Mediscope The Journal of GMC

ORIGINAL ARTICLE DOI: https://doi.org/10.3329/mediscope.v11i1.71637

Antimicrobial Susceptibility Pattern of Uropathogens Isolated at a Private Hospital in Khulna, Bangladesh

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Abstract

Background & objectives: Urinary tract infection (UTI) is one of the most common infectious diseases affecting all age & sex groups, causing significant morbidity & mortality with a substantial economic burden. Due to the irrational empiric use of antibiotics, resistance is increasing at an alarming rate. Bacteria causing UTIs & their antimicrobial susceptibility pattern varies among different areas & changes frequently over time. This study aimed to identify microorganisms causing UTI at a private hospital in the southern part of Bangladesh & to determine their sensitivity pattern towards commonly used antibiotics. **Methods:** A cross-sectional study was conducted in the clinical pathology & microbiology laboratory at Islami Bank Hospital (IBH), Khulna during the period of January'2021 to July'2021. Clean catch midstream urine samples (MSU) from 221 clinically suspected UTI cases of all age & sex groups were included in the study. Uropathogens were isolated & identified by standard microbiological techniques & susceptibility was determined by Kirby Kirby-Bauer disc diffusion method. **Results:** Among 221 suspected UTI cases, 108 (48.8%) were positive for urine culture, of which 103 (95.37%) showed antimicrobial growth. The majority 75 (69.4%) of the culture-positive cases were female. E. coli 50(44.24%) was the most predominant bacterial isolate, followed by Klebsiella 18(15.92%) & Enterococcus 16(14.15%). All Isolated gram-positive cocci (GPC) showed very high sensitivity to Vancomycin (83.3% to 100%), Linezolid (87.5% to 100%) & moderate sensitivity to Meropenem (66.7% to 75%). However, they showed relatively lower sensitivity to Ciprofloxacin, Doxycycline, Gentamicin, and Amoxiclav & very poor sensitivity to Nitrofurantoin (31.3% to 50% only). Levofloxacin had relatively better sensitivity against GPC (S. aureus- 83.3% & CONS- 75%), except Enterococcus. All gram-negative bacilli (GNB) showed a very good sensitivity towards Amikacin & Meropenem, ranging from 77.8% to 100%. E. coli & Pseudomonas were highly sensitive to Piperacillin-Tazobactam (90% & 88.9% respectively). GNB were poorly sensitive to commonly used 3rd generation cephalosporins, Azithromycin, Amoxiclav & Ciprofloxacin. Except for Pseudomonas & Klebsiella, Levofloxacin showed relatively good sensitivity against other GNB. Nitrofurantoin showed lower sensitivity against GNB, except for Pseudomonas (66.7%) & Enterobacter (75%). **Conclusion:** E. coli remains the most predominant uropathogen. Vancomycin, linezolid, Levofloxacin & Meropenem were very effective against GPC whereas Amikacin, Piperacillin- tazobactam & Meropenem showed good responses against GNB. Empiric antibiotics must be selected based on the current antibiogram of uropathogens in a particular area to prevent the increasing trends of antimicrobial resistance.

Keywords: Uropathogens, Gram-positive cocci, Gram-negative bacilli, Antibiotic resistance

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Mediscope 2024;11(1): 01-12

Introduction

Urinary tract infection (UTI) remains one of the most frequently encountered infectious diseases in medical practice, occurring from neonatal to geriatric age group.[1] It acts as a major cause of morbidity in both community & hospital settings affecting around 405 million people globally[2] with nearly 150 million diagnosed cases each year, costing the global economy over 6 billion US dollars.[3] UTI also accounts for more than 40% of the total cases of nosocomial infections reported by acute care hospitals & 66% to 86% of these infections are caused as an aftereffect of instrumentation of the urinary tract, mainly catheterization.[4]

Bacteria remain the major causative organisms of UTIs and are accountable for more than 95% of the cases.[5] Growth of more than 105 colony-forming unit (CFU) of bacteria per ml of urine for asymptomatic individuals & 103 for symptomatic individuals refers to significant bacteriuria.[6] Gram-negative bacilli are mostly accountable for UTI[7], of them E. coli is the predominant organism, which is responsible for more than 75% of the reported cases in both outpatient & inpatient facilities.[8] Other important Gram-negative organisms causing UTI are Klebsiella, Enterobacter, Citrobacter, Proteus, Serratia as well as Pseudomonas species. Among gram-positive organisms the most frequently isolated pathogens are Coagulase negative staphylococcus (CONS), S. aureus & Enterococcus species.[9] Nowadays, multidrug-resistant E. coli & K. pneumoniae are frequently recognized to be responsible for nosocomial infections including catheter-associated UTI (CA-UTI).[10] Most of the UTI cases are usually antimicrobial (caused by a single bacterial species) but polymicrobial infections (mixed bacterial infections) are also reported.[11]

