International Journal of Scientific and Technological Research www.iiste.org
ISSN 2422-8702 (Online), **DOI:** 10.7176/JSTR/6-03-10
Special Issue of Health Sciences, Vol.6, No.3, 2020

Evaluation of Antibiotic Resistance Rates of *Klebsiella pneumoniae* Isolated From Patients with Bloodstream Infection

Omer Akgul
Van Yuzuncu Yil University, Faculty of Pharmacy, Van, Turkey
E-mail: o.akgul@yyu.edu.tr

Abstract
Klebsiella pneumoniae accounts for more than 70% of human infections. Especially *K. pneumoniae* is considered as a significant cause of bloodstream-associated infections (BSIs), urinary tract infections (UTIs), and respiratory tract infections in neonatal and intensive care units. A total of 316 *K. pneumoniae*, 168 isolates from male and 148 isolates from female patients, were isolated from the blood cultures of intensive care patients in Van Training and Research Hospital of the University of Health Sciences. The highest isolation was detected in the age group of "72<" in the male and female patients. The lowest isolation rates were observed in the age group of "18-36" in the male patients and "36-54" in the female patients. Extended-spectrum β-lactamase (ESBLs) and Carbapenemase (CP) productions of 316 *K. pneumoniae* isolates were evaluated by antibiotic resistance results. Two hundred and fifty *K. pneumoniae* strains isolated from the patients were observed to be ESBL positive. CP productions of 132 of the 316 *K. pneumoniae* isolates were revealed to be positive. It was concluded that *K. pneumoniae* strains, which cause circulatory system infections in our region, had high ESBLs and CP resistance, and it was important to analyze them accurately by sex, age, and antibiotic resistance.

Keywords: ESBLs, carbapenemase, *K. pneumonia*, blood infection.

Special Issue of Health Sciences

DOI: 10.7176/JSTR/6-03-10

Introduction

Klebsiella spp. are identified within saprophyte bacteria, which are in the family Enterobacteriaceae and often isolated from the environment. Also, *Klebsiella pneumoniae* is the *Klebsiella* species that are most isolated from clinical infections and account for more than 70% of human infections (Hansen et al., 1998; Pitout et al., 2016). *K. pneumoniae* become colonized in humans often in the gastrointestinal tract, skin, and nasopharynx (Pitout et al., 2016). *K. pneumoniae* plays an important role in community-acquired infections such as necrotizing pneumonia, pyogenic liver diseases, and endogenous endophthalmitis (Broberg et al.,2014; Siu et al., 2012). Since 1970, *K. pneumoniae* has been regarded as a major cause of hospital infections, especially bloodstream-associated infections (BSIs), urinary tract infections (UTIs), and respiratory tract infections, in neonatal and intensive care units, (Hansen et al., 1998; Daikos et al., 2012; Broberg et al., 2014). Antibiotic resistance profiles of the bacteria (especially *K. pneumoniae*) that are cited among the causes of diseases such as bloodstream infections, diarrhea, pneumonia, UTIs, and gonorrhea have been emphasized in a report published by the World Health Organization (WHO), (World Health Organization, 2014). In some countries, more than half of the patients associated with *K. pneumoniae* have been reported to be incurable because of carbapenem resistance (Pitout et al., 2016).
β-lactam antibiotics are widely used in the treatment of bacterial infections. A considerable resistance is observed among gram-negative bacteria because of overuse or misuse of these antibiotics (Shaikh et al., 2015; Pitout and Laupland, 2008). In recent years, the increase in the multiple-drug resistant *K. pneumoniae* infections has raised concerns (Falcone et al., 2016; Man et al., 2017). *K. pneumoniae* that were isolated from infections have been reported to produce Extended-spectrum Beta-Lactamase (ESBL) and carbapenemase (CP) and cause considerable increases in mortality and morbidity rates (Meatherall et al., 2009; Man et al., 2017). ESBL-producing *K. pneumoniae* have been reported from various regions

