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Full Length Article

Antimicrobial Resistance and Sensitivity among Isolates of *Klebsiella pneumoniae* from Hospital Patients in Turkey

SEVİL TOROGLU AND DİLEK KESKİN[1]†
Department of Biology, Faculty of Arts and Science, Kahramanmaras Sütcü İmam University, 46100- Kahramanmaras, Turkey
†*Cine Vocational High School, Adnan Menderes University, 09500- Cine-Aydin, Turkey*
[1]Corresponding author's e-mail: dkeskin@adu.edu.tr

ABSTRACT

Klebsiella pneumoniae bacteria are significant agents of urinary system infections, upper respiratory tract infections and nosocomial infections. The aim of this study was to determine the antibiotic resistance to *K. pneumoniae* strains isolated in Microbiology Laboratory of different hospitals in Kahramanmaras between 2006-2007. Urine, vaginal fluid, wound, cerebrospinal fluid, blood, which send from various clinics were inoculated both Mac Conkey agar and Eosin Methylen Blue (EMB) agar. Twenty two *K. pneumoniae* were tested. Antibiotic resistance was determined by agar disc diffusion method using Mueller-Hinton agar according to Clinical and Laboratory Standards Institute recommendations and the production of β-lactamase was detected with the iodometric slide test. The Multiple antibiotic resistance (MAR) index values among 22 *K. pneumoniae* isolates were calculated. The results indicated that resistance rate of antibiotics was in the range of 95% Penicillin (PEN), 82% Amoxicillin (AMO), 77% Cefazolin (CEF), 59% Ceftriaxone (CEFT) and Tetracyclin (TET), 46% Gentamicin (GEN), 32% Nitrofurantoin (NIT), 27% Cefoxitin (CEFX & Ofloxacin (OFL), 23% Streptomycin (STR), 19% Chloramfenicol (CHL) and 9% Meropenem (MER). Among 22 isolates of *K. pneumoniae* 13 (59 %) showed beta lactamase activity especially isolated from urine, while 9 (41%) showed no beta lactamase activity. Out of 22 isolates, 18 (82%) isolates showed Multiple Antibiotic Resistance against four to ten antibiotics.

Key Words: *K. pneumoniae*; Antibiotic resistance; Beta lactamase activity

INTRODUCTION

Klebsiella pneumoniae strains are opportunistic pathogen and have been associated with various ailments such as urinary tract infection, septicemia, respiratory tract infection, wound infection, and diarrhea (Khadri *et al*., 2007).

Klebsiella pneumoniae is resistant to a number of antibiotics mainly extended-spectrum cephalosporin's and penicillin's due to acquisition of plasmid that encode for the production of extended spectrum beta lactamases (ESBL) especially TEM and SHV enzymes have been described worlwide (Lopes *et al*., 2005). Resistance of this species to third generation cephalosporins was first described in the early 1980s and a linear increase in resistance has occured since 1986 (Burwen *et al*., 1994; Monnet *et al*., 1997). These enzymes are derivatives of common β lactamases that have undergone one or more amino acid substitutions near the active site of the enzyme, thus increasing the affinity and the hydrolytic ability of enzyme for third-generation cephalosporins and monobactams (Jacoby & Medeiros, 1991). Genes encoding these enzymes are generally located in transferable plasmids, which are often such as aminoglycosides (Ferna'ndez-Rodri'guez *et al*., 1992).

In this study we determined the status of antimicrobial resistance, underlying conditions and determination of *K. pneumoniae* isolates with beta-lactamase production from patients, multiple antibiotic resistance ındex and also treatment of infections based on *K. pneumoniae,* which antibiotics could be better.

MATERIALS AND METHODS

Isolation of bacterial strains and identification: Twenty two isolates were collected from hospital patients in Kahramanmaras between 2006-2007 and recorded at specimens. Mac Conkey agar and EMBagar (Eosin Metilen Blue) agar used for *K. pneumoniae* isolation. Isolates were considered to be presumptive *Klebsiella* spp. gram-negative bacill, mucoid colonies and lactose positive. Confirmation of isolates was performed by using classic chemical tests (motility test, ure hydrolysis, acid production from mannitol, production of H_2S, IMVIC (Indol, Metil Red, Voges-Proskauer & Citrate), (Lassen, 1975; Krieg & Holt, 1984).