The incidence of UTI is more common in women than men & it is reported that about 35% of healthy women suffer from UTI at some point in their lifetime. Most UTI cases are caused by the retrograde ascent of fecal bacterial flora to the urinary bladder & kidney via the urethra, notably in females as their urethra is shorter & wider than men's. UTIs in female are also very common due to their vaginal colonization with uropathogens[7]. Susceptibility to trauma during coitus, pregnancy & obstruction may also contribute to the higher incidence of UTIs in females.[11]

Isolation & identification of uropathogens followed by their antibiotic susceptibility pattern is obtained by doing urine culture. As a common practice, empirical antibiotic therapy is initiated before the urine culture report is available, which leads to the indiscriminate use of antibiotics, resulting in the emergence of resistant microorganisms to one or more of the available drugs. As a result, there is a gradual narrowing of the scope for effective antibiotics to combat bacterial infections like UTIs.[7] In addition, the pattern of antimicrobial susceptibility of uropathogens is regularly changing due to ever-increasing uses of antibiotics for the treatment of different variety of infections outside the urinary tract.[1,11] Bacteria producing extended-spectrum beta-lactamases (ESBLs) are constantly increasing in the population, which shows resistance to most of the broad-spectrum antibiotics except carbapenem.[12]

An alarming picture has been reflected by a recent study in Bangladesh, which demonstrated more than 75% of the E. coli causing UTIs are resistant to third-generation cephalosporins.[13] In Bangladesh UTI is a significant public health problem & increasing antibiotic resistance even complicates the treatment of uncomplicated UTI by increasing patient morbidity & health care costs due to frequent treatment failure, recurrent infections & unnecessary use of broad-spectrum antimicrobials.[10,14] There is no large-scale prospective survey of UTIs in Bangladesh, that can reflect the up-to-date burden of the infections & the antimicrobial susceptibility pattern in the community.[10] Nationwide continuous monitoring of the etiology of the infections & susceptibility pattern is of paramount importance for not only selecting appropriate antibiotics but also for rational choice of empiric therapy to reduce the misuse or overuse of antibiotics.[11]

This study was carried out to determine the recent bacterial etiology for UTIs & to analyze their susceptibility pattern in an acute care hospital in Khulna City to disseminate information about the choice of appropriate antibiotics for empirical therapy, which will guide our physicians in treating UTIs.

Materials & methods

It was a retrospective cross-sectional study conducted in the clinical pathology & microbiology laboratory at Islami Bank Hospital (IBH), Khulna during the period of January'2021 to July'2021. Clinically suspected 221 UTI cases irrespective of age & sex, referred from outpatient & different inpatient departments of the hospital with the requisition of urine culture & sensitivity were included in the study.

Clean catch midstream urine samples (MSU) (4-5 ml) were collected in a sterile disposable leakproof container from all the enrolled suspected UTI cases and transported immediately to the laboratory. Urine culture was done by semi-quantitative method on MacConkey agar, Blood agar, and Chromogenic media by using calibrated loops and incubated aerobically for 24 hours at 37°C.[1,7] A routine microscopic examination of all urine samples was done to count pus cells. If no colony appeared after 24 hours of incubation, those culture plates were further incubated for 48 hours. Bacterial isolates were identified and confirmed by using standard microbiological and biochemical tests like Gram staining, examining colony morphology on culture media, motility indole urease test, citrate utilization test, by observing biochemical changes in TSI media, catalase, coagulase & oxidase test.[7]

Antimicrobial susceptibility testing was performed on Mueller Hinton agar using disk diffusion Kirby Bauer's technique according to Clinical and Laboratory Standards Institute (CLSI) guidelines. Antibiotics were interpreted as sensitive & resistant, based on the zone of inhibition of bacterial growth, recommended by the disc manufacturer. Gentamicin (10μg), Ciprofloxacin (5μg), Levofloxacin (5μg), Amoxiclav (30μg), Ceftriaxone (30μg), Meropenem (30μg) & Nitrofurantoin (300μg)- these 7 antibiotic discs were used for both gram-positive & gram-negative organisms. Doxycycline (30μg), Cefepime (30μg), Vancomycin (30μg) & Linezolid (30μg) discs were used only for gram-positive bacteria. On the other hand, Amikacin (30 μg), Azithromycin (15μg), Cefotaxime (30 μg), Cefuroxime (30 μg), Ceftazidime (30μg) & Piperacillin-tazobactam (110 μg) discs were used only for gram-negative organisms.

Results

Among the 221 suspected UTI cases of different ages & sex included in this study, 138 (62.44%) were female & 83 (37.56%) were male with a male-to-female ratio of 1:1.66 (Figure 01).

