiotic	E. coli n= 39 n (%)	Klebsiella n= 12 n (%)	Pseudomonas n= 9 n (%)	Proteus n= 6 n (%)
Ampicillin	39 (100)	12 (100)	9 (100)	6 (100)
Gentamycin	9 (23)	10 (83.3)	9 (100)	6 (100)
Amikacin	6 (15.4)	4 (33.3)	3 (33.3)	5 (83.3)
Amoxyclav	34 (87.2)	12 (100)	9 (100)	6 (100)
Amp. + Sulbactam	37 (94.9)	11 (91.7)	6 (66.7)	6 (100)
Pipzo (Piperacillin + Tazobactam)	2 (5.1)	8 (66.7)	9 (100)	5 (83.3)
Cefuroxime	33 (84.6)	10 (83.3)	9 (100)	6 (100)
Cefepime	9 (23)	4 (33.3)	3 (33.3)	3 (100)
Cefotaxime	6 (15.4)	6 (50)	8 (88.9)	5 (83.3)
Ceftriaxone	5 (12.8)	5 (41.6)	7 (77.8)	5 (83.3)
Ciprofloxacin	6 (15.4)	12 (100)	5 (55.6)	6 (100)
Levofloxacin	1 (2.6)	4 (33.3)	7 (77.8)	3 (50)
Imipenem	0 (0)	0 (0)	0 (0)	0 (0)
Meropenem	0 (0)	0 (0)	0 (0)	0 (0)
TMP + SMZ (Trimethoprim + Sulfamethoxazole)	27 (69.2)	1 0(83.3)	9 (100)	6 (100)
Norfloxacin	35 (89.7)	11 (91.7)	2 (22.2)	6 (100)
Cefoperazone + Sulbactam	0(0)	3 (25)	1 (11.1)	1 (16.7)
Nitrofurantoin	2 (5.1)	3 (25)	1 (11.1)	1 (16.7)
Tigecycline	0(0)	0 (0)	0 (0)	0 (0)
Ceftazidime	35 (89.7)	5 (41.6)	1 (11.1)	1 (16.7)

Table 5. Resistance Pattern of Gram Negative Isolates of Culture Positive UTI in the Present Study

Table 5 shows the antibiotic resistance pattern among gram negative isolates of our study. Majority of gram negative isolates in our study were found resistant to Ampicillin, Gentamycin, Amoxyclav, Ampicillin + Sulbactam, Cefuroxime and TMP + SMZ.

Antibiotic	E. coli n= 39 n (%)	Klebsiella n= 12 n (%)	Pseudomonas n= 9 n (%)	Proteus n= 6 n (%)
Ampicillin	0 (0)	0 (0)	0 (0)	0 (0)
Gentamycin	30 (76.9)	2 (16.7)	0 (0)	0 (0)
Amikacin	33 (84.6)	8 (66.7)	6 (66.7)	1 (16.7)
Amoxyclav	5 (12.8)	0 (0)	0 (0)	0 (0)
Amp. + Sulbactam	2 (5.1)	1 (8.3)	3(33.3)	0 (0)
Pipzo (Piperacillin + Tazobactam)	37 (94.9)	4 (33.3)	0 (0)	1 (16.7)
Cefuroxime	6 (15.4)	2 (16.7)	0 (0)	0 (0)
Cefepime	30 (76.9)	8 (66.7)	6 (66.7)	3 (50)
Cefotaxime	33 (84.6)	6 (50)	1 (11.1)	1 (16.7)
Ceftriaxone	34 (87.2)	7 (58.3)	2 (22.2)	1 (16.7)
Ciprofloxacin	33 (84.6)	0 (0)	4 (44.4)	0 (0)

