Yield of Urinary Pathogens and their Sensitivity Pattern at Paediatric Tertiary Care Facility, Karachi

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Abstract

Objective: To determine the yield of common pathogens isolated from urine specimens and their sensitivity pattern in children at National Institute of Child Health (NICH), Karachi.
Methods: This was a retrospective descriptive study conducted in the department of paediatric nephrology and pathology, National Institute of Child Health over a period of two years, from January 2014 to December 2015. All urine samples received in our laboratory from children admitted to nephrology and other departments during the study period were processed for culture and sensitivity. All samples were inoculated with cystine lactose electrolyte deficient (CLED) agar plates and biochemical characteristics of the specific pathogen were identified on biochemical tubes. The plates and tubes were incubated for 24 hours at 37ºC and growth of more than 10^5 CFU was considered as significant. These colonies were identified by morphology, lactose fermentation, Gram stain and biochemical tests. Antibiotic sensitivity was performed by Kirby-Bauer method as per CLSI (Clinical and Laboratory Standards Institute) guidelines and sensitivity was recorded after 24 hours' incubation at 37ºC.
Results: Out of 4107 samples processed, 1442 were positive giving a yield of 35% with 66% in girls and 34% in boys. E. coli was the most common pathogen (55%), followed by Pseudomonas (13.6%), Klebsiella (13,5%) and Candida albicans (11%). Majority of pathogens were sensitive to piperacillin-tazobactam (80-100%). Quinolones and aminoglycosides sensitivity was found in 65 to 85% and in 65 to 90% cases, respectively. Most of the pathogens (75%) were resistant to 3rd generation cephalosporins except Citrobacter species.
Conclusion: A high yield of common pathogens in urine samples and high resistance to common antibiotics was observed.

Keywords: Urine specimen collection, bacteria, bacterial sensitivity tests, children.
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Introduction

Urinary tract infection (UTI) is defined as growth of a single pathogen with colony forming units (CFU)>10^5 per ml of clean catch midstream urine[1,2]. UTI is the second most common infection after acute respiratory infections in children[2]. According to the American Academy of Paediatrics (2011), the prevalence of UTI is 5% in children aged 2-24 months[3]. Its occurrence is 2% in boys and 3-8% in girls[2]. Lifetime risk for symptomatic UTI is 3 to 5 times higher in girls than in boys. Asymptomatic bacteriuria is more common among girls. In UTI, there is tissue invasion and inflammation caused by proliferating bacteria resulting in renal parenchymal infection known as pyelonephritis. In fact, this acute or acute on chronic pyelonephritis is responsible for significant morbidity and mortality in

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children and if left untreated may result in renal scarring, hypertension and chronic kidney disease[3,4]. UTI may also be responsible for drug resistance, recurrence, hospitalisation and delay in surgical intervention. UTI is an indicator of underlying structural or functional abnormalities of the urinary tract in 30-40% of the cases[4].

UTI has been classified as typical or atypical (complicated) UTI according to the severity of illness. UTI may be classified according to predominant symptoms related to the upper urinary tract, known as pyelonephritis, or lower urinary tract symptoms, called cystitis. Clinical, presentation of UTI varies from patient to patient depending upon the age of the child, underlying causative pathogen, structural urinary tract defects and period after which the patient presents. Classical signs and symptoms include fever, abdominal pain, vomiting, frequency, dysuria, burning micturition and occasionally either retention of urine or frank pyuria. At times children present an atypical or complicated course when a child presents with signs and symptoms of uraemia (acidosis, anaemia, hypertension), or symptoms related to sepsis-like hypotension and convulsions. Such complicated cases (atypical UTI) require hospitalisation, the detailed evaluation including radio imaging, haematological, biochemical tests, and thorough septic work-up like urinalysis, blood and/or urine cultures and intensive care, including dialysis or urological interventions like catheterisation. Though interleukins (IL-6 and 8), C-reactive proteins and procalcitonin have been studied as biomarkers of UTI, they are not used in common practice. These at atypical cases are particularly responsible for significant morbidity and mortality in children with various congenital anomalies of kidneys and urinary tract (CAKUT)[1,4]. Among CAKUT, obstructive uropathies like posterior urethral valves, vesicoureteral reflux and neurogenic bladder are the major causes responsible for recurrent and complicated UTI[2-4]. Urolithiasis is the most common acquired obstructive uropathy responsible for recurrent UTI, urosepsis, acute kidney injury (12%) and chronic kidney disease (>20%) in our setup[5]. Therefore, proper diagnosis and identification of underlying cause are essential for prevention of renal damage and chronic kidney disease (CKD).