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Antibiotic resistance activity: Antibiotic resistance was determined by an agar disc diffusion test (Bauer *et al*., 1966) using Mueller-Hinton agar (Difco) according to Clinical and Laboratory Standards Institute (CLSI, 2005) recommendations. Twelve different antibiotics were used. For antibiotic resistance determination, the isolates were grown in Luria- Bertani (LB) broth until the turbidity equal to the 0.5 Mc Farland standart. Cultures were swabbed on to the Mueller–Hinton agar and all isolates were tested against Meropenem (MER, 10 µg/mL), Amoxicillin (AMO, 20 µg/mL), Penicilin (PEN, 10 µg/mL), Nitrofrantoin (NIT, 300 µg/mL), Cefazolin (CEF, 30 µg/mL), Cefoxitin (CEFX, 30 µg/mL), Ceftriaxone (CEFT, 30 µg/mL), Gentamicin (GEN, 10 µg/mL), Tetracycline (TET, 30 µg/mL), Streptomycine (STR, 10 µg/mL), Chloramfenicol (CHL, 30 µg/mL), Oflaxain (OFL, 5 µg/mL). The isolates those grown in inoculation were evaluated as resistant and the others were evaluated as susceptible (CLSI.2005). The antibiotic discs were dispensed sufficiently separated from each other so as to avoid overlapping of inhibition zones. The plates were incubated at 37°C and the diameters of the inhibition zones were measured after 18 h. All susceptibility tests were carried out in duplicate and were repeated twice if discordant results had been obtained.

β-lactamase production: The production of β-lactamase was detected with the iodometric slide test (MacFaddin, 2000; Toroglu & Toroglu, 2009). Previously, iodine solution was added to penicillin solution. Later, emulsify organism tested in a drop of freshly prepared penicillin-iodine solution on flamed side of a glass slide; made a heavy suspension. Then starch solution was added. Initially, solution of all samples will turn purple. An indication of β - lactamase production is clearing of solution, clearing of purple color to white within 5 min. But the entire mixture does not have to clear; clearing of definite clumps or areas is sufficient to denote a positive result. Starch and iodine react in solution to produce a purple color.

Multiple antibiotic resistance ındex: For all isolates, we calculated the MAR index values (a/b, where a represents the number of antibiotics the isolate was resistant to, b represents the total number of antibiotics the isolate tested against). A MAR index value ≥ 0.2 is observed when isolates are exposed to high risk sources of human or animal contamination, where antibiotics use is common; in contrast a MAR index value <or = 0.2 observed when antibiotics are seldom or never used (Krumperman, 1985; Matyar *et al.,* 2008).

RESULTS AND DISCUSSION

The results showed the resistance rate of antibiotics have shown in the range of 95% penicillin, 82% amoxicillin, 77% cefazolin, 59% each of ceftriaxone and tetracyclin, 46% gentamicin, 32% nitrofurantoin, 27% cefoxitin and oflaxacin, 23% streptomycin, 19% chloramfenicol and 9% meropenem (Table I & Table II).

Table I: Prevalence of the antibiotic resistance and beta lactamase production among 22 clinical *K. pneumoniae* ısolates

Antibiotics	Beta lactamase activity
Pen	-
Pen Tet	+
Pen Ofl	-
Amo Pen	+
Amo Pen Cef Cefx	+
Amo Pen Nit Cef	+
Amo Pen Cef Ceft	-
Amo Pen Cef Ceft	-
Amo Pen Nit Tet Ofl	+
Amo Cef Cefx Gent Ofl	-
Amo Pen Cef Ceft Gent Tet	+
Pen Cef Ceft Gent Tet Str	-
Amo Pen Cef Ceft Gent Tet	-
Amo Pen Nit Cef Ceft Tet Chl	+
Mer Amo Pen Nit Cef Cefx Ceft	+
Amo Pen Cef Cefx Ceft Gent Tet	+
Amo Pen Nit Cef Cefx Tet Str	-
Amo Pen Nit Cef Ceft Gent Tet Ofl	-
Mer Amo Pen Cef Cefx Ceft Gent Tet	+
Amo Pen Cef Ceft Gent Tet Str Chl	+
Amo Pen Cef Ceft Gent Tet Str Chl Ofl	+
Amo Pen Nit Cef Ceft Gent Tet Str Chl Ofl	+

There are many local studies about antimicrobial resistance and sensitivity among *K. pneumoniae* in Turkey like ours (Halit *et al*., 1999; Gonlugur *et al*., 2004; Yüksel *et al*., 2006; Aladag & Durak, 2009; Albayrak & Kaya, 2009) and other countries (Jones *et al*., 2004; Aiyegoro *et al*., 2007; Jean *et al.,* 2009; Romanus *et al*., 2009).

