IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS)
e-ISSN:2278-3008, p-ISSN:2319-7676. Volume 13, Issue 3 Ver. IV (May. – June. 2018), PP 41-47
www.iosrjournals.org

Emergence of Meropenem Resistance in Pathogens Recovered From Urine Cultures in Bangladesh

Mohammad Asaduzzaman*[1], Md. Mahbub Ullah[1], Sayed Md. Redwan[1], Md. Jahangir Alam[1], Farha Matin Juliana[2], Nazmul Hossain[1], Biswajit Das[1], Runa Asma[3], Manoj Mandal[4] and Khokon Kumar Dutta[4]

[1]*Department of Biochemistry, Primeasia University, Banani, Dhaka, Bangladesh*
[2]*Department of Biochemistry and Molecular Biology, Jahangirnagar University, Savar, Dhaka, Bangladesh*
[3]*Department of Laboratory Medicine, IBN SINA Diagnostic & Consultancy Center, Badda, Dhaka, Bangladesh*
[4]*Department of Biochemistry and Molecular Biology, Bangabandhu Sheikh Mujibur Rahman Science & Technology University, Gopalganj, Bangladesh*
Corresponding Auther: Mohammad Asaduzzaman

Abstract: *Meropenem is a broad spectrum antibiotic and it's efficacy is much higher against in Urinary tract Infection. It is a vital public health problem in the world along with developing country like Bangladesh is resistance of antibiotics to different types of bacteria and the rates of these bacterial resistances are changing for various antibiotic therapies. Our aim was to assess the efficacy of Meropenem against uropathogens. A total of 12943 urine samples were collected in 2016 (Jan-Dec) and out of which 1018 (8.0%) were bacteriologically positive. Among the isolated uropathogens, 94.7% were gram negative and 5.3% were gram positive organism. Male were found more prone to get UTI under 10 years and more than 50 years; and between 21-50 years of age females were more affected than male. E. coli was the most prevalent (83.5%) isolate followed by Klebsiella spp. (6.5%), Staphylococcus aureus (2.8%), Pseudomonas spp. (2.3%), Enterococcus spp. (2.2%) and Proteus spp. (1.2%). The most predominant resistance organism Pseudomonas spp. (25%) in male and Acinetobacter spp. (100%) in female were found but here number of UTI patients were very few. The most predominant organism E. coli resistant to Meropenem was around 2.5% in male and 4.0% in female.*
Keywords*: Meropenem, Carbapenem, UTI, Resistance, Uropathogen.*

Date of Submission: 06-06-2018 Date of acceptance: 24-06-2018

I. Introduction

Antibiotic resistance is an increasing threat to life and morbidity and mortality. Urinary Tract Infection (UTI) is a predominant infection all over the world but it is more prevalent in developing south Asian countries like Bangladesh. Urinary Tract Infection (UTI) represents as one of the most common diseases encountered in medical practices these days and encompasses a broad range of clinical fields that are associated with a common finding of positive urine cultures. Besides every year about 150 million people are affected by UTIs. Worldwide at a cost of about US$6 billion and even UTIs have demonstrated significant morbidity and mortality. (1)

They are the second most common types of infection in humans accounting for 8.3 million doctor's visit annually in USA.(2) UTI can be nosocomially ubiquitous in clinical environment so that prevalence rate of uropathogens is being alarmingly accelerated.(1) Urinary tract infection is more common in female than male, because of the short length of the urethra and its proximity to anus. Pregnancy and sexual activity also make female more susceptible to UTI. Different factors like age, sex, immunosuppression and urological instruments may affect prevalence of UTIs.(3)

To prevent these pathogens, different types of antibiotics and their super generations are used irrespectively with different doses in misused and overused forms. So uropathogens are getting resistant to efficacious drugs adopting different mechanisms of mutations and genetic transformations.(4) The etiology of UTIs and the antibiotic susceptibility of urinary pathogens, both in community and hospitals, have been changing over the past years and recently, the antibiotic resistance has become a major global problem.(5) A large proportion of uncontrolled antibiotic usage has contributed to the emergence of resistant bacterial infections.(6)

