

Antibiotic susceptibility of microbiota members *Escherichia coli* strains isolated from stool samples of patients attended Kırıkkale Yüksek İhtisas Hospital in ten months

Kırıkkale Yüksek İhtisas Hastanesine on aylık süreçte başvuran hastaların gaita örneklerinden izole edilen mikrobiyota elemanı *Escherichia coli* izolatlarının antibiyotik duyarlılıkları

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ABSTRACT

Objective: Antibiotic resistance has turned into a global public health problem in all over the world. Intestinal flora bacteria perform many important functions for human health. As a member of microbiota *Escherichia coli* cause many infections. This study was aimed to determine antibiotic susceptibility of microbiota member *E. coli* isolates against to the antibiotics that used in treatment.

Methods: One hundred and fifty stool samples, which were sent to Kırıkkale Yüksek İhtisas Hospital microbiology laboratory in a period of between March to December 2013 to study fecal occult blood test and were determined as "negative", were included in this study. *E. coli* isolates were performed antibiotic susceptibility test by the Kirby Bauer disk diffusion method according to the recommendations of the Clinical Laboratory Standards Institute (CLSI).

Results: A total of 70 out of 150 *E. coli* isolates were sensitive to all antibiotics that used in the study. Twenty four (16%) isolates were found to be ESBL producers. All isolates were found sensitive to carbapenems.

Conclusion: It was reached the conclusion that monitoring to resistance profiles of microbiota member *E. coli* isolates, especially in specific group patients in addition to infection agents, is important for giving direction to empirical therapy.

Key Words: Antimicrobial susceptibility, *E. coli*, microbiota

ÖZET

Amaç: Antibiyotik direnci, tüm dünyada global bir halk sağlığı sorunu haline dönüşmüştür. Bağırsak florası bakterileri, insan sağlığı adına birçok önemli görevi yerine getirirler. Mikrobiyota üyesi olarak *Escherichia coli* birçok enfeksiyona neden olmaktadır. Bu çalışmada mikrobiyota üyesi *E. coli* izolatlarının tedavide kullanılan antibiyotiklere karşı antibiyotik duyarlılıklarını belirlemeyi amaçladık.

Yöntemler: Kırıkkale Yüksek İhtisas Hastanesi, Mikrobiyoloji Laboratuvarına Mart-Aralık 2013 tarihleri arasında gaitada gizli kan araştırılması için gönderilen ve "negatif" sonuç çıkan 150 gaita örneği değerlendirmeye alındı. *E. coli* izolatlarının antibiyotik duyarlılık testi Kirby Bauer disk difüzyon yöntemiyle yapıldı ve sonuçlar Clinical Laboratory Standards Institute (CLSI) standartlarına göre değerlendirildi.

Bulgular: Yüz elli *E. coli* izolatının 70 tanesi çalışılan tüm antibiyotiklere duyarlı bulundu. İzolatların 24 (%16)'ünde genişlemiş spektrumlu betalaktamaz saptandı. İzolatların tümü karbapenemlere duyarlı bulundu.

Sonuç: Mikrobiyota elemanı *E. coli* izolatlarının direnç profillerinin özellikle spesifik hasta gruplarında izlenmesinin ve enfeksiyon ajanlarına karşı ampirik tedavinin belirlenmesinde önemli olacağı kanısına varılmıştır.

Anahtar Kelimeler: Antimikrobiyal duyarlılık, *E. coli*, mikrobiyota

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INTRODUCTION

Antibiotic resistance has turned into a global public health problem in all over the world (1). Many issues such as excessive or misused antibiotics, inadequately controlled antibiotic usage policy, tourism, refugees, international travel, and lack of hygiene are mediated on the development of antibiotic resistance (2). Antibiotic resistance caused by mutations, enzymes and mechanisms of change in the target region, may be transmitted to the other bacteria through the plasmids, transposons or other mobile resistance elements. This case is mediated with increasing resistance faster than expected (1, 2). *Escherichia coli* (*E. coli*) isolates located in the intestinal flora are involved as a source of resistance genes. These genes can be transferred quickly to other commensal or pathogenic bacteria (3). Microbiota *E. coli* isolates are considered to be a useful indicator in spread of acquired antibiotic resistance genes (4).

