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Antibiotic Resistance Profiles and ESBL Production in *E.coli* and *Klebsiella spp*. Isolated from Clinical Samples in a Tertiary Care Hospital

Üçüncü Basamak Bir Hastanedeki Klinik Örneklerden İzole Edilen *E.coli* ve *Klebsiella spp*. Türlerinde Antibiyotik Direnç Profilleri ve ESBL Üretimi

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Abstract

Aim Extended-spectrum beta-lactamases (ESBL) play an important role in the development of resistance to beta-lactam antibiotics in Gram-negative bacteria. ESBL-producing bacteria can cause outbreaks, especially in hospital infections, which can lead to inadequate treatment, prolonged hospital stay, and increased mortality rates. This study aimed to investigate the antibiotic resistance profiles and ESBL production rates in Escherichia coli and Klebsiella spp. species isolated from various clinical samples in a tertiary care hospital

Materials and Methods A total of 315 bacterial isolates were included in the study between September 2022-January 2023. 213 of them were E.coli (67.6%) and 102 were Klebsiella spp. (32.4%). Antibiotic susceptibilities of the isolates; ampicillin, amoxicillin-clavulanate, piperacillin/tazobactam, cefuroxime, cefixime, cefotaxime, gentamicin, amikacin, ciprofloxacin, trimethoprim-sulfamethoxazole, imipenem and meropenem were tested. ESBL production was evaluated with a double disk synergy test. The results were interpreted according to EUCAST criteria.

Results ESBL positivity rate was determined as 35.2% in E. coli isolates and 52.9% in Klebsiella spp. isolates. This rate was found as 22% in pediatric patients and 42% in adult patients. When evaluated according to gender, ESBL positivity was found to be significantly higher in male patients. According to clinical sample types, ESBL positivity was seen most in endotracheal aspirate and wound samples. According to the disk diffusion test, the highest resistance was detected against beta-lactam group antibiotics and the lowest resistance was detected against carbapenems.

Conclusions ESBL production continues to be a significant resistance problem in hospital infections. This study draws attention to the importance of detecting ESBL-positive isolates with the double disk synergy test. Incorrect and unnecessary antibiotic use is one of the main risk factors for increasing ESBL positivity rates. Therefore, early detection of ESBL-positive bacteria, isolation precautions and reconsideration of antibiotic policies are of great importance.

Keywords Extended spectrum beta-lactamase, double disk synergy test, E.coli, Klebsiella spp., antibiotic resistance

Öz

Anaç *Geniş spektrumlu beta laktamazlar (GSBL) gram negatif bakterilerde beta laktam antibiyotiklere direnç gelişmesinde önemli bir rol oynar. GSBL üreten bakteriler salgınlara, özellikle de hastane enfeksiyonlarına sebep olarak yetersiz tedaviye, uzun hastane yatışına ve artmış mortaliteye yol açabilir. Bu çalışma üçüncü basamak bakım hizmeti veren bir hastanede çeşitli klinik örneklerden izole edilen E.coli ve Klebsiella spp. türlerinde antibiyotik direnci profillerini ve ESBL üretimi oranını araştırmayı hedefledi*

Gereç ve Yöntem *Eylül 2022-Ocak 2023 tarihleri arasında toplam 315 bakteri çalışmaya dahil edildi. Bakterilerden 213 tanesi E.coli (%67.6), 102 tanesi Klebsiella spp. (%32.4) idi. İzolatların ampisilin, amoksisilin-klavulonat, piperasilin-tazobaktam, sefuroksim, sefiksim, sefotaksim, gentamisin, amikasin, siprofloksasin, trimetoprim-sulfametaksazol, imipenem ve meropenem duyarlılıkları test edildi. GSBL üretimi çift disk sinerji yöntemi ile değerlendirildi. Sonuçlar EUCAST kriterlerine göre değerlendirildi*

Bulgular *E.coli izolatlarında GSBL pozitiflik oranı %35.2, Klebsiella spp. izolatlarında ise %52.9 olarak belirlendi. Bu oran pediatrik hastalarda %22, erişkin hastalarda ise %42 olarak bulundu. Cinsiyete göre değerlendirildiğinde GSBL pozitifliği erkek hastalarda anlamlı olarak daha yüksek bulundu. Klinik örnek tiplerine göre GSBL pozitifliği en çok trakeal aspirat ve yara örneklerinde görüldü. Disk difüzyon testine göre en yüksek direnç beta-laktam grubu antibiyotiklere, en düşük direnç ise karbapenemlere karşı saptandı.*

