Original Article

Bacterial Aetiology and Antibiotic Resistance Pattern of Community-Acquired Urinary Tract Infections in Children in a Tertiary Care Hospital in Bangladesh

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Abstract

Background: Urinary tract infections (UTIs) in children are among the most common bacterial infections. Community-acquired urinary tract infections (CAUTI) are often treated empirically with broad-spectrum antibiotics. Pattern of aetiologic agents and their antibiotic sensitivity may vary according to geographical and regional location. So, knowledge of antibiotic resistance trends is important for improving evidence-based recommendations for empirical treatment of UTIs.

Objectives: To determine the common bacterial aetiologies of CAUTIs and their antibiotic resistance patterns in a tertiary care hospital, Savar.

Materials and Methods: This cross-sectional descriptive study was conducted at Enam Medical College Hospital, Savar from May 2016 to April 2017. We collected clean-catch mid-stream urine samples from 257 patients having clinical diagnosis of UTI and submitted to the clinical microbiology laboratory for culture and sensitivity.

Results: A total of 120 (46.7%) samples were positive for bacterial growth. Escherichia coli (79%) was the most common pathogen, followed by Klebsiella spp. (14%). Bacterial isolates showed high prevalence of resistance to multiple antibiotics. Resistance against amoxicillin/clavulanic acid, co-trimoxazole and ciprofloxacin was higher compared to newer quinolones and aminoglycosides.

Conclusion: Esch. coli and Klebsiella spp. were the predominant bacterial pathogens. The resistance pattern to commonly prescribed antibiotics was quite high and alarming.

Key words: UTI; Community acquired; Children; Esch. coli; Multi-drug resistance

Introduction

Urinary tract infections (UTI) are among the most common bacterial infections diagnosed in community health practice.1 Worldwide, an estimated 8% of girls and 2% of boys experience at least one episode of UTI by the age of seven years and recurrence occurs in 12–30% of them within a year.2 In both sexes, UTI caused by Esch. coli accounts for 75–90% of all infections followed by Klebsiella and Proteus. Staphylococcus and Enterococcus can also cause infection in both sexes.3 There may be variations in aetiologic agents of UTIs and their resistance patterns to antibiotics in different geographical areas.5,6

Paediatric UTIs remain underdiagnosed in many instances because of the absence of specific symptoms and signs, particularly in infants and young children.2,4 Therefore, accurate diagnosis and appropriate use of antimicrobials for treatment and prevention of urinary tract infections (UTI) are vital to reduce the burden and also to prevent the possible long-term consequences.7 Community-acquired UTIs (CAUTI) are often treated with different broad-spectrum antibiotics, when one with a narrow spectrum of activity may be appropriate, because of concerns about infection with resistant organisms.3,4 The extensive uses of antimicrobial agents have invariably resulted in the development of antibiotic resistance which, in recent years, has
become a major problem worldwide.\(^8\)

In Bangladesh, paediatric UTIs are usually treated empirically because of the unavailability of standard therapeutic guidelines and local susceptibility data. Knowledge of the aetiological agents of UTIs and their antimicrobial resistance patterns in our setting may help clinicians in choosing the appropriate antimicrobial treatment. Moreover, the aetiology of UTI and the pattern of antibiotic resistance have been changing over the past years.\(^9\) Most of the studies on paediatric urinary tract infections caused by multidrug resistant bacteria have been done in western world\(^10,11\), but these types of studies are scarce in South Asian region.\(^12\) However, there are not much information on aetiology and resistance pattern of community acquired UTIs in Bangladesh. But drug resistance is spreading fast mainly due to overuse or underuse of antibiotics, incomplete medications and widespread practice of feeding livestock with low levels of antibiotics to promote growth.\(^13\) The aim of this study was to determine the different bacterial pathogens and their resistance pattern causing community-acquired UTIs in children. This study is important for clinician in order to facilitate the empiric treatment and management of patients with symptoms of UTIs. Moreover, the data would also help authorities to formulate antibiotic prescription policies.

**Materials and Methods**

This cross-sectional descriptive study was conducted from May 2016 to April 2017. The study was conducted on 257 patients with symptoms of UTI attending Paediatric outpatient department and inpatient unit of Enam Medical College Hospital, Savar, Dhaka, Bangladesh. Freshly voided clean-catch midstream specimens of urine were submitted to the clinical microbiology laboratory for processing, subsequent culture and antimicrobial susceptibility test using the disk diffusion method as described by the National Committee for Clinical Laboratory Standards (presently called as Clinical Laboratory Standard Institute).\(^14\) The isolates were tested against commonly prescribed antibiotics: ampicillin, amoxicillin/clavulanic acid, cotrimoxazole, cefixime, cefuroxime, gentamicin, azithromycin, ciprofloxacin, levofloxacin, nitrofurantoin, ceftriaxone, meropenem, and imipenem.