Among the beta lactam antibiotics, penicillin resistance rate (95%) was the highest and amoxicillin resistance rate was 82% in the present study (Table II). Aladag and Durak (2009) has shown penicillin resistance rate 100% to *K. pneumoniae* isolated from urinary system infections. In their study, bacterial suspectibility to all antimicrobial agents was determined according to criteria of the National Committee for Clinical Laboratory Standarts by means of agar disc diffusion test like ours. A high resistance of beta lactam antibiotics is due to penisilinase coded by R factor inhibited it. (Sawai *et al.,* 1973). Generally urine isolates were resistant to only penicillin. Blood isolates were resistant to penicillin and amoxicillin. Cerebro Spinal Fluid (CSF) isolates were resistant to penicillin and cefazolin. Beta lactams were showed high resistance in this study.

Among the Cephalosporins group, as for the cefazolin resistance rate, it has been 77% (Table II). It was the highest in cephalosporins group. In Turkey, Sesli-Cetin *et al.* (2007) reported that cefazolin suspectibility rate has been 31.4%. *K. pneumoniae* isolated from intensive care unit. Gonlugur *et al.* (2004) has shown cefazolin suspectibility rate 64.3% to *Klebsiella* spp isolated from a Turkish university hospital by disc diffusion method. Our result was different from that reported by Jean *et al.* (2009) who also reported that *K. pneumoniae* showed a resistance of 31% to cefazoline. In their study, a total of 574 *Enterobacteriaceae* isolates

Table II: Antibiotic resistance of 22 isolates *K. pneumoniae* strains according to the disc diffusion

Antibiotic group:	Antibiotics	Resistance (%)
Beta-Lactams:	Penicilin (PEN),Amoxicillin (AMO), Meropenem (MER)	95%, 82%, 9%
Nitrofrantoins:	Nitrofrantoin (NIT)	32%
Cephalosporins:	Cefazolin(CEF), Ceftriaxone(CEFT), Cefoxitin(CEFX)	77%, 59%, 27%
Aminoglycosides:	Gentamycin (GEN), Streptomycine (STR)	46%, 23%
Tetracyclines:	Tetracycline (TET)	59%
Macrolides:	Chloramphenicol (CHL),	19%
Quinolones:	Ofloxacin (OFL)	27%

Table III: Multiple Antibiotic resistance index of 22 *K. pneumoniae* strains

Source of isolates	Total Isolates	Multiple Antibiotic Resistance Index (MAR)
Urine	15	0.08, 0.17(3 isl) 0.33((2 isl), 0.42(3 isl), 0.58(3 isl), 0.66, 0.75, 0.83
Blood	3	0.5, 0.58, 0.66
Vaginal Fluid	1	0.33
Cerebrospinal Fluid	2	0.66
Wound	1	0.33

isl:isolates

recovered from various clinical samples. *E. coli, K. pneumoniae, Enterobacter cloaceae, Serratia marcescens, Citrobacter freundii, Morganella moragnii, Proteus mirabilis* were tested 18 antimicrobial agents by the broth microdilution method. It can be suggested that difference of the method can be affect resistance's percentage of bacteria.

Among the Cephalosporins group, as for the ceftriaxone resistance rate, it has been 59% (Table II). Ceftriaxone resistance rate has reported from 0.6% to 79.6% in different studies (Karlowsky *et al*., 2002; Jones *et al*., 2004; Al-Zahrani & Akhtar, 2005; Romanus *et al*., 2009). Shukla *et al.* (2004) reported that *K. pneumoniae* showed a resistance of 62.5% to ceftriaxone among the different clinical isolates.

Tetracycline resistance was 59% (Table II). Resistance patterns of *K. pneumoniae* revealed that 88.5% to tetracycline (Romanus *et al*., 2009). In a similar study, all *K. pneumoniae* isolates were higly resistant to tetracycline 100% (Okonko *et al*., 2009). Our results are similar to that reported by Ahmed *et al.* (2000) who also reported that *K. pneumoniae* showed a resistance of 61% to tetracycline. In their study, a total of 155 common pathogenic bacteria were recovered from patients with diarrhea and 362 common bacterial organisms were recovered from patients with urinary tract infections. *E. coli, K. pneumoniae, Proteus mirabilis, Enterobacter, Acinetobacter* and *Pseudomonas* species were isolates obtained from this study.

