SAS Journal of Medicine
Abbreviated Key Title: SAS J Med
ISSN 2454-5112
Journal homepage: https://saspublishers.com

OPEN ACCESS

Medicine

Frequency of Carbapenem Resistance in UTI Patients in a Tertiary Level Hospital

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DOI: https://doi.org/10.36347/sasjm.2024.v10i09.025 | **Received:** 11.08.2024 | **Accepted:** 17.09.2024 | **Published:** 23.09.2024
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Abstract **Original Research Article**

***Background*:** Urinary tract infections (UTIs) remain the common infections diagnosed in outpatients as well as hospitalized patients. Current knowledge on antimicrobial susceptibility pattern is essential for appropriate therapy. Extended-Spectrum Beta-Lactamase (ESBL) producing bacteria may not be detected by routine disk diffusion susceptibility test, leading to inappropriate use of antibiotics and treatment failure. The aim of this study was to determine the distribution and antibiotic susceptibility patterns of bacterial strains isolated from patients with community acquired urinary tract infections (UTIs) at Comilla Medical College Hospital, Comilla as well as identification of ESBL producers in the population of different uropathogens. ***Objectives*:** To obseve the frequency of carbapenem resistance in UTI patients in a tertiary level hospital. ***Methods*:** This cross sectional observational study was done on inpatients and outpatients department of Comilla Medical College Hospital, Comilla in 6 months' period. Formal ethical approval was taken before commencement of the study. Adult patients presenting with features of UTI were approached and finally selected in accordance to selection criteria. Convenience sampling technique was applied to enroll the total 100 study population. Following describing the purpose, methods and benefits of study written consent was taken from each patient. All patients were subjected to detail history, clinical examination and relevant investigation. Value of clinical investigations were noted on questionnaire. Following data collection, all were verified and prepared for data entry. Final analysis was done by using SPSS version 19. ***Results*:** Out of 100 patients attending in Comilla Medical College Hospital with symptoms suggestive of UTI, 31% had culture positive. Our study showed a high prevalence of UTI in females (61%) than in males (39%). Most common symptom was urgency (88%) followed by abdominal pain (77%), dysuria (67%) and fever (66%). DM was an important comorbid condition which was present in 34% patients. In this study, the most predominant isolated organism was E. coli (86%). In this study the Carbapenems (e.g.meropenem, imipenem,) shows maximum efficacy. These antibiotics shows their efficacy against 96-99% of the uropathogens. ***Conclusion*:** Uropathogens resistance to antibiotic has now become a public health concern in Bangladesh [24]. This study showed that Carbapenems resistance is not so common in our country but resistance is increasing due to irrational use. According to the guideline of IDSA, most of the antibiotics used in our study should not be used as empirical treatment of UTI and our standard treatment guidelines for UTI is not sufficient which requires a large scale study.

Keywords: Urinary Tract Infections (UTIs), Antimicrobial Susceptibility Pattern, Extended-Spectrum Beta-Lactamase (ESBL), Carbapenems, Uropathogens.

INTRODUCTION

UTI is a common bacterial infection, often contributes to a frequent cause of morbidity in out-patients as well as hospitalized patients [1]. It is a serious ailment in human due to the frequency, recurrence and difficulty in eradication [2]. It poses great challenge because it may involve kidney, ureters, bladder and