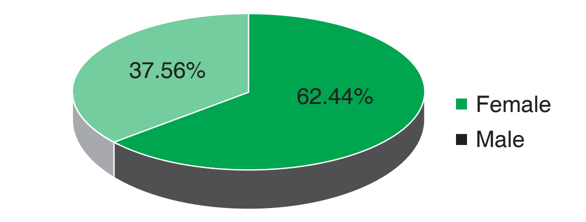

Figure 01: Sex distribution of suspected UTI cases enrolled in this study (N=221)

Out of 221 suspected UTI patients, 108 (48.87%) showed positive results for urine culture & the remaining 113 (51.13%) were negative (Figure: 02). Among the culture-positive patients, 75 (69.44%) were female & 33 (30.56%) were male. The majority [39 (36.12%)] of the culture-positive cases were in the age group 31-45 years, followed by 24 (22.22%) were in the group 16-30 years (Table 01).

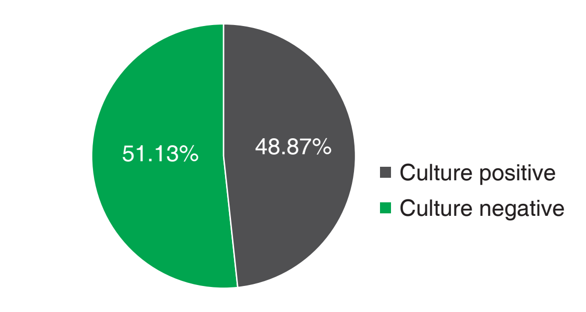

Figure 02: Percentage of positive & negative culture cases (N=221)

Table 01: Age & sex-wise distribution of culture-positive patients (n=108)

Age in years	Male (n= 33) (Number & %)	Female (n=75) (Number & %)	Total culture-positive patients (n=108)
≤ 15	4 (12.1%)	7 (9.33%)	11 (10.12%)
16 – 30	7 (21.21%)	17 (22.66%)	24 (22.22%)
31 – 45	11 (33.33%)	28 (37.33%)	39 (36.12%)
46 – 60	6 (18.18%)	10 (13.33%)	16 (14.82%)
≥ 60	5 (15.12%)	13 (17.33%)	18 (16.66%)
Total	**33 (30.56%)**	**75 (69.44%)**	**108 (100%)**

Among the 108 positive cultures, 103 (95.37%) had antimicrobial (single bacterial species) growth & only 5 (4.63%) showed polymicrobial (mixed) growth, each of which showed a pair of 2 different bacterial species. So, 108 culture-positive plates yielded a total of 113 bacterial isolates (Table 02). E. coli 50 (44.24%) was the most predominant bacterial isolate, followed by Klebsiella spp. 18 (15.92%), Enterococcus spp. 16 (14.15%), Pseudomonas spp. 09 (7.95%), Coagulase negative Staphylococcus (CONS)- 08 (7.07%), Staphylococcus aureus 6 (5.30%), Enterobacter spp. 04 (3.61%), & Proteus spp. 02 (1.70%) (Table 03).

Analyzing the bacterial isolates, it was evident that the majority 83 (73.45%) were gram-negative bacilli, whereas only 30 (26.54%) were gram-positive cocci (Table 03). 5 mixed growths showed, a pair of E. coli & Klebsiella in 02, E coli & Enterococci in 02, E. coli & pseudomonas in 01 culture positive plate. The susceptibility pattern of 11 selected antibiotics against gram-positive cocci & 13 selected antibiotics against gram-negative bacilli are shown in Table 04 & Table 05 respectively.

Table 02: Different nature of bacterial growths among positive culture (n=108) & total number of bacterial isolates

Nature of bacterial growth	Number of growth & percentage	Number of bacterial isolates
Unimicrobial (single bacterial species)	103 (95.37%)	103
Polymicrobial (mixed bacterial species)	5 (4.63%) Each of the mixed growths showed a pair of 2 different bacteria	10
Total	**108**	**113**

Table 03: Distribution of Gram-reactive organisms among total bacterial isolates (n=113)

Gram reactive bacteria	Bacterial isolates	Number & percentage
Gram-positive cocci	Enterococcus spp.	16 (14.15%)
	Coagulase -negative staphylococcus (CONS)	8 (7.07%)
	Staphylococcus aureus	6 (5.30%)
Total gram - positive cocci		**30 (26.54%)**

Gram negative bacilli	E. coli	50 (44.24%)
	Klebsiella spp.	18 (15.92%)
	Pseudomonas spp.	9 (7.96%)
	Enterobacter spp.	4 (3.61%)
	Proteus spp.	2 (1.70%)
Total gram - negative bacilli		**83 (73.45%)**

Table 04: Sensitivity pattern of isolated gram-positive bacteria causing UTI.