The early introduction of effective drugs against bacterial infections in the last century has changed the medical behavior and has significantly reduced the mortality rates due to these agents. However, the widespread use of antibiotics has induced different mechanisms of bacteria resistance to these drugs.(7) Bacterial resistance is naturally developed, being a consequence of bacteria adaptation to the environment. The exposure of

microorganisms to different antibiotics increases the selective pressure and favors the development of resistance.[8] The most frequently prescribed antibiotics to treat UTIs are Carbapenem, sulfamethoxazole+trimethoprim, fluoroquinolones (ciprofloxacin or norfloxacin), 1st , 2nd and 3rd generations of cephalosporins, amoxicillin + clavulanate and nitrofurantoin.[1]

However, Meropenem is an antibiotic and sold under the brand name Merrem among others, is a broad-spectrum antibiotic used to treat a variety of bacterial infections. Some of these include Urinary tract Infection, meningitis, intra-abdominal infection, pneumonia, sepsis, and anthrax. It is also sometimes used before surgery and following a bite wound to try to prevent infection. Meropenem can be given by injection into a vein. It is in the carbapenem family of medications. Meropenem usually results in bacterial death through blocking their ability to make a cell wall.[9] Meropenem was patented in 1983.[10] It was approved for medical use in the United States in 1996.[9] It is on the World Health Organization's List of Essential Medicines, the most effective and safe medicines needed in a health system.[11] The wholesale cost is the developing world is between 3.44 and 20.58 USD per one gram vial as of 2015.[12] In the United Kingdom this amount costs the NHS about 16 pound in 2015.[13]

The spectrum of action includes many Gram-positive and Gram-negative bacteria (including Pseudomonas) and anaerobic bacteria. The overall spectrum is similar to that of imipenem, although meropenem is more active against Enterobacteriaceae and less active against Gram-positive bacteria. It works against extended-spectrum β-lactamases, but may be more susceptible to metallo-β-lactamases.[14] In 2017 the FDA granted approval for the combination of meropenem and vaborbactam to treat adults with complicated urinary tract infections.[15]

Meropenem is bactericidal except against Listeria monocytogenes, where it is bacteriostatic. It inhibits bacterial wall synthesis like other β-lactam antibiotics. In contrast to other beta-lactams, it is highly resistant to degradation by β-lactamases or cephalosporinases. In general, resistance arises due to mutations in penicillin-binding proteins, production of metallo-β-lactamases, or resistance to diffusion across the bacterial outer membrane.[16] Unlike imipenem, it is stable to dehydropeptidase-1, so can be given without cilastatin. In 2016 a synthetic peptide-conjugated PMO (PPMO) was found to inhibit the expression of New Delhi metallo-beta-lactamase, an enzyme that many drug-resistant bacteria use to destroy carbapenems.[17, 18]

It is the most effective drugs for UTI patients in Bangladesh for treatment of UTI patients. But now a days we see the drugs does not work against uropathogens as before works. Our aim of the study to see the efficacy of Meropenem against Urinary Tract Infection patients in selected areas (Badda, Gulshan, Baridhara, Rampura, Doyagonj, Gandaria, Jatrabari and Sayedabad) of Dhaka and Narayanganj city, Bangladesh.

II. Materials And Methods

Materials

Study Location:

This was a retrospective analysis of laboratory data routinely collected from the microbiology department of IBN SINA Diagnostic & Consultation Center, Badda, Dhaka-1212, Bangladesh from 1st January, 2016 to 31st December, 2016. The total sample volumes were 12943.

Methods

Sample Collection and Bacteriological Assessment:

Early morning midstream urine samples were collected aseptically from 12943 (Male-3638 & female-9305) patients. The urine samples were collected into sterile wide container (China) with screw cap tops. On the label were the name, age, sex and time of collection. All the patients were instructed on how to collect the urine samples aseptically and taken to the laboratory immediately for culture. In the diagnostic laboratory, each well mixed urine sample (1µL) was inoculated on MacConkey agar (Oxoid) and Blood agar (Oxoid) media plate under class-II laminar airflow (NUVO Sanaji Malzemelzeni, Imalat Vc Ticaret A.S, Turkey). The inoculum on the plate was streaked out for discrete colonies with a sterile wire loop sterilized by auto loop sterilizer (Germany) following standard procedures. The culture plates were incubated at 37°C by an incubator (Germany) for 48 hours and observed for the growth of bacteria through formation of colonies. All the bacteria were isolated and identified using morphological, microscopy (Japan) and biochemical tests like TSI (HiMedia), MIU (HiMedia) and Simmons Citrate (HiMedia) agar following standard procedures.[19]

Antibiotic Susceptibility Assessment:

The disc diffusion technique was used for antibacterial susceptibility testing of the isolates using commercial antibiotics containing discs. We used the commercial antibiotic disc Meropenem (10µg, Oxoid). Interpretation of results was done using zone sizes. Zones of inhibition for *Enterobacteriaceae* ≥23 mm was considered sensitive, 20-22 mm intermediate and ≤19 mm resistant, for *Staphylococcus* spp., *Pseudomonas* spp. and *Acinetobacter* spp. ≥19 mm was considered sensitive, 16-18 mm intermediate and ≤15 mm resistant.

