JOURNAL OF PURE AND APPLIED MICROBIOLOGY, APRIL 2014. Vol. **8**(2), p. 985-991

Antimicrobial Resistance and Sensitivity among Isolates of *Esherichia coli* from Patients in Kahramanmaras, Turkey

Sevil Toroglu[1], Hatice Avan[1] and Dilek Keskin[2]*

[1]Department of Biology, Faculty of Arts and Science,
Kahramanmaras Sütcü Imam University, 46100- Kahramanmaras, Turkey,
[2]Cine Vocational High School, Adnan Menderes University, 09500- Cine-Aydin, Turkey.

(Received: 10 June 2013; accepted: 14 August 2013)

To determine the level of resistance to the widely used antibiotics in clinical isolates of *Esherichia coli.* 74 isolates were collected from different hospitals in Kahramanmaras and recorded at specimens. 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. This study was carried out in the laboratory of Kahramanmaras Sütcü Imam University, Biology Department. The results indicated that resistance rate of antibiotics was in the range of 91% Penicilin(PEN), 65% Tetracycline (TET) and Amoxicillin (AMX), 62% Cefazolin(CEFX), 59% Streptomycine(STR), 34% Oflaxain (OFL), 32% Chlorampenicol (CHL) and Ceftriaxone (CEFT), 27% Gentamycin (GEN), 24% Cefoxitin(CEFX), 18% Nitrofurantoin(NIT), %12 Meropenem(MER). Among the 74 isolates of *E.coli* were showed 38(51%) beta lactamase activity and 36(49%) isolates of *E.coli* were showed no beta lactamase activity. Out of 74 isolates, 50(68%) isolates showed Multiple Antibiotic Resistance three to twelve antibiotics.

Key words: *Esherichia coli*, Antibiotic, Resistance, Beta lactamase activity.

Escherichia coli is one of the main causes of nosocomial infections in humans. *E.coli* is also a common inhabitant of the human and animal gut and is considered an indicator of fecal contamination in food. Recently it is though that *E.coli* and certain other foodborne illnesses can sometimes trigger serious health problems months or years after patient survived that initial bout. The organisms is of clinical importance due to its cosmopolitan nature and ability to initiate, establish and cause various kinds of infections. Virulent strains of *E.coli* can cause gastroenteritis, urinary tract infections, blood stream infections and neonatal meningitis [1]. For example, more than 80% of urinary tract infections occur in outpatients and *E.coli* accounts for more than 50% of the infections in these patients[2,3]. In rare cases, virulent strains are also responsible for Haemolytic Uremic Syndrome (HUS), peritonitis, mastitis septicemia, and gram negative pneumoniae[1]. It is one of the organisms most frequently isolated from different clinical cases of diarrhea and others[4-6]. Antibiotic resistance is a major, increasing problem in clinical microbiology as a whole and in the therapy of hospital infections in particular. *E. coli* and other Enterobacteriaceae are more resistant to β-lactams[7,8]. *E.coli* often carry multi drug resistant plasmids and under stress readily transfer those plasmids to otherspecies[9-11].

We aimed in the present study to determine the status of antimicrobial resistance, underlying conditions, and determination of *E.coli* isolates with beta-lactamase from different hospitals in Kahramanmaras Turkey

* To whom all correspondence should be addressed.
E-mail:dkeskin@adu.edu.tr

MATERIALS AND METHOD

Isolation of bacterial strains and identification

74 isolates were collected from hospital patients in Kahramanmaras and recorded at specimens. Mac Conkey agar and EMBagar (Eosin Metilen Blue) agar used for *E.coli* isolation. Isolates were considered to be presumptive *Esherichia* 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 and Citrate)[12,13].

Antibiotic resistance activity

Antibiotic resistance was determined by an agar disc diffusion test[14] using Mueller-Hinton agar (Difco) according to Clinical and Laboratory Standards Institute[15] 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, 10µg/ml), Amoxicillin (AMO,20µg/ml), Penicilin (PEN, 10µg/ml), Nitrofrantoin (NIT,30µg/ml), Cefazolin(CEF,30µg/ml), Cefoxitin(CEFX,30µg/ml), Ceftriaxone (CEFT,30µg/ml), Gentamycin (GEN,10µg/ml), Tetracycline (TET,30µg/ml), Streptomycine (STR,10µg/ml), Chlorampenicol (CHL,30µg/ml), Oflaxain (OFL,5µg/ml). The isolates those grown in inoculation were evaluated as resistant and the others were evaluated as susceptible[15]. 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[16-17]. 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 Index

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[18,19].

