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Original Research Article

Prevalence of urinary tract infection and sensitivity pattern amongst children less than 3 years of age with fever in a tertiary care hospital in South Karnataka

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ABSTRACT

Background: Antimicrobial resistance is a major concern especially in urinary tract infections in children as improperly treated urinary tract infections (UTIs) on long term can cause renal scarring in young children, which leads to long term morbidities like hypertension, chronic renal disease and pre-eclampsia. The empirical therapy for UTI varies regionally due to their varied sensitivities and resistance pattern. This study aims to facilitate policy making in empirical antibiotic therapy of pediatric patients with urinary tract infections.

Methods: A cross sectional study, which included a group of 140 children's (6 months to 3 years) with fever were included in the study. All patients with colony count >1 lakh CFU/ml or colony count >50,000 CFU/ml, with leukocyturia (>5 WBCs/HPF in centrifuged urine) or colony count >1000 CFU/ml with urinary symptoms were diagnosed to be positive for urinary tract infection.

Results: The prevalence of UTI in febrile children less than 3 years in our study was 0.1%. Out of 140 patients with fever, 35 were UTI positive. *E. coli* was the most commonly isolated organism (60%), followed by MRSA (14.2%) and *Enterococci* (11.4 %). *E. coli* was found to be most sensitive to nitrofurantoin (85.7%), followed by gentamicin (61.9%) and norfloxacin (38%). *E. coli* showed high resistance to cefuroxime (76.2%) and ceftriaxone (71.4%). MRSA was found to be most sensitive to linezolid and vancomycin, and resistant to norfloxacin.

Conclusions: The data shows the increased resistance of *E. coli* to commonly prescribed antibiotics like cefuroxime and ceftriaxone. So, this study shows the empirical treatment of UTI in our region and the importance of having antibiotic prescription policies in every region.

Keywords: Urinary tract infection, *E. coli*, Nitrofurantoin

INTRODUCTION

Antimicrobial resistance is now growing as a major community health problem all over the world. The misuse of antibiotics is the major contributing factor to the emerging resistance pattern. As a result, infections caused by resistant microbes do not respond to existing treatment because of limited treatment options, resulting in prolonged illness and greater risk of death.¹ Urinary tract infections (UTIs) are one of the common bacterial

infections in childhood and may have significant adverse consequences, especially for young children. The importance of UTIs with fever in young children is that, it increases the probability of kidney involvement, like an increased risk of underlying nephrourologic abnormalities and consequent renal scarring. Kidney scarring is considered to cause long-term morbidity (hypertension, chronic renal disease, preeclampsia).² UTI can be treated adequately only by the definitive diagnosis of the local pathogen, the knowledge of the susceptibility

pattern and of any associated risk factors. The bacterial sensitivity pattern of the common pathogens keeps changing rapidly in all regions due to the inappropriate antibiotic use. As a result, UTI causing frequent bacteria like *E. coli* are gaining resistance to commonly prescribed antibiotics. Also, not so common pathogens could also emerge as causative organisms.³

In almost all cases of suspected UTI infection, empirical therapy (mostly a broad-spectrum antibiotic) will be initiated before the definitive diagnosis of the pathogen. This empirical therapy keeps changing rapidly due to the emergence of resistance and needs to be updated regularly through regular sensitivity studies.⁴ So, this study aims to look at the sensitivity and resistance pattern of the common UTI causing pathogen in our locality and in establishing the empirical therapy of UTI in children at the given period of time.

METHODS

This was a cross sectional observational study conducted in the pediatric OPD and wards of Mysore medical college and research institute, Mysore for a duration of 6 months (from November 2018 to April 2019). The study was conducted on 140 pediatric patients, in the age group of 6 months to 3 years with fever, with or without urinary symptoms.

The study was started only after obtaining approval from the institutional ethics committee. Written informed consent was taken from guardian/parent of the patients.

Inclusion criteria

Children (6 months to 3 years) with fever but without focus. Children (6 months to 3 years) with fever with excessive crying while passing urine or with urinary symptoms like burning micturition, straining, poor urinary stream, dribbling, frequency, change in urine colour, change in urine odour, blood in urine, diurnal incontinence.