Patients who presented with symptoms of UTI, such as fever, frequency of micturition, dysuria and abdominal pain/flank pain\(^3\) and showed significant bacterial growth (\(\geq 10^5\) CFU/mL) in urine sample were included. Patients who underwent antibiotic treatment or had been hospitalized within the previous week or whose urine samples showed no significant bacterial growth were excluded. UTI patients included in this study were classified as infants to early childhood (0–5 yrs) and late childhood to adolescents (>5 years to 18 years). Informed written consents were taken from the parents.

The Fisher Exact test was used for comparison of proportions; p values less than 0.05 were considered statistically significant. Results were summarised as percentages and presented in the form of tables.

**Results**

During the study period, total 257 patients with symptoms of UTI were included in this study. Among them, significant bacterial growth was found in urine samples of 120 patients, giving the prevalence of 46.7%. Of these 120 significant samples, 78 were from females and 42 were from males. Analysing prevalence with respect to sex, females (65%) had a higher prevalence of infection than males (35%). UTI prevalence was significantly related to sex (p value=0.027). Maximum number of cases was found in females (Table I).

**Table I: Distribution of culture positive cases according to age and sex (N=120)**

<table>
<thead>
<tr>
<th>Age groups</th>
<th>Male Number (%)</th>
<th>Female Number (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0−5 yrs</td>
<td>30 (25)</td>
<td>36 (30)</td>
<td></td>
</tr>
<tr>
<td>&gt;5 yrs</td>
<td>12 (10)</td>
<td>42 (35)</td>
<td>0.027</td>
</tr>
<tr>
<td>Total</td>
<td>42 (35)</td>
<td>78 (65)</td>
<td></td>
</tr>
</tbody>
</table>

We isolated three different bacterial species from the 120 urine samples that showed significant bacterial growth. *Esch. coli* (79%) and *Klebsiella spp.* (14%) accounted for the most prevalent bacterial isolates associated with UTI while *Staphylococci* were recovered less often (Table II).
Table II: Distribution of isolated bacteria in culture positive cases (N=120)

<table>
<thead>
<tr>
<th>Bacteria isolated</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Esch. coli</td>
<td>95</td>
<td>79</td>
</tr>
<tr>
<td>Klebseilla spp.</td>
<td>17</td>
<td>14</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>8</td>
<td>7</td>
</tr>
</tbody>
</table>

Table III showed the resistance pattern of antimicrobial drugs among the isolated bacteria. High level of drug resistance was noted in Esch. coli isolates. Esch. coli prevalence was highest for amoxicillin/clavulanic acid (64.3%) followed by cotrimoxazole (62.2%) and ciprofloxacin (52%). Intravenous drugs such as gentamicin (4%) and imipenem (4.5%) were the most effective antibiotics against Esch. coli, whereas ceftriazone showed 28% resistance. For oral agents, Esch. coli showed the lowest prevalence of resistance to cefuroxime (20%), nitrofurantoin (11%) and newer fluoroquinolones such as levofloxacin (7.1%). Among the other bacterial isolates, K. spp. had 100% susceptibility to imipenem, followed by gentamicin, levofloxacin, nitrofurantoin and cefuroxime. The least effective drugs with this isolate were the amoxicillin/clavulanic acid (93%) followed by azithromycin (60%) and ciprofloxacin (54.6%). Staphylococcus group showed the highest prevalence of resistance to cotrimoxazole (83.3%) and ciprofloxacin (66.7%). This isolate did not exhibit resistance to imipenem, levofloxacin and gentamicin.

Table III: Pattern of antibiotic resistance among the isolated bacteria (shown in %)

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>E. coli</th>
<th>Klebsiella spp.</th>
<th>Staphylococcus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin/</td>
<td>64.3</td>
<td>93</td>
<td>50</td>
</tr>
<tr>
<td>clavulanic acid</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azithromycin</td>
<td>40</td>
<td>60</td>
<td>33.3</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>28</td>
<td>23.5</td>
<td>10</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>52</td>
<td>54.6</td>
<td>66.7</td>
</tr>
<tr>
<td>Cotrimoxazole</td>
<td>62.2</td>
<td>44.4</td>
<td>83.3</td>
</tr>
<tr>
<td>Cefixime</td>
<td>26</td>
<td>21.4</td>
<td>16.7</td>
</tr>
<tr>
<td>Gentamicin</td>
<td>4</td>
<td>2.8</td>
<td>0</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>7.1</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>20</td>
<td>15.6</td>
<td>60</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>11</td>
<td>5.6</td>
<td>40</td>
</tr>
<tr>
<td>Imipenem</td>
<td>4.5</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Discussion