Antibiotics	Enterococcus (n= 16)		CONS (n=08)		S. aureus (n= 06)	
	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)
Gentamicin	7 (43.7%)	9 (56.3%)	4 (50%)	4 (50%)	3 (50%)	3 (50%)
Ciprofloxacin	8 (50%)	8 (50%)	3 (37.5%)	5 (62.5%)	3 (50%)	3 (50%)
Levofloxacin	7 (43.7%)	9 (56.3%)	6 (75%)	2 (25%)	5 (83.3%)	1 (16.7%)
Doxycycline	9 (56.3%)	7 (43.7%)	4 (50%)	4 (50%)	4 (66.7%)	2 (33.3%)
Amoxiclav	9 (56.3%)	7 (43.7%)	5 (62.5%)	3 (37.5%)	2 (33.3%)	4 (66.7%)
Ceftriaxone	7 (43.7%)	9 (56.3%)	4 (50%)	4 (50%)	4 (66.7%)	2 (33.3%)
Cefepime	10 (62.5%)	6 (37.5%)	3 (37.5%)	5 (62.5%)	3 (50%)	3 (50%)
Meropenem	11 (68.7%)	5 (31.3%)	6 (75%)	2 (25%)	4 (66.7%)	2 (33.3%)
Vancomycin	14 (87.5%)	2 (12.5%)	8 (100%)	0 (0%)	5 (83.3%)	1 (16.7%)
Linezolid	15 (93.8%)	1 (6.25 %)	7 (87.5 %)	1 (12.5%)	6 (100%)	0 (0%)
Nitrofurantoin	5 (31.3%)	11(68.7%)	4 (50 %)	4 (50%)	2 (33.3%)	4 (66.7%)

Enterococcus spp. was the most frequently isolated gram-positive cocci, which showed higher sensitivity to Linezolid (93.8%), Vancomycin (87.5%), Meropenem (68.7%), followed by Cefepime (62.5%). It showed lower sensitivity to Nitrofurantoin (31.3%), Levofloxacin (43.7%), gentamicin (43.7%), Ceftriaxone (43.7%) & Ciprofloxacin (50%). Enterococci spp. showed slightly higher sensitivity (56.3%) to both Doxycycline & Amoxiclav (Table 04).

Coagulase-negative staphylococcus (CONS) displayed higher sensitivity towards Vancomycin (100%), Linezolid (87.5%), Meropenem (75%), Levofloxacin (75%) & relatively lower sensitivity to Nitrofurantoin (50%), Doxycycline (50%), Ceftriaxone (50%), Gentamicin (50%) & very poor sensitivity towards Cefepime (37.5%) & Ciprofloxacin (37.5%). CONS showed slightly higher sensitivity to Amoxiclav (62.5%) (Table 04).

S. aureus had a very high sensitivity (100%) to Linezolid, followed by 83.3% sensitivity to Vancomycin, Levofloxacin & moderately high sensitivity (66.7%) to Meropenem, ceftriaxone, Doxycycline. Relatively lower sensitivity (50%) was documented towards Ciprofloxacin, Gentamicin & Cefepime. It had a very poor sensitivity (33.3%) towards Amoxiclav & Nitrofurantoin (Table 04).

All the Isolated Gram-negative bacilli (GNB) showed high sensitivity to Amikacin (E. coli-88%, Klebsiella-88.8%, Pseudomonas-77.8%, Enterobacter- 100% & Proteus-100%). GNB showed similar higher sensitivity towards Meropenem also. E. coli & Pseudomonas showed higher sensitivity (90 % & 88.9% respectively) to Piperacillin-Tazobactam. GNB also had a good sensitivity to Gentamicin (E. coli-74%, klebsiella & Pseudomonas- 66.7%, Enterobacter- 75%), except for the Proteus (only 50% sensitivity to gentamicin) (Table 05).

All isolated GNB displayed a lower sensitivity towards Amoxiclav (E. coli- 56%, klebsiella-38.8%, pseudomonas-11.1%, Enterobacter- 25% & proteus-00%), Azithromycin (E. coli- 34%, Klebsiella & proteus-50%, Pseudomonas- 33.3%, Enterobacter- 25%) & a very low sensitivity towards Cefuroxime (E. coli-38%, Klebsiella-27.7%, pseudomonas-11.1%, Enterobacter-25% & Proteus-0.0%) (Table 05).

3rd generation cephalosporins – Ceftriaxone & Cefotaxime were poorly sensitive against E. coli (50%, 42% respectively), Klebsiella (38.8% & 44.4% respectively), Pseudomonas (22.2% & 33.3% respectively), Enterobacter (50% & 50% respectively) & Proteus (50% & 50% respectively). Ceftazidime also displayed a very low sensitivity against Klebsiella (33.3%), Enterobacter (25%), and Proteus (0.0%) & relatively higher sensitivity against E. coli (58%) & Pseudomonas (66.6%) (Table 05).

Almost all isolated GNB showed poor sensitivity to Ciprofloxacin (Klebsiella & pseudomonas- 44.4%, Enterobacter & Proteus- 50%), except E. Coli which showed slightly higher sensitivity (64%) to ciprofloxacin. E. coli, Klebsiella & proteus showed relatively higher sensitivity to Levofloxacin (70%, 61.1% & 100% respectively) but the sensitivity pattern of Enterobacter & Pseudomonas towards Levofloxacin was as low as their sensitivity to ciprofloxacin (Table 05).