urethra [2]. It has been estimated that 150 million people are infected with UTI per annum worldwide [3]. In 2007, in the United States alone, there were an estimated 10.5 million office visits for UTI symptoms3. UTI is describes as a bacteriuria with urinary symptom. It is more common in female than in male as female urethra structurally found more effective for bacterial entry, proximity of genital tract and urethra, adherence of urethral mucosa to the mucopolysaccharide lining [4]. More than 95% of UTI are caused by bacteria [5]. Common bacterial pathogens causing UTI are Escherichia coli (E. coli) Klebsiella spp, Enterococci Pseudomonas, Proteus, Staphylococcus, Saprophyticus. Complicated UTI exhibits a broader bacterial spectrum as the cause of infection [6]. Gram negative bacteria are mostly responsible for UTI [7]. Among the gram negative bacteria E. coli is the most common etiological agent [8]. It is accounting for 75-90% of UTI in both outpatients and inpatients [9]. Most of these organisms are a normal part of the human gut flora. The etiology of UTI and its antibiotic resistance have been changing over the past years [10]. In most of the cases of UTI initially treated with empirical antimicrobial agents before getting the urine culture and sensitivity report. This empirical treatment may increase antibiotic resistance by frequent misuse which helps in emerging and spreading of resistant bacterial strains throughout the world [9-11]. There are various reports available in last two decades about changing pattern of pathogen and their sensitivity pattern to routinely used antibiotics which makes the situation miserable [5]. Increasing antibiotic resistance among uropathogens to commonly prescribed drugs has become a global reality. Resistance occurs in intestinal bacteria due to antibiotic therapy for treating infections outside the urinary tract [6]. The irrational use of antibiotics has an influence in the spread of antimicrobial resistance among bacteria [7, 8]. Different study shows that organisms are developing resistance to carbapenem class of antibiotics [1]. UTI with carbapenem resistant bacteria sometimes very difficult to treat. Persons with weakened immune systems or prolonged hospitalizations are at greater risk for acquiring carbapenem-resistant UTI. Carbapenem resistance to pathogenic organisms causing UTI were first identified in the United States around 2001[1]. In Bangladesh, carbapenem resistance are estimated to make up about 4% of gram negative infections [1] and it is responsible for approximately 9,000 infections per year [2]. Patients infected with unrecognized carbapenem resistant organism serves as reservoirs for transmission during health-care-associated infection outbreaks [2]. Pathogenic microorganisms causing UTI develope resistance to carbapenem in two ways. The first group produces carbapenemase enzymes that degrade carbapenems before they are able to kill the bacteria. Carbapenemase genes can easily be transferred between bacteria. The second group resist the effects of carbapenem through a combination of mechanisms, such as by way of beta-lactamase production and point mutations. It is unclear if the two groups differ in terms of transmissibility or virulence [3]. However, because carbapenamase producing microorganism can transfer carbapenemase genes to other gram negative bacteria, this group carries the added concern of spreading resistance to previously non-resistant bacteria. Carbapenem-resistant microorganism, and in particular, carbapenemase-producing KPC type have become globally endemic [12, 13]. One cohort study in Brazil described 118 patients were with Carbapenem resistant enterobacteriace infections in a period of almost four years [14]. Carbapenem resistance pattern is increasing day by day both globally and locally. Local data regarding this resistance pattern is not available. So it is necessary to find out Carbapenem resistance pattern in our region.

OBJECTIVES

General Objective

- To find out the frequency of Ccarbapenem resistance in UTI patients in a tertiary level hospital.

Specific Objective

- To study clinical profile and risk factors of urinary tract infections
- To study the antibiotic susceptibility pattern
- To assess the extent of drug-resistance in isolates.

Inclusion Criteria:

- All patients fulfilling the criteria of UTI (dysuria, frequency, fever and pain in lower abdomen)
- Age > 12 years
- Both sexes
- Urine culture positive for bacteria and/or urine for R/M/E –plus cell>10/HPF
- Those who are agree to take part in this study.

Exclusion Criteria:

- Age below 12 years.
- Those who refuse to take part in this study
- Those patients were on antibiotic advised to were excluded from this study
- Patients presented with active menstruation, PID, tubo-ovarian diseasge, appendicitis, colitis, severe other infections e.g. sepsis

Procedure of data analysis interpretation

After collection, data editing and clearing will be done manually and prepared for data entry and analysis by using SPSS version 19. Student t-test will be done to compare the groups. P values <0.5 will be considered as significant.

Procedure of preparing and organizing materials

Adult patients presenting with features of UTI were approached and finally selected in accordance to selection criteria. Convenience sampling technique was applied to enroll the total 100 study population.

Following describing the purpose, methods and benefits of study written consent was taken from each patient. All patients were subjected to detail history, clinical examination and relevant investigation. Freshly voided midstream clean-catch urine samples were collected from each patient of different age and sex groups in a sterile screw capped universal container. The specimen was labeled and transported to the microbiology laboratory for processing and cultured within half an hour of collection. A modified semi-quantitative technique using a standard calibrated bacteriological loop of urine was performed to transfer the 0.001 ml of sample on Blood agar and MacConkey agar media. After allowing the urine to be absorbed into the agar, the plates were then inverted and incubated aerobically at 37°C for 24 hours. The plates were then examined macroscopically for bacterial growth. The colony count was done using semi quantitative method. Number of colonies obtained is multiplied by 1000 to obtain the colony forming units (cfu)/ml [15]. A significant growth is considered if the number of colony is $>10^5$ colony forming unit (CFU)/ml. Colonial appearance and morphological characters of isolated bacteria was noted and Gram staining was done for identification of the isolated organisms. The characteristic bacteria on the culture media were aseptically isolated. Antimicrobial sensitivity tests were carried out by disc diffusion technique using Muller Hinton Agar. Interpretation of results was expressed in sensitive and resistant depending upon the size of the zone of inhibition. The antibiotics used for susceptibility testing in our study were meropenem and imipenem including amoxycillin, amoxyclav, cefotaxime, ceftriaxone, cephalexin, nalidexic acid, nitrofurantoin, mecillinum, amikacin, cefixime, ceftazidime, cefuroxime, cephradine ciprofloxacin cotrimoxazole, gentamycin, tazobactum.

