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In Children with Urinary Tract Infection, Organism and Its Sensitivity Patterns in Jharkhand – A Hospital Based Study

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Abstract:
Background: *Urinary tract infection is one of the most common infections in children. Early diagnosis and appropriate treatment can significantly decrease late serious complications.*
Aim & Objective: *The primary aim of this study was to see the causative organisms and their culture & sensitivity pattern, so that pediatrician can choose the most appropriate and safe antibiotic when treating a children with UTI in this area.*
Material and Methods: *All children from 1 month to 15 years of age with culture positive urinary tract infections who were admitted to Pediatric ward from 13th April 2018 to 12th February 2019 were included. The causative organisms for urinary tract infection along with its antibiotic sensitivity pattern were retrospectively reviewed and analyzed.*
Results: *Among 105 patients of suspected UTI, 48 cases of culture positive urinary tract infection were enrolled in this study in a period of 10 months. The most common causative organism was Escherichia coli (67%), followed by Klebsiella pneumoniae (21%), Non-hemolytics streptococcus (4%), Enterobacter (2%), Acinetobacter (2%), Proteus (2%) and Coagulase negative staphylococcus (2%). Out of 48 cases, 90% were sensitive to Amikacin and 85% were resistant to Ofloxacin.*
Conclusion: *Escherichia coli is the most common organism causing urinary tract infection in children. As resistant to first line antibiotic is increasing, antibiotic stewardship programme should be strengthened.*
Key words: *Antibiotics sensitivity, Organism, Resistance, UTI.*

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I. Introduction

Urinary tract infection (UTI) is one of the most common infections in children. Antibiotics are usually given empirically before the laboratory results of urine culture are available. To ensure appropriate therapy, current knowledge of the organisms that cause UTI and their antibiotic susceptibility is mandatory[1]. The spectrum of etiologic agents causing urinary tract infection and their antimicrobial resistance pattern has been continuously changing over the years, both in community and in hospitals[2]. *Escherichia coli* is still the most frequently isolated pathogen followed by *Klebsiella spp, Proteus*, and *Enterobacter spp*[3,4]. Especially, in the underdeveloped and developing countries, due to inappropriate use of antibiotics, antibiotic resistance is increasing and treatment of urinary tract infection is becoming more diffi cult. Physicians should understand the regional antibiotic resistance pattern for determining empirical therapy until the results for culture and sensitivity are available. The knowledge on local antibiotic susceptibility is not only helpful for empirical therapy but also necessary to cycle the antibiotics

regularly. According to the hospital policy and guideline, the first line antibiotic used for UTI in children in our hospital is Ofloxacin. Anecdotally, it was noted that children treated with oral Ofloxacin in the outpatient department were increasingly being admitted due to non-response to treatment. Therefore, the objectives of this study were to investigate the common microorganisms causing urinary tract infections and to identify the status of their antibiotic susceptibility in those children who were admitted with UTI[5].

II. Material and Methods

This retrospective study was performed on patients admitted to the children's ward of Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand with a diagnosis of culture positive UTI. All children aged from 1 month to 15 years with culture positive UTI who were admitted to children's ward from 13th April 2018 to 12th February 2019 were included. The clinical as well as demographic data of each case was reviewed and recorded in the patient proforma. The case notes were reviewed along with investigation reports to identify the most common pathogens causing urinary tract infection as well as the sensitivity pattern. Urine samples were collected according to Paediatric protocol. Catheter sample was collected in children with no urinary control and midstream clean catch collection in children with urinary control.

Criteria for culture positive UTI[5]	
Method of collection	**Colony count**
Suprapubic aspiration	Urinary pathogen in any number
Urethral catheterization	>=$50X10^3$ CFU/ml
Midstream clean catch	>10^5 CFU / ml

CFU: colony forming units

Bacterial isolates and antimicrobial testing:

A total 48 bacterial isolates were identified from 48 culture positive patients. Urine microscopy was sent in all cases along with culture and sensitivity. These isolates were identified in bacteriological laboratory of department of Microbiology in Rajendra Institute of Medical Sciences at Ranchi. Urine samples were plated out on selective agar plates. Antimicrobial susceptibilities were performed locally using Kirby disc diffusion method. In this method urine sample was collected in urine culture bottle. 1 micro litre (calibrated loop) of urine sample was inoculated on Blood and Mac Conkey agar and the plates were incubated at 37^0C for 24 hours. If there was growth of bacteria, the colony forming unit(CFU) was counted. And if no growth, then no growth after 24 hours of aerobic incubation was reported. For Gram negative bacilli, the biochemical identification was done by Motility Indole Urea (MIU), Triple Sugar Iron (TSI) and Citrate whereas for Gram positive cocci, Catalase and Coagulase test was done. The Antibiotic Susceptibility Test was done on Muller Hilton Agar (MHA) in which MHA plate was incubated for 16 to 18 hours and the zone of inhibition was measured. The results were recorded as susceptible (S), resistant (R) and intermediate (I) according to Clinical Laboratory Standard Institute (CLSI) Antimicrobial susceptibility testing guidelines. Antibiotics tested as first line were Penicillin/Amoxycillin, Erythromycin, Oxacillin, Cefotaxime, Cotrimoxazole, Nitrofurantoin, Nalidixic acid, Ciprofloxacin Ofloxacin, Amikacin, Gentamycin. The second line antibiotics tested were Chloramphenicol, Piperacillin-Tazobactum, Imipenem, Meropenem and Colistin. The data were recorded and analyzed using Microsoft excel 2010.

III. Results

here were forty eight patients with culture positive UTI admitted in children's ward from 13th April 2018 to 12th February 2019. The number of patients admitted with UTI according to the age group distribution is shown in ***Figure:1***. Among 48 confirmed culture positive UTI cases, 28 cases were female (58.4%) and 20 cases were male (41.6%). According to the seasonal variation, there were two peaks of increased admission of patients with UTI were noted. First peak was noticed in August in which 11 cases of culture positive UTI were admitted followed by second peak in December in which 9 cases were admitted. UTI was more common in summer (50%) followed by winter (23%), autumn (17.5%) and spring (17.5%) respectively.

Culture and Sensitivity Pattern of Urinary Tract Infection:

Out of 48 patients, 80% (N=38) had fever at the time of presentation. Those who didn't had fever at presentation were all less than two months of age. Other common symptoms at admission were vomiting, pain or crying during micturition and loose stool. Three patients had neonatal jaundice. Among 48 admitted culture positive UTI cases, three cases had one episode and one had two previous episodes of UTI. None of the patients had congenital abnormality of urinary tract like vesico-ureteric reflux. Out of forty eight patients, three also had pyelonephritis on ultrasonography. One had bilateral calcification of renal pelvicalyceal system, two had echogenic kidneys and one had mild hydronephrosis on ultrasonography.

The most common bacteria isolated in urine culture was *Escherichia coli* 67% (N=32) followed by *Klebsiella pneumoniae* 21% (N=10). The pattern of bacteria causing UTI is shown in ***Figure:2***.

Out of thirty two *Escherichia coli* positive cases, 30 cases (93%) were resistant to Amoxycillin followed by Nalidixic acid in 28 (87.5%) cases, Ciprofl oxacin in 27 (84.3%) cases, Cefotaxim in 26 (81.2%) cases, Ofloxacin in 26 (81.2%) cases, Cotrimoxazole in 22 (68.75%) cases, Gentamycin in 17 (53.1%) cases, Nitrofurantoin in 15 (46.8%) cases and Amikacin in 5 (15.6%) cases shown in ***Figure:3***. Out of eleven case of *Klebsiella pneumoniae*, Amoxycillin was resistant in 10 (100%) cases followed by Nitrofurantoin in 8 (80%) cases, Gentamycin in 7 (70%) cases, Cotrimoxazole in 7 (70%) cases, Cefotaxime in 7 (70%) cases, Nalidixic acid in 7 (70%) cases, Ciprofloxacin in 6 (60%) cases, Ofloxacin in 4 (40%) cases and Amikacin in 2 (20%) cases shown in ***Figure:4***.

In this study, the *Enterobacter* was sensitive only to Ofloxacin and Colistin. *Non-hemolytic streptococcus* was sensitive only to Amoxycillin and Chloramphenicol. *Coagulase negative*s *staphylococcus* was sensitive to Oxacillin, Erythromycin and Ofloxacin. *Acinetobacter* was sensitive only to Amikacin. Out of forty eight urine culture positive cases three organisms were resistant to all first line antibiotics. Out of three, two were *Klebsiella pneumoniae* and one was *Escherichia coli*. Both were sensitive only to Meropenem, Imipenem and Colistin. Among all the patients, 58% received Amikacin followed by Ofloxacin, Cefotaxime, Chloramphenicol, Vancomycin and Meropenem in 17%, 15%, 6%, 2%, 2% respectively.