Nitrofurantoin showed poor sensitivity against Klebsiella (27.7%) & Proteus (50%) but it displayed a relatively better sensitivity pattern against E. coli (58%), Pseudomonas (66.7%) & Enterobacter (75%).

Table 05: Sensitivity pattern of isolated gram-negative bacteria causing UTI.

Antibiotics	E. coli (n=50)		Klebsiella (n=18)		Pseudomonas (n=9)		Enterobacter (n=4)		Proteus (n=2)	
	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)	S (%)	R (%)
Amikacin	44 (88%)	6 (12%)	16(88.8%)	2 (11.2%)	7 (77.8%)	2(22.2%)	4 (100%)	0 (00%)	2 (100%)	0 (00%)
Gentamicin	37 (74%)	13 (26%)	12(66.7%)	6 (33.3%)	6 (66.7%)	3(33.3%)	3 (75%)	1 (25%)	1 (50%)	1 (50%)
Ciprofloxacin	32 (64%)	18 (36%)	8 (44.4%)	10(55.6%)	4 (44.4%)	5(55.6%)	2 (50%)	2 (50%)	1 (50%)	1 (50%)
Levofloxacin	35 (70%)	15 (30%)	11(61.1%)	5 (38.9%)	4 (44.4%)	5(55.6%)	2 (50%)	2 (50%)	2 (100%)	0 (00%)
Azithromycin	17 (34%)	33 (66%)	9 (50%)	9 (50%)	3(33.35%)	6(66.7%)	1 (25%)	3 (75%)	1 (50%)	1 (50%)
Nitrofurantoin	29 (58%)	21 (42%)	5 (27.7%)	13(72.2%)	6(66.7%)	3(33.3%)	3 (75%)	1 (25%)	1 (50%)	1 (50%)
Amoxiclav	28 (56%)	22 (44%)	7 (38.8%)	11(61.1%)	1 (11.1%)	8(88.9%)	1 (25%)	3 (75%)	0 (00%)	2 (100%)
Ceftriaxone	25 (50%)	25 (50%)	7 (38.8%)	11(61.1%)	2 (22.2%)	7(77.8%)	2 (50%)	2 (50%)	1 (50%)	1 (50%)
Cefotaxime	21 (42%)	29 (58%)	8 (44.4%)	10(55.6%)	3(33.35%)	6(66.7%)	2 (50%)	2 (50%)	1 (50%)	1 (50%)
Cefuroxime	19 (38%)	31 (62%)	5 (27.7%)	13(72.2%)	1 (11.1%)	8(88.9%)	1 (25%)	3 (75%)	0 (00%)	2 (100%)
Ceftazidime	29 (58%)	21 (42%)	6 (33.3%)	12(66.7%)	6 (66.7%)	3(33.3%)	1 (25%)	3 (75%)	0 (00%)	2 (100%)
Meropenem	43 (86%)	07 (14%)	16(88.9%)	2 (11.1%)	7(77.8%)	2(22.2%)	4 (100%)	0 (00%)	2 (100%)	0 (00%)
Piperacillin-Tazobactum	45 (90%)	05 (10%)	NU	NU	8(88.9%)	1(11.1%)	NU	NU	NU	NU

Discussion

The present study demonstrated a higher percentage of female patients (62.44%) over male patients (37.56%) among the total suspected UTI cases. This finding corroborates well with a recent report from a teaching hospital in Bangladesh, where among the suspected UTI cases majority (59.37%) were female & 40.63% were male.[11]

We documented 48.87% (108/221) cases were positive for urine culture, which is almost similar to the study done at a tertiary care hospital in Uttarakhand, India having 49.1% (166/338) positivity for urine culture.[15] Sharmin et al. documented 46.66% positive urine culture also among children, which is very much consistent with present findings.[16] In contrast, a slightly higher (55%) urine culture positivity was reported by Biswas et al.[17] & a relatively lower rate (36.1%) of positive urine culture was recorded by a study at a tertiary care hospital in Haripur, Pakistan. The inclusion of only outpatients' samples may explain this lower rate of positive urine culture in this study.[18] On the contrary to our study, a report from a tertiary care hospital in Dhaka city reflected a very high rate (90.37%) of positive urine culture. The inclusion of urine samples having significant pyuria (≥ 5 pus cells /HPF) from catheterized UTI patients can be a good explanation for this very high rate of positive culture.[19]

This study recorded that the majority (69.44%) of culture-positive patients were female. A study at a tertiary care hospital in Dhaka, Bangladesh also showed female predominance (58.2%) among culture-positive UTI patients.[1] Ascending infection due to short urethra, the wrong practice of cleaning the perineum forward from the anus to vulva & sexual intercourse may be responsible for this higher frequency of UTI in females.[7] Longer urethra & presence of some natural antimicrobial substances in the prostatic fluid may explain the lower frequency of UTI in the male population.[20] Present studies documented the highest number (39/108; 36.12%) of culture-positive UTI patients were in the middle age group 31-45 years, which is very much consistent with the findings of Arina et al[19]. A study from a tertiary care hospital in Dhaka city demonstrated that 32.9% of culture culture-positive UTI patients were middle-aged people (within 21-40 years)[1], which is very similar to our findings.