Exclusion criteria

Co-existence of any systemic disorder.

Procedure

A single group of subjects in the age group less than 3 years, presenting with fever with urinary symptoms or fever without any discernible cause were enrolled in the study. For all subjects, urine microscopy, Gram staining and urine culture were done.

Method of collection of urine

Clean catch mid-stream urine is used to minimize contamination by periurethral flora. Contamination can be minimized by washing the genitalia with soap and

water. Antiseptic washes and forced retraction of the prepuce are not advised. The urine specimen should be promptly plated by Kirby-Bauer disc diffusion method within one hour of collection. If delay is anticipated, the sample can be stored in a refrigerator at 4 degree Celsius for upto 12-24 hours.⁵

Antibiotic susceptibility pattern was obtained using Kirby-Bauer disc diffusion method. For all patients, the following criteria was used for the diagnosis as UTI positive: all patients with colony count >1 lakh CFU/ml or colony count >50,000 CFU/ml, with leukocyturia (>5 WBCs/HPF in centrifuged urine) or colony count >1000 CFU/ml with urinary symptoms were diagnosed to be positive for urinary tract infection.⁶

Statistical analysis

Sample size calculation: using estimation technique, sample size was calculated by the formula.

$$n = Z^2P(1-P)/d^2$$

where n is sample size, Z=1.96 (statistics for 95% confidence interval), p=10.2% (prevalence of UTI in febrile children less than 3 years), d=5% (significance level). The sample size was calculated to be 140.¹⁸

Statistical methods included both descriptive statistics like mean, standard deviation, frequency and percent and inferential statistics using chi square test. P value is calculated using chi square test and p<0.05 was considered significant.

RESULTS

In this study, we were able to identify the prevalence, sensitivity and resistance pattern of isolated organisms, proportion of UTI diagnosed children with fever alone or alongwith with urinary symptoms and the mean duration of fever in UTI.

140 patients were enrolled in the study that met both the inclusion and exclusion criteria, out of which 35 patients were diagnosed to be UTI positive. The prevalence of UTI among the children who attended our pediatric OPD and wards, during the study period (6 months) was found to be 35 out of 20,000 patients (0.17%), whereas incidence of UTI was found to be 25%.

Age wise distribution of UTI positive cases is illustrated in Figure 1, which shows 20% in 6 months to 1-year age group, 31% in 1-2 years and 49% in 2-3 years age group and statistically did not show higher incidence in any age group (p=0.1). Gender wise distribution of UTI positive cases is illustrated in Figure 2, which shows 48.6% in females and 51.4% in males. Symptomatically 74.2% (26 out of 35) of UTI positive patients presented only with fever and no other focus of infection, while 20% (7 out of 35) patients had fever with urinary symptoms, and 5.7%

(2 out of 35) patients had fever with urinary and nonspecific symptoms, as illustrated in Figure 3. Most of the children who were diagnosed with UTI had a mean duration of fever for 5 days. Of the 35 patients diagnosed with UTI, 10 children (28.5%) had febrile seizures.

The distribution of predominant organisms in various age group is illustrated in Figure 4, which shows *E. coli* (57.1%), *Enterococcus* (28.5%), and *Enterobacter* (14.2%) in the 6 months to 1 year age group, and *E. coli* (72.7%), *Enterococcus* (18.1%), and *Proteus* (9%) in 1-2 years age group and *E. coli* (41.1%), *Enterobacter* (5.8%), *Proteus* (11.7%), MRSA (29.4%), and *Klebsiella* (11.7%) in the 2-3 age group UTI positive children. Overall, *E. coli* predominated (60%), followed by MRSA (14.2 %) and *Enterococci* (11.4%). Other pathogens isolated were *Proteus* (8%), *Klebsiella* (5%), and *Enterobacter* (5%).