Isolates were classified as either sensitive or resistant based on the definition of the Clinical and Laboratory Standard Institute.[20] Some laboratory stains of known sensitivity of *Staphylococcus aureus* ATCC 29213, *Enterococcus faecalis* ATCC 29212, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853 and *Streptococcus pneumoniae* ATCC 49619 were used as quality control strains for the antimicrobial discs.

Statistical Analysis:

Data were assessed using the Statistical Package for Social Science (IBM SPSS Statistics, version 18, IBM Corporation, SPSS Inc. Chicago, III, USA). The Trend chi square test for statistical comparisons between the groups.

III. Results

The total 12943 urine samples collected from patients, 1018 (8.0%) samples were positive and 11925 (92.0%) samples were negative at 2016 (January-December) in selected areas (Badda, Gulshan, Baridhara, Rampura, Doyagonj, Gandaria, Jatrabari, Sayedabad) of Dhaka, Bangladesh.

Tabel-1: Distribution of Urinary Tract Infection (UTI) patients by age groups and gender (n=1018)

Age (Years)	<10	11-20	21-30	31-40	41-50	51-60	61-70	71-80	81-90	>90
Male	39	4	14	13	23	34	50	33	5	2
Female	82	70	154	92	120	107	108	51	11	6
Total	121	74	168	105	143	141	158	84	16	8

In our study, table-1 showed the distribution table of urinary tract infection affected patients by their age groups and gender. The highest of the study subjects under goes to the 21-30 years age group (168 patients=154 female + 14 male) and followed by 61-70 years age group (158 patients=108 female + 50 male), 41-50 years age group (143 patients=120 female + 23 male), 51-60 years age group (141 patients= 107 females + 34 males) and <10 years age group (121 patients= 82 females + 39 males) respectively. Most prevalent frequency of female and male patients affected by uropathogens was found in 21-30 years and 61-70 years age group respectively.

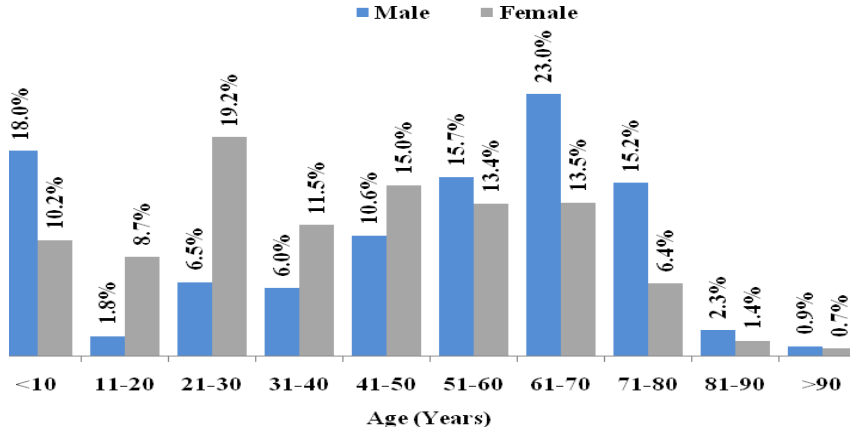

Figure-1: UTI percentage among different age groups of male (N=217) and female (N=801)

The percentage of male patients were more porne besides female patients (18.0% > 10.2%) under 10 years age groups. In between 11-20, 21-30, 31-40 and 41-50 years of age group female UTI infection (8.7%, 19.2%, 11.5% and 15.0% respectively) is higher than male (1.8%, 6.5%, 6.0% and 10.6% respectively). In between 51-60, 61-70 , 71-80 and 81-90 years age male infection (15.7%, 23.0%, 15.2% and 2.3% respectively) is higher than female (13.4%, 13.5%, 6.4% and 1.4% respectively). Above 90 years age male infection (0.9%) is higher than female (0.7%) but here number of patients were very few.