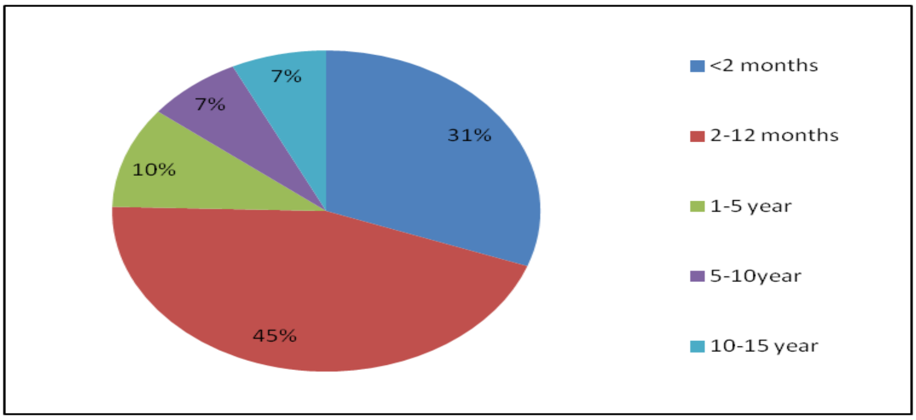

Fig 1: Showing age wise distribution of confirmed cases UTI among the study population.

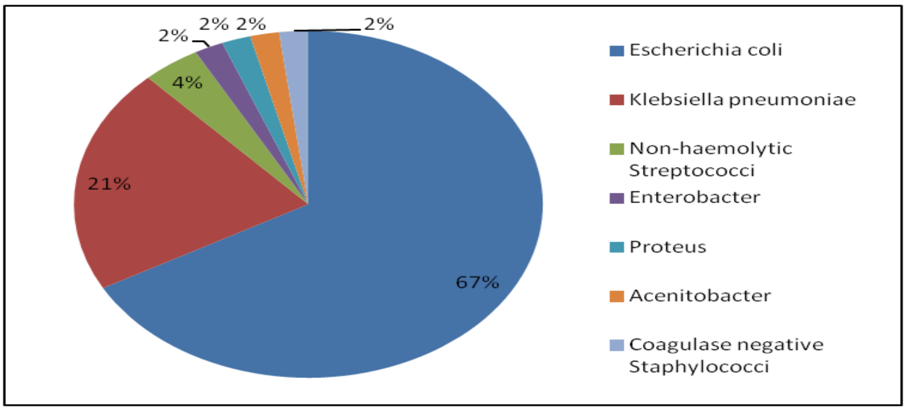

Fig 2: Showing percentage of pathogens causing urinary tract infections during the study.

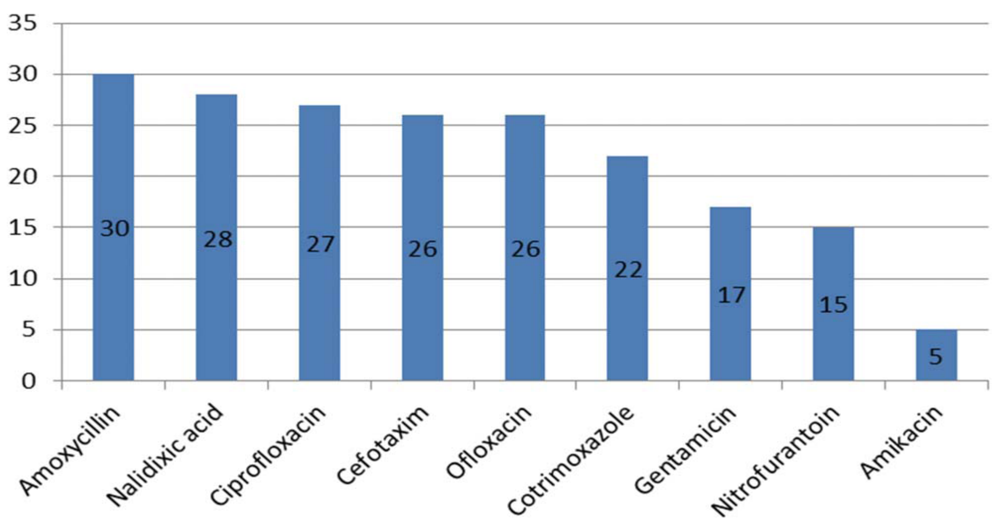

Fig 3: Resistance pattern of *Escherichia coli* (n=32) with first line antibiotics in the study.