RESULTS AND DISCUSSION

The resistance of *E.coli* isolates to antimicrobial agents (n=74) gave high resistance rates found that *E.coli* isolates diffusion tests for penicillin (91%), tetracycline and amoxicillin (65%), cefazolin (%62), streptomycine (59%), oflaxain(34%), chlorampenicol and ceftriaxone (32%) and gentamycin (27%). The most effective drugs against *E.coli* were meropenem (%12), nitrofurantoin (18%) and cefoxitin(24%) .The results were given table 1.

Among the beta lactam antibiotics, penicillin resistance rate was the highest (91%). The bactericidal antibiotics which inhibits bacterial cell wall synthesis, are penicillins.These bacteria offer resistance to penicillins by production of lactamases and by permeability barrier of the cell surface[20].

The fact that over 65% of *E.coli* isolates were resistant to amoxicillin is of great importance and means the antibiotic can not be used as empirical therapy for hospital patients infection. High frequency resistance to amoxicillin was also reported among *E.coli* isolates in Iran 83.7%[21] ; in Cameroon 89.2%-79.5%[22]; in Croatia 42%[23]; in Portugal and Spain 54.3%[24], as well as in USA 39%[25] and UK 38.4% [26]. Our results were in complyance with previous researchers.

As for the resistance rate of tetracycline, it was 65% (table1). Some researchers have reported

that tetracycline resistance rate from 44 to 94%[5,27,28]. Our results were in complyance with previous reserachers.

As for the resistance rate of cefazolin, it was 62% (table1). Some researchers have reported that cefazoline resistance rate from 12% to 78%[29-33]. Our results were in compliance with previous researchers.

With respect to resistance of streptomycine, it was 59% (table1). Some researchers have reported *E.coli* resistance rate to streptomycin 0%to 28.08 %[34-35]. In contrast to previous researchers, our results were very high percentage (59%). Many factors may have contributed to such high rates of resistance including misuse of antibiotics by health care professionals or non-skilled practitioners, misuse of antibiotics by the general public, and inadequate surveillance due to lack of information arising from routine antimicrobial susceptibility testing, like reports from other developing countries[4].

Table1. Antibiotic resistance pattern of *Esherichia coli* isolated from clinical samples

Antibiotics	Sensitive	Intermediate	Resistance
Pen	7(%9)	-	67(%91)
Amx	17(%23)	9(%12)	48(%65)
Tet	19(%26)	7(%9)	48(%65)
Cef	23(%31)	5((%7)	46(%62)
Str	24(%32)	6(%8)	44(%59)
Ofl	47(%64)	2(%3)	25(%34)
Chl	45(%61)	5(%7)	24(%32)
Ceft	39(%53)	11(%15)	24(%32)
Gen	46(%62)	8(%11)	20(%27)
Cefx	54(%73)	2(%3)	18(%24)
Nit	59(%79)	2(%3)	13(%18)
Mer	63(%85)	2(%3)	9(%12)

Fluoroquinolones are antibiotics that are very effective against many gram negative microorganisms, including *E.coli*. The resistance rate was in ofloxacin with 34% (table1). Ofloxacin resistance has been reported to be 13% and 60% in different studies[28,29,36]. Koksaldi-Motor *et al* (2010)[37] reported that resistance of quinolones have incresaed year by year. Our results are similar to that reported by Ates (2007)[36] who also reported that *E.coli* showed resistance of 30% to ofloxacin. In her study, a total of 200 common pathogenic bacteria were recovered from patient with urinary tract infections *E.coli, Klebssiella, Streptococci, Enterobacter, Proteus, Coagulase negative Staphylococci, Staphylococcus aureus, Enterococci, Pseudomonas, Citrobacter, Serratia* species were obtained from this study.