Sonuç *ESBL üretimi hastane enfeksiyonlarında önemli bir direnç sorunu olmaya devam etmektedir. Bu çalışma, GSBL pozitif izolatların çift disk sinerji testi ile tespit edilmesinin önemine dikkat çekmektedir. Yanlış ve gereksiz antibiyotik kullanımı, GSBL pozitiflik oranlarını artıran başlıca risk faktörlerinden biridir. Bu nedenle, GSBL pozitif bakterilerin erken tespiti, izolasyon önlemleri ve antibiyotik politikalarının yeniden değerlendirilmesi büyük önem taşımaktadır.*

Anahtar Kelimeler *Genişletilmiş Spektrumlu Beta-Laktamaz, Çift Disk Sinerji Testi, E.coli, Klebsiella spp., Antibiyotik Direnci*

INTRODUCTION

Antimicrobial resistance has become one of the most serious global problems threatening public health today. Increasing antibiotic resistance complicates the treatment of infections, prolongs the duration of treatment, and increases mortality and morbidity rates.[1] Third-generation cephalosporin-resistant Enterobacterales and carbapenem-resistant Enterobacterales are categorised as critical priority by World Health Organization (WHO).[2] In this context, infection control and appropriate antibiotic use in healthcare institutions are among the basic strategies in the fight against resistance.

Escherichia coli and Klebsiella spp. species, which are the main causes of hospital infections, can cause serious clinical conditions, especially in intensive care units (ICU) and immunosuppressed patients. Urinary tract infections, lower and upper respiratory tract infections, wound infections and sepsis caused by these bacteria are more complicated due to resistant strains.[3] Resistance to beta-lactam antibiotics, which are frequently preferred in such infections, limits treatment options.

Extended-spectrum beta-lactamases (ESBL) are enzymes that can eliminate the effectiveness of antibiotics, especially third-generation cephalosporins and aztreonam. ESBL production is usually easily transmitted via plasmid, which facilitates the transfer of resistance traits to different bacteria through horizontal gene transfer.[4,5] ESBL-positive bacteria can also be resistant to antibiotics such as aminoglycosides, quinolones and trimethoprim-sulfamethoxazole, which increases the risk of multidrug resistance (MDR).[6] Infections caused by ESBL-producing bacteria can lead to inadequate treatment, prolonged hospital stay, and increased healthcare costs. In addition, these strains can cause outbreaks because they can easily spread in hospital environments.[7] Regular monitoring of ESBL positivity rates and antibiotic resistance profiles is of great importance in order to prevent the spread of resistant bacteria and determine appropriate treatment approaches.

This study aimed to investigate antibiotic resistance patterns and ESBL production rates in *E.coli* and *Klebsiella spp.* isolated from various clinical samples in a tertiary care hospital. The relationship between ESBL positivity and age, gender, sample type, and clinical admission type were also evaluated. It is aimed that the obtained data will contribute to the determination of local resistance trends and to empirical antibiotic selection.

MATERIALS and METHODS

In this study, antibiotic resistance profiles and ESBL production status of a total of 315 strains isolated from urine, blood, sputum, endotracheal aspirate (ETA) and wound samples sent to the microbiology laboratory between September 2022 and January 2023 were evaluated. In patients with multiple positive cultures, only the first isolate was included in the study.

Samples were inoculated on 5% sheep blood agar (SBA) and eosin methylene blue (EMB) agar and incubated at 35°C for 18–24 hours under aerobic conditions. For urine cultures, samples with 105 or more "colonial forming units" (cfu)/ml growth were taken for bacterial identification and antibiotic susceptibility testing. Blood culture bottles were taken as a set, and patients with growth in both bottles were included in the study. Bottles were incubated in the Bactec FX40 (BD Diagnostics, USA) device for 5 days. Those giving positive signals were taken from the device and subcultured into SBA and EMB media.

Isolates were identified by colony morphology, Gram staining and oxidase test. Oxidase negative gram negative bacilli were taken into classical biochemical tests (indole, methyl red, Voges-Proskauer, citrate [IMViC] reactions). For strains that could not be identified by conventional methods, BD Phoenix™ (BD Diagnostics, USA) automatic identification system was used.

Antibiotic susceptibilities were performed by Kirby Bauer disc diffusion method and the results were interpreted

according to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) criteria.[8] ESBL production was tested by double disk synergy test (DDST). Bacterial suspensions were prepared in 0.5% McFarland standard and inoculated onto Mueller-Hinton agar. Ceftazidime, cefepime, ceftriaxone and amoxicillin-clavulanic acid discs were placed with a distance of at least 20 mm and incubated 18–24 hours at 35°C. Augmented zone of inhibition around beta-lactam discs or presence of keyhole in the direction of clavulanic acid disc was accepted as ESBL positivity.

The study was approved by the Lokman Hekim University Non-Interventional Clinical Research Ethics Committee on 12.05.2022 (Decision No: 2022/77) and supported by the Lokman Hekim University Scientific Research Projects Coordination Unit with project number TYL-2023-28.