Intestinal flora bacteria perform many important functions for human health however in cases of the suppression of the immune system, postsurgical infections and especially in urinary tract infections emerge as the pathogens (3, 5). Microbiota *E. coli* strains are agents of especially urinary tract infections (UTI) and sepsis or bacteremia (6). Infections caused by gram negative bacteria are the significant morbidity and mortality factors. Also for the last twenty years, extended spectrum beta lactamase (ESBL) producing gram negative bacteria leads to more serious health problems (7). At the same time both intestinal flora members and ESBL producing bacteria often emerges in hospital-acquired infections (8). These bacteria that carry ESBL enzymes may have an antibiotic-resistance gene to beta-lactam antibiotics and also to aminoglycosides, fluoroquinolones, and trimethoprim-sulfamethoxazole and the infections caused by these multi-drug resistant bacteria can be problem in the treatment (7).

Antibiotic susceptibility profiles of especially community acquired or nosocomial infections agents

are included in antibiotic resistance surveillance studies conducted in Turkey. We believe that the microbiota bacteria are important, because of being agents of nosocomial and community acquired infections and also being sources for transfer their resistance genes to the other bacteria. Due to, *E. coli* as a member of microbiota, is the most frequently encountered bacteria in Enterobacteriaceae family, and also cause many infections, this study was aimed to determine antibiotic susceptibility of microbiota member *E. coli* isolates against to the antibiotics that used in treatment.

MATERIAL and METHOD

One hundred and fifty stool samples, which were sent to Kırkkale Yüksek İhtisas Hospital microbiology laboratory in a period of between March to December 2013 to study fecal occult blood test and were determined as “negative”, were included in this study.

The first five negative stool samples in order of acceptance to laboratory in everyday were included in the study for randomization. Samples from the same patient were excluded. Single colony inoculation of examples was performed into Eosin Methylene Blue agar (EMB, Klasmed, Turkey) and cultures were incubated for 18-20 hours at 37°C. Lactose-positive and metallic green sheen colonies were studied by BBL Crystal E/NF ID System (Becton Dickinson, USA) and antibiotic susceptibility test was performed with bacteria identified as *E. coli*. Antimicrobial susceptibility test of the *E. coli* isolates was performed by the Kirby Bauer disk diffusion method according to the recommendations of the Clinical Laboratory Standards Institute (CLSI) using with Mueller Hinton Agar (MH, KlasMed, Turkey). Antibiotic susceptibility of bacteria was evaluated according to CLSI data and inhibition zone diameters were measured with millimetric ruler. Also ESBL production of bacteria was determined according

to the CLSI. Accordingly, phenotypic confirmatory test was performed to isolates with zone diameters for ceftazidime (30 µg) <22 and for cefotaxime (30 µg) <27. For this ceftazidime-clavulanic acid (30/10 µg) and cefotaxime-clavulanic acid (30/10 µg) discs were used. The test were considered ESBL positive if the inhibition zone diameter is ≥ 5 mm larger with clavulanic acid than without. The quality control of the media, bacterial identification tests and antibiotic discs was performed with *E. coli* ATCC 25922 strain.

RESULTS

A total of 150 stool samples, from 92 (61.33%) male and 58 (38.67%) female patients, were evaluated in the study. The age distribution of the patients ranged from 3 to 88. 121 (80.67%) samples were from outpatients and 29 (19.33%) from inpatients of all isolates. A total of 70 out of 150 *E. coli* isolates were sensitive to all 23 antibiotics that used in study. Antibiotic susceptibility results of *E. coli* bacteria isolated from intestinal flora are given in Table 1. Twenty four (16%) isolates were

Table 1. Antibiotic susceptibility of *E. coli* isolates

Antibiotics	Susceptibility		Resistance	
	n	%	n	%
Cefepime	150	100.00	0	0.00
Imipenem	150	100.00	0	0.00
Meropenem	150	100.00	0	0.00
Ertapenem	150	100.00	0	0.00
Amikacin	146	97.33	4	2.67
Cefoxitin	144	96.00	6	4.00
Cefeperozone	142	94.67	8	5.33
Gentamicin	140	93.33	10	6.67
Piperacillin-tazobactam	138	92.00	12	8.00
Levofloxacin	129	86.00	21	14.00
Ciprofloxacin	127	84.67	23	15.33
Cefuroxime (oral)	126	84.00	24	16.00
Cefotaxime	126	84.00	24	16.00
Ceftriaxone	126	84.00	24	16.00
Ceftazidime	125	83.33	25	16.67
Cefazolin	122	81.33	28	18.67
Amoxicillin-clavulanic acid	122	81.33	28	18.67
Ampicillin-sulbactam	116	77.33	34	22.67
Trimethoprim-sulfamethoxazole	112	74.67	38	25.33
Piperacillin	110	73.33	40	26.67
Doxycycline	106	70.67	44	29.33
Tetracycline	100	66.67	50	33.33
Ampicillin	80	53.33	70	46.67

found to be ESBL producers. Antibiotic susceptibility rates of ESBL positive isolates are given in Table 2. All isolates were found sensitive to carbapenems.

