Journal of Al Azhar University-Gaza *(Natural Sciences)*, 2018, 20 (2) : 81-98

Bacterial Etiology of Urinary Tract Infection and their Antimicrobial Resistance Profiles

Abdelraouf A. Elmanama, Anfal A. Alreqeb, Heba Kamal Kalloub, Mariam R. Al-Reefi, Rami J. Musallam, Samah A. Radi, Zyed M. Harara

Medical Laboratory Sciences Department Faculty of Health Sciences
Islamic University of Gaza

Received 20/10/2018 *Accepted* 23/12/2018

Abstract:

Background: *Urinary tract infections (UTI) are one of the most widespread infectious diseases in hospitalized and outpatients. Empirical therapy of UTI depend on the predictability of the agents causing UTI and knowing their antimicrobial susceptibility patterns.*
Objectives: *The aim of this study is to investigate the susceptibility pattern of different bacteria species isolated from urinary tract infection to commonly used antimicrobials from Al-Shifa hospital in Gaza strip.*
Methodology: *A total of 1,276 midstream urine samples from in and out patients suspected of UTI were cultured as per standard urine culture procedures. All positive cultures were tested further to identify isolates using conventional methods. Antimicrobial susceptibility test was performed by the disk diffusion method.*
Results: *Only 17.2% (219 out of 1.276) of samples were considered positive. The most frequently isolated urinary pathogens were Escherichia coli, Klebsiella spp. High percentage of Gram-negative bacterial isolates was resistant to amoxicillin/clavulanic acid, piperacillin. Gram positive bacterial isolates showed resistance to vancomycin, piperacillin. Of the Gram negative and Gram-positive isolates, 99.5% and 92.3% respectively were multidrug resistant, diversities in MDR patterns were observed among isolates.*
Conclusion: *Routine surveillance of antibiotic-resistant pattern must be a continuous process so as to provide physicians with up to date information about the local data of UTI antimicrobial resistance.*
Keywords*: Urinary tract infection, Antimicrobial resistance, and Gaza, Palestine.*

1. Introduction

Urinary tract infections (UTIs) remain the most common bacterial infection in human population and is also one of the most frequently occurring nosocomial infections (Gastmeier et al., 1998). Its annual global incidence is of almost 250 million (Ronald et al., 2001). Worldwide, about 150 million people are diagnosed with UTI each year, costing the global economy in excess of 6 billion US dollars (Akram, Shahid, & Khan, 2007). Proliferation of bacteria in the urinary tract is the cause of urinary tract infection. The clinical manifestations of UTI depend on the part of the urinary tract involved, the etiologic organisms, the severity of the infection and the patient's immunity (Foxman, 2002).

Urinary tract infection is the second most common clinical indication for empirical antimicrobial treatment in primary and secondary care, and urine samples constitute the largest single category of specimens examined in most medical microbiological laboratories. Healthcare practitioners regularly have to make decisions about prescription of antibiotics for UTI. Criteria for the diagnosis of UTI vary greatly, depending on the patient and the context (Shill, Huda, Moain, & Karmakar, 2010).

Urinary tract infection, including cystitis and pyelonephritis, are the most common infectious diseases in childhood (Robinson, Finlay, Lang, & Bortolussi, 2015). *E. coli* accounts for as much as 90% of the community-acquired and 50% of the nosocomial UTIs (Vila et al., 2002).

Urinary tract infections are responsible for more than 7 million patient visits and one million hospital admissions (due to complications) per year in the United States only (Saverino et al., 2011). (There are no similar statistics in Palestine). Urinary tract infections are classified as either mono or polymicrobial in nature depending on the part of the urinary tract colonized. UTIs are also classified as cystitis or pyelonephritis. In addition, UTIs are further classified as simple or complicated (Saverino et al., 2011).

Many different microorganisms can infect the urinary tract, but by far the most common agents are the Gram-negative bacilli. *Escherichia coli* causes ~80% of acute infections in patient without catheters, urologic abnormalities or calculi. Other Gram-negative rods, especially *Proteus* and *Klebsiella,* occasionally *Enterobacter* accounts for a smaller portion of uncomplicated infection. *Staphylococcus saprophyticus* accounts for 10% to 15% of acute symptomatic UTI in young females. In the hospitalized patient 10% to 15% develops UTI due to catheter caused by *E. coli, Proteus, Pseudomonas, Klebsiella, Serratia, Staphylococci, Enterococci* and *Candida* (Stamm, 2005).

