Background. The increased emergence of new resistant strains in most human pathogens has become one of the most serious global health threat. Empirical treatment of urinary tract infections (UTI’s) has become difficult in many parts of world. Therefore, local susceptibility patterns of uropathogens is of great importance to achieve cure and reduce the misuse of empirical antibiotics. This study presents the incidence of uropathogens and their antimicrobial susceptibility patterns in West bank of Palestine.

Methods. A total of 16,883 urine culture samples were included in this retrospective study. The incidence of recovered uropathogens was estimated over 12-year in the examined urine samples, as well as the sex and age groups of the patients. Antimicrobial susceptibility was performed for all identified bacterial isolates.

Results. A total of 6,539 /16,883 (38.7%) urine culture samples showed significant bacterial growth. The common isolates were E. coli, coagulase negative Staphylococci, Streptococcus spp, S aureus, and Klebsiella spp, and their frequencies were 47%, 19.6%, 18.4%, 4.9%, 2.9%, respectively. Gram positive uropathogens showed susceptibility towards amoxi/clav, cefuroxime, cephalothin, sulpha/trimethoprim, nitrofurantoin, ciprofloxacin, ofloxacin and norfloxacin as follow: 83.9%, 80.1%, 70.1%, 36.6%, 65.1, 57.6%, 51.6%, 47.8%, respectively. While Gram negative uropathogens were susceptible to ciprofloxacin, ofloxacin, norfloxacin, cefuroxim, nitrofurantoin, sulpha/trimethoprim, nalidixic acid, and amoxi/clav 76.1%, 71.8%, 72.9%, 64%, 67.5%, 48.7%, 57.6%, 42.1%, respectively.

Conclusions. This retrospective study shows high rates of antimicrobial resistance to all commonly used anti-urinary tract infection drugs, and demonstrates the importance to monitor the incidence of common uropathogens and their antimicrobial susceptibility patterns before starting treatment.

Introduction

Urinary tract infections (UTIs) have an estimated occurrence of 150 million infections each year worldwide (1). In the USA, UTI’s account for more than 7 million outpatient visits annually. Total costs for management of UTIs exceed one billion dollars in USA (2).

Gram negative aerobic bacteria represent the majority of uncomplicated UTI’s, with E. coli incidence rate (70-95%) , while the most commonly isolated gram positive aerobic bacteria are coagulase negative staphylococci accounts for around 5 to 10% (3-4).

Most pathogens of the urinary tract are coming from fecal normal flora that colonize the peri-urethral area and vagina in females.

Due to continuous and increased emergence of new bacterial resistance strains, antimicrobial susceptibility patterns of uropathogens are of great importance for successful treatment of UTIs. Local data on antimicrobial susceptibility patterns is becoming more necessary in countries where there is antimicrobial abuse especially when these: drugs can be obtained without medical prescription from pharmacies (5).
To our best knowledge, few local data on antimicrobial susceptibility patterns and epidemiology of uropathogens among Palestinian population were reported. A recent published study showed limited data from one local area (6). This study investigated large numbers of cultured UTI specimens which have been received over the last 12 years covering the whole Palestinian population of West Bank region.

Material and methods

This retrospective study is based on data obtained from the records of 11 centers of Medicare-Medipal laboratories. Data included 16,883 urine culture samples investigated over twelve years period (April 2001, to March 2013).

Urine Culture and identification of bacterial isolates

Most specimens were mid-stream clean catch urine collected upon request of examining physician, and not all cultured samples were examined for urinalysis. Urine samples were cultured on both 5% blood agar and MacConkey’s culture plates. Inoculation of plates was done by using one micro liter disposable calibrated loops. Plates were incubated for 24-48 hours at 37°C. After incubation, the urine cultures considered to be negative when bacterial growth was lower than $10^3$ CFU/mL; positive when pure growth was higher than $10^5$ CFU/mL. Growth of more than one type of bacteria was considered contamination and neglected.

Identification of bacterial isolates was based on the Gram staining characteristics of the bacteria, appearance of colonies on agar, Catalase test, Oxidase test, Staphylase test and their biochemical profile including Triple Sugar Iron (TSI), Sulphour-Indole-Mannitol (SIM), Urease, Citrate, Methyl-Red (MR) and VogesProskauer (VP).

Antimicrobial susceptibility test

All bacterial isolates were tested for their susceptibility to antimicrobials using modified Kirby-Bauer technique and guidelines used in England (7). The antimicrobials diffusion discs were obtained from (Bioanalyse, Yenimahalle ,Ankara / Turkey). Antimicrobials tested were the following: amikacin, amoxicillin-clavulanic acid, ampicillin, cefaclor, cefixime, cefotaxime, ceftazidime, ceftriaxone, cefuroxime, cephalexin, cefalothin, ciprofloxacin, ofloxacin, cotrimoxazole, gentamicin, nalidixic acid, norfloxacin, sulphamethoxazole-trimethoprim (SXT) and nitrofurantoin. Furthermore, other antibiotics were used less frequently and were mentioned in table 1.