Table-2: Distribution of specific uropathogen mediated UTI among UTI patients

Organisms	Percentage (n=1018)		
	Male	Female	Total
E. coli	176(17.3%)	674(66.2%)	850(83.5%)
Proteus spp.	4(0.4%)	8(0.8%)	12(1.2%)
Pseudomonas spp.	11(1.1%)	12(1.2%)	23(2.3%)
Klebsiella spp.	12(1.2%)	54(5.3%)	66(6.5%)
Enterobacter spp.	1(0.1%)	9(0.9%)	10(1.0%)
Staph.aureus	4(0.4%)	24(2.4%)	28(2.8%)

Enterococcus spp.	8(.8%)	14(1.4%)	22(2.2%)
Acinetobacter spp.	1(0.1%)	0(0.0%)	1(0.1%)
Citrobacter spp.	0(0.0%)	1(0.1%)	1(0.1%)
Group B *Streptococcus*	0(0.0%)	1(0.1%)	1(0.1%)
Serratia spp.	0(0.0%)	2(0.2%)	2(0.2%)
Staph. saprophyticus	0(0.0%)	2(0.2%)	2(0.2%)
Total	217(21.3%)	801(78.7%)	1018(100%)

Table 2 showed that the most predominant organism *E. coli* 850 (male 176 and female 674) found in UTI patients. According to number or percentage distribution, the second prevalent organism was *Klebsiell*a spp. 66 (male 12 & female 54) followed by *Staphylococcus aureus* 28 (male 4 and female 24), *Pseudomonas* spp. 23 (male 11 and female 12), *Enterococcus* spp. 22 (male 8 and female 14), *Proteus* spp. 12 (male 4 and female 8) and *Enterobacter* spp. 10 (male 1 and female 9) respectively. In total bacteriologically positive cases, the most prone organism in male and female were *E. coli* (17.3% and 66.2 %) respectively. Moreover, all the isolated organisms were found highest in female except *Acinetobacter* spp. in contrast male patients. On the other hand the study showed that the total 21.3% male patients and 78.7% female patients were found.

Table-3: Prevalence of different uropathogens among male and female patients

Organisms	**Male (n=217)**		**Female (n=801)**	
	Number	**Percentage**	**Number**	**Percentage**
E. coli	176	81.1%	674	84.1%
Proteus spp.	4	1.8%	8	1.0%
Pseudomonas spp.	11	5.1%	12	1.5%
Klebsiella spp.	12	5.5%	54	6.7%
Enterobacter spp.	1	0.5%	9	1.1%
Staph.aureus	4	1.8%	24	3.0%
Enterococcus spp.	8	3.7%	14	1.7%
Acinetobacter spp.	1	0.5%	0	0.0%
Citrobacter spp.	0	0.0%	1	0.1%
Group B *Streptococcus*	0	0.0%	1	0.1%
Serratia spp.	0	0.0%	2	0.2%
Staph. saprophyticus	0	0.0%	2	0.2%
Total	217	100.0%	801	100.0%

In this study, the urinary tract infections of female patients (801) were more prone to male patients (217). In male, the most predominant uropathogen were *E. coli* (81.1%) followed by *Klebsiella* spp. (5.5%), *Pseudomonas* spp. (5.1%), *Enterococcus* spp. (3.7%), *Staphylococcus aureus* (1.8%), *Proteus* spp. (1.8%). In female, the most prevalent uropathogen were *E. coli* (84.1%) followed by *Klebsiella* spp. (6.7%), *Staphylococcus aureus* (3.0%), *Enterococcus* spp. (1.7%), *Pseudomonas* spp. (1.5%). The study noted that female patients were more infected by all of the isolated organism except *Acinetobacter* spp. but here the number were very few.

Table-4: Susceptibility pattern of Meropenem against uropathogens among female UTI patients (n=801)

Name of organisms	**Sensitive**		**Resistant**	
	Number	**Percentage**	**Number**	**Percentage**
E. coli	657	97.5%	17	2.5%
Proteus spp.	8	100.0%	0	0.0%
Pseudomonas spp.	9	75.0%	3	25.0%
Klebsiella spp.	50	92.6%	4	7.4%
Enterobacter spp.	9	100.0%	0	.0%
Staph.aureus	21	87.5%	3	12.5%
Enterococcus spp.	11	78.6%	3	21.4%
Citrobacter spp.	1	100.0%	0	0.0%
Group B *Streptococcus*	1	100.0%	0	0.0%
Serratia spp.	2	100.0%	0	0.0%
Staph. saprophyticus	2	100.0%	0	0.0%
Total	771	96.3%	30	3.7%