In respect of resistance rate of chlorampenicol, it was 32% (table1). Some researchers have reported that chloramphenicol resistance rate from 2.17 to 60%[34,35,38]. Our results were in accordance with previous researchers.

Taking into account the total number of clinical isolates in the present study period 32% of

Table 2. Multiple Antibiotic Resistance Index of 74 *Esherichia coli* strains

Source of isolates	**Total Isolates**	**Multiple Antibiotic Resistance Index (MAR)**	**Beta lactamase**
Urine	52	0.08(6i), 0.17(3i), 0.25(4i), 0.33(5i), 0.42(8i),0.5 (8i) 0.58(6i), 0.67(3i), 0.75(5i), 0.83(1), 0.92(2),1(1i)	29(+) 23(-)
Drain	1	0.5(1i)	1(+)
Abscess	4	0.33(3i),0.67(1i)	3(+),1(-)
Blood	2	0.67(1i), 0.33(1i)	2(-)
Tissue	1	0.42(1i)	1(+)
Wound	6	0.17(1i), 0.25(1i),0.42(2i),0.58(1i), 0(1i)	6(-)
Appendicitis	1	0.33(1i)	1(+)
Vaginal fluid	4	0.08(1i), 0.5(1i),0.75(1i), 0(1i)	3(+),1(-)
Probe tip	1	0.42(1i)	1(+)
Abdominal Internal Fluid	1	0.08(1i)	1(+)
Tracheolaringeal aspirate	1	0.42(1i)	1(-)
Total	74		38(+),36(-)

i:isolates +:Present, -: Absent

the *E.coli* species were resistant to cefoxitin (table1). Some researchers have reported resistance rate of cefoxitin 2%-32.1% in different studies [22,29,34,39-41]. Our results were similar to Pieboji *et al* (2004)[22] who also reported that gram negative bacilli isolates (n=522), obtained from a wide range of clinical specimens (urine, pus and blood) from inpatients and outpatients at Yaounde Central hospital between March 1995 and April 1998, were evaluated for resistance to antibiotics.

As for resistance rate of ceftriaxone, it was 32% (table1). Many researchers have tested resistance of ceftriaxone to *E.coli*. According to previous studies resistance of *E.coli* was from 0%to 100% [29,31,36,38,42-45]. Our results were in complyance with previous researchers.

Among the aminoglycosides group, gentamycin resistance rate was 27% (table1). Some researchers have reported gentamycin resistance rate to *E.coli* from 1.5% to 54%[37,40,46,47]. Our results were similar to Cho *et al* (2011)[41] who also reported that gentamycin resistance rate was 29.2% patients with diarrhea. Koksaldi-Motor *et al*., (2010) reported that when it compared to previous year's data suspectibility of *E.coli* isolated from urine to gentamycin were decreased and also different resistance rate occured different locations[37].

In this study hospitalized patients *E.coli* isolates were found to be sensitive to nitrofurantoin 18% resistant (table1). Nitrofurantoin still exhibited low resistance frequencies in all countries investigated (0-25 %) despite many years of usage [24,30,32,48-50]. Our results were similar to Ay *et al*(2001)[48] who also reported that nitrofurantoin resistance rate was 22% in hospitalized patients.

Carbapenems, mainly meropenem, resistance rate of meropenem was showed in 12 % (table1). Some researchers have reported meropenem resistance rate to *E.coli* from 0% to 9.1%[29,33,45]. Our results were similar to Uzun *et al*.,(2006)[45] who also repoted that percentage of meropenem resistance was 9.1% in Turkey. It can be suggested that meropenem can be used for infections based on *E.coli*.

Among the 74 isolates of *E.coli* were showed 38 (51%) beta lactamase activity and 36(49%) isolates of *E.coli* were showed no beta lactamase activity (tableII). The main mechanism of bacterial resistance to the β -lactam class of antibiotics consists of the production of - β lactamases, which are hydrolytic enzymes with the ability to inactivate these antibiotics, before they reach the penicillin-binding proteins located at the cytoplasmic membrane[51]. Some researchers have reported beta lactamase activity rate to *E.coli* from 6.5% to 65.94%[27,42,52-54]. Our results were similar to Kumar *et a*l (2011)[54] who also reported that 57.69% beta lactamase activity rate to *E.coli*.