around the world (Girlich et al., 2001; Livermore and Hawkey, 2005; Mena et al., 2006; Carrer et al., 2008). In 2001, ESBL prevalence in Germany (*K. pneumoniae* 8,2%) has been reported to be lower when compared with the USA and Western Pacific regions (Sturenburg and Mack, 2003). In Taiwan, the annual incidence of ESBL-producing *K. pneumoniae* has been reported to be 12,1% between 2002 and 2010 (Cheng et al., 2016). According to the data of the National Antimicrobial Resistance Surveillance System (UAMDSS), where the data on blood cultures are collected in Turkey, GSBL positivity in *K. pneumoniae* in 2013 was found to be 49,9% (Saygılı and Akgüneş, 2017). In Europe, Carbapenem-resistant *K. pneumoniae* isolates have been observed to be spreading since 2006 (Mena et al., 2006; Gröbner et al., 2009). In Greece, it has been reported that CP-KP was isolated from 10% of the patients who had been admitted in intensive care units (Papadimitriou-Olivgeris et al., 2017; Man et al., 2017). In a multi-center study conducted in Turkey between 2000-2003, Gram-negative bacteria were found to be 99,3% susceptible to meropenem and 97,6% to imipenem (Çiftçi et al., 2013). In hospital-based studies, the mortality rate in cases of comorbid infection and *K. pneumoniae*-induced bacteremia has been reported to be 20-40% (Meatherall et al., 2009).

This study aimed to determine the presence and prevalence of *K. pneumoniae* in the blood culture samples obtained from the inpatients in the intensive care units of Van Training and Research Hospital of the University of Health Sciences. Also, the study aimed to reveal the antibiotic resistance profiles of the *K. pneumoniae* isolates and determine the risks they pose to human health in intensive care units.

Materials and Method

Isolation and Identification of Bacteria, and Antibiogram Test:

The inpatients in the intensive care units of Van Training and Research Hospital of the University of Health Sciences between February and December of 2018 were monitored. The distributions of the intensive care patients were classified by their sexes and average ages (<18, 18-36, 36-54, 54-72, 72<). Blood culture bottles were monitored in Bactec/Alert 3D (Biomerieux, USA) for 72 hours. Positive blood culture bottles were evaluated microbiologically. The blood culture bottles were inoculated on 5% sheep-blooded agar (Acumedia, USA), McConkey Agar (Oxoid, UK), and Eosin Methylene Blue agar (EMB, Oxoid, UK). The cultures were left for incubation at 37° C for 48 hours. The colony morphology of the cultures was evaluated. Their biochemical tests such as Gram staining, Catalase test, and Oxidase test were carried out. Vitek 2 Compact (Biomerieux, USA) device was used for the identification of the bacteria and antibiogram test.

Statistical Analysis:

Descriptive statistics for the studied variables (characteristics) were presented as count and percent. Proportions styled outfits were compared with the Z test for two proportions styled outfits. Statistical significance levels were set at 5% and MINITAB for windows (: 14) statistical program was used for all statistical computations.

Ethics:

The Ethics Committee of Van Training and Research Hospital of the University of Health Sciences approved this study.

Conclusion

Results of Isolation and Identification of Bacteria, and Antibiogram Test:

Three hundred and sixteen *K. pneumoniae*, 168 isolates from the male patients and 148 from the female patients, were isolated from the blood cultures of the intensive care patients. The highest isolation was detected in the age group of "72<" in the male and female patients. The second highest isolation rates were found to be at the age group of "36-54" in the male patients and "<18" in the female patients. The lowest isolation rates were observed in the age group of "18-36" in the male patients and "36-54" in the female patients (Table 1).

The antibiotic resistance rates of the *K. pneumoniae* isolates detected in the female and male patients were given in Table 2. The highest antibiotic resistance of the *K. pneumoniae* strains in the female patients was found to be against Ceftazidime (118, 80%) and Ampicillin (116, 78,4%). The lowest antibiotic resistance of the *K. pneumoniae* isolates isolated from the female patients was found to be against Nitrofurantoin (140, 94,6%). The highest intermediate resistance in female patients was found to be against Tigecycline (39, 26,3%). *K. pneumoniae* isolates isolated from the male patients were found to show the highest resistance against Ampicillin (126, 75%) and Ceftazidime (120, 71,4%). The highest antibiotic susceptibility of the *K. pneumoniae* isolates isolated from the male patients was found to be

against Fosfomycin (158, 94%). The highest intermediate resistance in male patients was found to be against Amikacin (51, 30,4%).