Table-4 showed that Meropenem sensitive against isolated uropathogenic bacteria in total male patients were 96.3% and rest of resistant 3.7%. All of them (100%) *Proteus* spp., *Enterobacter* spp., *Citrobacter* spp., Group B *Streptococcus*, *Serratia* spp and *Staph. saprophyticus* were sensitive to Meropenem but here the numbers were very few. On the other hand the most prevalent resistant organism was *Pseudomonas* spp. (25.0%). In contrast of frequency, *E. coli* was the most significant organism which was 97.5 % sensitive and 2.5 % resistant to Meropenem. However, the other isolated bacteria's sensitive pattern to Meropenem followed by *Pseudomonas* spp. (75.0%), *Klebsiella* spp. (92.6%), *Staphylococcus aureus* (87.5%) and *Enterococcus* spp.

(78.6%) and resistant pattern followed by *Staphylococcus aureus* (12.5%) , *Enterococcus* spp. (21.4 %) and *Klebsiella* spp. (7.4%) respectively.

Table-5: Susceptibility pattern of Meropenem against uropathogens among male UTI patients (n=217)

Name of organisms	Sensitive		Resistant	
	Number	Percentage	Number	Percentage
E. coli	169	96.0%	7	4.0%
Proteus spp.	4	100.0%	0	0.0%
Pseudomonas spp.	8	72.7%	3	27.3%
Klebsiella spp.	12	100.0%	0	0.0%
Enterobacter spp.	1	100.0%	0	0.0%
Staph. aureus	3	75.0%	1	25.0%
Enterococcus spp.	7	87.5%	1	12.5%
Acinetobacter spp.	0	0.0%	1	100.0%
Total	204	94.0%	13	6.0%

In our study table-5 showed that Meropenem sensitive against isolated uropathogenic bacteria in total female patients were 94.0% and rest of resistant 6.0%. All of them (100%) *Proteus* spp., *Klebsiella* spp. and *Enterobacter* spp. were sensitive to Meropenem but here the numbers were very few. On the other hand the most prevalent resistant organism was *Acinetobacter* spp. (100%) but here the numbers were very few. By contrast of frequency, *E. coli* was the most significant organism which was 96.0 % sensitive and 4.0 % resistant to Meropenem. However, the other isolated bacteria's sensitive pattern to Meropenem followed by *Pseudomonas* spp. (72.7%), *Staphylococcus aureus* (75.0%) and *Enterococcus* spp. (87.5%) and resistant pattern followed by *Pseudomonas* spp. (27.3%), *Staphylococcus aureus* (25.0%) & *Enterococcus* spp. (12.5%) respectively.

IV. Discussion

This study aimed to evaluate the pattern of antimicrobial susceptibility of bacteria isolated from patients with UTI seen at the IBN SINA diagnostic center, Badda, Dhaka, Bangladesh. Moreover, we have identified the crucial bacterial species associated with UTI and described the profile of resistance to Meropenem. It is important that clinicians are aware of the regional antibiotic resistance rates before initiating experimental antimicrobial therapy for UTI treatment, as it is well-described that urinary infection with a resistant pathogen is more likely to lead to bacteriological/clinical failures.[21] In our study, we tested total 12943 urine samples and 1018 (8.0%) were bacteriological positive and 11925 (92.0%) were bacteriological negative found.

In our study we found The highest of the study subjects under goes to the 21-30 years age group (168 patients=154 female + 14 male) and followed by 61-70 years age group (158 patients=108 female + 50 male), 41-50 years age group (143 patients=120 female + 23 male), 51-60 years age group (141 patients= 107 females + 34 males) and <10 years age group (121 patients= 82 females + 39 males) respectively. Most prevalent frequency of female and male patients affected by uropathogens was found in 21-30 years and 61-70 years age group respectively. According to frequency in total infected patients, we saw that mostly female patients are affected by uropathogens in all the age groups in contrast male patients. It was noted that the highest frequency of UTIs observed in women when compared to men, which is often attributed to a shorter urethra that facilitates colonization by these microorganisms.[1] Most prevalent frequency of female and male patients affected by uropathogens was found in 21-30 years and 61-70 years age group respectively. However, there were found significant difference between the age groups and sex of urinary tract infection patients at 5% ($P<0.05$).