Different factors like age, gender, immuno-suppression and urological instruments may affect prevalence of UTIs (Iqbal, Naqvi, & Akhter, 2010). Catheter-associated UTIs are one of the most dangerous health risks contributing 34% of all health care associated infections (Fink et al., 2012) The prevalence of infecting organism is influenced by the age of the patients. *S. saprophyticus* is recognized as causing approximately 10% of symptomatic lower urinary tract infections in young sexually active females whereas it rarely causes infection in males and elderly individual (Mollick, Dasgupta, Hasnain, & Ahmed, 2016). UTIs are among the most common postoperative nosocomial infections. Appropriate treatment could decrease mortality and morbidity in surgical patients and play a vital role in combating the ongoing crises of increasing antibiotic resistance (Oscarson, 2016).

Therefore, physicians who diagnose and treat patients with UTIs, should be aware of the commonest uropathogens responsible for community acquired and nosocomial UTIs (Oscarson, 2016). In Palestine, antibiotics are poorly regulated and available on the private market without a prescription (Kanapathipillai et al., 2018). Study in Palestine indicates emerging ciprofloxacin resistance among urinary tract infection isolates. Increasing resistance against ciprofloxacin demands coordinated monitoring of its activity and rational use of the antibiotics (El Astal, 2005).

This study aimed at identifying the most common microorganism that causes UTIs and to determine of the most effective antimicrobial agents. Area-specific monitoring studies aimed to gain knowledge about the type of pathogens responsible for UTIs and their resistance patterns may help clinicians in prescribing the right empirical treatment.

2. Materials and Methods

Sampling and microbiological investigation

The population of the study consists of all patients who were required to do urine culture by their attending physicians at Al-Shfia Hospital during the period from October, 2017 till end of January 2018.

Data, Sample Collection, and Analysis

The clean-catch midstream technique was used to collect urine samples of at least 20 mL into a sterile container, repetitive samples were excluded. For each sample, the information was recorded including patient name, age, sex, address date of sample collection, source (Inpatient or outpatient). All urine samples were cultured according to standard techniques. In short, a total bacterial count plate was inoculated with 1 µl of urine sample. In addition, one Blood Agar and one MacConkey agar plates were also inoculated with urine sample. Plates were incubated for 24-48 hours at 37 ^oC. A culture was considered positive if plate count showed counts of 10^5 cfu/ml or higher (in few cases cultures were considered positive even counts lower than 10^5 cfu/ml were obtained when MacConkey agar exhibited pure growth of common uropathogens). Isolated bacteria were streaked into in a Nutrient Agar slants and send to the Microbiology laboratories of the Islamic University of Gaza for identification. Subcultures were made onto Blood, HiCrome UTI Agar (HiMedia, India) and MacConkey agar. Two hundred and nineteen (17.2%) out of 1,276 patients suspected of having UTIs were culture positive.

Identification of isolates

The cultural characteristics from different media such as MacConkey agar, blood agar, and HiCrome media were recorded. Gram stain reaction for all isolated colonies was performed and results were recorded and guided the next step of identification. Isolates were tested biochemically for further confirmation of isolated bacteria, such as; Oxidase, Catalase, Coagulase, Indole production test, MR test, Citrate utilization test, Motility test, and Urease test.

Antimicrobial susceptibility testing

The susceptibility of isolates to various antimicrobials was determined using the disk diffusion method recommend by Clinical laboratory Sciences Institute (CLSI, 2017). Isolates were inoculated in Brain Heart Infusion Broth (BHIB) and incubated for 4 hours at 37°C. Their turbidities were compared and adjusted to 0.5 McFarland standard solutions. The surface of two sterile Mueller-Hinton agar (MHA) plates were entirely swabbed using the standardized inoculum. After drying for about 5-10 min, the antimicrobial disks (Table 1) were placed onto the surface of inoculated MHA. Maximum of six discs were used for each plate. The plates were incubated for 30 minutes in a refrigerator to allow diffusion prior to incubation at 37°C for 24 hours (Mollick et al., 2016).

Table (1): List of antimicrobials and their potency used in antimicrobial susceptibility of uropathogens.