Among the aminoglycosides, as for the gentamicin resistance rate, it was 46% (Table II). In Turkey, some researchers have reported gentamycin resistance rate from 15.2% to 77.9% (Urbarli *et al*., 2001; Yilmaz *et al*., 2005). Our results are in complyance with previous research. In Trinidad Orrett (2004) it showed gentamicin resistance rate was 16.7% among the *K. pneumoniae* isolated from intensive care unit. Gentamycin resistance rate change according to region. For example, while in westren Nigeria, Okonko *et al* (2009) reported that gentamicin resistance rate was 100%, In south-western Nigeria Okesola and Makanjula (2009) reported that 48.4%.

Resistance rate of nitrofurantoin was 32% in the present study (Table II). Romanus *et al.* (2009) reported that 31.2% nitrofurantoin resistance rate was like ours. In their study, a total of 300 clinical isolates of *K. pneumoniae* were isolated from 100 blood samples, 100 sputum samples, 100 urine samples. The isolates were subjected to susceptibility testing using agar disc diffusion test of determining antimicrobial susceptibility and the results were interpreted as per National Committee for Clinical Laboratory Standarts (NCCLS) recommendations like ours. Ay *et al.* (2003) reported that nitrofurantoin resistance rate was 48% and 30% among the *K. pneumoniae* isolated from urine samples. Yüksel *et al.* (2006) reported that nitrofurantoin could be included as a reasonable alternative in the empirical treatment of lower urinary tract infections in older children.

Taking into account the total number of clinical isolates in the present study period only 27% of the *K. pneumoniae* species isolated were resistant to cefoxitin (Table II). Goldstein *et al.* (1995) reported 2.8% cefoxitin resistance rate of *K. pneumoniae* isolated in community. In Turkey, Toroglu *et al.* (2005) reported that cefoxitin resistance rate was from 0% to 100% to *Klebsiella* sp isolated from Aksu river. Durmaz *et al.* (1997) have shown that out of 93 *Klebsiella* sp., 20 were resistant to cefoxitin.

Among the Quinolones group, ofloxacin resistance rate was 27% *K. pneumoniae* isolated from clinical samples (Table II). In Turkey, Ozbilge *et al.* (2004) reported that ofloxacin resistance rate was 6% *K. pneumoniae* isolated from urine samples. Aiyegoro *et al.* (2007) reported that all *Klebsiella* spp showed sensitivity to ofloxacin. Okonko *et al.* (2009) reported that *K. pneumoniae* showed 0% resistance to ofloxacin. Durak *et al.* (2007) also reported that *K. pneumoniae* showed a resistance of 25% to ofloxacin among the clinical isolates. In their study, the sensitivities of total 103 bacteria strains consisting of 52 Gram negative (*E. coli, Proteus* spp, *Pseudomonas aeruginosa, K. pneumoniae*) and 51 Gram positive (*Stpahylococcus aureus, Streptococcus pyogenes*) bacteria

isolated and identified from different patient material against to ofloxacin were determined by disc diffusion method. Durak *et al.* (2007) reported that ofloxacin is more effective to Gram negative strains than Gram positive bacteria and an increase on the number of resistant strains.

Taking into account the total number of clinical isolates in the present study period only 23% of the *K. pneumoniae* species isolated were resistant to streptomycin (Table II). Okonko *et al.* (2009) reported streptomycin resistance rate of 100% to *K. pneumoniae* isolated from clinical samples. Aladag and Durak (2007) also reported that *Klebsiella* spp showed a resistance of 22,4% to streptomycin, using the method similar to ours.

Macrolides antibiotics like chloramfenicol resistance rate was 19% in the present study (Table II). Okonko *et al.* (2009) reported chloramphenicol resistance rate of 100% in Abekuta, South western Nigeria. In a different study, the extended spectrum beta lactamase (ESBL) producing *Klebsiella* spp strains isolated from urinary system infections were determined to be 21% resistant to chloramphenicol (Kim *et al*., 2005). In Turkey, Aladag and Durak (2009) reported 17.8% chloramfenicol resistance rate among the ESBL producing *K. pneumoniae* and 20% chloramfenicol resistance rate among the non ESBL producing *K. pneumoniae*. Our results were similar to that reported by Aladag and Durak (2007) who also reported that *K. pneumoniae* showed a resistance 17.8% and 20% resistance to chloramphenicol. All samples strains of susceptibility of antibiotics were determined by using disc diffusion method as we did.