Ethical implication:

- The study was approved by the ethical review committee of Comilla Medical College Hospital.
- Helsinki declaration was followed during whole study.
- Consent was obtained after briefing the study purpose in Bangla to all respondents.
- It was made clear to them that they are free to take part or decline at any part of the study.
- All personal information related to patient was kept confidential.
- Investigation cost was from the patient who can afford and assistance for poor patient.

RESULTS

The study was conducted among 100 patients attending at indoor and outdoor of department of Medicine in Comilla Medical College Hospital to observe frequency of Carbapenem resistance.

Table 1: Age distribution of the study patients (N=100)

Variable	Age range	Frequency	Percentage
Age	20-30 years	16	16
	31-40 years	08	08
	41-50 years	12	12
	51-60 years	12	12
	61-70 years	28	28
	71-80 years	16	16
	81-90 years	04	04

Table 1 showed age distribution of the study patients. From this table it is seen that 28% patients of the study population were in the age group of 61-70 years followed by 16% in the age group of 20-30 years and 71-80 years. Only 4% were in the age group of 81-90 years.

Table 2: Residential habit and economic status of the study patients (N=100)

Factors	Frequency	Percentage	P Value
Residential habit			
Urban	33	33	P <0.05*
Rural	67	67	
Total	100	100	
Economic status			
Lower class	5	5	P <0.05*
Middle class	91	91	
Higher class	4	4	
Total	100	100	

Table 2 showed residential habit and economic status of the study population. In this study 67% of patients of the study population were from rural area which is statistically higher (p<0.05) than patients from urban area. Economic status of the study population shows 91% of the responders were from middle class

which was statistically higher than patients from higher and lower class group (P<0.05).

Table 3: Baseline characteristics of study patients (N=100)

Factors	Frequency	Percentage	P value
Marital status			
Married	82	82	P <0.05*
Unmarried	18	18	
Total	100	100	
Sexual activity			
Active	72	72	P <0.05*
Not active	28	28	
Total	100	100	
Education status			
Educated	68	68	P <0.05*
Not educated	32	32	
Total	100	100	

Table 3 showed marital status, sexual activity & educational status of study population. It can be seen from this table that 82% were married among the study patients which is statistically higher (p<0.05) than unmarried patients. It can also be seen from the table that 72% were sexually active which is also statistically higher than sexually inactive patients. This difference was also statistically significant (0<0.05). It was also observed most of the patients were educated which consists of 68% of the study patients. Number of educated patients were statically higher than illiterate patients (p <0.05).