In present study, the lowest MAR index was 0.008 obtained from urine, vaginal fluid and abdominal 1nternel fluid samples. In contrast to the highest MAR index was 1 obtained from urine. The lowest MAR index was 0 obtained from tissue samples, none of the isolates showed no resistance all tested antibiotics. Out of 74 isolates, 50 (68%) isolates showed Multiple Antibiotic Resistance three to twelve antibiotics. The MAR index were determined 0.25 and above (table 2). Some researchers have reported Multi Drug Resistance rate to *E.coli* from 2% to 97%[55-61]. Our results were in complyance with previous researchers. Study shows that multiple resistance is a common hospital pathogens. Higher resistance exhibited to penicilin, tetracycline and amoxicillin may have accounted due to increased use of these drugs in this area and referral hospital status of our hospital and prior treatment with multiple antibiotics.

In conclusion, it is suggested that meropenem and nitrofurantoin could be better for treatment of infections based on *E.coli* according to the present study. Penicilin, tetracycline and amoxicillin were non-advisible antibiotics for *E.coli* infections according to the MAR results. Also, the high number of multidrug resistant isolates gives rise to concern. Regular monitoring of antimicrobial drugs. Resistance seems to necessary to improve our guidelines for empirical antibiotic therapy.

ACKNOWLEDGEMENTS

This project financially supported by Kahramanmaras Sutcu Imam University Research Fund (BAP, Project Number: 2013/2-42 M).

REFERENCES

1. Gehlbach SH., Madormack JN, Drake BM, Thompson W.V.Spread of disease by fecal –oral route in day nurseries' *Health Service Reports*,

1978**: 88**(4):320-322.