Among the beta lactam antibiotics, resistance rate of meropenem has been 9% in the present study (Table II). Carbapenems are the drugs of choice for many infections caused by gram negative and gram positive bacteria (Nicolau, 2008; Shah, 2008). In our results, it was the lowest. Ay *et al.* (2003) reported that *Klebsiella* has the highest resistance among the bacteria isolated from urine samples. Imipenem antibiotics, third generation cephalosporins, kinolon and aminoglycozid have the most sensitive antibiotics *Klebsiella* (Ay *et al*., 2003). Al-Zahrani and Akhtar (2005) reported that *K. pneumoniae* showed highest susceptibility to meropenem (94.4%), which corroborates with the previous reports (Ay *et al*., 2003; Al-Zahrani & Akhtar, 2005; Ullah *et al*., 2009).

Among the isolates, 59% (13/22) were found to be beta-lactamase producers. There was no correlation between β lactamase production and resistance to the used antibiotics. The reason for this is that many isolates were determined to be β-lactamase negative in spite of their resistance to some of the antibiotics. On the other hand, some isolates were determined to be both β-lactamase positive and resistant to some antibiotics (Toroglu *et al.,* 2005). Some researchers reported that extended spectrum β-lactamase in *K. pneumoniae*. It reported that from 10.4% to 66.7% among *K. pneumoniae* isolated from different samples (Kader & Kumar, 2004; Kolar *et al.,* 2006; Aladag & Durak, 2009; Albayrak & Kaya, 2009; Kaskatepe & Yıldız, 2009).

In recent years, due to selection pressure of antibiotics in hospital enviroment multiple resistance to antibiotics has been seen in the enteric organisms. This is more so with *K. pneumoniae* (Eisentein, 1995). This organisms has been resistant to aminoglycosides beta lactams, fluoroquinolones and to other antibiotics and has the greatest ability to receive and disseminate resistant factors (French *et al.,* 1997). The presence of antimicrobial agents at low concentration through leaching or continued usage lead to the development of drug resistant isolates and multiple antibiotic resistance (MAR) in bacteria and reduced efficiency of antibiotic treatment for human and animal diseases (Tendencia & De la Pena, 2001). In present study, both vaginal fluid and wound samples showed 0.33 the MAR index value. Among the *K. pneumoniae* strains isolated from ürine, the lowest MAR index value was 0.08, the highest MAR index value was 0.83. In present study, the MAR indexes of *K. pneumoniae* were from 0.33 to 0.83. MAR index were given Table III. Out of 22 isolates, 18 (82%) isolates showed Multiple Antibiotic Resistance four to ten antibiotics. Some researchers found that multiple antibiotic resistance (MAR) index value were from 75 to 88.3% among *K. pneumoniae* isolates (Shukla *et al*., 2004; Manandhar *et al*. 2006). Our results were similiar to Shukla *et al.* (2004). In their study, 88.3% (106) of the isolates were found to be resistant to at least one of the 3rd Generation antibiotics (3GC) (cefotaxime, ceftazidime & ceftriaxone) and 72% of the isolates were resistant to all the 3GC tested.

Further studies need to be carried out to determine especially those, which haven't been studied on are resistant to *K. pneumoniae*. *K. pneumoniae* isolated from different clinical samples need to be tested to find out whether they produce β lactamase or not. While dealing with *K. pneumoniae* infections, extended spectrum antibiotics might be avoided. Before using the antibiotics, antibiotic sensitivity test should be done. Following usage of antibiotics and identification of antibiotics resistance evolution are vital for a good treatment.

CONCLUSION

It is suggested that meropenem, chloramphenicol and streptomycin could be better for treatment of infections based on *K. pneumoniae* according to the present study. Penicilin and amoxicillin were non-advisible antibiotics for *K. pneumoniae* infections according to the MAR results. Furthermore, *K. pneumoniae* infections is a serious opportunistic pathogens. There was no compatibility between β-lactamase production and antibiotic resistance.