ESBLs and CP production of the 316 K. pneumoniae isolates obtained from the blood cultures of the inpatients of intensive care units were evaluated by antibiotic resistance results (Table 2). While ESBLs of the 122 *K. pneumoniae* strains isolated from the female patients were observed to be positive, ESBLs of the 128 *K. pneumoniae* strains isolated from the male patients were observed to be positive. In the evaluation of the 316 *K. pneumoniae* strains, the CP production of the 63 *K. pneumoniae* isolates in the female patients and 69 *K. pneumoniae* isolates in the male patients were revealed to be positive.

Statistical Analysis Results:

Distribution of the *K.pneumonia* isolates by sex and age was examined and the difference between the incidence rates of the infection was found to be statistically significant between the age groups of <18 and 18-36 ages (Table 1). The statistical evaluation of the antibiotic resistance profiles of the *K.pneumonia* isolates in the males and females were expressed by P_R, P_I, and P_S. The P_R value was observed to be significant only in Meropenem and Fosfomycin by sex. The P_I value was found to be significant in Meropenem, Gentamicin, and Cefepime. When compared with the other antibiotics, only P_S values of the antibiotics Ciprofloxacin and Fosfomycin were revealed to be significant (Table 2).

Table 1. Distribution of the *K.pneumonia* isolates by sex and age

Yaş	Erkek (n=168,%)	Kadın (n=148,%)	*P* değeri
<18	18 (11)	40 (27)	0,001
18-36	8 (5)	22 (15)	0,002
36-54	32 (19)	21(14)	0,249
54-72	28 (17)	29 (20)	0,499
72<	62 (37)	56 (38)	0,864

Table 2. Antibiotic resistance profiles of the *K. pneumonia* isolates

	Woman (n=148) (%)			Man (n=168) (%)			*P*		
ANTİBİYOTİK	R	I	S	R	I	S	P_R	P_I	P_S
SXT*	63 (43)	-	85 (57)	77 (45,8)	-	91 (54,2)	0,560	-	0,560
Levofloksasin	31 (21)	3 (2)	114 (77)	30 (17,9)	1(0,6)	137 (81,5)	0,488	0,256	0,321
Ciprofloxacin	94 (63,5)	7 (4,7)	41 (31,8)	92 (54,8)	4(2,4)	72 (42,8)	0,115	0,256	0,005
Ampicillin	116 (78,4)	-	32 (21,6)	126 (75)	-	42 (25)	0,479	-	0,479
Piperacillin	22 (15)	-	126 (85)	21 (12,5)	-	147 (87,5)	0,541	-	0,541
Piperacillin/Tazobactam	97 (65,5)	11 (7,4)	40 (27,1)	98 (58,3)	15 (8,9)	55 (32,8)	0,188	0,629	0,269
Imipenem	32 (13,5)	23 (15,5)	93 (71)	35 (20,8)	24 (14,3)	109 (64,9)	0,864	0,754	0,790
Meropenem	56 (37,8)	7 (4,7)	85 (57,5)	46 (27,4)	23 (13,7)	99 (58,8)	0,047	0,007	0,871
Ertapenem	49 (33,1)	1 (0,7)	98 (66,2)	49 (29,2)	5 (3)	114 (67,8)	0,450	0,135	0,757
Amikacin	40 (38)	32 (21,6)	76 (40,4)	36 (21,4)	51 (30,4)	81 (48,2)	0,245	0,078	0,578
Netilmicin	17 (11,5)	-	131 (88,5)	18 (10,7)	-	150 (89,3)	0,827	-	0,827
Tobramycin	17 (11,5)	-	131 (88,5)	18 (10,7)	-	150 (89,3)	0,827	-	0,827
Gentamisine	43 (29)	27 (18,2)	78 (52,8)	56 (33,3)	17 (10,1)	95 (56,6)	0,413	0,037	O,493
Colistin	15 (10,1)	-	133 (89,9)	30 (17,9)	-	138 (82,1)	0,500	-	0,500
Nitrofurantoin	8 (5,4)	-	140 (94,6)	15 (8,9)	-	153 (91,1)	0,229	-	0,229
Tigecycline	12 (8,1)	39 (26,3)	97 (65,6)	13 (7,7)	32 (19)	123 (73,3)	0,903	0,121	0,139
Fosfomycine	22 (15)	-	126 (85)	10 (6)	-	158 (94)	0,009	-	0,009
Ceftazidime	118 (80)	4 (2,7)	26 (17,3)	120 (71,4)	8 (4,8)	40 (23,8)	0,088	0,339	0,173
Cefuroxime	102 (69)	-	46 (31)	111 (66)	-	57 (34)	0,590	-	0,590
CefuroximeAxetil	102 (69)	1 (0,7)	46 (30,3)	108 (64,2)	2 (1,2)	58 (34,6)	0,384	0,638	0,516
Cefoxitin	54 (36,5)	1 (0,7)	93 (62,8)	59 (35,1)	3 (1,8)	106 (63,1)	0,800	0,378	0,962
Cefepime	74 (50)	1 (0,7)	73 (49,3)	67 (39,9)	9 (5,4)	92 (54,7)	0,071	0,018	0,334
Cefixime	44 (29,7)	-	104 (70,3)	55 (32,7)	-	113 (67,3)	0,565	-	0,565
Aztreonam	20 (13,5)	-	128 (86,5)	19 (11,3)	1 (0,6)	148 (88,1)	0,552	-	0,552