The antibiotic susceptibility pattern of different UTI causing organisms is illustrated in Figure 5 and sensitivity pattern of *E. coli* and MRSA is illustrated in Figure 6 and 7 respectively. *E. coli* is sensitive to nitrofurantoin (85.7%), gentamicin (61.9%), norfloxacin (38%), amikacin (33.3%), ceftriaxone (23.8%), cefuroxime (23.8%), cotrimoxazole (23.8%), ciprofloxacin (23.8%), nalidixic acid (19%), ofloxacin (14.2%), cefotaxime (14.2 %), and azithromycin (9%), MRSA is sensitive to vancomycin (80%), linezolid (80 %), gentamicin (60%), nitrofurantoin (60%), and norfloxacin (20%). *Enterococci* shows sensitivity to linezolid (50%), vancomycin (50%), and Fosfomycin (25%). *Proteus* shows sensitivity to ceftriaxone (90%), cefuroxime and gentamicin (66.6%), norfloxacin, and ciprofloxacin (33.3%). *Klebsiella* shows sensitivity to norfloxacin (50%), ciprofloxacin (54%), ceftriaxone (62%), gentamicin (65%), and nitrofurantoin (40%) and lastly *Enterobacter* shows sensitivity to norfloxacin (60%), gentamicin (55%), and cotrimoxazole (40%).

The resistance pattern of *E. coli* and MRSA is illustrated in Figure 8 and 9 respectively. *E. coli* shows resistance to cefuroxime (76.1%), ceftriaxone (71.4%), Norfloxacin (61.9%), cotrimoxazole (57.1%), ciprofloxacin (42.8%), gentamicin (28.5 %), ceftriaxone (14.2%), nitrofurantoin (14.2%), and amikacin (4.7%). MRSA shows resistance to cotrimoxazole (80%), nitrofurantoin (60%), ciprofloxacin (60%), and gentamicin (20%). *Enterococci* shows resistance to norfloxacin (50%), ciprofloxacin (50%), gentamicin (40%), nitrofurantoin (25%), ceftriaxone (20%). *Proteus* shows resistance to nitrofurantoin (60%), norfloxacin (33.3%), amikacin (31%), and cefuroxime (30%). *Klebsiella* shows resistance to cefuroxime (50%), ceftriaxone (30%), nitrofurantoin (25 %) and norfloxacin (25%). And lastly *Enterobacter* shows resistance to cefuroxime (50%), ceftriaxone (40%), gentamycin (25%), nitrofurantoin (23%), norfloxacin (25%).

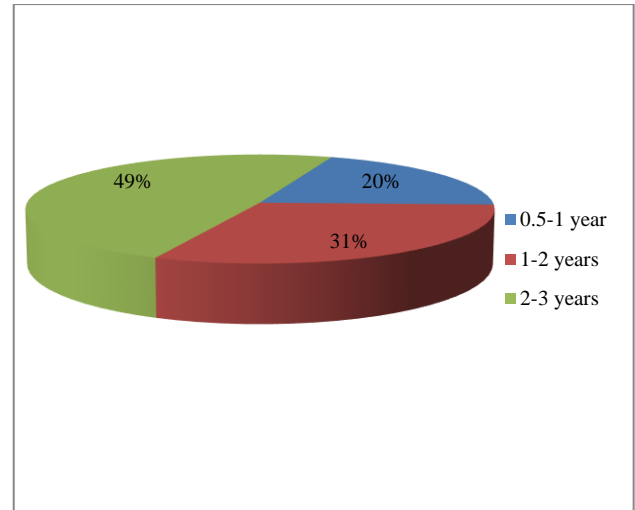


Figure 1: Percentage distribution of UTI based on age.

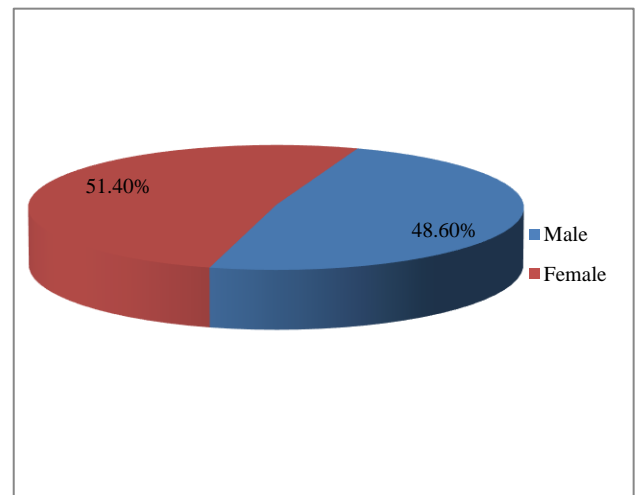


Figure 2: Percentage distribution of UTI based on gender.