REFERENCES

Ahmed, AA., H. Osman, A.M. Mansour, A.H. Musa, A.B. Ahmed, Z. Karrar and H.S. Hassan, 2000. Antimicrobial agent resistance in bacterial isolates from patients with diarrhea and urinary tract infection in the Sudan. *American J. Trop. Med. Hyg.*, 63: 259–263

Aiyegoro, O.A., O.O. Igbinosa, I.N. Ogunmwonyi, E.E. Odjadre, O.E. Igbinosa and A.I. Okoh, 2007. Incidence of urinary tract infections (UTI) among children and adolescents in Ile-Ife, Nigeria. *African J. Microbiol. Res*., 013–019

Aladag, M.O. and Y. Durak, 2007. Investigation of some Antibiotic Sensitivities *Klebsiella pneumoniae* Isolated From Urinary System Infections. *Fırat Sag. Hiz. Derg.*, 4: 40–49

Aladag, M.O. and Y. Durak, 2009. Investigation of some antibiotic susceptibilities, plasmid profiles and ESBL Characteristic of *Klebsiella pneumoniae* ısolated from urinary System Infections. *World Appl. Sci. J.,* 6: 630–636

Albayrak, N. and S. Kaya, 2009. Extended spectrum beta lactamases production and antimicrobial resistance ratio of the *Esherichia coli* and *Klebsiella pneumoniae* strains isolated from various clinical specimens. *Türk Microbiol. Cem. Derg*., 39: 16–21

Al-Zahrani, A.J. and N. Akhtar, 2005. Susceptibility patterns of extended spectrum ß-lactamase (ESBL)- producing *Escherichia coli* and *Klebsiella pneumoniae* isolated in a teaching hospital. *Pakistan J. Med. Res.,* 44: 64–67

Ay, S., L. Abut-İşeri and B. Duman, 2003. İdrar Örneklerinden İzole Edilen Gram Olumsuz Mikroorganizmaların Antibiyotiklere Duyarlılıkları**.** *Inönü Üniv. Tıp. Fak. Derg*., 10: 59–62

Bauer, A.W., W.M.M. Kirby, J.C. Sherris and M. Turck, 1966. Antibiotic susceptibility testing by a standardized single disk method. *American J. Clin. Pathol*., 45: 493–496

Burwen, D.R., S.N. Banerjee and R.P. Gaynes, 1994. The national nosocomial infections surveillance system. Ceftazidime resistance among selected nosocomial gram negative bacilli in the United States. *I. Infect. Dis*., 170: 1622–1625

Clinical and Laboratory Standart Institute (CLSI), 2005. *Performance Standards for Antimicrobial Susceptibility Testing, 15th İnformational Supplement*. Document M 100-S 15. Clinical and Laboratory Standards Institute, Wayne, Phladelphia

Durak, Y., M. Kır, B. Ozkalp and M.O. Aladag, 2007. The Sensitivity Research of Gram (Negative) and Gram (Positive) Bacteria Isolated From Different Clinical Material Against Ofloxacin. Fırat Saglık Hizmetleri Dergisi, Cilt 2. *Sayı,* 4: 85–92

Durmaz, B., I.H. Ozerol, K. Şahin, M.S. Tekerekoglu and M. Koroglu, 1997. The resistance of *Enterobacteriaceae* and *Pseudomonas* to β-lactam antibiotics. *J. Turgut Özal Med. Center*., 4: 193–196

Eisentein, B.I., 1995. Enterobacteriaceae. *In*: Mandell, G.L., J.E. Bennet, J.E. Bennet and R. Dolin (eds.), *Principle and Paractice of Infectious Diseases,* 4th edition, p: 79. Chırchill Livingstone, New York

Ferna´ndez-Rodrı´guez, A., J.C. Canto´n R. Pe´rez-Dı´az, J.J. Martı´nez-Beltra´n, J. Picazo and F. Baquero, 1992. Aminoglycoside-modifying enzymes in clinical isolates harboring extended-spectrum beta-lactamases. *Antimicrob. Agents Chemother.*, 36: 2536–2538

French, R.L., I. Philips, 1997. Antibiotic Resistance. *In*: O'Grady, F., R.G. Finch, H.P. Lambart and D. Greenwood (eds.) *Antibiotic and Chemotheraphy* 7th edition, pp: 23–42. Churchill Livingstone New York

Goldstein, F.W., Y. Pean, J. Gerter and Vigil'roc Study Group, 1995. Resistance to Ceftriaxone and Other β-Lactams in Bacteria Isolated in the Community. *Antimicrob. Agents Chemother.,* 39: 2516–2519

Gonlugur, U., M.Z. Bakici, I. Akkurt and T. Efeoglu, 2004. Antibitic susceptibility patterns among respiratory isolates of Gram negative bacilli in a Turkey university hospital. *BMC Microbiol.,* 4: 1–5

Halit, V., V. Sinci, S. Kalaycioglu, D. Erer, C. Sivrikoz, I. Fidan and I. Akyar, 1999. Meropenem Sensitivity of Bacteria Isolated From Thoracic and Cardiovascular Surgery Intensive Care Unit. *GKDC Dergisi*, 7: 21–24