Definitive diagnosis of UTI and sensitivity pattern of causative agents are essential for immediate treatment for selection of appropriate antibiotic, subsequent imaging workup for underlying conditions and long-term follow up for recurrence and CKD[4,6,7].

Management of UTI is complex in children with underlying obstructive conditions, refluxing kidneys, neurogenic bladder or in immunocompromised children, e.g. post-transplant[4].

Most UTIs are the result of ascending infections. Haematogenous spread occurs in a minority of infections. CAKUT is the major predisposing conditions for infection.

The most common causative organism of UTI is E. coli and is responsible for 80-85% of cases[1-3]. Other gram-negative pathogens are Klebsiella, Citrobacter, Enterobacter, Morganella Morgani and Pseudomonas. Among gram positive organisms, Enterococci, Streptococcus faecalis and rarely Staphylococci species are seen in renal or peri-renal abscesses. Candida albicans and Cryptococcus are responsible for complicated UTI[1,4].

Urine culture and sensitivity test is the gold standard method for diagnosis. Though urinalysis for microscopy (significant pyuria, gram stain for bacteriuria), rapid urine dipsticks tests (positive leuco cyteesterase and nitrite) are suggestive of UTI in 85-95% of cases[3,4]. But it will not give us the specific pathogen and microbial sensitivity. So, urine culture and sensitivity is the gold standard tool in the diagnosis of UTI. Generally, empirical antibiotic treatment is started based on clinical judgement and urinalysis pending the availability of result of bacterial culture and sensitivity[4,8,9].

Antimicrobial resistance is a big challenge in the management of UTI and resistant UTI is twice likely to be associated with high morbidity and mortality. Antibiotic-resistant UTI may be responsible for prolonged hospital stay as well as a delay in surgical interventions when required. Thus, change of antibiotic, prolonged hospital stay and delay in procedure will increase the burden of health care cost[1,4,7].

A high prevalence of antimicrobial resistance to various antibiotics has been reported in developing countries mostly due to irrational use in primary care setting for simple infections. Recently in a meta-analysis, reported resistance to E. coli UTI in children to commonly used antibiotics in primary care setting was up to 80% from developing countries[7]. In a local study from a tertiary care hospital, E. coli was found as the most common (63%) pathogen and overall a high sensitivity (82%) has been shown[10].

In developing countries, approach to identify gaps, upgrade and strengthen existing standard of care to provide ultimate benefit and enhance patient care in the real-life scenario is not very common. Therefore, the following study was planned to report the yield of microbial growth and their sensitivity pattern in children either hospitalised or being followed in the outpatient department of NICH, over two years.

The objective of our study was to determine the yield of common pathogens isolated from urine specimens and their sensitivity pattern in children with suspicion of urinary tract infection.

Material and Methods

This is a retrospective descriptive study conducted in the department of paediatric nephrology and department of pathology of National Institute of Child Health (NICH), Karachi from January 2014 to December 2015. This study included all urine samples received in our laboratory from children aged 1 month to 13 years with suspicion of UTI either admitted in different wards (medical or surgical) or attending OPD of NICH and processed for urinalysis and culture during the study period.