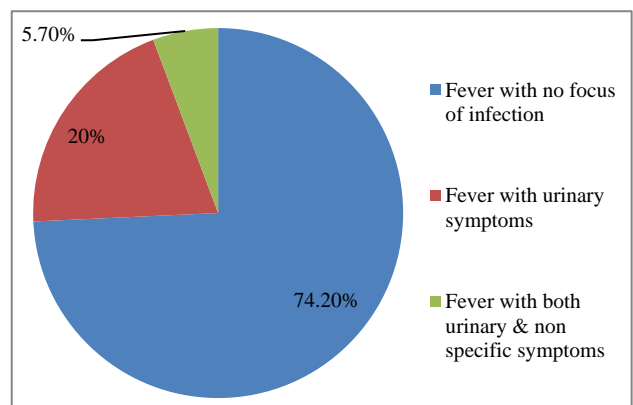


Figure 3: Percentage distribution of UTI based on various presenting symptoms.

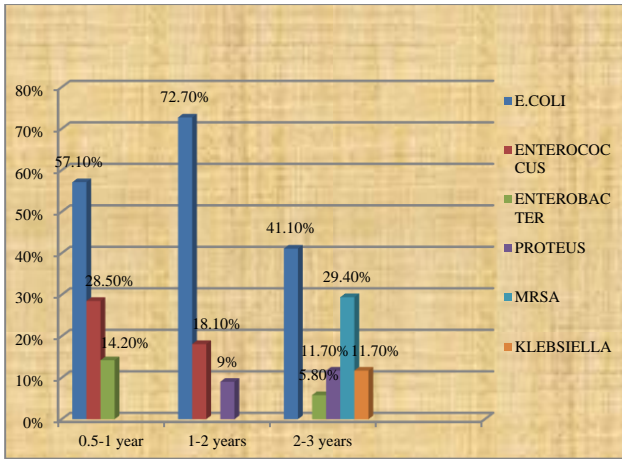


Figure 4: Percentage distribution of predominant UTI causing organisms.

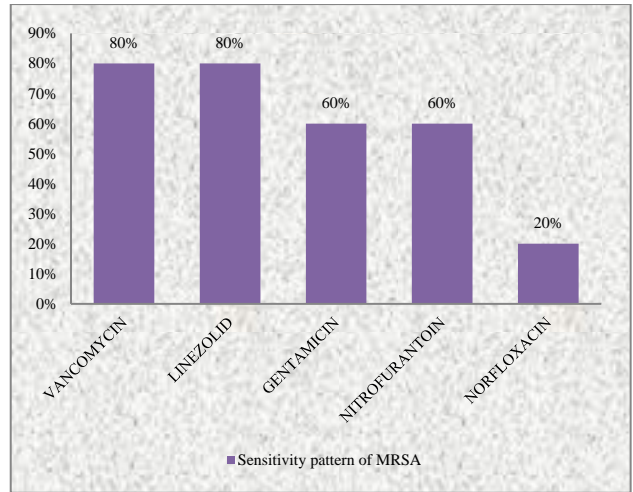


Figure 7: Sensitivity pattern of MRSA.

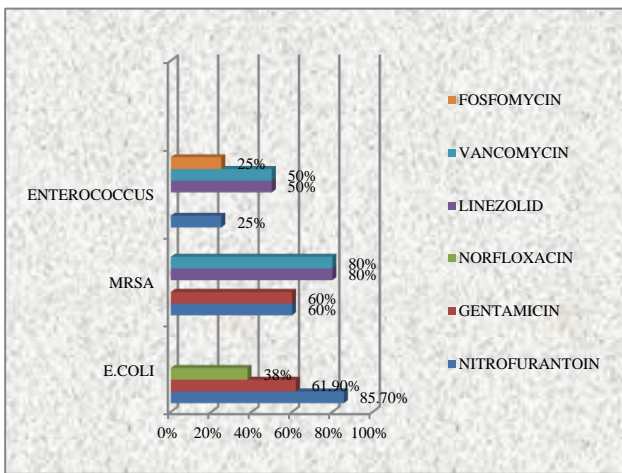


Figure 5: Antibiotic susceptibility pattern of common UTI causative organisms.