R: Resistant; I: Intermediate Susceptible; S: Susceptible; SXT*: Trimethoprim-sulfamethoxazole

Discussion

It has been revealed by various studies that *K. pneumoniae* isolated from blood cultures vary by sex and age (Meatherall et al., 2009; Boo et al., 2005; Pessoa-Silva et al., 2003). In Brazil, 55% of blood cultures were found to be isolated from male patients (Martins-Loureiro et al., 2001). Again, Leikin-Zach et al. found in their study that 65% of male patients were isolated. In a study Pessoa-Silva et al. conducted in 2003, *K. pneumoniae* isolation rate was reported to be higher in female patients. It was determined in several other studies that there was no difference between *K. pneumoniae* isolation rate and sex (Boo et al., 2005; Cassettari et al., 2009). In a study conducted in Canada between 2000 and 2007, 640 bacteraemic *K. pneumoniae* isolates were found to be highest in patients who were aged 60 and over (Meatherall et al., 2009). 853 *K. pneumoniae* were isolated from the blood cultures of intensive care unit patients in China and it was reported that the highest isolation rate was found in the male patients who were aged over 65 (Man et al., 2017). Melot et al. reported that 68 (57%) of the 119 *K. pneumoniae* isolates they isolated from blood between 2008 and 2013 were isolated from female patients. In this study, 316 *K. pneumoniae* were isolated from the blood cultures of intensive care patients and male patients aged over 72 were found to have the highest isolation (62, 19,6%).

The risk associated with ESBL and Carbapenem resistance of *K. pneumoniae* strains poses a significant problem in intensive care patients (Salmanov et al., 2019; Sharma et al., 2010). The isolation rate of ESBL positive *K. pneumoniae* isolated from hospitals in Germany between 2003 and 2007 was reported to be 66 (18%). 5 (7,6%) of the 66 ESBL positive *K. pneumoniae* isolates were found to produce carbapenemase (Gröbner et al., 2009). Espinar et al. (2011) revealed in their study, in which they used Vitek 2 automated system, that 72 *K. pneumoniae* isolates were ESBL positive. 25 (25%) of 100 *K. pneumoniae* isolates have been reported to be ESBL positive in the Nehru hospital of India (Sharma et al., 2010). *K. Pneumoniae* (21,8%) has been reported to be isolated at the highest rate from the samples collected from 642 patients in intensive care units in Ukraine. Third generation Cephalosporin resistance and carbapenem resistance of *K. pneumoniae* isolates have been reported to be 53,8% and 29,3%, respectively (Salmanov et al., 2019). In a retrospective study conducted in a pediatric intensive care unit in Israel between 2013 and 2014, it has been reported that 57 (65,5%) *K. pneumoniae* were isolated out of 87 blood cultures and ESBL resistance was observed in 5 (5,7%) *K. pneumoniae* (Leikin-Zach et al., 2018). 49 (70%) out of 70 *K. pneumoniae* isolates have been reported to be ESBL positive in the Al-Zahra hospital of Iran (Masjedian Jazi et al., 2007). It was observed in this study that 250 (79%) of the 316 *K. pneumoniae* isolates were ESBL positive and 132 (42%) were CP positive. When compared with the other studies, it was revealed that the people in our region were highly exposed to *K. pneumoniae* colonization and that health care professionals in intensive care units of hospitals should be provided more in-service training.

