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RESEARCH ARTICLE

Comparison of Antibiotic Sensitivity Pattern of *Escherichia coli* which Produce Extended Spectrum Beta-Lactamase Strains Isolated from Various Clinical Specimens in Intensive Care Unit

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Abstract

Objective: A retrospective analysis of the widely used antibiotics all susceptibility testing results from *Escherichia coli* (*E. coli*) cultured from clinical specimens' private hospital (from January 2017 to November 2018) was performed.

Methods: The VITEK 2 Compact automated microbiology system (bioMérieux) is designed for automated rapid antimicrobial susceptibility testing and identification of clinically relevant bacteria. Minimum inhibitory concentration (MIC) results previously obtained in recent clinical isolates with well-defined in isolates with well-characterized resistance mechanisms with the microdilution method were re-interpreted for the susceptible, intermediate and resistant categories using the 2018 EUCAST breakpoints. Clinical samples are most commonly isolated from blood, sputum and urine samples.

Results: The results of resistance pattern of *E. coli* isolates in our locality to antimicrobial agents showed that the 64 *E. coli* strains tested against fifteen antimicrobial agents. *E. coli* isolates were highly resistant to piperacillin, ceftazidime and aztreonam 98%, 61% and 61% respectively. The most sensitive antibiotics were colistin, tigecycline, imipenem and meropenem. In the present study, 73% (47) of the isolates were resistant to at least three to fourteen antibiotics. All the isolates showed resistance to at least one antibiotic. Thirty-nine per cent of *E. coli* isolates were extended spectrum beta-lactamase (ESBL) producers.

Conclusion: Considering the antibiogram, imipenem and meropenem should be preferred drugs for E. coli infection isolated from clinical samples.

Key words: *Esherichia coli*, antibiotic sensitivity, clinical specimens, intensive care unit

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Introduction

Esherichia coli is a diverse group of facultative anaerobic Gram-negative bacilli of the genus *Escherichia* in the family Enterobacteriaceae, and contains a variety of strains ranging from commensal organisms to highly pathogenic variants especially the intestine and the urinary tract (Mos et al., 2010).

The extended spectrum beta-lactamase (ESBL) enzymes are predominantly found in *E. coli* and *Klebsiella spp.* however, may also be found in other

species of *Enterobacteriaceae* (Khanfar et al., 2009). Fluoroquinolones, aminoglycosides and trimethoprim-sulfamethoxazole are used for treatment of infections caused by ESBL- producing bacteria (Falagas and Karageorgopoulos., 2009).

The aim of this study was to determine the characteristics and patterns of antibiotic resistance among isolates of *E. coli* recovered from clinical specimens in Giresun province.

Methods

Bacterial isolates

Ethical approval is were taken before study. Because of retrospective analysis, we did not patient approval. The sixty four *E. coli* were isolated from clinical specimens from intensive care unit of internal medicine in private hospital. Bacterial isolates were identified to level of species and subspecies by using the morphological and traditional biochemical tests and automatic diagnostic systems currently present in the market and commonly used for AST (Antimicrobial Susceptibility Testing) in clinical laboratories will therefore have to incorporate these criteria in their instruments to meet the needs of European microbiology laboratories according to standard methods described by (MacFaddin., 2000). In total, 64 *E. coli* were isolated from various clinical samples and detected by the VITEK 2 (bioMérieux) at the microbiology laboratory of our hospital between from January in 2017 to December in 2018. The VITEK 2 Compact Automated Microbiology System (bioMérieux) is designed for the rapid bacterial identification at the species level and determination of AST of clinically significant human bacterial pathogens (Ling et. al., 2001).

Antibiogram profile of E. coli

MIC results previously obtained in recent clinical isolates with well-defined in isolates with well-characterized resistance mechanisms with microdilution method were re-interpreted for the susceptible, intermediate and resistant categories using the 2018 EUCAST breakpoints. Fifteen different antibiotics were used. Antibiotics tested in AST-N326 (bioMérieux) card included piperacillin (PIP), ceftazidim (CAZ), aztreonam (ATM), levofloxacin (LEV), cefepime (FEP), trimethoprim-sulfamethoxazole (SXT), ciprofloxacin (CIP), tazobactam/piperacillin (TZP), netilmicin (NET), gentamicin (GEN), colistin (CT), amikacin (AK), imipenem (IPM), meropenem (MEM), tigecycline (TIG).

Detection of ESBL

VITEK 2 system with the antimicrobial susceptibility extend card AST-N326 (bioMérieux) card was designed to perform both screening and confirmatory tests for phenotypic detection of ESBL on the same plate. VITEK 2 system has two different ESBL detection procedures. The first one uses specific computer software called advanced expert system (AES), that performs analyzes and interpretation of MIC of the antibiotics used. The use of several antimicrobial agents increases the sensitivity of ESBL detection (Sorlózano et. Al., 2005) thus the second procedure was based on ESBL test on same AST-N326 card, where the antibiotic susceptibility of the isolates to FEP and 3rd generatin cephalosporin: cefotaxime (CTX) and ceftazidime (CAZ) with or without clavulanic acid were evaluated (Drieux et al., 2008).