All samples received (n= 4107) collected in a sterile container suitable for processing were included. A portion of the urine sample was initially centrifuged and looked for pus cells under microscopy and more than 8-10 pus cells/HPF were considered as significant pyuria. All samples with significant pyuria were inoculated on cystine lactose electrolyte deficient (CLED) agar plates and on a set of biochemical tubes. The plates and tubes were incubated in the incubator for 24 hours at 37ºC to see the morphological growth of the organism and its biochemical characteristics. The growth of more than 10^5 colony forming units (CFU)/ml were considered as significant bacterial growth. These colonies were identified by morphology and lactose fermentation. Gram stain of significant colonies was performed and categorised as gram-positive and gram-negative. Panel of biochemical tests in test tubes were performed to identify the bacterial pathogen. Antibiotic sensitivity testing was performed on sensitivity media by Kirby-Bauer method and per Clinical and Laboratory Standard Institution (CLSI) guidelines[11]. After 24 hours incubation at 37ºC, the plates were examined for sensitivity pattern and was recorded.

Since this was a retrospective data collected from the department of pathology, therefore main variables included; type of bacterial pathogen and their antimicrobial sensitivity pattern. A pre-designed proforma was used to collect data from hospital records. All collected data were coded and rechecked by principal investigator before final analysis.

Results

A total of 4107 urine samples were received for urinalysis and culture sensitivity over a period of two years. A total of 144 (35.1 %) samples were positive for either bacterial pathogens or candida.

Fig. 1 shows the frequency of different pathogens isolated in our study. E. coli was the most common pathogen grown in 794 samples (55%) followed by Klebsiella; 194(13.74%), Pseudomonas; 187(13.6%) and Proteus; 24(1.6%). Candida albicans were grown in 160 (11.1%) samples.

Considering gender, 66% samples were from female and rest were from males (34%). The growth of E. coli, Klebsiella and Pseudomonas were higher