Jacoby, G.A. and A.A. Medeiros, 1991 More extended-spectrum beta-lactamases. *Antimicrob. Agents Chemother*., 35: 1697–1704

Jean, S.S., P.R. Hsuesh, W.S. Lee, H.T. Chang, M.Y. Chou, I.S. Chen, J.H. Wang, C.F. Lin, J.M. Shyr, W.C. Ko, J.J. Ku, Y.C. Liu, W.K. Huang, L.J. Teng and C.Y. Liu, 2009. Nationwide surveillance of antimicrobial resistance among *Enterobacteriaceae* in intensive care units in Taiwan. *Eurpean J. Clin. Microbiol. Infect. Dis.,* 28: 215–220

Jones, M.E., D.C. Draghi, C. Thornsberry, J.A. Karlowsky, D.F. Sahm and R.P. Wenzel, 2004. Emerging resistance among bacterial pathogens in the intensive care unit - a European and North American Surveillance study (2000-2002). *Ann. Clin. Microbiol. Antimicrobials*., 3: 1–11

Kader, A.A. and A. Kumar, 2004. Prevalence and antimicrobial susceptibility of extended-spectrum β-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* in a general hospital in Saudi Arabia. *Saudi Med. J*., 25: 570–574

Karlowsky, J.A., M.E. Jones and D.C. Mayfield, 2002. Ceftriaxone activity aganist gram positive and gram negative pathogens isolted in US clinical microbiology laboratories from 1996 to 2000: results from the Surveillance net work(R) (TSN(R) Database –USA. *Int. J. Antimicrob. Agents*., 19: 413–426

Kaskatepe, B. and S. Yıldız, 2009. Antibiotic susceptibility and frequency of extended spectrum beta lactamase of *Klebsiella pneumoniae* strains isolated from urinary tract infections. *Türk Microbiol. Cem. Derg*., 39: 36–39

Khadri, H.C., S. Surekha, S. Laksmi and G. Narasima, 2007. Multidrug resistance and beta-lactamase production by *Klebsiella pneumoniae. African J. Biotechnol*., 6: 1791–1793

Kim, J., Y.M. Lim, I. Rheem, Y. Lee, J.C. Lee and S.Y. Seol, 2005. CTX-M and SHV-12 β lactamases are the most common extended spectrum enzymes in clinical isolates of *Esherichia coli* and *Klebsiella pneumoniae* collected from3 university hospitals within Korea. *FEMS Microbiol. Letters*, 245: 93–98

Kolar, M., T. Latal, P. Cermak, N. Bartonikova, E. Chmelarova, P. Sauer and M. Kesselova, 2006. Prevalence of extended –spectrum β lactamase–positive Klebsiella pneumoniae isolates in the Czech Republic. *Antimicrob. Agents*, 28: 49–53

Krieg, N.R. and J.G. Holt, 1984. *Bergey's Manual of Systematic Bacteriology*, Vol. 1, pp: 461–463. Williams and Wilkins, A Waverly company, Philadelphia

Krumperman, P.H., 1985. Multiple antibiotic resistance indexing of *Escherichia coli* to identify high-risk sources of fecal contamination of foods. *App. Environ. Microbiol*., 46: 165–170

Lassen, J., 1975. Rapid Identification of Gram-Negative Rods Using A Three-Tube Method Combined with A Dichotomic Key". *Acta Pathol Microbiol. Scandinevia Suppl.*, 83: 525–533

Lopes, A.C.S., J.F. Rodriques and M.A.M. Junior, 2005. Molecular typing of *Klebsiella pneumoniae* isolates from public hospitals in Recife. *Brazil Microbiol. Res*., 160: 37–46

MacFaddin, F.J., 2000. *Biochemical Tests for Identification of Medical Bacteria*, 3rd edition, p: 912. Philadelphia

Manandhar, T., J. Koirala, B.M. Pokhrel and P. Ghimire, 2006. Status of extended spectrum beta lactamase producing *Esherichia coli* and *Klebsiella* species in urinary tract infection. *J. Institute Med*., 28: 24–29

Matyar, F., A. Kaya and S. Dinçer, 2008. Antibacterial agents and heavy metal resistance in Gram-negative bacteria isolated from seawater, shrimp and sediment in Iskenderun Bay, Turkey. *Sci. Total Environ*., 407: 279–285