Cuzon et al. reported in their study that all of the 16 *K. pneumoniae* isolates they collected from five different countries were resistant against penicillin and cephalosporins. They reported that *K. pneumoniae* isolates showed the highest resistance against Tetracyclin (87,5%) and the lowest against Gentamicin (75%) among the other antibiotics. In a study in Portugal, 72 *K. pneumoniae* isolates were reported to show the highest antibiotic resistance against Trimethoprim–sulfamethoxazole (87,4%) and the lowest against Levofloxacin (44,2%) (Espinar et al., 2011). Meatherall et al. reported that the 640 bacteraemic *K. pneumoniae* strains showed the highest resistance against Ampicillin (100%). In this study, the *K. pneumoniae* strains isolated from the female and male patients were found to show the highest resistance against Ceftazidime (118, 80%; 120, 71,4%) and Ampicillin (116, 78,4%; 126, 75%). The lowest antibiotic resistance of the *K. pneumoniae* isolates isolated from the female and male patients were found to be against Nitrofurantoin (140, 94,6%) and Fosfomycin (158, 94%), respectively. The highest intermediate resistances in the female and male patients were found to be against Tigecycline (39, 26,3%) and Amikacin (51, 30,4%), respectively. It was detected that the antibiotic susceptibilities of the K. pneumoniae isolates isolated from the blood cultures collected from the female and male patients might vary and resistance should be revealed correctly in the selection of the antibiotic to be used in treatment.

The statistical evaluation of the *K. pneumoniae* strains isolated from the blood cultures of the patients was carried out regarding their sex and age distributions and antibiotic resistance patterns. The difference between the *K. pneumoniae* isolates isolated from the female and male patients who were aged "<18" and "18-36" was found to be statistically significant. Based on this, the female patients were found to be more susceptible to *K. pneumoniae*-induced circulatory system infections at young ages. It was determined that no such difference occurred in the other age groups. In statistically evaluating the differences in the antibiotic resistance by sex, the P_R value was found to be significant only in Meropenem and Fosfomycin. It was revealed that the resistance of the *K. pneumoniae* isolates isolated from the female patients against Meropenem and Fosfomycin might be higher. The P_I value was found to be significant

in Meropenem, Gentamicin, and Cefepime by sex. The intermediate resistance of the *K. pneumoniae* strains isolated from the male patients against the antibiotics Meropenem and Cefepime was found to be higher. The *K. pneumoniae* isolates isolated from the female patients showed higher resistance against Gentamicin. In the evaluation of the P_S value by sex, the difference between the antibiotics Ciprofloxacin and Fosfomycin was found to be significant. The *K. pneumoniae* strains isolated from the male patients were found to be more susceptible to Ciprofloxacin and Fosfomycin. It was observed that the sex, age, and resistance characteristics of K. pneumoniae-induced circulatory system infections might vary and it was important to perform annual follow-ups regularly in light of this information.
In conclusion, it was observed that *K. pneumoniae*-induced circulatory system infections that people in our region are exposed to posed a high risk in female and male patients. Especially, it was found that ESBLs and CP positive *K. pneumoniae* isolation rates were high and the patients were at serious risk. Based on this, it was revealed that the distribution of antibiotic resistance of circulatory system-induced *K. pneumoniae* isolates by age and sex might vary and that it was important to use antibiotic susceptibility results in correctly forming treatment methods to be prepared. It has been concluded that it is important to improve in-service training in hospitals and share the association between antibiotic resistance and agent with specialists.

References

Hansen, D.S., Gottschau, A., Kolmos, H.J. (1998). Epidemiology of Klebsiella bacteraemia: a case control study using Escherichia coli bacteraemia as control. J Hosp Infect, 38, 119–132.