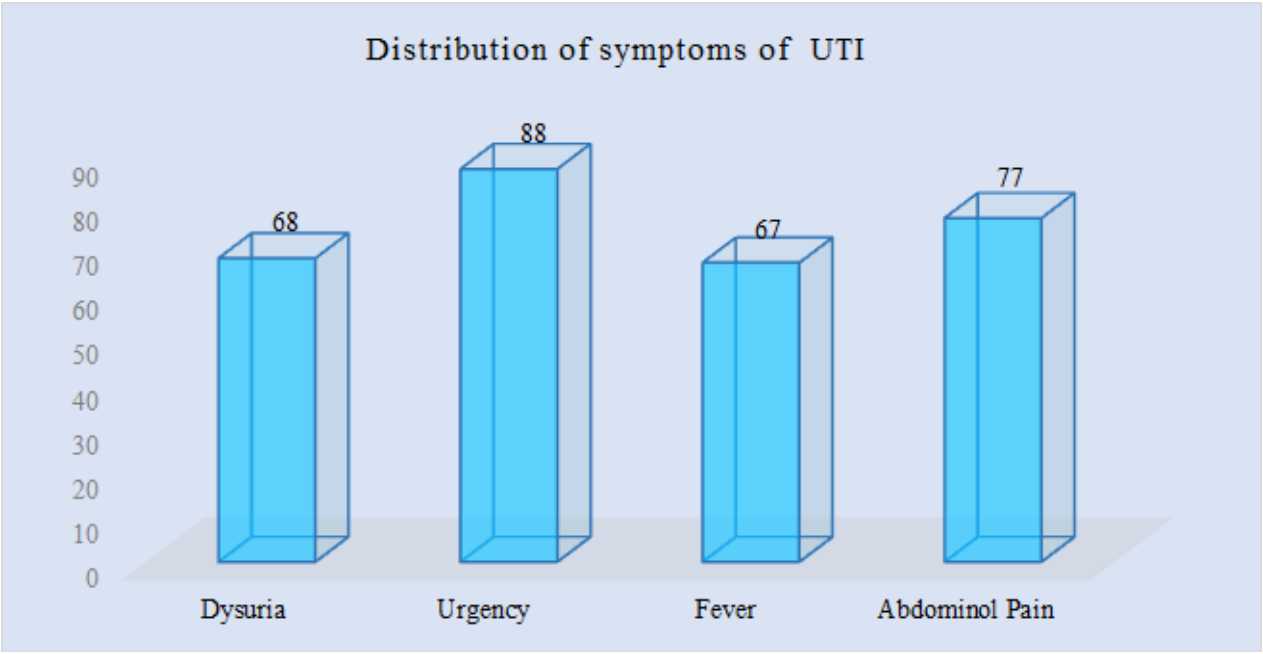

Figure I: Column chart showed frequency of different symptoms of UTI of the study patients (N=100)

Figure I showed it can be seen from the bar diagram that most frequently observed symptoms was urgency which was found among 88% of the study patients. Second most common symptom was abdominal pain which was found in 77% of the study patients. Dysuria and fever were noted in 68% and 67% of study patients respectively.

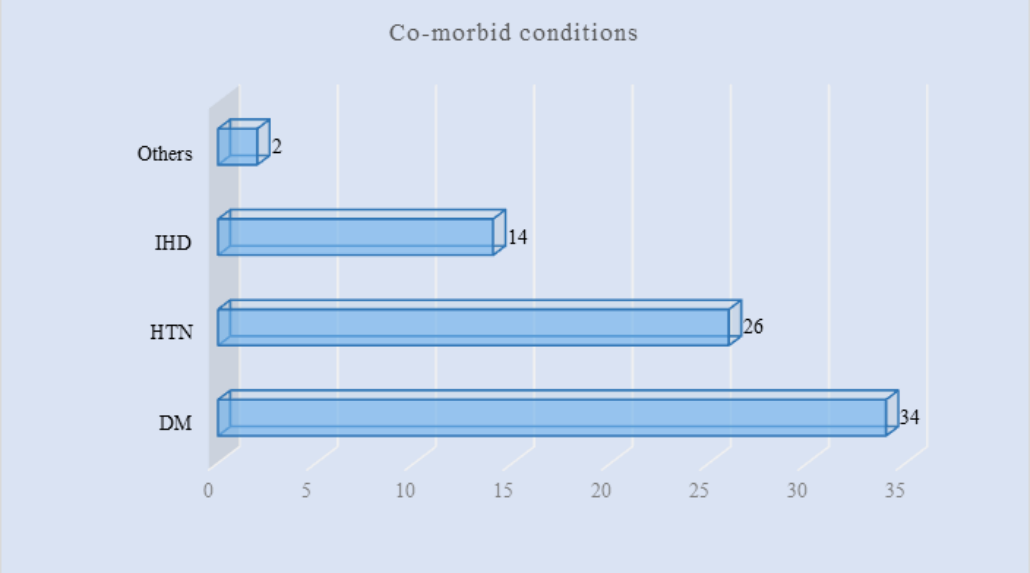

Figure II: Bar chart showed comorbidity in UTI patients (N=100)

Figure II showed comorbidity among the UTI patients. Most common comorbid condition was DM which was found in 34% of the study patients. From this figure hypertension and IHD were observed in 23% and 14% of the patients respectively.