Antimicrobial	Code	Potency	Gram negative	Gram positive	Manufacturer
Amikacin	AK	30 µg		X	
Amoxi/clavc	AMC	30 µg	X		
Azithromycin	AZM	15 µg		X	
Ceftriaxone	CTR	30 µg	X		
Cefuroxime	CXM	30 µg	X		
Doxycycline	DO	30 µg		X	
Gentamicin	CN	10 µg	X	X	
Meropenem	MRP	10 µg	X		
Nitrofurantoin	NIT	100 µg	X		
Norfloxacin	NX	10 µg		X	Liofilchem, Italy

Piperacillin	PRL	100 µg	X	X	
Tetracycline	TE	10 µg	X		
SXT/TM	SXT	25 µg	X	X	
Vancomycin	VA	5 µg		X	

SXT/TM; Trimethoprim/sulfamethoxazole, Amoxi/clavc; Amoxicillin/clavulanic acid

MDR determination

An isolates were considered as MDR if they were resistant to one or more antibiotics from each of at least three different classes.

Data analysis

Data collected was summarized, tabulated and analyzed using Statistical Package for Social Sciences (SPSS) software, version 22. The results were presented through tables and histograms

3. Results

Uropathogens

Only 17.2% (219 out of 1.276) of samples were considered positive. 94.5% of the isolates were Gram-negative isolates while the rest were Gram-positive. Six different UTI organisms were identified among the 219 urine cultures that yielded significant microbial growth. The Gram-negative bacteria were (*E. coli*, *Klebsiella* spp., *Pseudomonas aeruginosa* and *Proteus* spp.) and Gram-positive bacteria were *Enterococcus* and *Staphylococcus*. Staphylococcal isolates were coagulase negative and were identified as *S. saprophyticus* The predominant bacterial isolate from Gram negative were *E. coli*, *Klebsiella* spp., *Pseudomonas aeruginosa*, and *Proteus* spp. (131, 59.8%), (50, 22.8%), (16, 7.3%), (9, 4.1%) respectively. And from Gram positive, the predominant bacterial isolate was *Enterococcus* spp. 7 (3.2%), followed by *S. saprophyticus* 6 (2.7%).

Outpatient contributed the highest percentage of isolates (59%), followed by Internal Medicine Department (30%), Surgical

Department (6.8%), The least numbers of isolates came from various other departments (4.2%).

Antibiotic susceptibility pattern

Antibiotic susceptibility pattern of Gram-negative bacteria isolates

High resistance among Gram negative isolates was observed against amoxicillin/clavulanic acid (99%), piperacillin (93.2%), cefuroxime (87.4%) and ceftriaxone (68.9%) followed by trimethoprim/sulfamethoxazole (59.7%), and tetracycline (44.2%). Table (2) illustrates the summary of total number of antibiotics used with the sensitivity and resistance patterns of the uropathogens isolated in this study. Nitrofurantoin, gentamicin and meropenem were the most effective drugs with 93.7%, 85.9%, and 71.4% activity, respectively.

Table 2. Antibiotic resistance pattern of Gram-negative bacterial isolates recovered from urine samples.

Antimicrobial agent	**Antibiotic resistance**					
	Resistant		**Susceptible**		**Intermediate**	
	No	%	No	%	No	%
Amoxi/Clav	204	99	2	1.0	0	0.0
Ceftriaxone	142	68.9	62	30.1	2	1.0
Cefuroxime	180	87.4	25	12.1	1	0.5
Gentamicin	23	11.2	177	85.9	6	2.9
Meropenem	54	26.2	147	71.4	5	2.4
Nitrofurantoin	13	6.3	193	93.7	0	0
Piperacillin	192	93.2	10	4.9	4	1.9
Tetracycline	91	44.2	94	45.6	21	10.2
SXT/TM	123	59.7	82	39.8	1	0.5

SXT/TM; Trimethoprim/sulfamethoxazole, Amoxi/clavc; Amoxicillin/clavulanic acid

Most of the *E. coli* isolates were non-susceptible to the antimicrobial agents used in the study; and 99% (130) showed resistance to the Amoxicillin/Clavulanic acid. A notable exception was observed against Nitrofurantoin (only 3.2% resistance).

Of the 50 isolates of *Klebsiella* spp., 49 isolates found resistance to Amoxicillin/Clavulanic acid. Resistance to Ceftriaxone was highest among *Proteus* spp. isolates (55%). All of the *Proteus* spp. isolates were resistant to the Amoxicillin/Clavulanic acid while 100% were susceptible to Nitrofurantoin.

E. coli resistance to cefuroxime was (86.2%), *Klebsiella* spp. (96%), *Pseudomonas aeruginosa* (87.5%), and *Proteus* spp. (55.5%). Antibiotic resistance profiles of the isolated organisms are presented in figure (1).