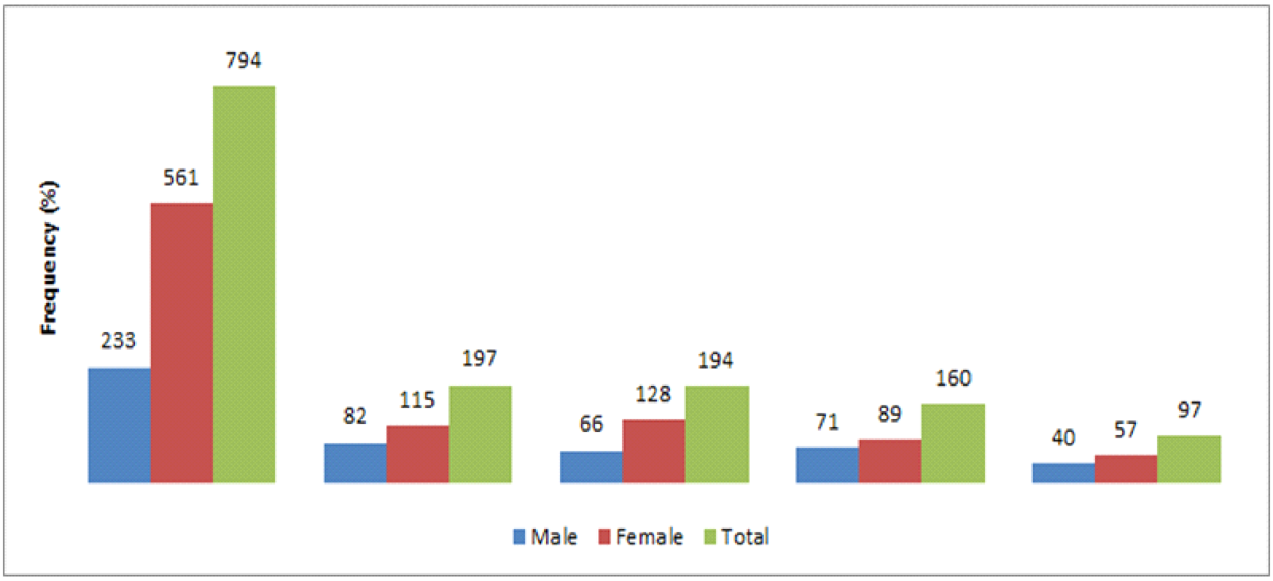

Fig. 1. Yield of urinary pathogens in 1442 samples

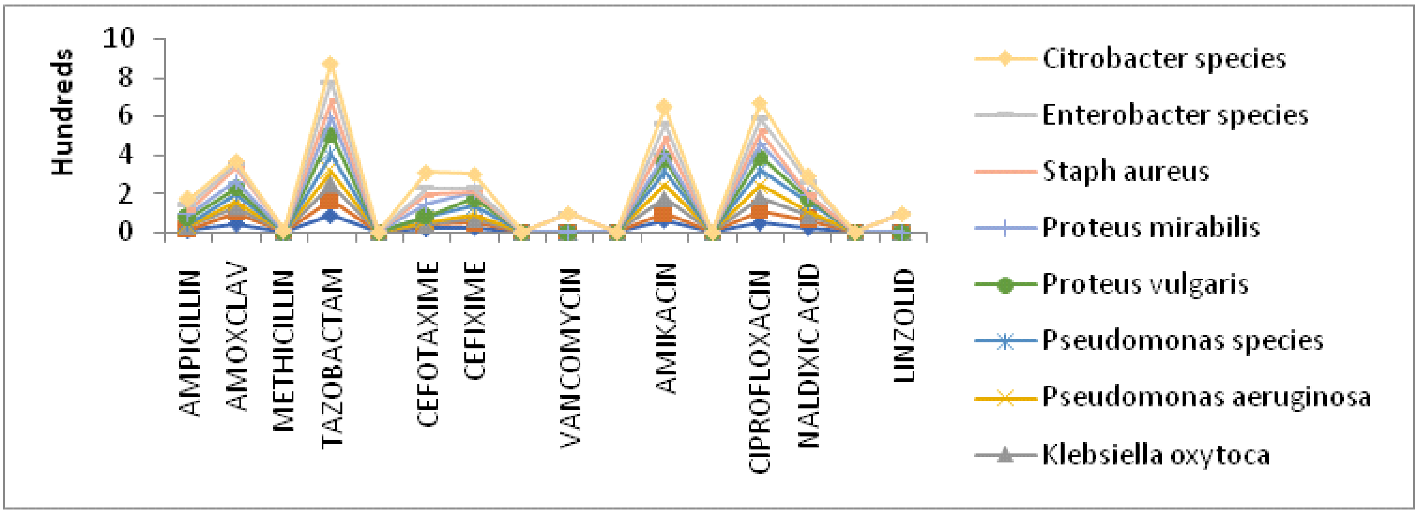

Fig. 2. Antibiotic sensitivity pattern of urinary pathogens

in females, accounting for 70.7%, 68.8% and 59.5% of cases, respectively.

Antimicrobial sensitivity pattern of isolated pathogens is shown in Fig. 2. Gram-negative pathogens were sensitive to piperacillin-tazobactam in 80-100% of cases, to ciprofloxacin and amikacin in 65-85% of cases. Other antibiotics like amoxiclav (Augmentin) sensitivity pattern of gram-negative pathogens was 25-40% except for Klebsiella pneumonia which was 60%. Gram-positive pathogens like Staphylococcus aureus were sensitive to glycopeptides (Vancomycin) in 99% and lincosamide (Lincocin) in 98%. S. aureus has shown high sensitivity to tazobactam (83%), amoxiclav (77%), amikacin (77%) and ciprofloxacin (66%).

Discussion

Confirmatory diagnosis of UTI with the specific pathogen and its sensitivity is essential for selection of appropriate antibiotic for optimal response in children with UTI in addition to other specific measures for the underlying cause of UTI. Therefore, it is imperative to understand the culture sensitivity patterns for optimal management and outcome in children with UTI.

Our study showed a high frequency of an isolation of bacterial growth in 35% of urine specimens. This represents samples from hospitalised children mainly from nephrology ward (65.6%) with various nephro-urological disorders who may have undergone catheterisation or had surgical interventions or have been exposed to the antibiotic treatment. The growth of Candida albicans (11%) also reflects that children have been exposed to prolonged or repeated antibiotics in the recent past.