This study recorded that most of the positive urine culture (95.37%; 103/108) yielded single bacterial species (unimicrobial growth) & only 4.63% (5/108) had polymicrobial growths, which is almost similar to the documentation by Haque et al.[11] Another study at a tertiary care hospital in Dhaka, Bangladesh documented 94.05% (95/101) of the culture-positive plates showed unimicrobial bacterial isolate & only 5.95% (6/101) had polymicrobial growth which is again in agreement with present findings.[21] 5 polymicrobial growths of our study showed a pair of E. coli & Klebsiella in 2, E. coli & Enterococci in 2, E. coli & Pseudomonas in 1 culture-positive plates which is almost similar to the report by R Parveen et al.[21]

In our study, E. coli (44.24%) was the most frequently isolated bacterial pathogen, followed by Klebsiella spp. (15.92%) & Enterococcus spp. (14.15%) which is nearly similar to the isolation pattern reported by Sohely et al., where E. coli (53.57%) was the most predominant pathogen, followed by Klebsiella spp. (17.86%) & Enterococcus spp. (10.71%).[16] Ritu Saha et al. also reported E. coli (42.8%) as the most frequently isolated bacteria in urine culture[7] & a study at a teaching hospital in Bangladesh again documented E. coli (59.30%) as the predominant bacterial pathogen among the UTI cases.[11] Apart from E. coli, Klebsiella spp. & Enterococcus spp. this study also reported Pseudomonas (7.96%), Enterobacter spp. (3.61%) & Proteus spp. (1.70%), which is very much consistent with the findings of Sohely et al.[16]

We also isolated Coagulase negative staphylococcus (CONS) (7.07%) as uropathogen, which is almost similar to the findings of Arina et al., showing 6.96% CONS isolated from catheterized patients in a tertiary care hospital in Dhaka, Bangladesh.[19] In contrast to our documentation, Haque et al. found a relatively higher (19.09%) isolation rate of CONS (S. saprophyticus).[11] Ritu Saha et al. also showed a much higher percentage of CONS (35.4%) in their study, which was done at a maternal & child healthcare hospital in Bangladesh.[7] CONS like S. saprophyticus which is a frequent colonizer in rectum, urethra, cervix & gastrointestinal tract, is considered as the 2nd most common bacterial etiology of UTI in sexually active young women of reproductive ages.[22] This may explain the very high isolation rate of CONS in this study.

Apart from CONS, 5.30% of S. aureus was also isolated in our study. Similar to our findings, 10.6% of S. aureus was documented in a study at a tertiary care hospital in Dhaka.[1] Sabita R. et al. reported a relatively lower percentage of S. aureus (2%) causing UTI in adolescent & adult women in their study.[23] From our study it is evident that gram-negative bacilli (73.45%) had predominated over gram-positive cocci (26.54%) as the etiology of UTI, which is very similar to the findings of Arina et al. showing a majority of the isolates (78.69%) were gram-negative bacilli. Ritu Saha et al. also reported that 61.7% of the bacterial isolates were gram-negative bacilli causing UTI in a maternal & child healthcare hospital in Bangladesh.[7]

Analyzing the sensitivity pattern of isolated Gram-positive organisms, it becomes evident that Enterococcus spp. showed higher sensitivity to Linezolid (93.8%) & Vancomycin (87.5%), moderate sensitivity to Meropenem (68.7%), Cefepime (62.5%), Doxycycline (56.3%) & Amoxiclav (56.3%), lower sensitivity to Ciprofloxacin (50%), Gentamicin (43.7%), Levofloxacin (43.7%), Ceftriaxone (43.7%) & a very poor sensitivity towards Nitrofurantoin (31.3%), which corroborates well with the documentation of Ritu Saha et al.[7] In our study, sensitivity pattern of S. aureus was more or less similar to Enterococci, except that it showed higher sensitivity to Levofloxacin (83.3%), Ceftriaxone (66.7%) & relatively lower sensitivity to Amoxiclav (33.3%) & cefepime (50%). Arina et al. reported that S. aureus was highly sensitive to Levofloxacin (100%) & poorly sensitive to Amoxiclav (25%)[19], which is very much in agreement with present findings. Ritu Saha et al. documented S. aureus was moderately sensitive to Ceftriaxone (62.5%) & it had lower sensitivity (31.1%) to cefepime[7] which is also in consistent with our study.