Most *E. coli isolates* (84.7%) were sensitive for gentamicin while all *Pseudomonas aeruginosa* (100%) were susceptible.
Meropenem demonstrated an excellent *in vitro* activity against 15/16 (93.7%) *Pseudomonas aeruginosa* isolates (one isolate was intermediate and no resistance) and (74.0%) against *E. coli*. The highest resistance to meropenem was demonstrated among *Klebsiella* isolates (36%) followed by *Proteus* (33%). Trimethoprim/sulfamethoxazole demonstrated moderate activity (51.9% resistance) against *E. coli* isolates and even lower against all other isolates (Figure 1).

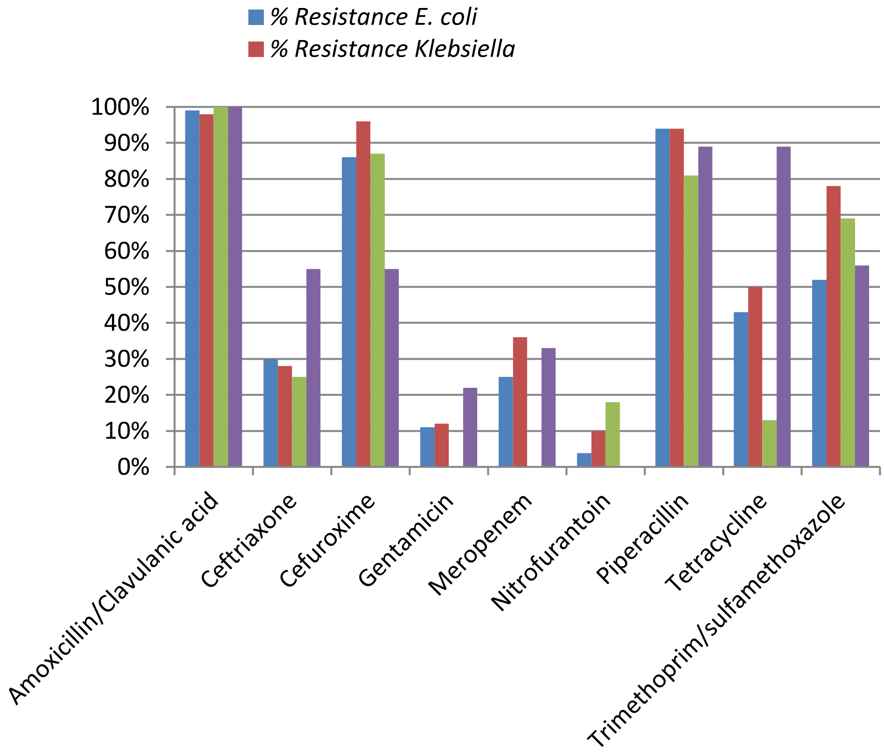

Figure (1): Percentage of Resistance Gram negative bacterial isolates from urine samples to antimicrobial agent.

Antibiotic susceptibility pattern of Gram-positive bacteria isolates

The highest percentage of Gram-positive isolates were sensitive to amikacin, azithromycin, gentamicin, norfloxacin, and trimethoprim-sulfamethoxazole (84.6%, 76.9%, 76.9%, 61.5% and 61.5%) respectively. High resistance was observed against vancomycin (76.9%), piperacillin (69.2%), norfloxacin, and trimethoprim/sulfamethoxazole (38.5%) respectively (Table 3).

Table (3): Percentage of Resistance Gram-positive bacterial isolates from urine samples to antimicrobial agent.

Antimicrobial	Results					
	Resistant		***Susceptible***		***Intermediate***	
	N	***%***	***N***	***%***	***N***	***%***
Amikacin	2	15.4	11	84.6	0	0
Azithromycin	3	23.1	10	76.9	0	0
Doxycycline	4	30.8	7	53.8	2	15.4
Gentamicin	2	15.4	10	76.9	1	7.7
Norfloxacin	5	38.5	8	61.5	0	0
Piperacillin	9	69.2	4	30.8	0	0
SXT/TM	5	38.5	8	61.5	0	0
Vancomycin	10	76.9	3	23.11	0	0

SXT/TM; Trimethoprim/sulfamethoxazole

All of the 6 *Staphylococcus* isolates screened showed 100% susceptibility to Gentamicin, and 100% resistance to Piperacillin. *Enterococcus* resistance to Vancomycin was very high (85.7%), 57.1% to Norfloxacin, 42.8% to Doxycycline. The least resistance was to Amikacin (14.2%) followed by Gentamicin (28.5%) as shown in Figure (2).