Table 4: Distribution of bacterial pathogen among the study patients, (N=100)

Pathogen	Male (%)	Female (%)	Total
E. coli	35	51	86
Klebsiella	2	7	9
Enterococcus	1	4	5

Table 4 showed distribution of uropathogens among the study patients. Culture report of urine samples shows most common pathogen is E. coli which was found in 86% as of the study patients. It was also observed that Klebsiella and Enterococci were isolated from 9% and 5% of the urine sample respectively. It can also be noted that maximum number of isolates were distributed among the females. Number of isolates from urine samples of female were stastically ($p<0.05$) than that of male.

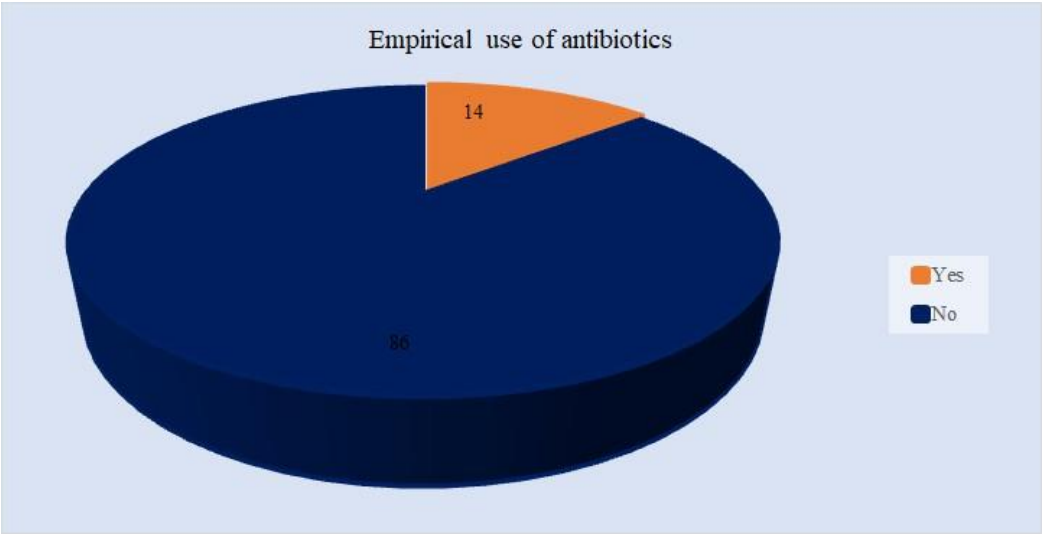

Figure III: Pie chart showed Empirical use of Antibiotic by study population before inclusion in the study (N=100)

Figure III showed about 10% persons were treated with antimicrobials before inclusion in the study. However, majority (90%) of them were not treated before the culture and sensitivity.

Table 5: Antibiotic resistant pattern among the UTI patients (N=100)

Antibiotics	Resistance (%)	Total (%)
Imipenum	1	100
Meropenum	4	100
Amicacin	8	100
Tazobactum	1	100
Gentamycin	10	100
Nitrofurantine	12	100
Mecillium	12	100
Colistin	16	100
Ceftazidim	47	100
Cotrimazole	47	100
Ciprofloxacin	48	100
Ceftriaxon	55	100

Table 5 showed antibiotic resistance pattern of the study patients. It is seen from the table that imipenem and meropenem resistance were found in 1% and 4% of the study patients respectively. It can also be observed that high degree of resistance against commonly used antibiotics-ceftazidime, cotrimazole, ciprofloxacin, and Ceftriaxone were found. In vitro resistance of the isolates to these antibiotics were varied from 47% to 55%.

Table 6: Antibiotic sensitivity pattern among the UTI patients (N=100)

Antibiotics	Sensitivity (%)	Total (%)
Imipenum	99	100
Meropenum	96	100
Amicacin	92	100
Tazobactum	99	100
Gentamycin	90	100
Nitrofurantine	88	100
Mecillium	88	100
Colistin	84	100
Ceftazidim	53	100
Cotrimazole	53	100
Ciprofloxacin	52	100
Ceftriaxon	45	100

Table 6 showed antibiotic sensitivity pattern of the study patients. From this table it is seen that, Carbapenems that include imipenems (99.5%), meropenum (96%) were more sensitive for UTI patients than others. It was also noted that amikacin, tazobactum, gentamycin, nitrofurantoin, and mecillinum, were found to be highly effective antibiotic against most of the uropathogens.