Pitout, J.D., Nordmann, P., Poirel, L. (2015). Carbapenemase-producing Klebsiella pneumoniae, a keypathogen set for globalnosocomialdominance. Antimicrob. Agent Chemother, 59, 5873-84.

Broberg, C.A., Palacios, M., Miller, V.L. (2014). Klebsiella: a longway to go towards understanding this enigmatic jet-setter. F1000Prime Rep, 6, 64.

Siu, L.K., Yeh. K.M., Lin, J.C., Fung, C.P., Chang, F.Y. (2012). Klebsiella pneumoniae liver abscess:a new invasive syndrome. Lancet Infect Dis, 12, 881– 887.

Daikos, G.L., Markogiannakis, A., Souli, M., Tzouvelekis, L.S. (2012). Bloodstream infections caused by carbapenemase-producing Klebsiella pneumoniae: a clinical perspective. Expert Rev Anti Infect Ther, 10, 1393–1404.

World Health Organization. Antimicrobial resistance: global report on surveillance 2014. WHO, Geneva, Switzerland, 2014.

Shaikh, S., Fatima, J., Shakil, S., Rizvi, S.M.D., Kamal, M.A. (2015). Antibiotic resistance and extended spectrum beta-lactamases: Types, epidemiology and treatment. Saudi J Biol Sci 22: 90-101.

Pitout, J.D., Laupland, K.B. (2008). Extended-spectrum β-lactamase-producing Enterobacteriaceae: an emerging public-health concern. Lancet Infect Dis, 8, 159-166.

Falcone. M., Russo, A., Iacovelli, A., Restuccia, G., Ceccarelli, G., Giordano, A. (2016). Predictors of outcome in ICU patients with septic shock caused by Klebsiella pneumoniae carbapenemase–producing K. pneumoniae. Clin Microbiol Infect, 22, 444-450.

Man, M.Y., Shum, H.P., Chan, Y.H., Chan, K.C., Yan, W.W., Lee, R.A., (2017). Clinical predictors and outcomes of Klebsiella pneumoniae bacteraemia in a regional hospital in Hong Kong. J Hosp Infect, 97, 35-41.

Meatherall, B.L., Gregson, D., Ross, T., Pitout, J.D., Laupland, K.B. (2009) Incidence, risk factors, and outcomes of Klebsiella pneumoniae bacteremia. Amerikan J Med, 122, 866-873.

Carrër, A., Poirel, L., Eraksoy, H., Cagatay, A.A., Badur, S., Nordmann, P. (2008). Spread of OXA-48-positive carbapenem-resistant Klebsiella pneumoniae isolates in Istanbul, Turkey. Antimicrob Agents Chemother, 52, 2950-54.

Girlich, D., Poirel, L., Leelaporn, A., Karim, A., Tribuddharat, C., Fennewald, M. (2001). Molecular epidemiology of the integrin located VEB-1 extended-spectrum β-lactamase in nosocomial enterobacterial isolates in Bangkok, Thailand. J Clin Microbiol, 39, 175–182.

Livermore, D.M., Hawkey, P.M. (2005). CTX-M: changing the face of ESBLs in the UK. J. Antimicrob. Chemother, 56, 451-4.

Mena, A., Plasencia, V., Garcıa, L., Hidalgo, O., Ayestaran, J.I., Alberti, S. (2006). Characterization of a large outbreak by CTX-M-1-producing Klebsiella pneumoniae and mechanisms leading to in vivo carbapenem resistance development. J Clin Microbiol, 44, 2831–2837.

Stürenburg, E., Mack, D. (2003). Extended-spectrum β-lactamases: implications for the clinical microbiology laboratory, therapy, and infection control. J Infect, 47, 273-295.

Cheng, W.L., Hsueh, P.R., Lee, C.C., Li, C.W., Li, M.J., Chang, C.M. (2016). Bacteremic pneumonia caused by extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae: Appropriateness of empirical treatment matters. J Microbiol Immunol Infect, 49, 208-215.

Saygılı Pekintürk, N., Akgüneş, A. (2017). Yatan hastalardan izole edilen Escherichia coli ve Klebsiella spp. suşlarında genişlemiş spektrumlu beta-laktamaz üretimi ve antibiyotik direnç oranları: 2011-2015 verileri. Turk Hij Den Biyol Derg, 74, 3, 221 – 228.