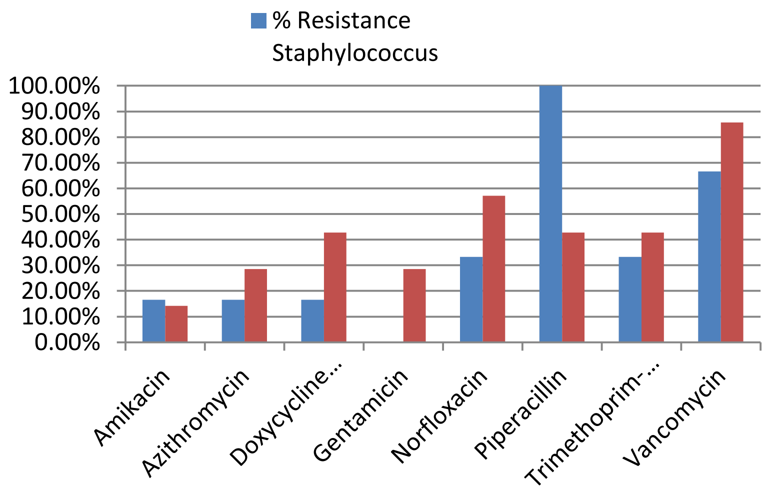

Figure (2): Percentage of Resistance Gram positive bacterial isolates from urine samples to antimicrobial agent.

Of the Gram-negative tested isolates, 99.5% (205) were multidrug resistant (MDR). A total of 131 *E. coli* isolates were analyzed, 130 isolates MDR to The antibiotics tested. All of the *Klebsiella* spp., *Pseudomonas aeruginosa*, and *Proteus* spp. isolates were MDR. Of the Gram-positive tested isolates, 92.3% (12) were MDR. A total of 6 *Staphylococcus* isolates were analyzed, 5 isolates MDR. All of the *Enterococcus* isolates were MDR.

Discussion

Six different genera of UTI pathogens were identified from the 219 positive urine cultures. The predominant bacterial isolate from Gram negative was *E. coli* 131 (59.8%) followed by *Klebsiella* spp. 50 (22.8%), *Pseudomonas aeruginosa,* and *Proteus* spp. 16, 9 (7.3, 4.1%) respectively. And from Gram positive the predominant bacterial isolate was *Enterococcus* 7 (3.2%), followed by *Staphylococcus* 6 (2.7%).

Higher frequency of *E. coli* (82.3%) has been obtained in a similar study which also reported Coagulase Negative Staphylococci (2.4%), *Pseudomonas aeruginosa* (1.2%), *Proteus mirabilis* (0.8%), *Klebsiella pneumoniae* (0.4%), and *Staphylococcus aureus* (0.4%)(Khatri, Basnyat, Karki, Poudel, & Shrestha, 2012). A similar result to that of our study was also obtained from a study conducted in Latin America. They reported *E. coli* 67.21 % followed by *P. aeruginosa* (2.4%) (Vranic, Zatric, Rebic, Aljicevic, & Abdulzaimovic, 2017).

A study done in Gaza strip, Palestine revealed similar result with Gram-negative bacteria represented 437 (91.0%) of the positive bacterial cultures (480), whereas Gram-positive were 43 (9.0%). *E coli* was the predominant uropathogen (52.5%) causing UTI followed by *Proteus mirabilis* (9.8%) and *Klebsiella pneumonia* (9.2%) whereas *E faecalis* was the most common uropathogen (5.2%) isolated among the Gram positive bacteria (El Astal, 2005).

E. coli predominated all other pathogens uropathogen (being implicated in more than one half of all the UTI) in most studies. Similar frequency of isolates of *E. coli* has been obtained in studies performed in Latin American (52%), Norway (56.7%), England

(65.1%) and USA (68%) (De Backer et al., 2008; Kamat, Fereirra, Kulkarni, & Motghare, 2008; Linhares, Raposo, Rodrigues, & Almeida, 2013; Peterson, Kaul, Khashab, Fisher, & Kahn, 2007; Zhanel et al., 2005) *E. coli* was also been found to be a common pathogen causing UTI (Beyene & Tsegaye, 2011; Khatri et al., 2012). A study conducted in Palestine wherin three hundred *E. coli* isolates were collected from outpatient females (Tunyapanit & Pruekprasert, 2006). A study conducted in Egypt, *E. coli* was higher frequency of all isolates (Elsayed, Ismail, & Elgamal, 2017).