In the fugure we saw the percentage of male patients were more porne in contrast female patients (18.0% > 10.2%) under 10 years age groups. Our finding is supported by the fact that uncircumcised male infants appear to be at increased risk of UTIs in the first three months of life. In a study of 100 otherwise healthy infants ranging in age from five days to eight months and admitted to the hospital because of a first known UTI. Most of the UTIs in infants younger than three months of age were in males, but female infants predominated thereafter. We also found in between 11-20, 21-30, 31-40 and 41-50 years of age group female UTI infection (8.7%, 19.2%, 11.5% and 15.0% respectively) is higher than male (1.8%, 6.5%, 6.0% and 10.6% respectively). In between 51-60, 61-70 , 71-80 and 81-90 years age male infection (15.7%, 23.0%, 15.2% and 2.3% respectively) is higher than female (13.4%, 13.5%, 6.4% and 1.4% respectively). Above 90 years age male infection (0.9%) is higher than female (0.7%) but here number of patients were very few. The most predominat age gorup was 21-20 years in female patients. Incidence of infection in females increases directly with sexual activity and child-bearing. In the women, 25-30% of women between 20-40 years of age will get UTIs. The anatomical relationship of the female urethra and the vagina makes it liable to trauma during sexual intercourse as well as bacteria been massaged up the urethra into the bladder during pregnancy and child birth. It has been reported in several studies that women who are sexually active, and especially if they use contraceptives, foams,

gels, diaphragm and spermicides which are known to promote greater colonization of the vagina are at higher risk of developing UTIs. Furthermore, another mechanism that could explain the lower frequency of UTI in men would be the prostatic fluid, which has antibacterial substances. We got 801 (78.7%) female and 217 (21.3%) male patients. However, there were found significant difference between the percentage of age groups and sex of urinary tract infection patients at 5% ($P<0.05$).

Table 2 showed that the most predominant organism *E. coli* 850 (male 176 and female 674) found in UTI patients. According to number or percentage distribution, the second prevalent organism was *Klebsiella* spp. 66 (male 12 and female 54) followed by *Staphylococcus aureus* 28 (male 4 and female 24), *Pseudomonas* spp. 23 (male 11 and female 12), *Enterococcus* spp. 22 (male 8 and female 14), *Proteus* spp. 12 (male 4 and female 8) and *Enterobacter* spp. 10 (male 1 and female 9) respectively. In total bacteriologically positive cases, the most prone organism in male and female were *E. coli* (17.3% and 66.2 %) respectively. Moreover, all the isolated organisms were found highest in female except *Acinetobacter* spp. in contrast male patients. On the other hand the study showed that the total 21.3% male patients and 78.7% female patients were found. There is fecal contamination of periurethral area, then the bacteria spreads on ascending through the bladder and causes cystitis. These infections of the lower urinary tract, in some cases, can affect the kidneys and cause acute pyelonephritis, which consequently may result in bacteremia and sepsis.[22]. However, there were found significant difference between the isolated organism and sex of urinary tract infection patients at 5% ($P<0.05$).

In this study, the urinary tract infections of female patients (801) were more prone to male patients (217). In male, the most predominant uropathogens were *E. coli* (81.1%) followed by *Klebsiella* spp. (5.5%), *Pseudomonas* spp. (5.1%), *Enterococcus* spp. (3.7%), *Staphylococcus* aureus (1.8%), *Proteus* spp. (1.8%). In female, the most prevalent uropathogens were *E. coli* (84.1%) followed by *Klebsiella* spp. (6.7%), *Staphylococcus aureus* (3.0%), *Enterococcus* spp. (1.7%), *Pseudomonas* spp. (1.5%). Several studies have shown that Escherichia coli is the major bacterial species associated with UTIs, and Klebsiella pneumoniae is the second most important bacteria in this type of infection[1]. The study noted that female patients were more infected by all of the isolated organism except Acinetobacter spp. but here the number were very few. However, there were found significant difference between the percentage and frequency of isolated organism and sex of urinary tract infection patients at 5% ($P<0.05$).