The present study documented that CONS had 50% sensitivity towards Gentamicin and ceftriaxone & only 37.5% sensitivity to Ciprofloxacin, which is nearly very similar to the report of Haque et al. where the sensitivity of CONS (S. saprophyticus) towards Gentamicin, Ceftriaxone & Ciprofloxacin was 52.63%, 55.26% & 36.84% respectively.[11] In contrast to these reports, Arina et al. documented relatively much lower sensitivity of CONS to Ceftriaxone (11.17%) & Ciprofloxacin (29.42%).[19] We found that CONS was moderately sensitive to Amoxiclav (62.5%), Doxycycline (50%) & poorly sensitive to Cefepime (37.5%). Ritu Saha et al.[7] also reported a very similar sensitivity pattern of CONS towards Amoxiclav (66.95), Doxycycline (46.5%) & cefepime (26.1%). CONS showed good sensitivity to Levofloxacin (75%), Meropenem (75%) & a very high sensitivity to Vancomycin (100%), Linezolid (87.5%). Similar to this report, Arina et al. also recorded that CONS had a higher sensitivity towards Levofloxacin (82.36%), Vancomycin (100%) & Linezolid (100%).[19] In our study CONS displayed relatively good sensitivity to Nitrofurantoin (50%) than Enterococcus spp. (31.3%) & S. aureus (33.3%). Similarly, Ritu Saha et al. documented that 56.4% of CONS were sensitive to Nitrofurantoin.[7] In contrast, Haque et al. reported much higher sensitivity (81.58%) of CONS (S. saprophyticus) to Nitrofurantoin.[11]

All Isolated Gram-negative bacilli (GNB) showed higher sensitivity to Amikacin (E. coli-88%, Klebsiella- 88.8%, Pseudomonas-77.8%, Enterobacter- 100% & Proteus-100%) & they displayed a very similar sensitivity pattern towards Meropenem also. Similar to our findings, Ritu Saha et al. documented that GNB was highly sensitive to Amikacin & Meropenem, except

Pseudomonas, which showed relatively decreased sensitivity towards Amikacin (68.8%).[7] Arina et al. reported that all GNB were highly sensitive to Meropenem (E. coli- 85.7%, Klebsiella- 80.9%, Pseudomonas- 87.1%, Enterobacter- 93.7% & Proteus- 94.4%)[19], which is again in accordance to present findings. A study done at a tertiary care hospital in Dhaka showed that GNB had relatively lower sensitivity towards Meropenem (E. coli-59.1%, Klebsiella-66.7% & Pseudomonas-40%)[1], which is completely in contrast to our documentation.

E. coli & Pseudomonas showed higher sensitivity (90 % & 88.9% respectively) to Piperacillin-Tazobactam. All GNB also showed good sensitivity towards Gentamicin (E. coli-74%, klebsiella & Pseudomonas- 66.7%, Enterobacter- 75%), except Proteus, which had only 50% sensitivity to gentamicin. Ritu Saha et al. also documented a very similar pattern of sensitivity of GNB towards Piperacillin-Tazobactam & Gentamicin.[7] In contrast to our findings, Arina et al. reported that all GNB were highly resistant to Gentamicin (E. coli- 57.8%, Klebsiella- 57.1%, Pseudomonas- 56.41% & Proteus- 61.1 resistant), except Enterobacter which was only 31.2% resistant to Gentamicin.[19]

We found a lower sensitivity pattern of GNB towards Amoxiclav (E. coli- 56%, klebsiella -38.8 %, pseudomonas -11.1 %, Enterobacter- 25% & proteus-0.0%). GNB had a very similar lower sensitivity trend to Cefuroxime also. GNB were also poorly sensitive to Azithromycin (E. coli- 34%, Klebsiella & proteus- 50%, Pseudomonas- 33.3%, Enterobacter- 25%). This is in agreement the with study of Khanam et al., who also reported a much lower sensitivity pattern of GNB towards Amoxiclav, azithromycin & cefuroxime.[1] Isolated GNB showed poor sensitivity to Ciprofloxacin (Klebsiella & pseudomonas- 44.4%, Enterobacter & Proteus- 50%), except E. coli which showed slightly higher sensitivity (64%), which is very much consistent with the findings of Sohely et al.[16] E. coli, Klebsiella & proteus showed relatively higher sensitivity to Levofloxacin (70%, 61.1% & 100% respectively) but sensitivity pattern of Enterobacter & Pseudomonas towards Levofloxacin was as low as their sensitivity to ciprofloxacin. This is also true for the study done by Ritu Saha et al.[7] & Nahar et al.[24]

The present study showed that Klebsiella & Proteus had lower sensitivity to nitrofurantoin (27.7% & 50% respectively) but E. coli, Pseudomonas & Enterobacter displayed a much better sensitivity (58%, 66.7% & 75% respectively). Haque et al. showed a very similar sensitivity pattern of GNB towards nitrofurantoin, except for Enterobacter which had relatively poor sensitivity to nitrofurantoin (50%)[11] than our documentation. Akram et al. reported that Klebsiella was 24% sensitive to nitrofurantoin, which is very similar to our findings but E. coli had only 20% sensitivity, which is very much oppositive to our result.[25] Biswas et al documented that E. coli was 100 % resistant to nitrofurantoin, whereas Proteus & Klebsiella were 100% sensitive[17], which is a contrast in comparison to our study. So, the sensitivity pattern of GNB towards nitrofurantoin varies among different studies.