Multiple Antibiotic Resistance (MAR) index

For all isolates, MAR index values were tested according to Matyar et al., (2008).

Results

The results of resistance pattern of *E. coli* isolates in our locality to antimicrobial agents showed that the 64 *E. coli* strains tested against fifteen antimicrobial agents in Table 1. *E. coli* isolates were highly resistant to PIP, CAZ and ATM 98%, 61% and 61% respectively. Resistance rate of CIP was showed in 52%. When we compared to resistance of TZP, *E. coli* isolates showed 38% resistance rate. Among the aminoglycosides group, GEN resistance rate was 28%. In respect of resistance rate of CT, it was 11%. The most sensitive antibiotics were CT, TIG, IPM and MER, as is illustrated in Table 1 and Table 2 shows the antimicrobial susceptibility of all *E. coli* isolated from urine, blood, and sputum. Of the total *E. coli* isolates, 25 (39%) isolates were ESBL producers and 39 (61%) isolates were non-ESBL producers in Table 2.

Table 1. Antibiotic resistance pattern of 64 *E. coli* isolated from clinical specimens in intensive care unit.

Antibiotics	Resistance	Intermediate	Sensitive
PIP	63 (98%)	-	1 (2%)
CAZ	39 (61%)	2 (3%)	23 (36%)
ATM	39 (61%)	3 (15%)	22 (34%)
LEV	36 (56%)	-	28 (44%)
FEP	34 (53%)	6 (9%)	24 (38%)
SXT	34 (53%)	1 (2%)	29 (45%)
CIP	33 (52%)	2 (3%)	29 (45%)
TPZ	24 (38%)	37 (58%)	3 (4%)
NET	22 (34%)	2 (3%)	40 (63%)
GEN	18 (28%)	1 (2%)	45 (70%)
CT	7 (11%)	-	57 (89%)
AK	7 (11%)	10 (16%)	47 (73%)
IPM	5 (7%)	9 (14%)	50 (78%)
MEM	4 (6%)	9 (14%)	51 (80%)
TIG	4 (6%)	4 (6%)	56 (88%)

Abbreviation; PIP, Piperacillin, CAZ; Ceftazidim, ATM; Aztreonam, LEV; Levofloxacin, FEP; Cefepime, SXT; Trimethoprim sulfamethoxazole, CIP; Ciprofloxacin, TPZ; Tazobactam/Piperacillin, NET; Netilmicin, GEN; Gentamicin, CT; Colistin, AK; Amikacin, IPM; Imipenem; MEM; Meropenem, TIG; Tigecycline.

Discussion

In our study, when we compared to resistance of PIP, *E. coli* isolates showed high antibiotic resistance with 98% PIP. Some researchers have reported resistance rate PIP from 100% to17.2% to *E. coli* in clinical samples (Kafilzadeh and Farsimadan., 2016; Batarseh et al., 2013). Our results were lower than Batarseh et al., (2013) who also reported that resistance rate of PIP with 100%.

When it comes to resistance of CAZ, *E. coli* isolates showed high antibiotic resistance with 61% CAZ. Some researchers have reported that CAZ resistance rate from 7.3% to 98.9% to *E. coli* in clinical samples (Ozsahin et al., 2005; Al-Mijali et al., 2017). Our results were lower than Al-Mijali et al., (2017) who also reported that resistance rate of CAZ with 98.9%.

In our study, when we compared to resistance of ATM, *E. coli* isolates showed high antibiotic resistance with 61% ATM. Some researchers have reported that ATM resistance rate from 89% to 98.9% to *E. coli* in clinical samples (Akter et al., 2012; Al-Mijali et al., 2017). Our results were lower than Akter et al., (2012) who also reported that resistance rate of ATM with 89%.

Table 2. Distribution of 64 *E. coli* clinical samples, Sexuality, source, MAR Index and ESBL Producers

Name of Clinic	Number of samples	Source of isolates	Sexuality F/M	ESBL Producers	MAR İndex
Anesthesia and Reanimation	34	5 Sputum 29 Urine	18F 16M	21- 12+	0.07(8isl);0,14(2isl);0.2(4isl); 0.27;0.33;0.4(7isl);0.47;0.53(3isl);0 .87;0.67;0.6(2isl); 0.8(2isl); 0,93
Internal medicine	9	9 Urine	9F	6+ 3-	0.07; 0.14; 0.47; 0.53 (3 isl) 0.6; 0.67(2isl)
Chest diseases	6	2 Sputum 4Urine	4F 2M	2- 4+	0.2;0.27;0.33(2);0.6;0.67
Neurology	7	2 Sputum 5Urine	3F 4M	5- 2 +	0.07;0.27; 0.4; 0.47; 0.53(2); 0.67
Infectious Diseases	2	2Urine	1M 1F	2-	0.07(2 isl)
Cardiology	3	1Blood	3M	1+ 2-	0. 0.4;0.93
Gynecology	1	1Urine	1F		0.07
General Surgery	1	1Urine		1-	0.8
Brain and Nerve Diseases	1	1 Sputum	1F	1-	0.07
Total	64	53 Urine, 10 Sputum 1 Blood		25+ (39%) 39- (61%)	