In the present study, we sought to determine the aetiology and resistance patterns in prevailing bacterial aetiologic agents of community acquired urinary tract infection (CAUTI). The prevalence (46.7%) of UTI, among symptomatic patients, in this study is close to the prevalence of 54% recorded in Bamenda by Akoachere et al. Prevalence rates were reported 10.9% in India and 39.7% in Nigeria. This difference in prevalence could be due to differences in methodology and sample size between these latter studies and our study. The prevalence of UTI was significantly higher in females than in males; these findings agree with earlier similar studies on CAUTIs. In our study, 79% of all clinically significant urinary isolates are Esch. coli, followed by Klebsiella spp. (14%). This result is similar to findings by Bahadin et al in Singapore. Our prevalence rate (79%) of Esch. coli is close to the findings reported by other studies in different parts of Asian region. Chinnasami et al found it 83% in India, Masud et al found 53.8% in Bangladesh, Shah et al found 50.9% in Pakistan and Moore et al found it 44% in Cambodia. Worldwide, paediatric UTIs due to Esch. coli are an important part of this problem because they limit therapeutic choices and increase morbidity of infection. However, lower rates of Esch. coli were also reported, particularly from developed countries—9.3% from USA, 10.2% from Korea. In the present study 14% of Klebsiella isolates were found present among all uropathogens studied. Our findings were different from those of Akoachere et al in Cameroon. They found Klebsiella spp. to be the least isolated organism (1.2%). However, Klebsiella spp are rarely encountered in cases of community-acquired UTI in several other studies. But, in a study by Akram et al in India higher prevalence (27.3%) of Klebsiella spp. was found. These variations in aetiologic agents could be due to the different bacterial ecology in these different regions.

This study reveals a relatively high prevalence of resistance to most antibiotics tested. Resistance to cotrimoxazole, amoxicillin/clavulanic acid and ciprofloxacin is far above the 20% rate recommended for empirical use of antibiotics for community-acquired UTIs. This result is consistent with findings from other studies in Uganda and Buea. Such high levels of resistance are probably due to antibiotic
misuse by poorly trained health workers as has been documented in many developing countries.\textsuperscript{26,28} It is also observed in this study that cefixime and azithromycin, the commonly prescribed antibiotics now-a-days used as empirical therapy in paediatric UTI, are becoming resistant against the commonest organisms. Almost 45\% of \textit{Esch. coli} isolates were resistant to at least one cephalosporin. Similar rates of antimicrobial resistance were documented in other studies from Bangladesh\textsuperscript{19}, Iran\textsuperscript{29} and India\textsuperscript{30}. However, compared to reports from Nepal, we observed a considerable increase in resistance against penicillins, aminoglycosides, quinolones and ceftriaxone.\textsuperscript{12} Lower rates of resistance among the paediatric isolates causing UTI have been documented in western countries.\textsuperscript{31}

In the present study \textit{Klebsiella} isolates showed resistance against broad spectrum cephalosporin, macrolides and amoxicillin/clavulanic acid which is consistent with the previous data of other community-based studies.\textsuperscript{32}

The most potent drugs were gentamicin, imipenem, nitrofurantoin and levofloxacin. This result is similar to the findings of Akoachere et al\textsuperscript{6} except that the latter did not test levofloxacin. Higher resistance rate to all antibiotics used in this study with the exception of imipenem and gentamicin may be explained as uncontrolled consumption of these antibiotics during the past decade in our region.\textsuperscript{29,30}

The level of drug resistance in microorganism among paediatric patients in this study is a serious issue. Previous reports have suggested that higher resistance is likely to be occurring in the communities with higher proportion of young children and high antibiotic consumption.\textsuperscript{30} Resistance to the broad spectrum cephalosporins, fluoroquinolones, macrolides and other oral antibiotics among the isolates in this study necessitates the use of intravenous drugs like gentamicin, carbapenem as alternative choice for paediatric UTIs. Among oral drugs nitrofurantoin and levofloxacin showed effectiveness against both \textit{Esch. coli} and \textit{Klebsiella spp}. Although we found carbapenems as the most effective agent against almost all the organism but the high rate of resistance from similar studies is of special concern.\textsuperscript{33} Therefore, evidence-based therapy with broad spectrum antibiotics for serious or critical cases to prevent bacterial resistance is needful.

It is quite alarming to note that almost all of the isolates included in this study were found resistant to four or more antibiotics. Moreover, this study concludes that the antibiotics like cefuroxime, nitrofurantoin and levofloxacin, which exhibited greater potencies than ciprofloxacin and amoxicillin/clavulanic acid, might be a better choice for the empirical treatment of CAUTI for children suspected with UTIs in our scenario. Therefore, it is an important issue to be addressed by the policy makers to formulate a strict antibiotic prescription policy in our country. Further multicentred studies might be needed for a specific treatment recommendation.

References