DISCUSSION

This observational cross sectional study was done among 100 patients in medicine department of Comilla Medical College Hospital. This study shows that 28% patients of the study population were in the age group of 61-70 years followed by 16% in the age group of 20-30 years and 71-80 years. Only 4% were in the age group of 81-90 years. From previous study Ferede G *et al*., and Harsha TR also found that elderly patients were more in risk of development of UTI and antibiotic resistance [2-4]. Therefore, this study was similar with the previous one. We also found that most of the patients were female which consists of 61% of total study population. It has been extensively reported that adult women have a higher prevalence of UTI than men, principally owing to anatomical and physical factors [15-17]. This finding corresponds with the finding of medical textbook like Medical bacteriology that UTI is common for females [18-20]. In this study 67% of patients of the study population were from rural area than patients from urban area. Economic status of the study population shows 91% of the responders were from middle class groups because lower class groups may not able to attend tertiary level hospital due to their poverty and higher class groups attend private hospital for their ailment. This similar kind of findings were found in previous studies like Harsha TR *et al*., and Arjunan M *et al*., where the study was conducted in the rural area and had middle class patients more [4, 5]. In this study, 82% were married among the study population than unmarried population. Again among the study population 72% were sexually active which is also statistically higher than sexually inactive patients. In previous study like Prakash D *et al*., (2013) and Harsha TR *et al*., (2013) also found the similar findings [3, 4]. Which also matched the findings of sexual active persons were vulnerable for UTI. In this study it is shown that 68% responders were educated because educated patients are more conscious

about their health status and they admitted themselves in hospital much more than illiterate patients. This study shows that the common symptoms of UTI were urgency, abdominal pain, burning sensation, dysuria, fever [21-23]. This typical finding matched with our findings regarding the symptoms among the study patients. Where we found, most frequently observed symptoms was urgency which was found among 88% of the study patients. Second most common symptom was abdominal pain which was found in 77% of the study patients. Dysuria and fever were noted in 68% and 67% of study patients respectively. Some studies show UTI is common in diabetic patients [24]. Though it is not being found significantly associated with other co-morbidities like HTN, IHD. That is likely dissimilar with our findings. We found DM was the most common co-morbidities among the study population which is 34% of patients. From this figure hypertension and IHD were observed in 23% and 14% of the patients respectively. Culture report of urine samples shows most common pathogen is E. coli which was found in 86% as of the study patients. It was also observed that Klebsiella and Enterococci were isolated from 9% and 5% of the urine sample respectively. From previous studies this finding matched with that. However, prevalence of this study much higher than previous studies in 2011 where E. coli was 75% [9]. In this study the Carbapenems (e.g.meropenem, imipenem,) shows maximum efficacy where meropenem and imipenem show their efficacy against 96% and100% of the uropathogens respectively. A retrospective cohort study was conducted in Premier Perspective database (2009-2013) of 175 US hospitals. They included all adult patients with community-onset culture-positive urinary tract infection (UTI), among 40,137 patients and found (3.1%) were Carbapenem resistance [25, 26]. In our study we also found that amikacin, tazobactum, gentamycin, nitrofurantoin, and mecillinum were found to be highly effective antibiotic against most of the uropathogens. In this study it was shown that, imipenem and meropenem resistance were found in 1% and 4% of the study patients respectively. It can also be observed that high degree of resistance against commonly used antibiotics- ceftazidime, cotrimazole, ciprofloxacin, and Ceftriaxone were found. In vitro resistance of the isolates to these antibiotics were varied from 47% to 55%. Kyle D *et al*., found cases of UTI diagnosed at Cleveland Clinic, a 1,400-bed academic medical center in Cleveland, Ohio, between 2006 and 2012 through a retrospective review of microbiology. They identified 108 individuals; 22 (20%) had UTIs due to Carbapenem-resistance [27, 28]. In others study, Senewiraten *et al*., [29] found in1624 hospitalized patients, a total of 454 (25%) isolates were recovered [29]. The most common isolate was E. coli (n=276, 61%). Out of 276 E. coli isolates, 156 (57%) were multi-drug resistant isolates and 21 (7.6%) of the isolates were resistant to carbapenems. All of carbapenem-resistant E. coli (CRE) were MDR. Significant drug resistances were observed among CRE compared to other MDR E. coli. This study showed that the resistance is more than that of our study. However, the dissimilarities of drug resistance and sensitivities were different or present due to different causal organism found in different studies.

LIMITATION OF THE STUDY

The study has some limitation which are as follows:

- The study was conducted upon a small size of population which is too small to conclude over this commonest and burning issue.
- The study was conducted in a very limited area to represent.
- The study time was very limited to represent as overall result.