Treatment of urinary tract infections is becoming more complicated with an increase of the number of resistant strains to antibiotics and prevalence of antibiotic resistance mechanisms. Table-4 showed that Meropenem sensitive against isolated uropathogenic bacteria in total male patients were 96.3% and rest of resistant 3.7%. All of them (100%) *Proteus* spp., *Enterobacter* spp., *Citrobacter* spp., Group B *Streptococcus*, *Serratia* spp and *Staph. saprophyticus* were sensitive to Meropenem but here the numbers were very few. On the other hand the most prevalent resistant organism was Pseudomonas spp. (25.0%). In contrast of frequency, *E. coli* was the most significant organism which was 97.5 % sensitive and 2.5 % resistant to Meropenem. As Meropenem is in the carbapenem family of medications, It was very effective in most of the uropathogens, But it is very alarming subject to resistant a wide range of this drugs. It had observed that horizontal gene transfer is a factor in the emergence and spread of antimicrobial resistance in clinical isolates. Consequently, it has been suggested that the high prevalence of resistance to a particular antibiotic does not always reflect antibiotic consumption in a given environment.[1,23] However, the other isolated bacteria's sensitive pattern to Meropenem followed by *Pseudomonas* spp. (75.0%), *Klebsiella* spp. (92.6%), *Staphylococcus aureus* (87.5%) and *Enterococcus* spp. (78.6%) and resistant pattern followed by *Staphylococcus aureus* (12.5%) , *Enterococcus* spp. (21.4 %) and *Klebsiella* spp. (7.4%) respectively. There were no significant difference among the susceptibility pattern of Meropenem, isolated organism and sex of the patients at 5% ($P>0.05$).

In our study table-5 showed that Meropenem sensitive against isolated uropathogenic bacteria in total female patients were 94.0% and rest of resistant 6.0%. All of them (100%) *Proteus* spp., *Klebsiella* spp. and *Enterobacter* spp. were sensitive to Meropenem but here the numbers were very few. On the other hand the most prevalent resistant organism was *Acinetobacter* spp. (100%) but here the numbers were very few. By contrast of frequency, E. coli was the most significant organism which was 96.0 % sensitive and 4.0 % resistant to Meropenem. However, the other isolated bacteria's sensitive pattern to Meropenem followed by *Pseudomonas* spp. (72.7%), *Staphylococcus aureus* (75.0%) and *Enterococcus* spp. (87.5%) and resistant pattern followed by *Pseudomonas* spp. (27.3%), *Staphylococcus aureus* (25.0%) and *Enterococcus* spp. (12.5%) respectively. There were no significant difference among the susceptibility pattern of Meropenem, isolated organism and sex of the patients at 5% ($P>0.05$).

The knowledge on the regional pattern of bacterial resistance is critical to guide the medical staff to choose an appropriate antibiotic for the treatment of UTI patients.[24] Bacterial resistance has become a public health issue and has increasingly been associated with risk factors that put life in danger.[1] Awareness is needed of both the population and health professionals about the importance for the correct use of antibiotics, and it is mandatory to take into account the result of antibiotics susceptibility tests. The Meropenem use should be performed only after the microbial susceptibility confirmation, and it is necessary to find other alternatives for

the empirical treatment. The bacterial resistance prevention can be performed through control measures that limit the spread of resistant bacteria and the rational use of antimicrobial policy.

V. Conclusion

In conclusion, the results showed that there was a high prevalence of occurrence of urinary tract infection among patients of areas (Badda, Gulshan, Baridhara, Rampura, Doyagonj, Gandaria, Jatrabari and Sayedabad) of Dhaka and Narayanganj city, Bangladesh. Most of the bacteria were susceptible to Meropenem. The prescribed Meropenem antibiotic were still effective and safe against the uropathogens, but should be reserved for only complicated UTIs and should use to follow the antibiotic guidelines in order to prevent emergence of multi drug resistant organisms.

Reference

[1]. Jahangir Alam, Farha Matin Juliana, Md Rahimgir, Mohammad Nazir Hossain, Babry Fatema, Mohammad Asaduzzaman (2017). "Resistance Pattern of Ciprofloxacin against common Uropathogens in Selected Area of Dhaka city, Bangladesh." IOSR Journal of Nursing and Health Science(IOSR-JHNS), 6:5:52-57.

[2]. Annabelle TD, Jennifer AC (1999). Surveillance of pathogens and resistance patterns in urinary tract infection. Phil J Microbial Infect Dis. 28:11-4.

[3]. Iqbal T, Naqvi R and Akhter SF (2010). Frequency of urinary tract infection in renal transplant recipients and effect on graft function. J Pak Med Assoc. 60(10):826-829.

[4]. Laisa Ahmed Lisa, Dipak Kumar Paul, Sudhangshu Kumar Biswas, Nirmal Chandra barman and Shital Kumar Barman (2015). Drug Resistance Profiles of Potential Gram Negative Rods Isolated from Urinary Tract Infected (UTI) Patients of Bangladesh with Four South Asian Countries. Int J Pharma Sciences, 5(4):1160-1166.

