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*

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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

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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)

Age groups	Male Number (%)	Female Number (%)	p value
0−5 yrs	30 (25)	36 (30)	0.027
>5 yrs	12 (10)	42 (35)	
Total	42 (35)	78 (65)	

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)

Bacteria isolated	Number	Percentage
Esch. coli	95	79
Klebseilla spp.	17	14
Staphyloccus aureus	8	7

Table III showed the resistance pattern of antimicrobial drugs among the isolated bacteria. High level of drug resistance was noted in *Eshc. coli* isolates. *Eshc. 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 %)

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

Discussion

In the present study, we sought to determine the aeitiology 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.[6] Prevalence rates were reported 10.9% in India[15] and 39.7% in Nigeria[16]. 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.[6,16] In our study, 79% of all clinically significant urinary isolates are *Esch. coli*, followed by *Klebseilla spp*. (14%). This result is similar to findings by Bahadin et al[17] 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[18] found it 83% in India, Masud et al[19] found 53.8% in Bangladesh, Shah et al[20] found 50.9% in Pakistan and Moore et al[21] 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.[22] However, lower rates of *Esch. coli* were also reported, particularly from developed countries — 9.3% from USA[23], 10.2% from Korea[24]. In the present study14% of *Klebsiella* isolates were found present among all uropathogens studied. Our findings were different from those of Akoachere et al[6] in Cameroon. They found *Klebseilla spp*. to be the least isolated organism (1.2%).[6] However, *Klebsiella spp*. are rarely encountered in cases of community-acquired UTI in several other studies.[9,25] But, in a study by Akram et al[17] 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.[26] This result is consistent with findings from other studies in Uganda[27] and Buea[6]. Such high levels of resistance are probably due to antibiotic

misuse by poorly trained health workers as has been documented in many developing countries.[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 *Esch. coli* isolates were resistant to at least one cephalosporin. Similar rates of antimicrobial resistance were documented in other studies from Bangladesh[19], Iran[29] and India[30]. However, compared to reports from Nepal, we observed a considerable increase in resistance against penicillins, aminoglycosides, quinolones and ceftriaxone.[12] Lower rates of resistance among the paediatric isolates causing UTI have been documented in western countries.[31]

In the present study *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.[32]

The most potent drugs were gentamicin, imipenem, nitrofurantoin and levofloxacin. This result is similar to the findings of Akoachere et al[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.[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.[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 *Esch. coli* and *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.[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, nitrofurantioin 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

1. Foxman B. The epidemiology of urinary tract infection. Nature Reviews Urology 2010; 7(12): 653–660.
2. Desai DJ, Gilbert B, McBride CA. Paediatric urinary tract infections: diagnosis and treatment. Aust Fam Physician 2016; 45(8): 558–563.
3. Elder JS. Urinary tract infection. In: Nelson textbook of paediatrics. First South Asia edition. India: Thomson Press, 2016: 2556−2562.
4. Robinson JL, Le Saux N. Management of urinary tract infections in children in an era of increasing antimicrobial resistance. Expert Rev Anti Infect Ther 2016; 14(9): 809–816.
5. Gupta K. Emerging antibiotic resistance in urinary tract pathogens. Infectious Disease Clinics of North America 2003; 17: 321–323.
6. Akoachere JFTK, Yvonne S, Akum NH, Seraphine EN. Etiologic profile and antimicrobial susceptibility of community-acquired urinary tract infection in two Cameroonian towns. BMC Research Notes 2012; Vol 5. doi: 10.1186/1756-0500-5-216.
7. Hay AD, Sterne JA, Hood K, Little P, Delaney B, Hollingworth W et al. Improving the diagnosis and treatment of urinary tract infection in young children in primary care: results from the DUTY prospective diagnostic cohort study. Ann Fam Med 2016; 14(4): 325–336.
8. Kumar MS, Lakshmi V, Rajagopalan R. Related articles, occurrence of extended spectrum beta-lactamases among Enterobacteriaceae spp. isolated at a tertiary care institute. Indian J Med Microbiol 2006; 24: 208–211.
9. Manges AR, Natarajan P, Solberg OD, Dietrich PS, Riley LW. The changing prevalence of drug-resistant

Escherichia coli clonal groups in a community: evidence for community outbreaks of urinary tract infections. Epidemiol Infect 2006; 134: 425–431.

10. Uyar Aksu N, Ekinci Z, Dundar D, Baydemir C. Childhood urinary tract infections caused by ESBL-producing bacteria: risk factors and empiric therapy. Pediatr Int 2017; 59(2):176−180.

11. Flokas ME, Detsis M, Alevizakos M, Mylonakis E. Prevalence of ESBL-producing Enterobacteriaceae in paediatric urinary tract infections: a systematic review and meta-analysis. J Infect 2016; 73(6): 547–557.

12. Singh SD, Madhup SK. Clinical profile and antibiotics sensitivity in childhood urinary tract infection at Dhulikhel Hospital. KUMJ 2013; 11(44): 319–324.