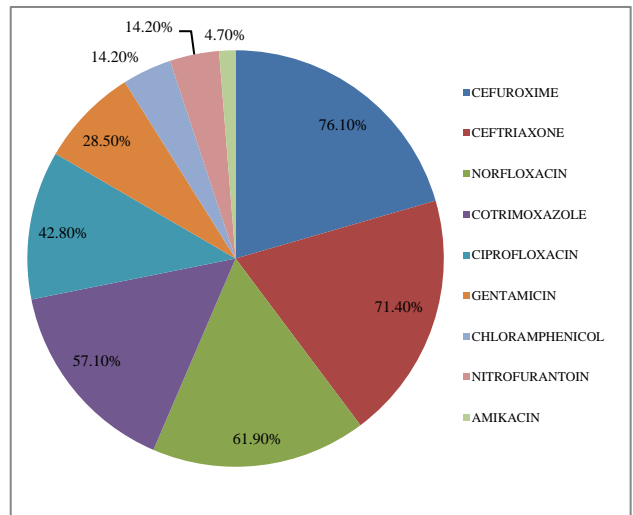


Figure 8: Resistance pattern of E. coli.

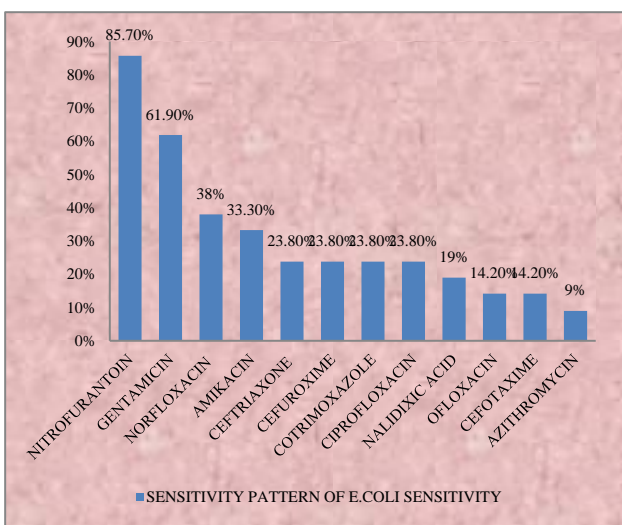


Figure 6: Sensitivity pattern of E. coli.

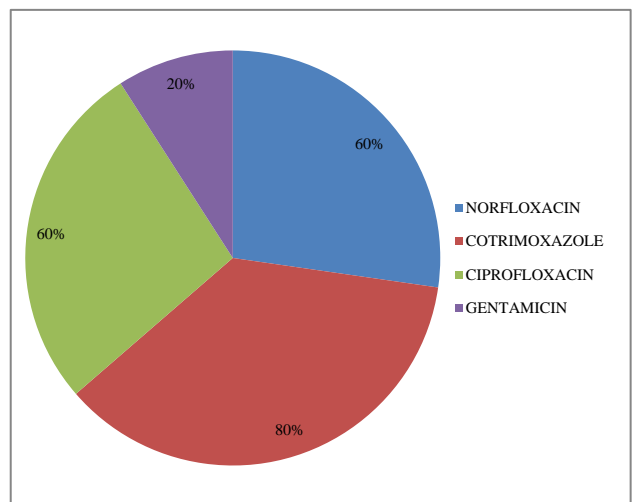


Figure 9: Resistance pattern of MRSA.

