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Antibiotic resistance rates of *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Klebsiella pneumoniae* isolated from a university-affiliated hospital in North Cyprus

Kuzey Kıbrıs'taki bir üniversite hastanesinden izole edilen *Pseudomonas aeruginosa*, *Acinetobacter baumannii* ve *Klebsiella pneumoniae* bakterilerinin antibiyotik direnç oranları

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ABSTRACT

Objective: Infections caused by resistant gram-negative bacteria to antimicrobials occur at increasing rates. Therefore, routine screening of resistance patterns is crucial for treatment approaches using proper antibiotics. Nevertheless, there is not enough data with respect to antibiotic resistance profiles in North Cyprus. This study was conducted in order to investigate the resistance rates of *Pseudomonas aeruginosa*, *Acinetobacter baumannii* and *Klebsiella pneumoniae* which were isolated from the Near East University (NEU) Hospital, North Cyprus.

Method: It was included in this study *P. aeruginosa*, *A. baumannii* and *K. pneumoniae* which were isolated in the NEU Hospital Clinical Microbiology Laboratory between 01 August 2010 and 31 December 2014. Identification and susceptibility tests were performed by using the BD Phoenix 100 system (software version 6.01A). The antimicrobial susceptibility test results were determined according to the Clinical and Laboratory Standards Institute (CLSI) guidelines, and the resistance rates of bacterial isolates to antibiotics were examined retrospectively.

Results: It was evaluated that the antibiotic resistance rates of 186 *P. aeruginosa*, 61 *A. baumannii*, and 204 *K. pneumoniae* strains which were isolated

ÖZET

Amaç: Antimikrobiyallere dirençli Gram-negatif bakterilere bağlı gelişen enfeksiyonlar gittikçe artan oranlarda görülmektedir. Bu nedenle direnç paternlerinin rutin olarak taranması tedavide uygun antibiyotik verilmesi için önemlidir. Ancak, Kuzey Kıbrıs'taki antibiyotik direnç profiline ilişkin yeterli veri mevcut değildir. Bu çalışma Kuzey Kıbrıs'taki Yakın Doğu Üniversitesi (YDÜ) Hastanesi'nde izole edilen *Pseudomonas aeruginosa*, *Acinetobacter baumannii* ve *Klebsiella pneumoniae* bakterilerindeki direnç oranlarının araştırılması amacıyla yapılmıştır.

Yöntem: YDÜ Hastanesi Klinik Mikrobiyoloji Laboratuvarı'nda 01.08.2010 ve 31.12.2014 tarihleri arasında izole edilen *P. aeruginosa*, *A. baumannii* ve *K. pneumoniae* bakterileri bu çalışmaya dâhil edilmiştir. Tanımlama ve duyarlılık testleri BD Phoenix 100 sistemi (6.01A yazılım programı) kullanılarak yapılmıştır. Antimikrobiyal duyarlılık test sonuçları Clinical and Laboratory Standards Institute (CLSI) kılavuzuna göre belirlenmiş ve bakteri izolatlarının antibiyotiklere direnç oranları retrospektif olarak incelenmiştir.

Bulgular: YDÜ Hastanesi'nde Ağustos 2010 ve Aralık 2014 tarihleri arasında izole edilen 186 *P. aeruginosa*, 61 *A. baumannii*, ve 204 *K. pneumoniae*

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between August 2010 and December 2014 at the NEU Hospital. *P. aeruginosa* isolates were mostly resistant to aztreonam (42.9%), ceftazidime (19.5%), levofloxacin (20.2%) and ciprofloxacin (18.8%). In contrary, resistance rates for imipenem and meropenem were lower (11.8% and 6.5%, respectively). *A. baumannii* displayed high resistance (32.8%-92.7%) to most of the antibiotics tested, while the resistance rate for colistin was 5.1%. The highest antimicrobial resistance rates in *K. pneumoniae* isolates were detected in ampicillin-sulbactam (39.9%), cefazolin (35.3%), cefuroxime (34.2%) and tetracycline (30.8%); while the lowest rates of resistance were recorded for ertapenem (4.6%), imipenem (0.0%), meropenem (1.0%) and amikacin (0.0%). Besides, extended-spectrum beta-lactamase (ESBL) positive results were obtained among 16.7% of *K. pneumoniae* isolates.