2. Blomgran, R., Zheng L , Stendhal O. Uropathogenic *Esherichia coli* trigger oxygen-dependent apoptosis in human neutrophils through the cooperative effect of type 1 fimbriae and lippolysaccharide. *Infect Immun*., 2004: **72**:4570-4578.
3. Jha, N and Bapat SK.A study of sensitivity and resistance of pathogenic microorganisms causing UTI in Kathmandau valley. *Kathmandu Univ Med J*., 2005: **3**:123-129.
4. Okeke IN, Lamikanra A, Edelman R. Socioeconomic and behavorial factors leading to acquired bacterial resistance to antibiotics in developing countries. *Emerg Infect Dis*. 1999: **5**:18-27.
5. Olowe OA, Olayemi AB, Eniola KIT and Adeyeba AO..Aetiological agents of diarrhoea in children under 5 years of age in Osogbo. *Afr J Clin and Exp Microbiol*, 2003: **4**(3):62-66.
6. Tobih JE, Taiwo SS,Olowe OA, Olaosun OA, Adejumo SO. Microbiological profiles of discharging ears in Osogbo, Nigeria. *Trop. Doc*, 2006: **36**(3):165-166
7. Sogaard P. The epidemiology of antibiotic resistance in three species of Enterobacteriaceae and the relation to consumption of antimicrobial agents in Odense University Hospital. *Dan Med Bull*, 1989: **36**:65-84
8. Jensen TG.Antibiotikaforbrug og resistens pa Odense Universitetshospital 1987-92, thesisKMA,OUH and Odense University, DK 5000 Odense C,1995.
9. Johhnson J, Kuskowski M, Meanerd M, Gajewski A, Xercavins M, Garau J. Similarly between human and chicken *E.coli* isolates in relation to ciprofloxacin resistance status. *Infect Dis*, 2006: **194** (1) 71-78.
10. Toroglu S and Keskin D. Antimicrobial Resistance and Sensitivity among Isolates of *Klebsiella pneumoniae* from Hospital Patients in Turkey. *Int JAgri Biol*, 2011: **13**(6) 941–946.
11. Aktürk S, Dincer S., and Toroglu S. Determination of microbial quality and plasmid-mediated multidrug resistant bacteria in fountain drinking water sources in Turkey. *J Environ Biol.*, 2012 **33**,1127-1136.
12. Cowan SF, Steel KJ Manual for the Identification of the Medical Bacteria Cambridge: Cambridge University Press. pp. 7-122 ,1970.
13. Prakash S, Dayalan JA and Edison N. Prevalence of Bacteriuria In Jeyaseharan Hospital of South India and their antibiogram. *Asian Pacific J Trop Biomed*, 2011: 105-108.
14. Bauer, A.W, Kirby, WM.M, Sherris, JC., Turck, M. Antibiotic susceptibility testing by a standart.. CLSI., Performance standards for antimicrobial susceptibility testing; 15th informational supplement. 1966.
15. CLSI.,. Performance standards for antimicrobial susceptibility testing; 15th informational supplement. CLSI / NCCLS M 100- S 15. Clinical and Laboratory Standards Institute, Wayne, PA.2005.
16. MacFaddin F.J.. Biochemical Tests for Identification of Medical Bacteria. 3 rd Edn., *Philadelphia*, USA, p.912, 2000.
17. Toroglu, E, and Toroglu, S.. Microbial pollution of water in Golbasi lake in Adiyaman, Turkey. *J Environ Biol .*, 2009: 30(1), 33-38.
18. Matyar, F., Kaya, A and Dinçer, S.. Antibacterial agents and heavy metal resistance in Gram-negative bacteria isolated from seawater, shrimp and sediment in Iskenderun Bay, Turkey. *Sci Total Environ*., 2008: **407**:279-285.
19. Krumperman, PH. Multiple antibiotic resistance indexing of *Escherichia coli* to identify high-risk sources of fecal contamination of foods. *App Environ Microbiol*., 1985: **46**:165–170.
20. Suginaka H, Ichikawa A, and Kotani S., Penicillin-Resistant Mechanisms in *Pseudomonas aeruginosa*: Binding of Penicillin to *Pseudomonas aeruginosa* KM 338. *Antimicrob Agents Chemother*., 1975: **7**(5): 629–635.
21. Mohammadi M, Ghasemi E, Mokhayeri H, Pournia Y, Boroun H. Antimicrobial resistance patterns of *E. coli* detected from hospitalized urine culture samples. *Asian J Biol Sci*, 2010: **3**(4) 195-201.
22. Piéboji JG, Koulla-Shiro S, Ngassam P, Adiogo D, Njine T, Ndumbe P.Antimicrobial resistance of Gram-negative bacilli isolates from inpatients and outpatients at Yaounde Central Hospital, Cameroon. *Int J Infect Dis*, 2004: **8**(3):147-54.
23. Bariši Z, Babi-Erceg A, Borzi E, Zorani V, Klaiterna V, Carev M. Urinary tract infections in South Croatia: aetiology and antimicrobial resistance. *Int J Antimicrob Agents*, 2003: **22**, 61-64.
24. Kahlmeter G. The ECO-SENS project: a prospective, multinational multicentre epidemiological survey of the prevalence and antimicrobial susceptibility of urinary tract pathogens/interim report. *J Antimicrob Chemother*, 2000: **46**(Suppl. S1):15-22.
25. Dyer IE, Sankary TM, Dawson JA. Antibiotic resistance in bacterial urinary tract infections, 1991_/1997. *West J Med* 169:265_/8,1998.
26. MacGowan AP, Brown NM, Holt HA, Lovering AM, McCulloch SY, Reeves DS.. An 8-year

survey of the antimicrobial susceptibility patterns of 85 971 bacteria isolated from patients in a district general hospital and the local community. *J Antimicrob Chemother;* 1993: **31**:543_/57.