Bacteriological studies usually reveal the involvement of Gram negative enteric organisms that commonly cause UTI, such as *E. coli, Klebsiella* and *Proteus* species (Casqueiro, Casqueiro, & Alves, 2012). Gram- negative bacteria were more prevalent >50% in many studies (Fredrick, Francis, Fataki, & Maselle, 2013; Tessema, Kassu, Mulu, & Yismaw, 2007; Zorc, Kiddoo, & Shaw, 2005). This could be due to the presence of unique structure in Gram-negative bacteria which facilitates attachment to the uroepithelial cell, with resultant high prevalence in the gastrointestinal tract. It is this unique structural characteristic that prevent elimination of bacteria with urinary lavage, and allow its multiplication and tissue invasion ensuing in invasive infection and pyelonephritis (Khatri et al., 2012).

Gram positive cocci contributed less UTIs than Gram-negative (Khatri et al., 2012). In our study, among Gram positive, the predominant bacterial isolate was *Enterococcus* spp. (7, 3.2%), followed by *Staphylococcus* spp. (6, 2.7%). Similar frequency of isolates of Gram positive has been obtained from various studies (Ayelign et al., 2018; Farajnia, Alikhani, Ghotaslou, Naghili, & Nakhlband, 2009; Fredrick et al., 2013).
The high Gram-negative bacterial resistance observed in this study against wide variety of antimicrobials, yet a high percent of bacterial isolates was sensitive to Nitrofurantoin (93.7%), and Gentamicin (85.9%) followed by Meropenem (71.4%). This is comparable to a study, wherein, nitrofurantoin was found to be the most effective antibiotic against gram negative (Khatri et al., 2012). However, our results are not comparable to a study which

reported resistance rate to Gram-negative bacilli of 96% to amoxicillin– clavulanic acid, 66.9% to tetracycline, 64.7% to trimethoprim-sulfamethoxazole, 37.6% to chloramphenicol, and 22.4% to ceftriaxone (Getachew, 2010).
In this study, only 6 *Staphylococcus* isolates were analyzed, 33.3% resistance to Norfloxacin, this is not comparable to a similar study which reported 100% susceptibility of *S. aureus* isolates to Norfloxacin (Khatri et al., 2012). In this study, all of the 6 *Staphylococcus* isolates screened showed 100% susceptibility to Gentamicin, and 66.7% to Trimethoprim-sulfamethoxazole. This is comparable to a study obtained by Farajnia et al. (Farajnia et al., 2009), for Gentamicin, but not for Trimethoprim-sulfamethoxazole 2% (Farajnia et al., 2009).

Multidrug resistance was seen in 99.5% of the Gram negative, 92.3% of Gram- positive isolates which raises serious concerns. Similar result has been obtained in studies performed in Palestine, a high percentage of multiple-drug resistance was observed for the majority of the isolates (Astal, El-Manama, & Sharif, 2002) This suggests a high resistance gene pool perhaps due to general misuse, and inappropriate usage of antibiotics, and increase in the production of bacterial enzymes such as beta- lactamases, and lack of good controlling mechanism, which can increase the prevalence of multidrug resistant microorganisms (Ndihokubwayo et al., 2013).

Data concerning the etiology and the antimicrobial resistance patterns of the agents causing UTIs may help clinicians to choose appropriate antimicrobial treatments (Kengne, Dounia, & Nwobegahay, 2017). The Infectious Diseases Society of America guidelines suggest that 10-20% resistance warrants a change in the recommended antibiotic used as the first line therapy (Warren et al., 1999).
The decreased susceptibility rates found for many agents in the current study is worrying, since some of them are currently prescribed in Gaza as agents for treating UTIs. The current data may reflect the extensive use of prescribed agents. This overuse

may select for multidrug resistant strains which will spread within a particular region.

Conclusions

There is an increasing risk for individuals to have a UTI with MDR pathogens, thus, an eminent need for continuous monitoring and reporting of uropathogens susceptibility profiles. Empirical treatment protocols should be reviewed periodically based on local data which in turn should be used as guides for treating physicians.

Acknowledgment

We would like to take this opportunity to express the profound gratitude to the Medical Laboratory Sciences Department of the Islamic University of Gaza for making available of their facilities and supporting the project with equipment and disposables, and many thanks to Al-Shifa'a Hospital.

References:

Akram, M., Shahid, M., & Khan, A. U. (2007). Etiology and antibiotic resistance patterns of community-acquired urinary tract infections in JNMC Hospital Aligarh, India. *Annals of clinical microbiology and antimicrobials, 6*(1), 4.

Astal, Z., El-Manama, A., & Sharif, F. (2002). Antibiotic resistance of bacteria associated with community-acquired urinary tract infections in the southern area of the Gaza Strip. *Journal of chemotherapy, 14*(3), 259-264.