E. coli was the most common bacterial pathogen isolated in 55% of samples and it has been reported as a causative pathogen in more than 80% of children with UTI in most of studies[2,3,6]. However, in a recent systemic review on the global prevalence of antibiotic resistance in paediatric urinary tract infections in primary care setting has shown declining trends of E. coli isolation. Meta-analysis of the same review comprising of 58 observational studies investigated 77783 E. coli isolates in urine and showed a prevalence of resistance ranging from 54 to 67% of E. coli in urine cultures[7]. The high variability can be justified with study design, duration, urine sample collection methods and site of study. These recent figures are consistent with our finding of growth of E. coli in 55% of samples. Our study has shown Klebsiella in 13.74%, Pseudomonas in 13.6% and Proteus in 1.6%. Similar figures have also been reported in other published studies[11-15]. The growth of Pseudomonas reflects a high frequency of complicated UTI in children hospitalised with various urological disorders. Around 2.4% urine samples grew gram-positive organisms which are rare causative agents of UTI and may also suggest complicated UTI or renal or perirenal abscess with possible haematogenous route[9,15-17].

The resistant pattern of antibiotics to different organisms is alarming. Most of the first line drugs used in the treatment of urinary tract infection were not effective as 70-80% of pathogens were resistant to cefixime, cefotaxime, nalidixic acid and amoxiclav. A high resistance of urinary pathogens has been reported globally and from developing countries including India and Pakistan[17-21]. However, in a local study from a tertiary care hospital, growth of E. coli in 63% and it was sensitive to amikacin in 82% of cases[6]. Similar figures (65-85%) of E. coli sensitivity to amikacin was found in our study[11]. The variation in antibacterial sensitivity of other bacterial pathogens could be explained based on the difference in the study population, use of antibiotic pattern in primary health care and prevalent bacterial sensitivity. Since in current study majority of samples were taken from children admitted with different nephrological and urological problem and many of them have already received antibiotics.

This resistance to primary drugs may be due to irrational use of antibiotics in primary care setting due to the availability of antibiotics over-the-counter in Non-Organisation for Economic Co-operation and Development (N-OECD) countries compared to OECD countries[7]. This practice of antibiotic use is not uncommon in our country which may have contributed to high resistance in our study as was reported from Ghana and Nigeria[7]. Resistance has been found higher in children who received antibiotics during last 6 months and in children younger than 5 years. Other important reasons for high resistance are prolonged and repeated use of antibiotic in children with different febrile illnesses other than urological problems. Similar reasons have been reported in a recently published meta-analysis on prevalence of antibiotic resistance in UTI in children and it was shown that E. coli has high resistance to first line treatment such as ampicillin (73.0-87.7%), co-trimoxazole (59.8-89.8%) and co-amoxiclav (40.9-79%) in studies from developing countries[7]. However, piperacillin-tazobactum, ciprofloxacin and amikacin showed a comparative good sensitivity pattern against gram-negative pathogens (69-89%). Reported resistance of E. coli to ciprofloxacin was 28.6% in different studies[7,11,22-25]. Recently, aminoglycosides, piperacillin tazobactum, cefoperazone-sulbactum have been recommended for complicated UTI[16,25]. Our results also suggest that in children hospitalised for UTI along with other complications like urinary retention, uraemia and urosepsis, glycopeptides (Vancomycin) and lincosamide (linezolid) showed a very effective sensitivity against gram-positive organisms (98-99%). This is consistent with other studies[16]. Further studies may be carried out to find out the factors responsible for high antibiotic resistance pattern to rationalise the use of antibiotics in children with UTI.

Since this is a laboratory data analysis, there are many limitations. Most important are lack of clinical information regarding renal functions, acute inflammatory markers like C-reactive protein, underlying structural (posterior urethral valves) or functional abnormalities (vesicoureteral reflux), blood cultures, use of antibiotics and type of urine sample collection methods, both of which affect the yield of bacterial growth and sensitivity pattern.

Conclusion

A high yield of common bacterial pathogens in urine samples of children with suspicion of UTI was recorded. A high bacterial resistance was observed to the common antimicrobial agents in our study, however, tazobactum, ciprofloxacin and amikacin showed a comparatively better sensitivity pattern.

Conflict of Interest

Authors have no conflict of interests and no grant/funding from any organisation for this study.

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