Conclusion: According to literature review, this is the first study that evaluated the antimicrobial resistance rates of *P. aeruginosa*, *A. baumannii* and *K. pneumoniae* isolates in a centre in North Cyprus. Among the antibiotics tested, particularly the carbapenem resistance in *P. aeruginosa* and *K. pneumoniae* strains, and colisitin resistance in *A. baumannii* were detected at lower rates in comparison to the other studies where high rates of resistance were documented. Nevertheless, the results of this study indicate that antibiotic resistance in our hospital cannot be ignored, and the test results should be monitored routinely. By conducting multi-centered studies, more comprehensive data on antimicrobial resistance patterns and the underlying genetic mechanisms should be documented in North Cyprus.

Key Words: drug resistance, North Cyprus *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*

suşunun antibiyotik direnç oranları değerlendirilmiştir. *P. aeruginosa* izolatlarında en yüksek direnç oranları aztreonam (%42,9), seftazidim (%19,5), levofloksasin (%20,2) ve siprofloksasin (%18,8) antibiyotiklerinde görülmüştür. İmipenem ve meropenem için ise daha düşük direnç oranları (sırasıyla %11,8 ve %6,5) saptanmıştır. *A. baumannii* izolatlarının, test edilen antibiyotiklerin çoğuna karşı yüksek seviyede dirençli (%32,8-%92,7) olduğu görülmüş; bu izolatlar arasındaki kolistin direnci ise %5,1 olarak belirlenmiştir. *K. pneumoniae* izolatlarında en yüksek direnç oranları ampisilin-sulbaktam (%39,9), sefazolin (%35,3), sefuroksim (%34,2) ve tetrasiklin (%30,8) antibiyotiklerinde; en düşük oranlar ise ertapenem (%4,6), imipenem (%0,0), meropenem (%1,0) ve amikasin (%0,0) antibiyotiklerinde saptanmıştır. Ayrıca, *K. pneumoniae* izolatları arasında %16,7 oranında genişlemiş spektrumlu beta-laktamaz (GSBL) pozitifliği görülmüştür.

Sonuç: Bu çalışma, araştırmalarımıza göre Kuzey Kıbrıs'taki bir merkezde *P. aeruginosa*, *A. baumannii* ve *K. pneumoniae* izolatlarının antibiyotiklere karşı direnç oranlarını değerlendiren ilk çalışmadır. Çalışmamızda, test edilen antibiyotikler arasında özellikle *P. aeruginosa* ve *K. pneumoniae* suşlarında karbapenem direnci; *A. baumannii*'de ise kolistin direnci, yüksek direnç oranlarının bildirildiği diğer çalışmalara göre daha düşük oranlarda bulunmuştur. Ancak, bu çalışmanın bulguları hastanemizde antibiyotik direncinin gözardı edilmemesi ve test sonuçlarının rutin olarak taranması gerektiğine işaret etmektedir. Çok merkezli çalışmalar yürütülerek Kuzey Kıbrıs'taki antimikrobiyal direnç paternleri ve altta yatan genetik mekanizmalar ile ilgili daha geniş kapsamlı verilerin elde edilmesi gerekmektedir.

Anahtar Kelimeler: ilaç direnci, Kuzey Kıbrıs *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Klebsiella pneumoniae*

INTRODUCTION

Infections developed by antibiotic-resistant Gram-negative bacteria occur at increasing rates. Apart from being difficult to treat, these infections are associated with high morbidity and mortality and pose a threat to the global public health (1).

Due to the presence of outer membrane structure and defense mechanisms such as periplasmic beta-lactamases, Gram-negative bacteria are more resistant to antimicrobial agents than Gram-positive bacteria. This also makes it more difficult to develop

novel antibiotics against Gram-negative bacteria (2).

Pseudomonas aeruginosa is a non-fermenting Gram-negative bacterium which is an opportunistic pathogen (3). This bacterium, which causes nosocomial infections such as pneumonia, urinary tract infection and sepsis, is resistant to many antibiotics including beta-lactams, aminoglycosides and fluoroquinolones (4). Infections caused by multidrug-resistant *P. aeruginosa* are regarded as a serious clinical problem and are seen relatively common (5).