27. Shibi AM.. Incidence of beta lactamase production and antibiotic susceptibilities among clinical isolates in Saudi arabian hospitals. *Current Therap Res*, 1995: **56**(4) 407-414.
28. M1sra SCR, Chander LCY, Debata LCNK, Ohri BVC.Antibiotic resistance pattern of isolates from wound and soft tissue infections. *MJAFI*, 2000: **56**(3); 205-208
29. Inan N U, Gurler N. Investigation of Antibiotic Resistance and Some Virulence Factors of *Escherichia coli* Strains Isolated from Children with Urinary Tract Infections. *Ankem Derg*; 2004: **18**(2):89-96.
30. Kutlu S, Kutlu M. Antibiotic susceptibility of *Escherichia coli* strains isolated in urinary tract infections in Didim, Turkey. *Turk J Infect*; 2007: 21(2): 81-83.
31. Koken G, Asik G, Ciftci H, Cetinkaya Z, Aktepe O.C, Yilmazer M. Efficiency of Fosfomycin Trometamol on *Escherichia coli* Strains from Community Acquired Urinary Tract Infections. *Ankem Derg*, 2008: **22**(1):23-27.
32. Eryilmaz M., Eylül –Bozkurt M., Yildiz MM., Akin A. Antimicrobial resistance of urinary *Esherichia coli* isolates. *Trop J of Pharm Res*, 2010: **9**(2) 205-209.
33. Yilmaz N., Köse ^., Au_ N., Ece G., Akkoçlu G., K1rakl1 C. Microorganisms Isolated from Blood Cultures of Intensive Care Unit Patients, their Antimicrobial Susceptibility and Etiological Agents in Nosocomial Bacteremia. *Ankem Derg*, 2010: **24**(1):12-19.
34. Barreto A., Bruno Guimarães B.,Hajer Radhouani H, Araújo C, Gonçalves A, Gaspar E, Rodrigues J, Igrejas G and Poeta P.Detection of antibiotic resistant E. coli and Enterococcus spp. in stool of healthy growing children in Portugal. *J Basic Microbiol*, 2009: **49**, 503–512.
35. Khan AU and Zaman MS. Multiple drug resistance pattern in Urinary Tract Infection patients in Aligarh. *Biomed Res*; 2006: **17** (3): 179-181.
36. Ates F: The analyse of urine culture results in patients with lower urinary tract infection, *Türk Üroloji Derg*; 2007: **33**(2):223-7.
37. Koksaldi-Motor V., Tutanç M., Arica V., Arica S., Ay B. Suspectibility of Uropathogen *Esherichia coli* strains to commonly used antibacterail agents in urinary tract infections. *Ankem Derg*, 2010,**24**(4) 198-201.
38. Kalantar E, Motlagh ME, Lornejad H, Reshadmanesh N. Prevalence of urinary tract pathogens and antimicrobial susceptibility patterns in children at hospitals in Iran. *Iran J Clin Infect Dis*, 2008: **3**(3):149-153.
39. Cetin ES, Demirci M, Kaya S, Ar1dogan BC, Adiloglu AK, Goksu Y, Gonulates N. Antibiotic susceptibilities of *Escherichia coli*, *Klebsiella pneumoniae* and *Enterobacter* strains isolated from blood specimens. *Turk Mikrobiyol Cem Derg*, 2006: **36**(1) : 20-24.
40. Gönüllü N., Canberk MB., Filiz O., Altinkum S., Kucükbasmac1 O., Aygun G., Altas K.. Antimicrobial susceptibilities and beta lactam resistance phenotypes of *Esherichia coli* strains isolated from various clinical samples.*Ankem Derg*, 2008: **22**(2) 64-68.
41. Cho SH, Lim YS , Park MS,Kim SH a, Yeon-Ho Kang YH.. Prevalence of Antibiotic Resistance in Escherichia coli Fecal Isolates From Healthy Persons and Patients With Diarrhea. *Public Health Res Perspect* , 2011: **2**(1), 41-45.
42. Albayrak, N. and S. Kaya,. 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*., 2009: **39**: 16–21.
43. Matute AJ, Hak E, Schurink CA, McArthur A, Alonso E, Paniagua M, Van Asbeck E, Roskott AM, Froeling F, Rozenberg-Arska M, Hoepelman IM. Resistance of uropathogens in symptomatic urinary tract infections in León, Nicaragua. *Int J Antimicrob Agents.*, 2004: **23**(5):506-9.
44. Kumarasinghe G, Chow C, Tambyah PA. Widespread resistance to new antimicrobials in a university hospital before clinical use. *Int J Antimicrob Agents* ., 2001;**18**(4):391-393.
45. Uzun K., Teke T., Yavuz Z. ., G..Surveillance of antimicrobial resistance and susceptibility in bacterai isolated from pulmonart critical care. *T1p Arast Derg*., 2006: **4**(3) 8-13.
46. Vlieghe E., Phoba MF., Muyembe Tamfun JJ., Jacobs J.. Antibiotic resistance among bacterial pathogens in Central africa: a review of the published literatue between 1995 and 2008. *Int J Antimicrob Agents*, 2009: **34**, 295-303.
47. Duman Y., Güçlüer N., Serindag A., Tekerekoglu MS. Antimicrobial suspectibility of *E.coli* strains and presence of extended-spectrum beta lactamase. *F1rat T1p Derg*., 2010: **15**(4) 197-200.
48. Ay S, Iseri LA, Duman B. Antibiotic Susceptibilities of Gram Negative Microorganisms Isolated from Urine Samples. *0nönü ÜnivT1p Fak Derg*., 2003: **10**(2) 59-62.