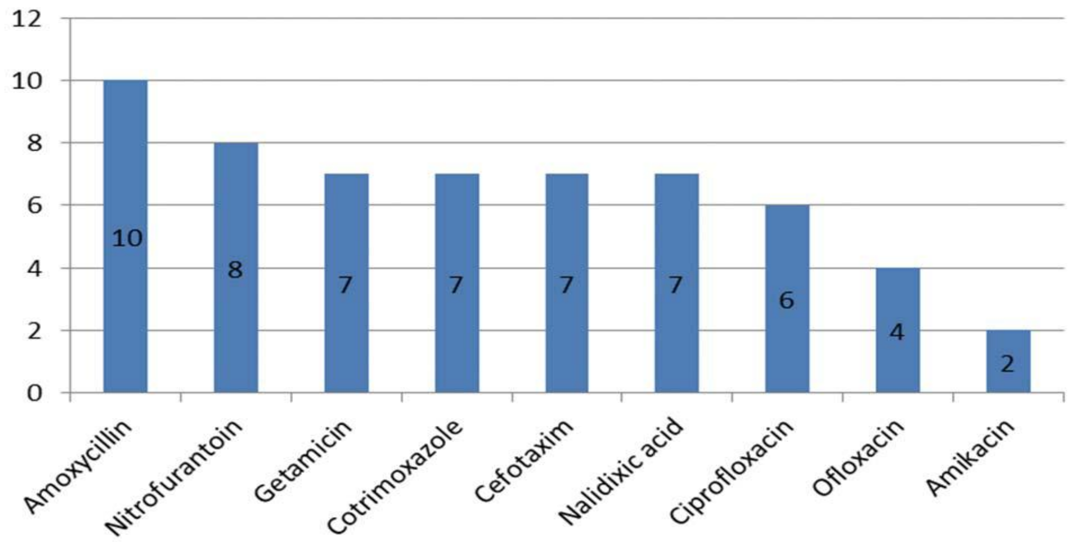

Fig 4: Resistance pattern of *Klebsiella pneumoniae* (n=10) with first line antibiotics in the study.

IV. Discussion

Escherichia coli is the most commonly reported pathogen causing UTI[6,7,8,9,10]. This is also reflected in this study. In the study done by Durgesh et al[7], *Escherichia coli* was the predominant (31.25%) isolates causing UTI, followed by *Staphylococcus aureus* (25%), *Pseudomonas aeruginosa* (15.62%), *Proteus mirabilis* (15.62%), *Klebsiella pneumoniae* (6.25%) and *Serratia marcescens* (6.25%) where as in our study the most common organism causing UTI was *Escherichia coli* (67%) followed by *Klebsiella pneumoniae* (21%), *Non haemolytic streptococcus* (4%), *Enterobacter* (2%), *Acinetobacter* (2%), *Proteus* (2%) and *Coagulase negative staphylococcus* (2%). Similarly, in the study done by Yolbas et al[6] and Mostafa et al[8], *Escherichia coli* was the most common organism causing urinary tract infection followed by *Klebsiella* which was similar to our study. Similar results were observed in studies done by Rehaman et al[9] and CW kwan et al[10]. This difference may be due to the variation in geographical distribution.

Study done by Haller et al[11] showed the effective empirical intravenous and oral antibiotics for the treatment of community-acquired UTIs include Ampicillin and Aminoglycosides, whereas the oral antibiotic of choice by Prais D et al[12] and Hoberman et al[13] showed Amoxicillin-Clavulanate or Cefuroxime and Cefixime respectively. In our study, uropathogens showed Culture and Sensitivity Pattern of Urinary Tract Infection increased resistant pattern to oral antibiotics ***(Fig: 3 & 4).*** The reason may be easy availability to antibiotics from pharmacy. We haven't seen the sensitivity with oral Cefixime as this disc was not available while this study was done. Hence this study cannot recommend the choice of empirical oral antibiotic.