Eight samples included in present study were from patients under 16 years. ESBL production is not detected in any of these samples but 2 isolates were found resistant against to quinolone that not recommended for children. In this group, while the ampicillin susceptibility rate was 50% and ampicillin sulbactam rate was 75%, amoxicillin clavulanate

sensitivity rate was found 100%. Fifty percent of the strains isolated from children were resistant to at least one antibiotic.

DISCUSSION

The antimicrobial susceptibility studies aim to susceptibility profiles of infection agents as phenotypically or genotypically. The aim of this study was to determine the phenotypic antibiotic susceptibility of microbiota members *E. coli* isolates as a possible source of infection and resistance genes. Although microbiota create beneficial effects on human health, the same bacteria overtake as infectious agents that threaten human health. Besides being a factor for many bacterial infections, it is a resource in terms of antibiotic resistance genes for many bacteria. Moreover, these resistance genes transfer not only between the flora bacteria but also can be transfer to the passes-by bacteria (3). In this respect, the investigation of the resistance profiles of bacterial flora may guide for the basis of empirical therapy, especially both in terms of person and community.

In several studies that shown whether particularly the fecal flora members are UTI factor or not (9, 10). Uropathogenic *E. coli* isolates are located phylogenetically in group B2 and less frequently in the group D. However non-pathogen *E. coli* isolates are often in group A and B1 and often have less virulence factors. All of these isolates are in human intestinal flora but dominantly are included in group B2 and D (11, 12). Also the studies have shown that flora in the elderly population consist of the more virulent isolates (11). In another similar study it was reported that fecal flora related with the group B2 (3). The study conducted in Taiwan has shown that fecal *E. coli* isolates have high levels antibiotic resistance gene cassette containing class 1 integrons (6, 13). In addition, it was indicated that these integrons can be effective to horizontal spread of antibiotic resistance in the intestine. In these studies it was emphasized

Table 2. Antibiotic susceptibility of ESBL positive *E. coli* isolates (%)

Antibiotics	Susceptibility	
	n	(%)
Ampicillin	0	0
Cefazolin	0	0
Cefuroxime (oral)	0	0
Cefotaxime	0	0
Ceftriaxone	0	0
Ceftazidime	0	0
Piperacillin	4	16.67
Ampicillin-sulbactam	4	16.67
Amoxicillin-clavulanic acid	8	33.33
Trimethoprim-sulfamethoxazole	8	33.33
Ciprofloxacin	11	45.83
Levofloxacin	11	45.83
Doxycycline	12	50.00
Tetracycline	12	50.00
Piperacillin-tazobactam	14	58.33
Cefoxitin	18	75.00
Cefeperozone-sulbactam	18	75.00
Gentamicin	20	83.33
Amikacin	22	91.67
Cefepime	24	100.00
Imipenem	24	100.00
Meropenem	24	100.00
Ertapenem	24	100.00

that studying normal flora surveillance in healthy people may be useful especially for estimating antibiotic resistance of infection agents *E. coli* isolates (6).

Lowest antibiotic susceptibility rate was found for ampicillin (53.33%) between all antibiotics included this study. In the period of the study limited reporting of infectious agents in the laboratory was done on the basis of CLSI. Accordingly gentamicin (93.33%) has the highest sensitivity rate in antibiotics group of A to all isolates included in the study. All isolates in this study were found sensitive to imipenem, meropenem, ertapenem and cefepime and also sensitivity rates were found (97.33%) and (92.00%) for amikacin and piperacillin tazobactam respectively.

Similarly, in studies aimed to determine of antibiotic resistance in fecal flora *E. coli* isolates, different resistance rates are reported to ampicillin. Yang et al. (6) in their study made in China they found 50.42% resistance rates to ampicillin. In a different study in the United States conducted with cervicovaginal and rectal *E. coli* isolates they found no differences between antimicrobial susceptibility and resistance rates of these isolates and determined to antimicrobial resistance rate to ampicillin as 39.50% (14). Ampicillin resistance rates of fecal flora *E. coli* isolates are determined in Germany 16.70% in Serbia 42.00% in Korea 43.70% in Spain 58.50% and in Mexico 100% (15-19).