Acinetobacter baumannii is a non-fermenting Gram-negative bacterium and this opportunistic pathogen is generally isolated from the infections in intensive care units (6). *A. baumannii* has been recognised as an important cause of nosocomial infections with high morbidity and mortality rates (7). This bacterium is most commonly encountered in septicemia, pneumonia and urinary tract infections (8). *A. baumannii* is capable of developing resistance against antimicrobial agents, and there has been an increase in the rates of multidrug-resistant isolates in the last decade (6).

Gram-negative bacteria that belong to *Enterobacteriaceae*, are part of the normal intestinal flora and besides, are among the most commonly encountered pathogens in clinical practice. These bacteria can easily be transmitted between individuals and they tend to receive genetic information typically by plasmids and transposons (9). *Klebsiella pneumoniae*, a member of *Enterobacteriaceae*, is an opportunistic pathogen and is involved in septicemia, pneumonia, urinary tract infections and soft tissue infections among hospitalized and immunosuppressed patients. Multidrug-resistance in *K. pneumoniae* is generally caused by the production of extended-spectrum beta-lactamases (ESBL) and carbapenemases. The spread of multidrug-resistant isolates usually results in the failure of antibiotic therapy given for these infections (10).

In order to control the infections caused by resistant Gram-negative bacteria, the risk factors should be determined, the resistant isolates should be identified, and preventive measures should be taken. Determination of the local antibiotic resistance profiles can guide the options of empirical therapy for the antibiotic-resistant Gram-negative infections (1).

There have been many publications on antimicrobial drug resistance in the literature. However the resistance patterns of *P. aeruginosa*, *A. baumannii* and *K. pneumoniae* strains in North Cyprus remain unclear. For this reason, *P. aeruginosa*, *A. baumannii* and *K. pneumoniae* isolates which were reported between August 2010 and December 2014 at the Near East University (NEU) Hospital in North Cyprus were included in this study. Therefore, a data on the antibiotic resistance patterns of these important bacteria isolated from the NEU Hospital was obtained in this research.

MATERIAL and METHOD

The present study was conducted at the NEU Hospital Clinical Microbiology Laboratory. The NEU Hospital was established in Nicosia, capital of North Cyprus, in July 2010. During the period of August 2010 and December 2014, the bed capacity of the hospital was 120 and the occupancy rate was 50%. The 12-bed general intensive care unit and six-bed cardiovascular surgery intensive care unit had an occupancy rate of 50%. Bacterial isolates, *P. aeruginosa*, *A. baumannii* and *K. pneumoniae* which were isolated at the NEU Hospital Clinical Microbiology Laboratory between 01.08.2010 and 31.12.2014 were included in this study. The isolated bacteria were collected from specimens sent by various departments during this time period. Identification of bacterial isolates and the antimicrobial susceptibility testing were performed using the BD Phoenix 100 system (software version 6.01A). The susceptibility test results were determined according to the Clinical and Laboratory Standards Institute (CLSI) guidelines (11). The presence of ESBL among *K. pneumoniae* isolates was also evaluated according to the test

results obtained from the Phoenix instrument. Demographic information of the patients, types of clinical specimens bacteria were isolated from, and the antibiotic resistance rates were investigated retrospectively. Repetitive isolates which were recovered from identical specimens of the same patient in a short period of time were excluded from the study. However, repetitive strains isolated over an extended period of time were included in the study. In addition, strains isolated from different specimens of the same patient were also included in the study. The data obtained were analyzed using the Microsoft Excel software.

RESULTS

Two hundred and twenty-four *P. aeruginosa*, 79 *A. baumannii* and 229 *K. pneumoniae* strains were isolated at the NEU Hospital Clinical Microbiology Laboratory between 01.08.2010 and 31.12.2014. The repetitive isolates recovered in a short period of time were excluded from the analysis, thus 186 *P. aeruginosa*, 61 *A. baumannii* and 204 *K. pneumoniae* strains were evaluated in the study. Distribution of the bacterial isolates among the patient specimens is given in the Table 1.