3rd generation cephalosporins – ceftriaxone & cefotaxime were poorly sensitive against E. coli (50%, 42% respectively), Klebsiella (38.8% & 44.4% respectively), Pseudomonas (22.2% & 33.3% respectively), Enterobacter (50% & 50% respectively) & Proteus (50% & 50% respectively). Haque et al. showed a very similar low sensitivity pattern of isolated GNB towards ceftriaxone in their study done at a teaching hospital in Bangladesh.[11] Ritu Saha et al. also documented poor sensitivity of GNB to both ceftriaxone & cefotaxime, except for Proteus, which had slightly increased sensitivity to ceftriaxone (64.5%) & cefotaxime (67.7%).[7] Kumar et al. reported a lower sensitivity of E. coli (37.5%) & a very poor sensitivity of Klebsiella (14.2%) towards ceftriaxone[26], which is again in agreement with our study.

We found that another 3rd generation of cephalosporin-ceftazidime displayed a very low sensitivity against Klebsiella (33.3%), Enterobacter

(25%), Proteus (0.0%) & relatively higher sensitivity against E. coli (58%) & Pseudomonas (66.6%). Akram et al. reported that ceftazidime showed good sensitivity against E. coli (69%) & Pseudomonas (67%), which is almost similar to our documentation.[25] On the contrary, Khanam et al. reported relatively lower sensitivity of E. coli (50%) & Pseudomonas (30%) to ceftazidime.[1] A study done on catheterized patients in a tertiary care hospital in Bangladesh, documented lower sensitivity of Klebsiella (33.34%), and Enterobacter (25%) to ceftazidime, which is completely consistent with our report. That study also showed lower sensitivity of E. coli (22.1%) & Pseudomonas (28.2%) to ceftazidime[19], which is much opposite to our findings.

Gradually, uropathogens are acquiring resistance to the most frequently used antimicrobials[16], which is reflected in our as well as in other studies. Selective drug pressure is one of the most important causes behind the occurrence of resistant bacterial strains. The use of antibiotics (like- cotrimoxazole, and ciprofloxacin) in livestock is also responsible for the emergence of antimicrobial resistance.[27] In Bangladesh, dispensing of antibiotics is not restricted to prescriptions of registered physicians only, rather they are widely available over the counter throughout the country. It leads to the irrational use of many life-saving antibiotics, triggering the emergence of drug-resistant mutants.[28] Actually, antibiotic Sensitivity patterns are altering day by day, which varies from one healthcare center to another even within the same city[16] & also significantly varies between different geographic areas.[29] So, proper knowledge of the antimicrobial sensitivity pattern of uropathogens in a particular area is of paramount importance in designing effective antibiotic therapy.[7]

This study was done by analyzing the retrospective laboratory data only. So, one of the important shortcomings of our study was that we failed to categorize UTI patients whether complicated or uncomplicated, due to lack of clinical information. Moreover, we could not separate community-acquired, nosocomial & catheter-associated UTIs. We admit that some bacterial species could not be isolated & identified due to lack of laboratory facilities. Furthermore, MIC was not done for the determination of antimicrobial susceptibility.

Conclusion & Recommendations

E. coli, Klebsiella & Enterococcus spp. are the most frequently isolated uropathogens at our hospital. UTI with CONS cannot be overlooked also. Amikacin, meropenem, piperacillin-tazobactam & sometimes gentamicin can be a good choice for UTIs caused by gram-negative bacilli. Levofloxacin can also be considered except for Pseudomonas spp. For gram-positive cocci vancomycin, linezolid are most sensitive molecule, but it must be used with caution to avoid the emergence of resistance. 3rd generation cephalosporins failed to show promising responses to both gram-positive & negative organisms. Nitrofurantoin was not so effective against gram-positive organisms but it showed a good response to some gram-negative bacilli.

As uropathogens are gaining resistance to commonly used antimicrobials in developed as well as developing countries, sensitivity patterns in a defined geographical area should be determined annually to establish an effective guideline for physicians. For treating UTIs, antibiotics must be selected according to the culture & sensitivity report. Physicians should prescribe empirical therapy, considering the recent antibiogram of a particular area. Moreover, it is also very essential to develop a national policy to undertake ‘Antimicrobial stewardship programs’ including all levels of healthcare providers to prevent the occurrence of drug resistance.

Acknowledgment

We are very much grateful to all doctors, technicians & staff of the clinical pathology & microbiology laboratory of Islami Bank Hospital (IBH), Khulna.

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