Ayelign, B., Abebe, B., Shibeshi, A., Meshesha, S., Shibabaw, T., Addis, Z., . . . Dagnew, M. (2018). Bacterial isolates and their antimicrobial susceptibility patterns among pediatric patients with urinary tract infections. *Turkish journal of urology, 44*(1), 62.

Beyene, G., & Tsegaye, W. (2011). Bacterial uropathogens in urinary tract infection and antibiotic susceptibility pattern in jimma university specialized hospital, southwest ethiopia. *Ethiopian journal of health sciences, 21*(2), 141-146.

Casqueiro, J., Casqueiro, J., & Alves, C. (2012). Infections in patients with diabetes mellitus: A review of pathogenesis. *Indian journal of endocrinology and metabolism, 16*(Suppl1), S27.

De Backer, D., Christiaens, T., Heytens, S., De Sutter, A., Stobberingh, E. E., & Verschraegen, G. (2008). Evolution of bacterial susceptibility pattern of Escherichia coli in uncomplicated urinary tract infections in a country with high antibiotic consumption: a comparison of two surveys with a 10 year interval. *Journal of Antimicrobial Chemotherapy, 62*(2), 364-368.

El Astal, Z. (2005). Increasing ciprofloxacin resistance among prevalent urinary tract bacterial isolates in Gaza Strip, Palestine. *BioMed Research International, 2005*(3), 238-241.

Elsayed, T., Ismail, H., & Elgamal, S. (2017). The Occurrence of Multidrug Resistant E. coli which Produce ESBL and Cause Urinary Tract Infections. *J Appl Microbiol Biochem, 2*(1).

Farajnia, S., Alikhani, M. Y., Ghotaslou, R., Naghili, B., & Nakhlband, A. (2009). Causative agents and antimicrobial susceptibilities of urinary tract infections in the northwest of

Iran. *International Journal of Infectious Diseases, 13*(2), 140-144.

Fink, R., Gilmartin, H., Richard, A., Capezuti, E., Boltz, M., & Wald, H. (2012). Indwelling urinary catheter management and catheter-associated urinary tract infection prevention practices in Nurses Improving Care for Healthsystem Elders hospitals. *American journal of infection control, 40*(8), 715-720.

Foxman, B. (2002). Epidemiology of urinary tract infections: incidence, morbidity, and economic costs. *The American journal of medicine, 113*(1), 5-13.

Fredrick, F., Francis, J. M., Fataki, M., & Maselle, S. Y. (2013). Aetiology, antimicrobial susceptibility and predictors of urinary tract infection among febrile under-fives at Muhimbili National Hospital, Dar es Salaam-Tanzania. *African Journal of Microbiology Research, 7*(12).

Gastmeier, P., Kampf, G., Wischnewski, N. a., Hauer, T., Schulgen, G., Schumacher, M., . . . Rüden, H. (1998). Prevalence of nosocomial infections in representative German hospitals. *Journal of Hospital infection, 38*(1), 37-49.

Getachew, T. (2010). Bacterial pathogens implicated in causing urinary tract infection (uti) and their antimicrobial susceptibility pattern in Ethiopia. *Revista CENIC. Ciencias Biológicas, 41*.

Iqbal, T., Naqvi, R., & Akhter, S. F. (2010). Frequency of urinary tract infection in renal transplant recipients and effect on graft function. *JPMA-Journal of the Pakistan Medical Association, 60*(10), 826.

Kamat, U. S., Fereirra, A., Kulkarni, M., & Motghare, D. (2008). A prospective study of surgical site infections in a teaching hospital in Goa. *Indian Journal of Surgery, 70*(3), 120.

Kanapathipillai, R., Malou, N., Baldwin, K., Marty, P., Rodaix, C., Mills, C., . . . Saim, M. (2018). Antibiotic resistance in Palestine: an emerging part of a larger crisis. *bmj, 363*, k4273.

Kengne, M., Dounia, A. T., & Nwobegahay, J. M. (2017). Bacteriological profile and antimicrobial susceptibility patterns of urine culture isolates from patients in Ndjamena, Chad. *Pan African Medical Journal, 28*(1).

Khatri, B., Basnyat, S., Karki, A., Poudel, A., & Shrestha, B. (2012). Etiology and antimicrobial susceptibility pattern of bacterial pathogens from urinary tract infection. *Nepal Med Coll J, 14*(2), 129-132.

Linhares, I., Raposo, T., Rodrigues, A., & Almeida, A. (2013). Frequency and antimicrobial resistance patterns of bacteria implicated in community urinary tract infections: a ten-year surveillance study (2000–2009). *BMC infectious diseases, 13*(1), 19.