DISCUSSION

This study gives an understanding of the prevalence pattern of UTI, most common presenting symptom in UTI cases, major organisms in each age group and lastly antibiotic sensitivity and resistance pattern in children less than 3 years, attending OPD and wards in our hospital. The prevalence of UTI in febrile children less than 3 years of age in our study was found to be 0.1%. Similar to our study, a study done by Freedman, the pediatric UTIs account for 0.7% of OPD visits and 5% of emergency visits by children annually.⁷ Another study done by Schlager, also shows a low prevalence of 1.7% of UTI in children less than 5 years of age.⁸ In a study done in India on prevalence of UTI in children less than 5 years by Kaushik et al, the prevalence rate of UTI was found to be 5%.⁹ The low prevalence rate of UTI in our study may probably be due to the short duration of study (6 months) and also due to the empirical treatment with antibiotics prior to the diagnosis of UTI.

The proportion of UTI in males were 51.4% and in females were 48.6%, but there was no statistical difference between the 2 genders in the distribution of UTI ($p>0.05$). In a similar study done by Badhan et al, there was a higher proportion of UTI in female gender compared to males.¹⁰ In another similar study done by Kalantar et al, there was a higher distribution of males with UTI.¹¹ This could be due to the existing gender bias in our country, where febrile male children are given more attention and given medical care than the female children.

Age wise distribution of UTI shows that the most common age group presenting with UTI was 2-3 years and the least affected was infant age group (6 months to 1 year). Also, another study done by Nair and Rai et al, showed similar findings to our study where infant age group were the least affected by UTI and children above 2 years had a higher percentage of UTI.¹² In contrast to our study, a study done by Mathivanan et al, showed that there is a higher UTI incidence in the infant age group and least in the 2-3 years age group.¹³ The low incidence of UTI in infant age group, could be attributed to the small sample size of infants as compared to older age group and also due to the fact that infants with fever, will be started empirically on antibiotics, as a precautionary measure, before identifying the definitive diagnosis by urine culture.

The mean duration of fever in our study was approximately 5 days in all urine culture positive patients as compared to urine culture negative patients, which had a mean duration of fever for 2 days, before showing other specific symptoms ($p<0.05$). So, any child presenting with fever for more than 4 days with or without other symptomatic presentation, there is a definite need to do urine culture and sensitivity for such children.

The most common presenting symptom in majority of our UTI positive cases were fever with no other symptoms (74.2%) as compared to fever with urinary symptoms (only 20%), whereas a small proportion of children showed fever with both urinary and non-specific symptoms like diarrhea, vomiting, throat infection etc. A study done by Brkic et al on clinical characteristics of UTI in childhood, it says that fever was the most common presenting symptom in children diagnosed with UTI and only a few proportion of UTI diagnosed children presented with urinary symptoms.¹⁴ According to American academy of pediatrics, the clinical presentation of UTI in young children tends to be non-specific in nature, most of them presenting with fever alone.¹⁵

In contrast, a study done by Badhan et al, the main presenting symptom in UTI diagnosed children were fever with urinary symptoms while Sharma et al, says that fever with abdominal pain were the most common presenting feature.^{16,17} In our study, around 30%, i.e., one third of the febrile patients diagnosed with UTI also presented with febrile seizures. So, this study implicates the need to rule out UTI, in all cases presenting with febrile seizures, as UTI can be the underlying etiology.

In our study, *E. coli* was the most predominant organism isolated (21 out of 35 cases, 60%), followed by MRSA (5 out of 35, 14.2%) and *Enterococci* (4 out of 35, 11.4%). Other pathogens isolated were *proteus* (8%), *klebsiella* (5%), and *Enterobacter* (5%). A similar study done by Saheb, says that the predominant organism isolated in their study was *E. coli*.¹⁸ Another study by Rai et al says that *E. coli* was the predominant isolated pathogen in 93.3% of the cases.¹⁹ MRSA was the next predominant organism (14.2%). A similar study done by Thaddanee et al, shows a 10% prevalence of MRSA in their study.²⁰ Other organisms like *Enterococci* showed a prevalence of 11.4%, which was similar to a study done by Badhan et al, which showed a prevalence of 13.5%.¹⁶ In our study *Klebsiella* was isolated in only 5% of our cases. In contrast, *Klebsiella* was present in 12% of the cases in a study done by Thaddanee et al.²⁰ This variation in species isolated probably be due to the regional variation (geographical and ethnical).