RECOMMENDATIONS

- This study shows that Carbapenems have some resistance in that local community. So we have to be more cautious to rational use of Carbapenems.
- Community awareness program should be undertaken for adherence to treatment protocol considering bacterial resistance and emerging multidrug resistant strains.
- It is necessary to conduct a regional research on the culture and sensitivity patterns of the bacteria

CONCLUSION

Out of 100 patients attending in Comilla Medical College Hospital with symptoms suggestive of UTI, 31% had culture positive. Our study showed a high prevalence of UTI in females (61%) than in males (39%). Most common symptom was urgency (88%) followed by abdominal pain (77%), dysuria (67%) and fever (66%). DM was an important comorbid condition which was present in 34% patients. In this study, the most predominant isolated organism was E. coli (86%). In this study the Carbapenems (e.g.meropenem, imipenem,) shows maximum efficacy. These antibiotics shows their efficacy against 96-99% of the uropathogens. Uropathogens resistance to antibiotic has now become a public health concern in Bangladesh [24]. This study shows that Carbapenems resistance (which considered last and powerful antimicrobials) are not uncommon in our country due to irrational use. According to guideline by Infectious Diseases Society of America (IDSA) in the year 2011, an antibiotic is no longer recommended for empirical treatment of acute UTI if there is > 20% resistance prevalence to that particular antibiotic[26]. According to this guideline of IDSA, most of the antibiotics used in our study should not be used for empirical treatment of acute UTI and our standard treatment guidelines for UTI is not sufficient which requires a large scale study.