Demographic information of the patients and the antibiotic resistance rates of *P. aeruginosa*, *K. pneumoniae* and *A. baumannii* were identified. The findings were stated individually for each pathogen.

One hundred and eighty-six *P. aeruginosa* isolates were detected from 123 patients. Distribution of the patients according to the age groups were nine (7.3%) for age zero; 14 (11.4%) for age 1-14; six (4.9%) for age 15-24; 12 (9.8%) for age 25-44; 17 (13.8%) for age 45-64; and 65 (52.8%) for age 65+. Numbers of female and male patients were noted to be 54 (43.9%) and 69 (56.1%), respectively.

The antibiotic resistance rates of 186 *P. aeruginosa* isolates were evaluated. The highest

Table 1. Distribution of *P. aeruginosa*, *K. pneumoniae* and *A. baumannii* isolates according to the patient specimens (NEU Hospital 2010-2014).

Specimen	P. aeruginosa		A. baumannii		K. pneumoniae	
	n	(%)	n	(%)	n	(%)
Wound material	34	18.3	7	11.5	9	4.4
Sputum	25	13.4	10	16.4	18	8.8
Cerebrospinal fluid	8	4.3	-	-	-	-
Deep tracheal aspirate	30	16.1	24	39.3	16	7.8
Urine	57	30.6	9	14.8	122	59.8
Blood	15	8.1	3	4.9	24	11.8
Catheter	9	4.8	6	9.8	10	4.9
Other	8	4.3	2	3.3	5	2.5
Total	**186**	**100.0**	**61**	**100.0**	**204**	**100.0**

resistance rates were recorded against aztreonam (42.9%), ceftazidime (19.5%), levofloxacin (20.2%) and ciprofloxacin (18.8%). However, resistance rates for imipenem (11.8%) and meropenem (6.5%) were found to be lower (Table 2).

Sixty-one *A. baumannii* isolates were reported from 40 patients. Distribution of the patients according to the age groups were three (7.5%) for age 1-14; five (12.5%) for age 15-24; five (12.5%) for age 25-44; 11 (27.5%) for age 45-64; and 16 (40.0%) for age 65+. There was no patient (0.0%) in the age group zero. Number of female patients was 17 (42.5%), and number of male patients was 23 (57.5%).

Antimicrobial resistance rates of 61 *A. baumannii* isolates were assessed. High levels of resistance (32.8%-92.7%) were detected against most of the antibiotics tested. Colistin resistance among *A. baumannii* isolates was noted to be 5.1% (Table 3).

In this study, 204 *K. pneumoniae* strains were isolated from 155 patients. Distribution of the patients according to the age groups were 18 (11.6%) for age zero; seven (4.5%) for age 1-14; six (3.9%) for age 15-24; 25 (16.1%) for age 25-44; 31 (20.0%) for age 45-64; and 68 (43.9%) for age 65+. Numbers of female and male patients were found to be 88 (56.8%) and 67 (43.2%), respectively.

Table 2. Antimicrobial resistance rates of *P. aeruginosa* isolates (NEU Hospital 2010-2014).

The antibiotics tested	P. aeruginosa (n: 186)		
	Number of the isolates tested	Number of the resistant isolates	
		n	(%)
Piperacillin-tazobactam	185	12	6.5
Ticarcillin-clavulanic acid	86	8	9.3
Ceftazidime	185	36	19.5
Cefepime	184	9	4.9
Aztreonam	184	79	42.9
Imipenem	186	22	11.8
Meropenem	184	12	6.5
Colistin	128	14	10.9
Gentamicin	185	23	12.4
Amikacin	185	13	7.0
Ciprofloxacin	186	35	18.8
Levofloxacin	129	26	20.2
Norfloxacin	57	8	14.0

Table 3. Antimicrobial resistance rates of *A. baumanii* isolates (NEU Hospital 2010-2014).