We were also able to identify the antibiotic susceptibility pattern of various pathogens isolated. *E. coli* was most sensitive to nitrofurantoin (85.7%), gentamicin (61.9%). The commonly used fluoroquinolones norfloxacin showed a poor sensitivity of only 38%, ciprofloxacin 23.8% and ofloxacin (14.2%). Azithromycin showed the least sensitivity of only 9%. In a study done by Badhan et al, *E. coli* was shown to be most sensitive to nitrofurantoin, amikacin, and cefotaxime.¹⁶ In contrast, a study done by Patel et al and Gupta et al, *E. coli* was found to be most sensitive to imipenem.^{21,22}

E. coli showed high resistance to cefuroxime (76.1%) and ceftriaxone (71.4%), followed by norfloxacin (61.9%). Other fluoroquinolones like ciprofloxacin showed a

resistance of 42.8%. In a similar study done by Angami et al, *E. coli* showed a high resistance pattern to ceftriaxone and fluoroquinolones like norfloxacin and ciprofloxacin. Other studies, also shows high resistance to fluoroquinolones.^{11,16} But our study showed least resistance to amikacin and nitrofurantoin similar to another study.^{20,23}

MRSA shows high sensitivity to vancomycin and linezolid, each 80% respectively and 60% sensitivity to nitrofurantoin and gentamicin each. A similar study, also says that MRSA is 100% sensitive to linezolid and 40 % sensitive to aminoglycosides.¹⁹ In a study done by Wattal et al, MRSA species only responded to vancomycin, linezolid, tigecycline and daptomycin and not to any other antibiotics.²⁴

In our study MRSA showed resistance to cotrimoxazole (80%), norfloxacin (60%), ciprofloxacin (60%), and least resistance (20%) to gentamicin. In contrast, another study, says that MRSA was sensitive to fluoroquinolones in 60% of the cases.¹⁹

Other organisms like *Enterococci* also showed sensitivity mostly to vancomycin and linezolid in 50% of the cases. *Klebsiella* similar to another study, showed high sensitivity to fluoroquinolones and cephalosporins.¹⁹ *Proteus* showed high sensitivity to cephalosporins mostly. *Enterobacter* shows most sensitivity to norfloxacin and gentamicin.

Strengths of the study

This study gives a clear picture on the symptomatic presentation of UTI in a febrile child, the most common pathogens in UTI in the study region, the antibiotic sensitivity of the doubtful organisms and their resistance pattern. This study also emphasizes on the need to have a definitive diagnosis of UTI with their sensitivity pattern by urine culture and sensitivity, in febrile children before initiation by empirical treatment, in order to avoid antibiotic resistance in the community.

Limitations of the study

Our study only involved a small sample size and it was conducted for a short duration of time. This study was a single centre study. It was not a placebo-controlled study. And we had to eliminate any contaminated samples. We did not comment on the diagnostic accuracy of urine microscopy in the identification of the UTI cases, confirmed by culture and sensitivity. Also, we excluded cases with presumed diagnosis of fever with specific focus like ear pain, pneumonia etc. We did not comment on the route of administration of various antibiotics, the clinical improvement after administration of sensitive antibiotics (by culture and sensitivity) and the duration of recovery for the affected cases.

So, here in our study we are seeing an emerging resistance to fluoroquinolones and cephalosporins among the most predominant organism like *E. coli*. So, there is a high need to implement the antibiotic stewardship program in all the regions of our country as the pattern, varies according to the ethnic and geographical variation. Also, there is a need to conduct similar studies in each region, every 6 months, due to the rapid changing pattern seen in the antibiotic sensitivity and resistance pattern.

CONCLUSION

In our study, *E. coli* was the predominant organism in children less than 3 years and diagnosed as UTI. Most of the isolates respond to nitrofurantoin, and gentamicin. So, any child presenting with fever for 4-5 days, with no other symptoms, its empirical to send urine for culture and sensitivity. Also, its ideal to do similar studies on the bacteriological sensitivity and culture for any region from time to time, as it helps in determining empirical treatment of UTI and helped to avoid misuse of antibiotics.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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