Compared to the study done by Yolbas et al[6], in which *Escherichia coli* was resistant to Amikacin in 3%, Nitrofurantoin 9%, Trimethoprim/Sulfamethoxazole 58% and Cefotaxime 51%, in our study *Escherichia coli* showed more resistant pattern to these antibiotics i.e Amikacin (15.6%), Nitrofurantoin (46.8%), Cotrimoxazole (68.75%) and Cefotaxime (81%). The reason for increase in resistance may be due to the excessive use of third generation Cephalosporins both as oral and intravenous route. In the study done by Durgesh et al[7], the mean sensitivity to Penicillin and Ciprofloxacin were 70.83% and 60% respectively. *Staphylococcus aureus* showed 75% resistance to Methicillin, Oxacillin and Vancomycin. Uropathogens were sensitive to Norfloxacin, Cotrimoxazole and Ofloxacin. These results were in contrast to our study in which *Escherchia coli* was sensitive to Amoxycillin and Ciprofloxacin in only 6% and 15.6% respectively, and in case of *Klebsiella pneumoniae* none was sensitive to Amoxycillin and only 40% were sensitive to Ciprofloxacin. The reason for this difference may be due to the injudicious over the counter use of antibiotics. In the study done by Mostafa et al[8], *Escherichia coli* had a sensitivity rate of 97.8% to Ceftriaxone and 95.2% to Cefotaxime in contrast to our study in which Cefotaxime was sensitive only in 18.7% of cases.

The highest resistance rate of *Escherichia coli* was to Penicillin (95.2%) followed by Amoxycillin and Cotrimoxazole (79% and 74.2% respectively) in the study by Mostafa et al[11] whereas in our study *Escherichia coli* showed high resistant to Amoxycillin (93%) followed by Nalidixic acid (87.5%). According to Mostafa et al[8] *Klebsiella spp.* showed the highest sensitivity to Ciprofloxacin (95.1) and Ceftriaxone 90.7% which was in contrast to our study in which *Klebsiella* was sensitive to Ciprofloxacin and Cefotaxime only in 40% and 30% respectively. In our study *Klebsiella* showed highest resistant to Amoxycillin which was simiar to study done by Mostafa et al[8]. In study done by Rehaman et al[9], 59.9% isolates of *Escherichia coli* were multidrug resistant where as in our study only one *Escherichia coli* was multidrug resistant. In our study *Escherichia coli* showed increase in resistant to oral antibiotics; Amoxycillin (93%), Ofloxacin (81.2%), Ciprofloxacin (84.3%) Cotrimoxazole (68.75%), and Nitrofurantoin (46.8%) which was similar to the results in study done by Rehaman et al[9]. The reason may be easy access to oral antibiotics from pharmacy.

In our study E. coli was sensitive to Cefotaxime in only 18.75% where as in study done by CW Kwan et al[10], *Escherichia coli* was sensitive to greater than 95% of third-generation Cephalosporins (Ceftriaxone and Ceftazidime). In their study bacteria were frequently resistant to ampicillin (54.4%) and Trimethoprim/Sulfamethoxazole (40.4%) which was comparable to our study. In our study *Escherichia coli* (81.2%) and *Klebsiella pneumoniae* (70%) showed increase in resistance pattern to Cephalosporins which was comparable to study done by Stephanie et al[14] in which there was high rate of resistance to third generation Cephalosporins in subpopulations of children admitted to the hospital for UTIs. In the study done by Rasoul et al[15], most isolates showed high resistance against Ampicillin, Cotrimoxazole, Nalidixic acid, and Nitrofurantoin and *Klebsiella* isolates showed more resistance against tested antibiotics than *Escherichia coli* isolates which was comparable to our study. Although our study suggested high resistance to oral antibiotics, there was a caveat that this study included in-patients only. This might have caused some selection bias. However, this information raises an important issue regarding antibiotic resistance in UTI. A future study including both in-patients and out-patients would help clarify if resistance to oral antibiotics has indeed emerged in the organisms causing UTI in the community.

V. Conclusion

Escherichia coli is the most common organism causing urinary tract infection in children. Urine microscopy as well as urine culture sensitivity should be sent before starting antibiotics. Knowledge of the sensitivity and resistance pattern of uropathogens in specific geographical locations is an important factor for choosing suitable antibacterial treatment. Uropathogens showed increased resistance to oral antibiotics. Amikacin remains the first line intravenous antibiotic in hospitalized patient.

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