The antibiotics tested	*A. baumannii* (n: 61)		
	Number of the isolates tested	Number of the resistant isolates	
		n	(%)
Ampicillin-sulbactam	61	8	13.1
Piperacillin-tazobactam	61	46	75.4
Ceftazidime	61	48	78.7
Cefepime	61	20	32.8
Cefotaxime	55	51	92.7
Imipenem	61	45	73.8
Meropenem	61	45	73.8
Colistin	59	3	5.1
Gentamicin	61	44	72.1
Amikacin	61	40	65.6
Tetracycline	55	42	76.4
Ciprofloxacin	61	47	77.0
Levofloxacin	59	44	74.6
Trimethoprim-sulfamethoxazole	61	44	72.1

Resistance rates of 204 *K. pneumoniae* against antibiotics were analyzed. The resistance levels of these isolates varied among different antibiotics. The highest rates of resistance in *K. pneumoniae* isolates were detected against ampicillin-sulbactam (39.9%), cefazolin (35.3%), cefuroxime (34.2%) and tetracycline (30.8%). The lowest rates of resistance were recorded for ertapenem (4.6%), imipenem (0.0%), meropenem (1.0%) and amikacin (0.0%) (Table 4). Besides, 34 (16.7%) of 204 *K. pneumoniae* isolates were noted to be positive for ESBL.

DISCUSSION

Infections caused by antimicrobial-resistant microorganisms lead to higher mortality, morbidity and treatment costs than those of antibiotic-susceptible pathogens (12). Besides, increase in the antimicrobial resistance can lead to ineffectiveness of the antibiotics used for the empirical therapy (2). For this reason, countries should establish data on their local antibiotic resistance profiles.

P. aeruginosa, *A. baumannii* and *K. pneumoniae* are Gram-negative bacteria which cause nosocomial

Table 4. Antimicrobial resistance rates of *K. pneumoniae* isolates (NEU Hospital 2010-2014).

The antibiotics tested	*K. pneumoniae* (n: 204)		
	Number of the isolates tested	Number of the resistant isolates	
		n	(%)
Amoxicillin-clavulanic acid	111	33	29.7
Ampicillin-sulbactam	203	81	39.9
Piperacillin-tazobactam	203	22	10.8
Ticarcillin-clavulanic acid	69	16	23.2
Cefazolin	201	71	35.3
Cefepime	203	44	21.7
Cefotaxime	26	4	15.4
Ceftriaxone	170	38	22.4
Cefoxitin	203	26	12.8
Cefuroxime	111	38	34.2
Ceftazidime	204	43	21.1
Aztreonam	203	44	21.7
Ertapenem	197	9	4.6
Imipenem	203	0	0.0
Meropenem	204	2	1.0
Gentamicin	204	29	14.2
Amikacin	204	0	0.0
Tetracycline	26	8	30.8
Ciprofloxacin	204	41	20.1
Levofloxacin	95	16	16.8
Norfloxacin	111	20	18.0
Trimethoprim-sulfamethoxazole	204	63	30.9

infections (2). The other significant feature of these bacteria is their ability to develop resistance against antibiotics (3,10,13). In North Cyprus, antibiotic resistance patterns of *P. aeruginosa*, *A. baumannii* and *K. pneumoniae* isolates remain unclear. Therefore, the findings of these bacteria isolated from the NEU Hospital between August 2010 and December 2014 were analyzed retrospectively. In this period, 186 *P. aeruginosa* from 123 patients, 61 *A. baumannii* from 40 patients, and 204 *K. pneumoniae* from 155 patients were reported.

Demographic information of the patients revealed that, the pathogens in this study were isolated most commonly from the patients aged 65 and over. The prevalence of *P. aeruginosa*, *A. baumannii* and *K. pneumoniae* in the age group 65+ was 52.8%, 40.0% and 43.9%, respectively. The reason of greater rates of infection in this age group can be explained by the weakened immune response in the elderly people which results in increased sensitivity against the pathogens (14). The proportions of female and male patients infected with *P. aeruginosa* were 43.9%-56.1%; while the percentages for *A. baumannii* were 42.5%-57.5%, respectively. These findings were similar for both of the pathogens. Among the patients infected with *K. pneumoniae*, the rates of female and male patients were 56.8% and 43.2%, respectively.