Monnet, D.L., J.W. Biddle and J.R. Edwards, 1997. Evidence of interhospital transmission of extended spectrum β lactam resistant *Klebsiella pneumoniae* in the United States, 1986 to 1993. *Infect. Control Hosp. Epidemiol*., 18: 492–498

Nicolau, D.P., 2008. Carbapenems: a potent class of antibiotics. *Expert Opin. Pharmacother*, 9: 23–27

Okesola, A.O. and O. Makanjula, 2009. Resistance to Third-Generation Cephalosporins and Other Antibiotics by Enterobacteriaceae in Western Nigeria. *American J. Infec. Dis*., 5: 17–20

Okonko, I.H., F.A. Soleye, T.A. Amusan, A.A. Ogun, T.A. Ogunnusi and J. Ejembi, 2009. Incidence of multi-Drug resistance (MDR) organisms in Abeokuta, southwestern Nigeria. *Global J. Pharmacol*., 3: 69–80

Orrett, F., 2004. Resistance patterns aong selective Gram-negative bacilli fro an intensive care unit in Trinidad, West Indies. *Saudi Med. J*., 25: 478–483

Ozbilge, H., F.Y. Zeyrek, A. Uzala and Y. İnanç, 2004. İdrar örneklerinden izole edilen *Klebsiella* suşlarının çeşitli antibiyotiklere direnç durumu. *Hr. Ü. Tıp Fak. Derg.,* 1: 24–28

Ullah, F., S.A. Malik and J. Ahmed, 2009. Antimicrobial susceptibility pattern and ESBL prevalence in *Klebsiella pneumoniae* from urinary tract infections in the Nort-West of Pakistan. *African J. Microbiol. Res.*, 3: 676–680

Romanus, I.I., O.A. Egwu, A.T. Ngozi, N.A. Chidiebube and E.P. Chika, 2009. Extended Spectrum Beta-Lactamase (ESBL) Mediated Resistance to Antibiotics Among *Klebsiella Pneumoniae* in Enugu Metropolis. *Macedonian J. Med. Sci*., 2: 196–199

Sawai, T., S. Yamagishi and S. Mitsuhashi, 1973. Penicillinases of *Klebsiella pneumoniae* and Their Phylogenetic Relationship to Penicillinases Mediated by R Factors. *J. Bacteriol*., 115: 1045–1054

Sesli-Cetin, E., S. Kaya, İ. Pakbas and M. Demirci, 2007. Microorganisms isolated from patients in intensive care units and their antibiotics susceptibilities. *İnönü Unv. Tıp Fakültesi Derg*., 14: 69–73

Shah, P.M., 2008. Parenteral carbapenems. *Clin. Microbiol. Infect. Suppl*., 14: 175–180

Shukla, I., R. Tiwari and M. Agrawal, 2004. Prevalence of extended specrtum-lactamase producing *Klebsiella pneumoniae* in a tertiary care hospital. *Indian J. Med. Microbiol*., 22: 87–91

Tendencia, E.A. and L.D. De la Pena, 2001. Antibiotic resistance of bacteria from shrimp ponds. *Aquaculture*, 193: 193–204

Toroglu, E. and S. Toroglu, 2009. Microbial pollution of water in Golbasi lake in Adiyaman, Turkey. *J. Environ. Biol*., 30: 33–38

Toroglu, S., S. Dincer and H. Korkmaz, 2005. Antibiotic resistance in Gram negative bacteria isolated from Aksu River in (Kahramanmaraş) Turkey. *Ann. Microbiol*., 55: 229–233

Urbarli, A., A. Ari, M. Erdenizmenli, N. Fidan and O. Özgenc, 2001. Idrar örneklerinden soyutlanan gram olumsuz bakteriler ve antibiyotik direnç oranlari. *Infeks Derg*., 15: 249–253

Yilmaz, E., C. Ozakin, M. Sinirtas and S. Gedikoglu, 2005. Uludag Universitesi Tip Fakultesi Bakteriyoloji Laboratuvari'nda 1999-2002 Yillari Arasinda idrar Orneklerinden izole Edilen Mikroorganizmalar ve Antibiyotik Duyarlilıkları. *Infeksiyon Derg*., 19: 91–96

Yüksel, S., B. Ozturk, A. Kavaz, Z.B. Ozcakar, B. Acar, H. Güriz, D. Aysev, M. Ekim and F. Yalcınkaya, 2006. Antibiotic resistance of urinary tract pathogens and evaluation of empirical treatment in Turkish children with urinary tract infections. *Int. J. Antimicrob. Agents*, 28: 413–416

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