Mollick, S., Dasgupta, T., Hasnain, M. J., & Ahmed, M. (2016). Isolation and Characterization of Pathogens Responsible for Urinary Tract Infection in Bangladesh and Determination of their Antibiotic Susceptibility Pattern. *Journal of Applied Pharmaceutical Science Vol, 6*(04), 072-076.

Ndihokubwayo, J. B., Yahaya, A. A., Dester, A., Ki-Zerbo, G., Asamoah-Odei, E., & Keita, B. (2013). Antimicrobial resistance in the African Region: Issues, challenges and actions proposed. *African Health Monitor, 16*, 27-30.

Oscarson, A. (2016). Urinary tract infections–Etiology, antibiotic susceptibility, and treatment in surgical patients in Nepal.

Peterson, J., Kaul, S., Khashab, M., Fisher, A., & Kahn, J. B. (2007). Identification and pretherapy susceptibility of pathogens in patients with complicated urinary tract infection or acute pyelonephritis enrolled in a clinical study in the United States from November 2004 through April 2006. *Clinical therapeutics, 29*(10), 2215-2221.

Robinson, J. L., Finlay, J. C., Lang, M. E., & Bortolussi, R. (2015). Prophylactic antibiotics for children with recurrent urinary tract infections. *Paediatrics & child health, 20*(1), 45-47.

Ronald, A., Nicolle, L., Stamm, E., Krieger, J., Warren, J., Schaeffer, A., . . . Chambers, S. (2001). Urinary tract infection in adults: research priorities and strategies. *International journal of antimicrobial agents, 17*(4), 343-348.

Saverino, D., Schito, A. M., Mannini, A., Penco, S., Bassi, A. M., & Piatti, G. (2011). Quinolone/fluoroquinolone susceptibility in Escherichia coli correlates with human polymicrobial bacteriuria and with in vitro interleukine-8 suppression. *FEMS Immunology & Medical Microbiology, 61*(1), 84-93.

Shill, M. C., Huda, N. H., Moain, F. B., & Karmakar, U. K. (2010). Prevalence of uropathogens in diabetic patients and their corresponding resistance pattern: results of a survey conducted at diagnostic centers in Dhaka, Bangladesh. *Oman medical journal, 25*(4), 282.

Stamm, W. E. (2005). Urinary tract infections and pyelonephritis. *HARRISONS PRINCIPLES OF INTERNAL MEDICINE, 16*(2), 1715.

Tessema, B., Kassu, A., Mulu, A., & Yismaw, G. (2007). Pridominant isolates of urinary tract pathogens and their antimicrobial susceptiblity patterns in Gondar University Teaching Hospital, nothwest Ethiopia. *Ethiopian medical journal, 45*(1), 61-67.

Tunyapanit, W., & Pruekprasert, P. (2006). Extended-spectrum beta-lactamases in Escherichia coli isolated from patients with community-acquired urinary tract infection at Songklanagarind hospital, Thailand. *Journal of Infectious Diseases and Antimicrobial Agents, 23*(2), 51-56.

Vila, J., Simon, K., Ruiz, J., Horcajada, J. P., Velasco, M., Barranco, M., . . . Mensa, J. (2002). Are quinolone-resistant uropathogenic Escherichia coli less virulent? *The Journal of infectious diseases, 186*(7), 1039-1042.

Vranic, S. M., Zatric, N., Rebic, V., Aljicevic, M., & Abdulzaimovic, A. (2017). The Most Frequent Isolates from Outpatients with Urinary Tract Infection. *Materia socio-medica, 29*(1), 17.

Warren, J. W., Abrutyn, E., Hebel, J. R., Johnson, J. R., Schaeffer, A. J., & Stamm, W. E. (1999). Guidelines for antimicrobial treatment of uncomplicated acute bacterial cystitis and acute pyelonephritis in women. *Clinical Infectious Diseases, 29*(4), 745-759.

Zhanel, G. G., Hisanaga, T. L., Laing, N. M., DeCorby, M. R., Nichol, K. A., Palatnick, L. P., . . . Nicolle, L. E. (2005). Antibiotic resistance in outpatient urinary isolates: final results from the North American Urinary Tract Infection Collaborative Alliance (NAUTICA). *International journal of antimicrobial agents, 26*(5), 380-388.

Zorc, J. J., Kiddoo, D. A., & Shaw, K. N. (2005). Diagnosis and management of pediatric urinary tract infections. *Clinical microbiology reviews, 18*(2), 417-422.