In our study, the patient specimens used for the isolation of these pathogens were also analyzed (Table 1). *P. aeruginosa* was mostly isolated from the urine samples (30.6%), which was followed by wound material (18.3%), deep tracheal aspirate (DTA) (16.1%) and sputum (13.4%) samples. This pathogen was also isolated from blood samples (8.1%), and these findings were consistent with the infections where *P. aeruginosa* is commonly encountered (4,15). The specimens which *A. baumannii* was mostly isolated were DTA (39.3%), sputum (16.4%), urine (14.8%) and wound material (11.5%). These findings were compatible with the previous studies where *A. baumannii* was stated to be isolated most commonly from the respiratory specimens followed by wound materials (16). In our study, *K. pneumoniae* was most frequently detected in urine samples (59.8%). This is not surprising since this pathogen is the second most common cause of community-acquired urinary tract infections developed by *Enterobacteriaceae* (17). The other samples where *K. pneumoniae* isolates were reported were blood (11.8%), sputum (8.8%) and DTA (7.8%), and these findings were consistent with the infections caused by this pathogen (10).

In the study, antimicrobial resistance patterns of *P. aeruginosa*, *A. baumannii* and *K. pneumoniae* isolates which were reported at the NEU Hospital betwen August 2010 and December 2014 were analyzed.

P. aeruginosa is intrinsically resistant to many antibiotics due to the presence of outer-membrane, efflux-pumps and intracellular mechanisms of antimicrobial inactivation. Although antibiotics such as carbapenems were introduced against *P. aeruginosa*, this organism can easily develop resistance as a result of mutations in the chromosome and acquisition of extracellular genes (3).

Data obtained in this study revealed that, the highest resistance in *P. aeruginosa* isolates was against aztreonam (42.9%) (Table 2). This can be explained by the emergence of ESBL and/or AmpC beta-lactamase producing strains which can hydrolyse aztreonam, cephalosporins and penicillins. Aztreonam resistance in *P. aeruginosa* is an obstacle for the administration of appropriate therapy. Many studies from Turkey, Europe and other countries reported high resistance rates (32.0%-52.0%) against aztreonam (18-20).

In the present study, aminoglycoside (gentamicin: 12.4%; amikacin 7.0%), fluoroquinolone (ciprofloxacin: 18.8%; levofloxacin: 20.2%; norfloxacin: 14.0%) and ceftazidime (19.5%) resistance among *P. aeruginosa* isolates were

found similar with the rates documented in the antimicrobial resistance report of South Cyprus in 2010 (21). The only difference between the findings was observed for the carbapenem antibiotics. Resistance rate in the 2010 report was declared to be 29.2%, while the percentages for imipenem and meropenem resistance in this study were found 11.8% and 6.5%, respectively (Table 2). In a recent meta-analysis from Turkey, *P. aeruginosa* isolates were reported to have decreased resistance rates to all antibiotics tested, with the exception of cefepime and monobactam, during 2010-2013 in comparison with the period before 2013 (22).

Apart from being intrinsically resistant to many antibiotics, *A. baumannii* has the ability to develop resistance against most antimicrobial agents. Presence of the outer-membrane, alteration of the drug target, enzymatic degradation of the antibiotics, and the efflux-pumps are responsible for the antimicrobial resistance (13).

In our study, *A. baumannii* isolates exhibited high resistance (32.8%-92.7%) against most of the antimicrobial agents tested (Table 3). This finding is consistent with those of many other studies where *A. baumannii* was shown to develop resistance to most of the antibiotics (23-27). In this study, the lowest resistance rates in *A. baumannii* isolates were detected for colistin (5.1%) and ampicillin-sulbactam (13.1%) (Table 3).

Among the antimicrobial agents used for *A. baumannii*, colistin is the most active antibiotic. However, because of increased incidence of colistin resistant *A. baumannii* isolates, today there is a suspicion regarding the use of this antibiotic against the infections caused by A. baumanii (28). Colistin resistance in our study was 5.1%. Nevertheless, this result should be confirmed by alternative methods (11). In the literature, varying rates of colistin resistance (as high as 40.6%) in *A. baumannii* isolates were documented by different countries (29). On the other hand, ampicillin-sulbactam is an alternative drug for *A. baumannii* infections (30). The resistance rate (13.1%) in this study was much lower than the result (51.6%) obtained from European countries which was published in 2008 (31).