MAR, Multiple Antibiotic Resistance Index, isl; ısolates, +; ESBL Producing, -Non-ESBL Producing F; Female, M; Male

In our study, when we compared to resistance of LEV, *E. coli* isolates showed high antibiotic resistance with 56% LEV. Some researchers have reported resistance rate LEV from 63,23% to 82% (Sohail et al., 2015; Al-Mijali et al., 2017). Our results were lower than Al-Mijali et al., (2017) who also reported that resistance rate of LEV with 63.23% to *E. coli* in clinical samples.

As for the resistance rate of FEP to *E. coli* islates it showed high resistance with 53%, Some researchers have reported resistance rate from 4,1% to 47.5% FEP to *E. coli* in clinical samples (Albayrak and Kaya, 2009; Batarseh et al., 2013). Our results were higher than Batarseh et al., (2013) who also reported that resistance rate of FEP with 47.5% to *E. coli* in clinical samples.

As for the resistance rate of AK, it was 11%. Some researchers have reported that AK resistance rate from 21.2% to 91% to *E. coli* in clinical samples (Albayrak and Kaya, 2009; Sohail et al., 2015). In other studies which conducted in Italy (Tinelli et al., 2012), Brazil (Abreu et al., 2011), and Nepal (Chander et al., 2013), the resistance rates were lower compared to our results.

Being a highly beta-lactamase stable carbapenem, with an unusual property of causing a post antibiotic effect on Gram negative bacteria resistance to IPM was found to be very low (7%). On the other hand, higher resistances were shown by (Jafri et al., 2014) and (Sabir et al., 2014) were 43.3% and 32.5% respectively. Some researchers have reported that IPM resistance rate to *E. coli* in clinical samples (Al-Mijali et al., 2017).

Carbapenems, especially MEM, resistance rate of MEM was showed in 6 % (table1). Some researchers have reported that MEM from 3% to 1.20% resistance rate to *E. coli* in clinical samples (Sohail et al., 2015; Al-Mijali et al., 2017). Our results were higher than Sohail et al., (2015) who also reported that resistance rate of MEM with 3%.

In our study, when we compared to resistance of TIG, *E. coli* isolates showed antibiotic resistance with 6% TIG. Some researchers have reported that TIG from 6.59% to 9.8% resistance rate to *E. coli* in clinical samples (Batarseh et al., 2013; Al-Mijali et al., 2017). Our results were equavalent to Al-Mijali et al., (2017) who also reported that resistance rate of TIG with 6,59%.

As for the ESBL producers, our results were similiar to El Sayed et al. (2017) who also reported that out of 100 isolates of *E. coli*, 36 were detected as ESBL producers and 64 were non-ESBL producers. In studies performed throughout the world, the frequency of ESBL positive. *E. coli* was from 0.2% to 95.4% (Shadid et al., 2008; Kaftandzhieva et al., 2009). For example, in a study Tasli ve Bahar, in Turkey producing ESBL enzymes in *Escherichia coli* strains of 17%, in the study Villegas, in Colombia 3.3-4.7% (Villegas et al., 2004), in the study Duttaroy and Mehta (2005), in India 29.1% in study Lavigne et al., (2004), in France 16.2%, have been reported.

On the other hand, study of Zhou, in Shanghai show that 47.4% of *E. coli* isolated from patients were ESBL producers (Zhou., 2001), in another study by the Wu, be was conducted in Taiwan hospitals, a rate of 18.18% of ESBL-producing *E. coli* (Wu et al., 2003), While in Lebanon the amount of at 28.1 percent, respectively (Daoud and Hakime, 2003).

In the present study, 73% (47) of the isolates showed Multiple Antibiotic Resistance three to fourteen antibiotics. All of the isolates showed resistance to at least one antibiotics.

The antimicrobial resistance of bacteria is a problem of global concern. There is a correlation between antibiotic use and subsequent resistance (Jensen et al., 2009). In the present study, it was observed that the isolates of *E. coli* showed different degree of resistance to different antimicrobials. The samples were isolated from different clinical specimens. Maximum numbers of isolates were collected from urine indicating that urinary tract is more prone to infection by *E. coli* which corresponds to the findings of other researchers (Sharafi et al., 1996; Paterson and Bonomo., 2005; Kumar et al., 2014).

Conclusion

Considering the antibiogram, CT, TIG, IPM and MER should be preferred drugs for *E. coli* infection isolated from clinical samples from Giresun region.

Ethics Committee Approval: Patients' consent was obtained in the use of microbiological data.
Peer-review: Externally peer-reviewed.
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