13. Islam MB, Hasan M. Antibiotic sensitivity pattern of the isolated of urinary pathogens at Dhaka National Medical College & Hospital. J Dhaka National Med Coll Hos 2012; 18(1): 4–6.

14 . National Committee for Clinical Laboratory Standards. Methods for disk susceptibility test for bacteria that grow aerobically, Volume NCCLS Document M2-A7. 7th. Wayne, Pa, USA: National Committee for Clinical Laboratory Standards; 2006.

15. Akram M, Shahid M, Khan AU. Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in J N M C Hospital Aligarh, India. Annals of Clinical Microbiology and Antimicrobials 2007; 6: 4.

16. Oladeinde BH, Omoregie R, Olley M, Anunibe JA. Urinary tract infection in a rural community of Nigeria. North American Journal of Medical Sciences 2011; 3(2): 75–77.

17. Bahadin J, Teo SSH, Mathew S. Aetiology of community-acquired urinary tract infection and antimicrobial susceptibility patterns of uropathogens isolated. Singapore Medical Journal 2011; 52(6): 415–420.

18. Chinnasami SSB, Sadasivam K, Pasupathy S. Pathogens causing urinary tract infection in children and their in vitro susceptibility to antimicrobial agents– a hospital based study. Biomed Pharmacol J 2016; 9(1): 7.

19. Masud MR, Afroz H, Fakruddin M. Prevalence of extended-spectrum beta-lactamase positive bacteria in radiologically positive urinary tract infection. Springer Plus 2014; 3: 216.

20. Ullah SSAAG, Gohar IR. Etiology and antibiotic resistance pattern of community-acquired urinary tract infections in children. KJMS 2015; 8(3): 428.

21. Moore CE, Sona S, Poda S, Putchhat H, Kumar V, Sopheary S et al. Antimicrobial susceptibility of uropathogens isolated from Cambodian children. Paediatr Int Child Health 2016: 1–5.

22. Wu CT, Lee HY, Chen CL, Tuan PL, Chiu CH. High prevalence and antimicrobial resistance of urinary tract infection isolates in febrile young children without localizing signs in Taiwan. J Microbiol Immunol Infect 2016; 49(2): 243–248.

23. Degnan LA, Milstone AM, Diener-West M, Lee CK. Extended-spectrum beta-lactamase bacteria from urine isolates in children. J Pediatr Pharmacol Ther 2015; 20(5): 373–377.

24. Han SB, Lee SC, Lee SY, Jeong DC, Kang JH. Aminoglycoside therapy for childhood urinary tract infection due to extended-spectrum beta-lactamase-producing Escherichia coli or Klebsiella pneumoniae. BMC Infect Dis 201; 15: 414.

25. Pourakbari B, Ferdosian F, Mahmoudi S, Teymuri M, Sabouni F, Heydari H et al. Increase resistant rates and ESBL production between E. coli isolates causing urinary tract infection in young patients from Iran. Braz J Microbiol 2012; 43(2): 766–769.

26. Hillier SL, Magee JT, Howard AJ, Palmer SR. How strong is the evidence that antibiotic use is risk factor for antibiotic-resistant, community -acquired urinary tract infection? J Antimicrob Chemother 2002; 50: 241–247.

27. Odongo CO, Anywar DA, Luryamamoi K, Odongo P. Antibiograms from community-acquired uropathogens in Gulu, northern Uganda—a cross-sectional study. BMC Infectious Diseases 2013; 13: 193.

28. Bryce A, Hay AD, Lane IF, Thornton HV, Wootton M, Costelloe C. Global prevalence of antibiotic resistance in paediatric urinary tract infections caused

by Escherichia coli and association with routine use of antibiotics in primary care: systematic review and meta-analysis. BMJ 2016; 352: i939.

29. Mirsoleymani SR, Salimi M, ShareghiBrojeni M, Ranjbar M, Mehtarpoor M. Bacterial pathogens and antimicrobial resistance patterns in pediatric urinary tract infections: a four-year surveillance study (2009−2012). Int J Pediatr 2014; Article ID 126142. doi: 10.1155/2014/126142.

30. Sharma S, Kaur N, Malhotra S, Madan P, Ahmad W, Hans C. Serotyping and antimicrobial susceptibility pattern of escherichia coli isolates from urinary tract infections in pediatric population in a tertiary care hospital. J Pathog 2016. doi:10.1155/2016/2548517.

31. Stultz JS, Doern CD, Godbout E. Antibiotic resistance in pediatric urinary tract infections. Curr Infect Dis Rep 2016; 18(12): 40.

32. Dimitrov TS, Udo EE, Emara M, Awini F, Passadilla R. Etiology and antibiotic susceptibility patterns of community-acquired urinary tract infections in Kuwait hospital. Med Princ Pract 2003; 13: 334–339.

33. Ansari S, Nepal HP, Gautam R, Shrestha S, Neopane P, Gurung G et al. Community acquired multi-drug resistant clinical isolates of Escherichia coli in a tertiary care center of Nepal. Antimicrob Resist Infect Control 2015; 4: 15.