Nearly 10% of the nosocomial infections are developed by *K. pneumoniae*. Multidrug-resistance caused most commonly by ESBLs and carbapenemases in this pathogen generally results in treatment failure (10). ESBLs which belong to Ambler Class A beta-lactamases can hydrolyse monobactams and cephalosporins, but do not affect carbapenems or cephamycins (15). Rate of infections particularly caused by ESBL producing *E. coli* and *K. pneumoniae* has increased (32). On the other hand, carbapenems have been used as the last resort treatment for the infections caused by multidrug-resistant *Enterobacteriaceae* (33). However, the incidence of carbapenemase-producing *Enterobacteriaceae* has risen globally over the last decade. *K. pneumoniae* carbapenemase (KPC) enzymes (for which *K. pneumoniae* isolates are the major sources) are the most frequent cause of antibiotic resistance in carbapenemase-producing *Enterobacteriaceae* (34).

Antibiotic resistance rates detected among *K. pneumoniae* in this study were noted to be different from the data of South Cyprus in the 2010 report (21). In that publication, resistance of *K. pneumoniae* against fluoroquinolones, carbapenems and the third-generation cephalosporins were documented as 38.8%, 16.4%, and 34.3% respectively, while the isolates in our study exhibited lower resistance rates for these antibiotics. In our *K. pneumoniae* isolates, ciprofloxacin, levofloxacin and norfloxacin resistance were recorded as 20.1%, 16.8% and 18.0%, respectively. While low levels of resistance were detected for ertapenem and meropenem (4.6% and 1.0%, respectively), none of *K. pneumoniae* isolates (0.0%) were resistant against imipenem. Among the third-generation cephalosporins, prevalence of resistance for cefotaxime, ceftriaxone and ceftazidime were found to be 15.4%, 22.4% and 21.1%,

respectively. Resistance rate of *K. pneumoniae* isolates against azteronam was 21.7% (Table 4). In this study, the data from Phoenix instrument revealed that 34 (16.7%) of 204 *K. pneumoniae* isolates were positive for ESBL. However, this result should be confirmed by alternative methods (35). Yet, our finding is comparable with the data reported from Turkey in 2008. In that study, ESBL prevalence among Klebsiella spp. isolated from urine cultures was found to be 12.0% (36).

The antimicrobial resistance report in 2010 indicated that aminoglycoside resistance of *K. pneumoniae* in South Cyprus was 19.4% (21). According to the results of our study, gentamicin resistance among *K. pneumoniae* isolates was found to be 14.2%, while none (0.0%) of these isolates was resistant to amikacin. The highest levels of resistance in *K. pneumoniae* isolates were detected for ampicillin-sulbactam (39.9%), cefazolin (35.3%), cefuroxime (34.2%) and tetracycline (30.8%) (Table 4). Because of the increased incidence of cefazolin resistance, today there is a suspicion regarding the use of this antibiotic against the infections caused by *Enterobacteriaceae* (37). Besides, a study conducted in the USA revealed an increase in the resistance rates of *K. pneumoniae* isolates against antibiotics except for tetracycline between 1998 and 2010 (38).

Our study presented a data on the antimicrobial resistance rates of *P. aeruginosa*, *A. baumannii* and *K. pneumoniae* isolates reported between August 2010 and December 2014 at the NEU Hospital in North Cyprus. These bacteria are clinically important pathogens and investigation of their antimicrobial resistance patterns is crucial. To our knowledge, this is the first study that analyzed the antimicrobial resistance rates of *P. aeruginosa*, *A. baumannii* and *K. pneumoniae* isolates in a centre from North Cyprus. Among the antibiotics tested, particularly the rates of carbapenem resistance in *P. aeruginosa* and *K. pneumoniae* isolates, and the level of colistin resistance in *A. baumannii* were found to be lower in comparison with the other studies where high rates of resistance were reported. Relatively lower rates of resistance in these bacteria could be a result of implementation of accurate infection control programme and administration of proper antibiotic treatment protocols in our hospital. Yet, the results obtained from this study suggest that antibiotic resistance in our hospital cannot be ignored and the susceptibility test results should be analyzed regularly. By additional multi-centered studies, more comprehensive data on antimicrobial resistance profiles of bacteria and the genetic backgrounds of resistance should be reported from North Cyprus.

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