Table 1. Distribution of antimicrobial susceptibility for the main uropathogens.

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>E. coli No.(%)*</th>
<th>Streptococcus spp. No.(%)</th>
<th>C.N.S No.(%)</th>
<th>S. aureus No.(%)</th>
<th>Proteus spp. No.(%)</th>
<th>Klebsiella spp. No.(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amox / Clav</td>
<td>2571(43)</td>
<td>1028(91.1)</td>
<td>1077(79.1)</td>
<td>278(76.3)</td>
<td>116(60.3)</td>
<td>148(31.8)</td>
</tr>
<tr>
<td>Cefaclor</td>
<td>1755(44)</td>
<td>720(64.7)</td>
<td>801(61)</td>
<td>165(60)</td>
<td>85(50.6)</td>
<td>124(54.8)</td>
</tr>
<tr>
<td>Cefixime</td>
<td>666(72.1)</td>
<td>313(33.2)</td>
<td>286(10.8)</td>
<td>52(7.7)</td>
<td>27(88.9)</td>
<td>54(72.2)</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>408(75.2)</td>
<td>60(70)</td>
<td>76(57.9)</td>
<td>31(71)</td>
<td>22(77.3)</td>
<td>21(81)</td>
</tr>
<tr>
<td>Ceftazidime</td>
<td>1638(79.7)</td>
<td>442(50.9)</td>
<td>491(25.9)</td>
<td>100(28)</td>
<td>76(85.5)</td>
<td>112(78.6)</td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>1164(79.3)</td>
<td>440(77.7)</td>
<td>520(55.2)</td>
<td>86(59.3)</td>
<td>55(90.9)</td>
<td>76(77.6)</td>
</tr>
<tr>
<td>Cefuroxime</td>
<td>2386(66.1)</td>
<td>1018(85.3)</td>
<td>1071(76.4)</td>
<td>227(74.9)</td>
<td>97(71.1)</td>
<td>160(58.8)</td>
</tr>
<tr>
<td>Cephalexin</td>
<td>1465(29.9)</td>
<td>602(51.2)</td>
<td>713(59.6)</td>
<td>153(49)</td>
<td>62(40.3)</td>
<td>94(47.9)</td>
</tr>
<tr>
<td>Cefalothin</td>
<td>702(16.4)</td>
<td>250(73.2)</td>
<td>262(69.8)</td>
<td>85(61.2)</td>
<td>22(27.3)</td>
<td>22(18.2)</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>1534(77)</td>
<td>575(55.1)</td>
<td>557(60.5)</td>
<td>173(56.1)</td>
<td>68(76.5)</td>
<td>92(76.1)</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>475(71.2)</td>
<td>61(52.5)</td>
<td>79(79.7)</td>
<td>51(70.6)</td>
<td>26(57.7)</td>
<td>24(58.3)</td>
</tr>
<tr>
<td>Nalidixic Acid</td>
<td>192(59.9)</td>
<td>212(7.5)</td>
<td>258(8.1)</td>
<td>83(6)</td>
<td>81(34.6)</td>
<td>90(62.2)</td>
</tr>
<tr>
<td>Nitrofurantoin</td>
<td>2477(74.4)</td>
<td>894(61.9)</td>
<td>968(67.5)</td>
<td>226(69.5)</td>
<td>107(84)</td>
<td>154(43.5)</td>
</tr>
<tr>
<td>Ofloxacin</td>
<td>425(73.2)</td>
<td>173(46.2)</td>
<td>175(52.6)</td>
<td>69(62.3)</td>
<td>18(72.2)</td>
<td>26(69.2)</td>
</tr>
<tr>
<td>Sulpha../Trime..</td>
<td>2488(49.3)</td>
<td>976(30.5)</td>
<td>1083(40.7)</td>
<td>242(46.7)</td>
<td>107(29)</td>
<td>160(53.1)</td>
</tr>
</tbody>
</table>

* No(%): Total number and percentage of each bacteria isolates
IBM-SPSS software (version 17 for Windows) was used to calculate the frequencies, cross-tables, and risk estimations.