49. Goker G, Kaya I, Ayd1n O, Gürler N. Investigation of *Escherichia coli, Klebsiella* and *Enterococcus* spp. Susceptibilities to Fosfomycine Tromethamole in Urinary Tract Infections. *Ankem Derg*; 2007: **21**(4): 219-222.
50. Kalem F, Gündem NS, Arslan U, Tuncer I. Antimicrobial susceptibility of *Escherichia coli* strains isolated from urinary tract infections. *Ankem Derg*; 2008: **22**(4): 193-197.
51. Falagas ME, Karageorgopoulos DE. Extended-spectrum beta-lactamase-producing organisms. *J Hospital Infection.* 2009;**73**(4):345-54.
52. Sami, A.A., Abd- el- Hamid, T., Sabbour, M.S. Incidence of beta lactamase Producing E. coli in urinary tract infection, *J Chemother,* 1985: **4** (6): 429-430.
53. Kader, A.A. and A. Kumar,. Prevalence and antimicrobial susceptibility of extended-spectrum ²-lactamase-producing Escherichia coli and Klebsiella pneumoniae in a general hospital in Saudi Arabia. *Saudi Med J.,* 2004: **25**: 570-574.
54. Kumar V, Mishra RK, Chandra A, Gupta P.. Incidence of ²-lactamase producing gram-negative clinical isolates and their antibiotic susceptibility pattern: A case study in Allahabad. *Int J Res Pure and Appl Microbiol,* 2011: **1**(3) 36-39.
55. Ahmed AA, Osman H., Mansour AM, Musa HA, Ahmed AB,Karrar Z and Hassan HS.. Antimicrobial agent resistance in bacterial isolates from patients with diarrhea and urinary tract infection in Sudan. *The American Soc Trop Med Hygiene*, 2000: **63**(5, 6), , pp. 259-263.
56. Moniri R, Khorshidi A, Akbari H.Emergence of Multidrug Resistant Strains of *Escherichia coli* Isolated from Urinary Tract Infections. *Iran J Publ Hlth*, 2003**, 32**:4, pp42-46.
57. Saeed A., Khatoon H and Ahmed FA.. Multidrug resistant gram negative bacterai in clinical isolates from Karachi. *Pakistan Journal of Pharm. Sci*. , 2009: **22**:1, January pp.44-48.
58. Al-Mardeni RI, Batarseh A, Omaish L, Shraideh M, Batarseh B, Unis N. Empirical treatment for pediatric urinary tract infection and resistance patterns of uropathogens, in Queen Alias Hospital and Prince A'lsha Military Center. Jordan. *Saudi J Kidney Dis Transplant;* 2009: **20**: 135-9.
59. Mathai E, Chandy S, Thomas K, Antoniswamy B, Joseph I, Mathai M, Sorensen TL, Holloway K.. Antimicrobial resistance surveillance among commensal Escherichia coli in rural and urban areas in Southern India. *Trop Med Int Health*.2008;**13**(1):41-5.
60. Al-Tawfiq JA. Increasing Antibiotic Resistance Among Isolates of *Escherichia coli* Recovered From Inpatients and Outpatients in a Saudi Arabian Hospital. *Infect Control Hosp Epidemiol;* 2006: **27**:748-753.
61. Rawat DV, Umesh D, Paul MP. Antibiotic Resistance Pattern of Urinary Tract Isolates of *Escherichia coli* from Kumaun Region. *N J I R M* **,** 2010: **1**(4): 43-46.