Levofloxacin	38 (97.4)	8 (66.7)	2 (22.2)	3 (50)
Imipenem	39 (100)	12 (100)	9 (100)	6 (100)
Meropenem	39 (100)	12 (100)	9 (100)	6 (100)
TMP + SMZ (Trimethoprim + Sulfamethoxazole)	12 (30.8)	2 (16.7)	0 (0)	0 (0)
Norfloxacin	4 (10.3)	1 (8.3)	7 (77.8)	0 (0)
Cefoperazone + Sulbactam	39 (100)	9 (75)	8 (88.9)	5 (83.3)
Nitrofurantoin	37 (94.9)	9 (75)	8 (88.9)	5 (83.3)
Tigecycline	39 (100)	12 (100)	9 (100)	6 (100)
Ceftazidime	4 (10.3)	7 (58.3)	8 (88.9)	5 (83.3)

Table 6. Sensitivity Pattern of Gram Negative Isolates of Culture Positive UTI in the Present Study

Table 6 shows the antibiotic sensitivity pattern of gram negative isolates of our study. 94.9% (37/39) of E. coli were found sensitive to Piperacillin + Tazobactam (Pipzo) and Nitrofurantoin. 97.4% (38/39) of E. coli were found sensitive to Levofloxacin. Almost, all the Gram negative isolates (100%) namely E. coli, Klebsiella, Pseudomonas and Proteus were found sensitive to Imipenem, Meropenem and Tigecycline. Next to them Cefoperazone + Sulbactam has shown good sensitivity against all the gram negative isolates of our study.

Antibiotic	Staph. aureus (n= 3) (S/R)	(S) Sensitivity (%)	(R) Resistance (%)
Penicillin	0/3	0	100
Ampicillin	0/3	0	100
Amoxyclav	0/3	0	100
Erythromycin	1/2	33.3	66.7
Clindamycin	2/1	66.7	33.3
Cefepime	3/0	100	0
Cefotaxime	3/0	100	0
Ceftriaxone	3/0	100	0
Vancomycin	3/0	100	0
Linezolid	3/0	100	0
Azithromycin	3/0	100	0
Clarithromycin	3/0	100	0
Chloramphenicol	2/1	66.7	33.3
Levofloxacin	1/2	33.3	66.7
Ofloxacin	3/0	100	0
Gatifloxacin	3/0	100	0
Tetracycline	2/1	66.7	33.3

Table 7. Antibiogram (Sensitivity/ Resistance Pattern of Culture Positive UTI in Febrile Children) of Gram Positive Isolates (Staphylococcus aureus) in the Present Study

Table 7 showing the "Antibiogram," i.e. the Sensitivity/Resistance pattern of Staphylococcus aureus isolates in our study. In our study 100% (3/3) of Staph. aureus was found to be sensitive to Cefepime, Cefotaxime, Ceftriaxone, Vancomycin, Linezolid, Azithromycin, Clarithromycin, Ofloxacin and Gatifloxacin. 33.3% (1/3) of Staph. aureus was found to be sensitive to Erythromycin and Levofloxacin, and 66.7% (2/3) of them were found to be sensitive to Clarithromycin, Chloramphenicol and Tetracycline. All the 3 Staph. aureus (100%) isolates in our study were found resistant to Penicillin, Ampicillin and Amoxyclav.

DISCUSSION

Urinary tract infection (UTI) is one of the most important causes of long-term morbidity and mortality with an estimated 150 million UTIs annually (Globernado et al 2007). It is associated with renal damage reported in about 5% of affected children and is common both in the community and hospitalised patients.[4] Uropathogenic E. coli (UPEC) is the most common aetiological agent responsible for 80 to 85% of community acquired UTIs with other significant uropathogens including Klebsiella pneumonia, Proteus mirabilis and Staphylococcus aureus etc.[5,6] In our study, the most common bacterial isolate found in culture positive childhood UTI was Escherichia coli (E. coli) accounting for 56.5% (39/69). This finding was in agreement with the previous studies such as Hussain M et al (57.2%),[7] Ravikiran CH et al (65.7%),[8] Amatya P et al (67%)[9] and Sumit Gupta et al (42.76%).[10] Whereas in Ashoka et al study, they found 80% isolates were E. coli as predominant bacterial isolate.