As known, infections caused by ESBL positive *E. coli* isolates, caused serious epidemiological changes in infectious diseases in recent years (20, 21). Sixteen percent of the isolates included in the study were the ESBL-positive, the ESBL resistance was not observed in strains isolated from children. But due to the number of children in the study are low, the obtained results may not reflect the real situation. French researchers in their study investigated ESBL changes in fecal flora of healthy individuals; they showed ESBL production rate increased from 0.6% to 6% over a period of 5 years (22). Studies with

healthy individuals in different countries, ESBL rates of fecal *E. coli* isolates were determined as 3.7% in Spain (23) and 5.8% in Switzerland (24). Considering the differences between these ratio and our country results, although in the other study the people selected from healthy individuals, in our study people who admitted to hospital were included the study so this can be the reason of the differences. In India in 2013, antibiotic susceptibility of *E. coli* strains isolated from stool samples of children aged 3-14 were determined and evaluated the relationship between demographics data of children and the resistance. In the study it was observed that antibiotic resistance rates of *E. coli* isolated from stool samples were higher in children lives in rural and have mothers with low level education than children lives in city and have mothers higher level education. The study also indicated that ESBL rate was low (9%) (1). Another result that obtained in this present study should be underlined although the less number of participants, quinolone resistance was observed in children. In this study 5D flora members *E. coli* strains evaluated quinolone resistance gene and found *aac(6')Ib-cr* gen positivity 20%. *QnrB* positivity was determined in flora members *E. coli* as 6% (25).

Fecal flora elements frequently emerge as factor of UTI. Therefore, in this study antibiotic susceptibility of the *E. coli* isolates against to the antibiotics commonly used in UTI determined and compared the other studies results about the antibiotic susceptibility rates of uropathogen *E. coli* isolates. The susceptibilities of *E. coli* isolates to ampicillin, cefazolin, gentamicin, ampicillin-sulbactam, trimethoprim - sulfamethoxazole, ciprofloxacin, amikacin and imipenem are found 53.33%, 81.33%, 93.33%, 77.33%, 74.67%, 74.67%, 84.67, 97.33%, 100%, respectively. Balasar et al in their study made in Konya, they reported 62.2% *E. coli* rates in uropathogen agents and susceptibility rates to ampicillin 27.2%, cephalothin 37%, gentamicin 68%, trimethoprim-sulfamethoxazole 46.5%, ciprofloxacin 48%, amikacin 97% and imipenem 99.4% (26). In another

study made in Erzurum, Saracoglu et al. isolated 71.3% *E. coli* from urine samples and susceptibility rates to ampicillin, trimethoprim-sulfamethoxazole, ampicillin sulbactam, ciprofloxacin, gentamicin and amikacin reported as 47.9%, 60.5%, 77.3%, 80.4%, 96.7%, 92.4%, respectively (27). Terek and Basoglu in their study made in İzmir, found susceptibility rates to ampicillin 34.2%, gentamicin 71.8%, trimethoprim-sulfamethoxazole 51%, ciprofloxacin 51.3%, imipenem 100% (28). In our study ESBL positivity rate was found 16%. In the other study in Turkey, it was detected as 38.6% in İzmir (28), 13,9% in outpatient and 27.5 in inpatient group in Malatya (29) and 20.2% in Ordu. The data obtained in this study are observed compatible in other studies that conducted with UTI agent *E. coli* isolates in Turkey.

In the study made in Kırkkale, they were tested fecal flora *E. coli* in 2004. They found that the resistance rate of Amikacin was 1% and the rate of ESBL positive isolates were 3% (31). In our study, after nine years we have found that the resistance of Amikacin is 4%, the rate of ESBL positive isolates are 16%. This results are shown that the resistance is higher in time.

As a result, determination of antibiotic susceptibility of fecal *E. coli* isolates that source of infection and resistance genes, is very important for country surveillance studies. We believe monitoring to resistance profiles of fecal flora *E. coli* isolates especially in specific group patients in addition to infection agents is important for giving direction to empirical therapy.

CONFLICTS of INTEREST

The authors declare no conflicts of interest.

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