REFERENCES

1. Wagenlehner, F. M., & Naber, K. G. (2006). Treatment of bacterial urinary tract infections:

presence and future. *European urology*, *49*(2), 235-244.
2. Ferede, G., Yismaw, G., Wondimeneh, Y., & Sisay, Z. (2012). The prevalence and antimicrobial susceptibility pattern of bacterial uropathogens isolated from pregnant women. *Eur J Exp Biol*, *2*(5), 1497-1502.
3. Prakash, D., & Saxena, R. S. (2013). Distribution and antimicrobial susceptibility pattern of bacterial pathogens causing urinary tract infection in urban community of meerut city, India. *International scholarly research notices*, *2013*(1), 749629.
4. Harsha, T. R., Vijaya, D., & Nagarathnamma, T. (2013). Bacteriological profile & comparison of antibiotic susceptibility pattern of uropathogens by conventional disk diffusion and Rapid mini API method. Journal of pharmaceutical and biomedical sciences. *J Pharm Biomed Sci*, *30*(30), S7-S12.
5. Arjunan, M., Al-Salamah, A. A., & Amuthan, M. (2010). Prevalence and antibiotics susceptibility of uropathogens in patients from a rural environment, Tamilnadu. *Am J Infect Dis*, *6*(2), 29-33.
6. Kashef, N., Djavid, G. E., & Shahbazi, S. (2010). Antimicrobial susceptibility patterns of community-acquired uropathogens in Tehran, Iran. *The Journal of Infection in Developing Countries*, *4*(4), 202-206.
7. Adler, A., & Carmeli, Y. (2011). Dissemination of the Klebsiella pneumoniae carbapenemase in the health care settings: tracking the trails of an elusive offender. *MBio*, *2*(6), 10-1128.
8. Munoz-Price, L. S., Poirel, L., Bonomo, R. A., Schwaber, M. J., Daikos, G. L., Cormican, M., ... & Quinn, J. P. (2013). Clinical epidemiology of the global expansion of Klebsiella pneumoniae carbapenemases. *The Lancet infectious diseases*, *13*(9), 785-796.
9. Saleh, A. A., Ahmed, S. S., Ahmed, M., Sattar, A. N. I., & Miah, M. R. A. (2009). Changing trends in uropathogens and their antimicrobial sensitivity pattern. *Bangladesh Journal of Medical Microbiology*, *3*(2), 9-12.
10. Dyer, I. E., Sankary, T. M., & Dawson, J. A. (1998). Antibiotic resistance in bacterial urinary tract infections, 1991 to 1997. *Western journal of medicine*, *169*(5), 265-268.
11. Kallen, A. (2013). Vital signs: CRE. *MMWR*, *62*(9), 165-170.
12. Bhargava, A., Hayakawa, K., Silverman, E., Haider, S., Alluri, K. C., Datla, S., ... & Kaye, K. S. (2014). Risk factors for colonization due to carbapenem-resistant Enterobacteriaceae among patients: exposed to long-term acute care and acute care facilities. *Infection Control & Hospital Epidemiology*, *35*(4), 398-405.
13. Goodman, K. E., Simner, P. J., Tamma, P. D., & Milstone, A. M. (2016). Infection control implications of heterogeneous resistance mechanisms in carbapenem-resistant Enterobacteriaceae (CRE). *Expert review of anti-infective therapy*, *14*(1), 95-108.
14. De Oliveira, M. S., De Assis, D. B., Freire, M. P., do Prado, G. B., Machado, A. S., Abdala, E., ... & Levin, A. S. (2015). Treatment of KPC-producing Enterobacteriaceae: suboptimal efficacy of polymyxins. *Clinical Microbiology and Infection*, *21*(2), 179-e1.
15. Urine Culture-General Procedure: University of Nebrasaka Media Center division of Laboratory Science Clinical Lab.Scince Program CLS 418/CLS 419.
16. Gonzalez, C. M., & Schaeffer, A. J. (1999). Treatment of urinary tract infection: what's old, what's new, and what works. *World journal of urology*, *17*, 372-382.
17. Stamm, W. E., & Norrby, S. R. (2001). Urinary tract infections: disease panorama and challenges. *The Journal of infectious diseases*, *183*(Supplement_1), S1-S4.
18. Kumar, M. S., Lakshmi, V., & Rajagopalan, R. (2006). Occurrence of extended spectrum ß-lactamases among Enterobacteriaceae spp. isolated at a tertiary care institute. *Indian journal of medical microbiology*, *24*(3), 208-211.
19. Khan, A. U., & Musharraf, A. (2004). Plasmid-mediated multiple antibiotic resistance in Proteus mirabilis isolated from patients with urinary tract infection. *Medical science monitor: international medical journal of experimental and clinical research*, *10*(11), CR598-602.
20. Sleigh, J. D., & Timbury, M. C. (1986). Notes on Medical Bacteriology. 2nd edition. 1986, pp. 212-218. Churchill Livingstone Inc., 1560 Broadway, New York.
21. Better Health Channel, (2014). Urinary tract infections (UTI) - Better Health Channel. [online] Available at: http://www.betterhealth.vic.gov.au/bhcv2/bhcarticles.nsf/pages/urinary_tract_infections [Accessed 8 Apr. 2015].
22. Jerry, R., & Balentine, F. (2013). Urinary Tract Infection: UTI Symptoms and Treatment. [online] MedicineNet. Available at: http://www.medicinenet.com/urinary_tract_infection/article.htm [Accessed 8 Apr. 2015].
23. Karriem-Norwood, V. (2012). Urinary Tract Infections (UTIs) Causes, Symptoms, Treatments. [online] Webmd.com. Available at: http://www.WebMD.com/women/guide/your-guide-urinary-tract-infections [Accessed 8 Apr. 2015].
24. Jarvis, T. R., Chan, L., & Gottlieb, T. (2014). Assessment and management of lower urinary tract infection in adults. *Australian Prescriber*, *37*(1), 7-9.
25. Yasmeen, B. N., Islam, S., Islam, S., Uddin, M. M., & Jahan, R. (2015). Prevalence of urinary tract infection, its causative agents and antibiotic sensitivity pattern: A study in Northern International Medical College Hospital, Dhaka. *Northern*

International Medical College Journal, *7*(1), 105-109.

26. García-Morúa, A., Hernández-Torres, A., Salazar-de-Hoyos, J. L., Jaime-Dávila, R., & Gómez-Guerra, L. S. (2009). Community-acquired urinary tract infection etiology and antibiotic resistance in a Mexican population group. *Revista Mexicana de Urología*, *69*(2), 45-48.
27. Majumder, M. I., Ahmed, T., Hossain, D., & Begum, S. A. (2014). Bacteriology and antibiotic sensitivity patterns of urinary tract infections in a tertiary hospital in Bangladesh. *Mymensingh Med J*, *23*(1), 99-104.
28. Urine Cultures- General Procedure: University of Nebraska Medical Center Division of Laboratory Science Clinical Laboratory Science Program CLS 418/CLS 419.
29. Senewiratne, B., Senewiratne, K., & Hettiarachchi, J. (1973). Bacteriology and Antibiotic Sensitivity in Acute Urinary-Tract Infections in Ceylon. *The Lancet*, *302*(7823), 222-225.