Gröbner, S., Linke, D., Schütz, W., Fladerer, C., Madlung, J., Autenrieth, I.B. (2009). Emergence of carbapenem-non-susceptible extended-spectrum β-lactamase-producing Klebsiella pneumoniae isolates at the university hospital of Tübingen, Germany. J Med Microbiol, 58, 912-22.

Papadimitriou-Olivgeris, M., Fligou, F., Bartzavali, C., Zotou, A., Spyropoulou, A., Koutsileou, K. (2017). Carbapenemase-producing Klebsiella pneumoniae bloodstream infection in critically ill patients: risk factors and predictors of mortality. E J Clin Microbiol Infect Dis, 36, 1125-31.

Çiftci, İ.H., Karakeçe, E., Aşık, G., Demiray, T., Er, H. (2013). Karbapenem Dirençli Klebsiella Pneumoniae Suşlarında Oxa-48 ve Kpc Varlığının Araştırılması. Ankem Derg, 27, 49-54.

Boo, N.Y., Nag, S.F., Lim, V.K. (2005). A case-control study of risk factors associated with rectal colonization of extended-spectrum beta-lactamase producing Klebsiella sp. in newborn infants. J Hosp Infect, 61, 68-74.

Pessoa-Silva, C.L., Meurer Moreira, B., Câmara Almeida, V. (2003). Extended-spectrum beta-lactamase-producing Klebsiella pneumoniae in a neonatal intensive care unit: risk factors for infection and colonization. J Hosp Infect, 53, 198-206.

Martins-Loureiro, M., de Moraes, B.A., de Mendonça, V.L., Rocha-Quadra, M.R., dos Santos-Pinheiro, G., Dutra-Asensi, M. (2001). Molecular epidemiology of extendedspectrum beta-lactamase-producing Klebsiella pneumoniae isolated from neonatal intensive care unit patients involved in hospital infection cases in Rio de Janeiro, Brazil. Rev Latinoam Microbiol, 43, 88-95.

Leikin-Zach, V., Shany, E., Yitshak-Sade Eshel, R., Shafat, T., Borer, A. (2018) Neonatal Risk Factors for Colonization with Extended-Spectrum Beta-Lactamase-Producing Bacteria in the Neonatal Intensive Care Unit. Isr Med Assoc J, 5, 286-90.

Cassettari, V.C., da Silveira, I.R., Dropa, M. (2009). Risk factors for colonisation of newborn infants during an outbreak of extended-spectrum β-lactamase producing Klebsiella pneumoniae in an intermediate-risk neonatal unit. J Hosp Infect, 71, 340-7.

Melot, B., Colot, J., Guerrier, G. (2015) Bacteremic community-acquired infections due to Klebsiella pneumoniae: clinical and microbiological presentation in New Caledonia, 2008–2013. Inter J Infect Dis, 41, 29-31.

Salmanov, A., Litus, V., Vdovychenko, S., Litus, O., Davtian, L., Ubogov, S. (2019). Healthcare-associated infections in intensive care units. Wiadom Lekar, 72, 963- 9.

Sharma, J., Sharma, M., Ray, P. (2010). Detection of TEM & SHV genes in Escherichia coli & Klebsiella pneumoniae isolates in a tertiary care hospital from India. Indian J Medical Res, 132, 332-7.

Espinar, M.,. Rocha. R, Ribeiro., M., Rodrigues, A.G., Pina-Vaz, C. (2011). Extended-spectrum β-lactamases of Escherichia coli and Klebsiella pneumoniae screened by the VITEK 2 system. J Med Microbiol, 60, 756-760.

Masjedian Jazi, F., Valehi, F., Talebi, A., Rastegar Lari, A. (2007). Molecular evaluation of resistance to extended spectrum B lactamases producing E. coli and K. pneumonia. Med Microbiol J Iran, 1, 27-34.

Cuzon, G., Naas, T., Truong, H., Villegas, M.V., Wisell, K.T., Carmeli, Y. (2010). Worldwide diversity of Klebsiella pneumoniae that produce β-lactamase blaKPC-2 gene. Emerg Infect Dis, 16: 1349.