[5]. Savita Jadhav, Arif Hussain, Savita Devi, Ashutosh Kumar, Sana Parveen, Nageshwari Gandham, Lothar H. Wieler, Christa Ewers, and Niyaz Ahmed (2011). Virulence characteristics and genetic affinities of multiple drug resistant uropathogenic Escherichia coli from a semi urban locality in India. PLoS One. 6(3):ee18063.

[6]. Grude N, Tveten Y and Kristiansen BE (2001). Urinary tract infections in Norway: bacterial etiology and susceptibility, a retrospective study of clinical isolates. Clin Microbiol Infect. 7:543-547.

[7]. Silveira GP, Nome F, Gesser JC, Sá MM and Terenzi H (2006). Estratégias utilizadas no combate a resistência bacteriana. Quím Nova. 29:844-55.

[8]. Santos NQ (2004). A resistência bacteriana no contexto da infecção hospitalar. Texto Contexto Enferm. 13:64-70.

[9]. "Meropenem". The American Society of Health-System Pharmacists. Retrieved 8 December 2017.

[10]. Fischer, Janos; Ganellin, C. Robin (2006). Analogue-based Drug Discovery. John Wiley & Sons. p. 497. ISBN 9783527607495.

[11]. "WHO Model List of Essential Medicines (20th List)" (PDF). World Health Organization. March 2017. Retrieved 29 June 2017.

[12]. "Single Drug Information". International Medical Products Price Guide. Retrieved 9 December 2017.

[13]. British national formulary : BNF 69 (69 ed.). British Medical Association. 2015. p. 379. ISBN 9780857111562.

[14]. AHFS Drug Information (2006 ed.). American Society of Health-System Pharmacists. 2006.

[15]. Commissioner, Office of the. "Press Announcements - FDA approves new antibacterial drug". www.fda.gov.

[16]. Mosby's Drug Consult 2006 (16 ed.). Mosby, Inc. 2006.

[17]. "New molecule knocks out superbugs' immunity to antibiotics". newatlas.com. Retrieved 2017-01-25.

[18]. K., Sully, Erin; L., Geller, Bruce; Lixin, Li,; M., Moody, Christina; M., Bailey, Stacey; L., Moore, Amy; Michael, Wong,; Patrice, Nordmann,; M., Daly, Seth. "Peptide-conjugated phosphorodiamidate morpholino oligomer (PPMO) restores carbapenem susceptibility to NDM-1-positive pathogens in vitro and in vivo". Journal of Antimicrobial Chemotherapy. doi:10.1093/jac/dkw476/2691388/peptide-conjugated-phosphorodiamidate-morpholino.

[19]. Cheesborough M (2006). District Laboratory practice in Tropical Countries, Cambridge United Press, UK, part 2, 7-106.

[20]. Clinical and Laboratory Standard Institute (2006). Methods for the Dilution Antimicrobial Susceptibility Tests for Bacteria. That Grow Aerobically. Approved Standards, Seventh Edition (M07), Villanova, MO 7-A 7.

[21]. Zhanel GG, Hisanaga TL, Laing NM, DeCorby MR, Nichol KA, Weshnoweski B, Johnson J, Noreddin A, Don E.Low DE, Karlowsky JA, Hoban DJ (2006). Antibiotic resistance in Escherichia coli outpatient urinary isolates: final results from the North American Urinary Tract Infection Collaborative Alliance (NAUTICA). Int J Antimicrob Agents. 27(6):468-75.

[22]. Mobley H (2016). Measuring Escherichia coli Gene Expression during Human Urinary Tract Infections. Pathogens. 5(1):7.

[23]. Ako-Nai AK, Adeyemi FM, Aboderin OA, Kassim OO (2005). Antibiotic resistance profile of staphylococci from clinical sources recovered from infants. Afr. J. Biotechnol. 4(8):816-822.

[24]. The knowledge on the regional pattern of bacterial resistance is critical to guide the medical staff to choose an appropriate antibiotic for the treatment of UTI patients.

Mohammad Asaduzzaman "Emergence of Meropenem Resistance in Pathogens Recovered From Urine Cultures in Bangladesh "IOSR Journal of Pharmacy and Biological Sciences (IOSR-JPBS) 13.3 (2018): 41-47.