In the present study next to E. coli we found Klebsiella (17.4%), Pseudomonas (13%), Proteus (8.7%) and Staphylococcus (4.4%) in the order. Similar order of findings was found in previous studies such as Ravikiran CH et al, Amatya P et al and Hussain M et al studies. In the present scenario, the essence of antimicrobial drug resistance of major uropathogens has posed a global threat. The prevalence of antimicrobial resistance among microorganisms that causes UTI is increasing worldwide. Resistance rates vary from country to country.[11] The results of urine culture sensitivity tests to different antibiotics show that all four bacterial isolates in our study were found resistant to Ampicillin. In our study we found 100% isolates of Klebsiella, Pseudomonas and Proteus were resistant to Amoxyclav. 100% isolates of Pseudomonas and Proteus in our study were found resistant to Gentamycin, Cefuroxime and TMP + SMZ. 100% isolates of Klebsiella and Proteus of our study were found resistant to Ciprofloxacin. In the present study 100% Pseudomonas species (9/9) showed resistance to commonly used antibiotics such as Ampicillin, Amoxyclav, Gentamycin, Cefuroxime, Pipzo and TMP + SMZ. 100% Proteus isolates (6/6) from culture positive UTI in our study were resistant to Ampicillin, Gentamycin, Amoxyclav, Ampicillin + Sulbactam, Cefuroxime, Ciprofloxacin, TMP + SMZ and Norfloxacin. Whereas in Sumith Guptha et al study resistance patterns of Klebsiella and E. coli were found to be 82.02% and 85.56% for Amoxicillin, 80.78% and 93.17% for Tetracycline, 78.95% and 81.76% for TMP + SMZ, 84.57% and 68.29% for Ciprofloxacin. Majority of Gram negative isolates in our study showed higher resistance to Ampicillin, Amoxyclav, Gentamycin, Cefuroxime and TMP + SMZ. The only Gram positive isolates in our study was Staph. aureus (3/69) which was found 100% resistant to Penicillin, Ampicillin, Amoxyclav and 66.7% of them were found resistant to Erythromycin and Levofloxacin as well. This finding was in agreement with findings of Sumith Guptha et al study.[10]

In our study 100% E. coli isolates were found sensitive to Imipenem, Meropenem, Cefoperazone + Sulbactam and

Tigecycline. 84.6% of E. coli (33/39) in our study were found sensitive to Amikacin, Cefotaxime and Ciprofloxacin. 97.4% of E. coli (38/39) in the present study were found sensitive to Levofloxacin. All the four types of Gram negative isolates of our study were found to be sensitive to Imipenem, Meropenem and Tigecycline. 77.8% (7/9) of Pseudomonas species in our study were found sensitive to Norfloxacin. Similar findings were found in Sumith Guptha et al study.

Most of the uropathogens isolated in our study were found to be resistant to commonly used first line antibiotics especially Ampicillin, Gentamycin, Amoxyclav, Cefuroxime, Ciprofloxacin, TMP + SMZ and Norfloxacin, while most of them were sensitive to Imipenem, Meropenem, Tigecycline, Cefoperazone + Sulbactam and Nitrofurantoin.

CONCLUSION

Urinary tract infection should be considered as a potential cause of fever in children, because most of the times UTI in children present with non-specific symptoms and signs. Therefore, Urine culture sensitivity testing should be considered as part of diagnostic evaluation of fever in children. As resistance to first line antibiotics is increasing, the paediatricians should appreciate the need for urine culture sensitivity as a part of standard evaluation of febrile children and also, they should monitor the antimicrobial culture sensitivity patterns to choose the appropriate antibiotics to treat the febrile UTI in children to prevent long-term complications. Regular monitoring is required to establish reliable information about susceptibility (Sensitivity/ Resistance) patterns of urinary pathogens for selecting optimal empirical therapy for patients with UTI. It is suggested that empirical antibiotic selection for treatment of UTI should be based on the knowledge of local prevalence of bacterial isolates and their antibiotic sensitivities rather than on universal guidelines.

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