**Result**

A total number of 6,539/16,883 (38.7%) was positive for a significant and pure bacterial growth from urine samples over the 12-year period. The distribution of bacterial isolates is shown in figure 1. Gram negative isolates accounted for 3627 (57.1%), while Gram positive isolates accounted for 2730 (42.9%). *E. coli* represented the vast majority of gram negative bacterial isolates (83.2%), followed by *Klebsiella* spp. (5.1%), *Proteus* spp. (3.6%), *Pseudomonas* spp. (3.4%), *Citrobacter* spp. (1.8%), *Enterobacter* spp. (1.6%), and other less frequent uropathogens. Gram positive bacterial isolates are dominated by coagulase negative staphylococci (CNS) (46%), followed by *Streptococci* spp. (42.3%), and *S. aureus* (11.5%).

**Figure 2** shows the distribution of gender and uropathogen isolates. There is a significant in the incidence (P < 0.05) of *E. coli* (50.7% vs 46.1%), *Citrobacter* spp.

(1.5% vs 0.9%), and *Pseudomonas* spp. (2.9% vs 1.8%) in males compared to females, but a significant incidence (P < 0.05) was observed in females than males due to infection with *Streptococci* spp. (18.9 vs 16.4%), *Klebsiellas*pp (3.1% vs 1.9%), & coagulase negative staphylococci (20.1% vs 17.3%) . The results of antimicrobial susceptibility patterns of uropathogen isolates are shown in **table 1**.

**Discussions**

This study shows generally that the results of bacterial isolates from urine cultures are much similar to other recent findings published in the neighboring country of Jordan (8-10). *Escherichia coli* is still the leading uropathogen, with overall (47%) of all bacteria isolated from urine samples obtained from patients suspected to have UTI. Also, *E. coli* represented (83.2%) of all Gram negative isolates, and its incidence was significantly higher among males than females (50.7% vs 46.1%). This result is different than findings reported from Turkey and Jordan (3, 8, 9), where women more often develop urinary tract infections due to *E.coli*. However, it is important to note that most of our patients developed community ac-
quired urinary tract infection. Remarkable high incidence of *E. coli* was found among children (62.1%) and elderly (55.2%) when compared to other age groups.

The present study demonstrates that the incidence rate of coagulase negative staphylococci (CNS) (19.6%) was common among females (20.1%) and similar to many other studies worldwide (3,11,12). Young adults and adolescents females had the highest incidence rates of CNS isolates (24.8%, 23.3%), respectively. Moreover, the incidence rate of Streptococcus species (18.4) was slightly higher among females than males (18.9 vs. 16.4%). The same observation is noticed with CNS which caused more UTIs among females compared to males (20.1% vs. 17.3%) especially among sexually active young persons. While the incidence rate of *S. aureus* (4.9%) was much similar among males and females (5.5% vs 4.8%). These results may reflect the fact that UTI is remarkably increased among sexually young active age groups as reported by Vincent et al. (12).

The incidence rates of *Klebsiella* spp., *Enterobacter* spp., and *Pseudomonas* spp. as cause of UTIs in this study were low and similar to many other studies (9-10). It is well established that these bacteria spp. are often associated with hospitalized patients and cause complicated cystitis and pyelonephritis (13). These three species are often associated with hospitalized patients and less with community acquired UTI. Age groups also did not show significant difference in incidence of these organisms among males and females as indicted by other studies (5,14). Other bacterial isolates were found in (<1%) including citrobacter spp., *Pantoea* spp., *Acinetobacter* spp., *Serratia* spp.

In general, all bacterial isolates from urine culture samples showed the lowest susceptibility in vitro to ampicillin (28.3%), while imipenem has the highest activity (93.8%). However, imipenem used mainly in hospitalized patients.

Gram positive bacteria showed better susceptibility rates in vitro to commonly used drugs in UTIs such as amoxicillin, cefuroxime and nitrofurantoin, whereas less susceptibility rate was detected against ciprofloxacin, sulpha/trimethoprim and cephalaxin (Table 1).

The results of this study demonstrated that *E. coli* isolates have the lowest susceptibility to the following drugs: amoxi/clav, cephalaxin, cephalothin, and sulphatherapem (Table 1). While *E. coli* was moderately susceptible to ciprofloxacin, nitrofurantoin, cefuroxime and nalidixic Acid, (Table 1). The low susceptibility to amoxi/clav and sulphatherapem in this study is similar to the results reported from Jordan and other Middle East countries (8,9,10,15,16). The other Gram-negative isolates (*Klebsiella* spp., *Enterobacter* spp., *Proteus* spp., *Citrobacter* spp. and *Pseudomonas* spp.) showed more resistance.
to antibiotics and mostly were multidrug resistance (Table 1). In conclusion, this study suggests that further periodic multi-center surveys are needed to control the spectrum of antimicrobial resistance in common clinical bacterial isolates in our region, since such available local data will help physicians to select the proper empiric therapy in treatment of UTIs and other infections and contribute to control the misuse of antimicrobial agents.

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References