Statistical Analysis

Statistical analyses were performed using the IBM SPSS Statistics v21.0 (IBM Corp., USA) program. Statistical significance level was accepted as $p<0.05$ in all tests. The distribution of the age variable was evaluated with the Shapiro-Wilk test. Since the age variable showed a normal distribution for all participants, it was summarized with the mean and standard deviation; however, since the distribution was not normal based on ESBL groups, median (min–max) values were used. The age difference between ESBL positive and negative groups was examined with the Mann-Whitney U test. The relationship between gender and ESBL results was evaluated with the Chi-square test. Antibiotic resistance distributions and descriptive variables were reported as frequency (n) and percentage (%).

RESULTS

Between September 2022 and January 2023, 315 bacteria isolated from clinical samples were investigated for their antibiotic resistance profiles and extended-spectrum β-lactamase activity. Of these, 67.6% (n: 213) were *E. coli*, and 32.4% (n: 102) were *Klebsiella spp*. (*K. pneumoniae* 91, *K.oxytoca* 11). The median age of the patients was 63.65±24.27 (min:2, max:101). Out of 315 participants, 69.2% (n: 218) were female and 94.3% (n: 297) were adults. Urine was the most frequently obtained clinical sample (n: 228, 72.4%), followed by ETA (n: 57, 18.1%), wound (n:18, 5.7%), and blood samples (n: 12, 3.8%). The clinical samples were primarily from the ICU, followed by the outpatient clinic and hospital wards. Where the majority of E. coli strains were isolated from outpatient clinics and urine samples, *Klebsiella spp*. strains were most commonly isolated from ICUs and ETAs. The distribution of isolates by sex, age, sample type, clinical setting, and ESBL results is summarized in Table 1.

Table 1. The Distribution of İsolates By Sex, Age, Sample Type, Clinical Setting, and ESBL Results

	E. coli **n (%)***	***Klebsiella spp.*** **n (%)***	**Total n (%)****
Gender			
Female	168 (78.9)	50 (49.0)	218 (69.2)
Male	45 (21.1)	52 (51.0)	97 (30.8)
Age			
<18 yrs	18 (8.5)	0 (0.0)	18 (5.7)
>18 yrs	195 (91.5)	102 (100)	297 (94.3)
Sample Type			
Urine	193 (90.6)	35 (34.3)	228 (72.4)
ETA	8 (3.8)	49 (48.0)	57 (18.1)
Blood	4 (1.8)	8 (7.9)	12 (3.8)
Wound	8 (3.8)	10 (9.8)	18 (5.7)
Clinical Setting			
Outpatient Clinics	126 (59.1)	5 (4.9)	131 (41.6)
Wards	21 (9.9)	13 (12.8)	34 (10.8)
ICU	66 (31.0)	84 (82.3)	150 (47.6)
ESBL			
Positive	75 (35.2)	54 (52.9)	129 (41.0)
Negative	138 (64.8)	48 (47.1)	186 (59.0)
Total	213	102	315

* column percentage
** row percentage

According to the results of the DDST, ESBL positivity was found in 41.0% (n: 129) of study group. ESBL positivity

was 35.2% (n: 75) in *E. coli* isolates, and was 52.9% (n: 54) in Klebsiella spp. ESBL positivity was 22.2% in pediatric patients, while this rate was 42.1% in adults. ESBL positivity was 37.2% in female patients and 49.5% in males and this difference was statistically significant (p = 0.040). ESBL positivity was significantly higher in *E.coli* and *Klebsiella spp*. isolates from male patients. ESBL positivity was found to be significantly higher in ETA and wound samples compared to other samples (p = 0.045). When ESBL positivity was examined according to patient presentation type, it was found to be 50% (n: 75) in ICU patients, 55.9% (n: 19) in ward patients, and 26.7% (n: 35) in outpatient clinic patients. This difference was statistically significant (p < 0.001) (Table 2). The median age was 75.0 (min: 7 – max: 98) in ESBL-positive patients and 68.0 (min: 2 – max: 101) in negative group; this difference was statistically significant (p = 0.006).

A comparative analysis of the antibiotic resistance profiles of ESBL-positive and ESBL-negative *E.coli* strains were presented in Table 3. Overall, ESBL-positive isolates exhibited significantly higher rates of resistance to most antibiotics. Furthermore, resistance to commonly used antibiotics such as ciprofloxacin, aminoglycosides and trimethoprim-sulfamethoxazole was also notable in positive strains. In contrast, resistance to carbapenem antibiotics (meropenem and imipenem) was low in both groups, and no statistically significant difference was found.

Antibiotic resistance rates of *Klebsiella spp*. isolates based on their ESBL were analysed in Table 4. Generally, ESBL-positive strains exhibit significantly higher resistance to many antibiotics. Ampicillin, piperacillin-tazobactam, amoxicillin-clavulanate have significantly higher resistance rates in ESBL-positive isolates. Among carbapenem antibiotics, resistance to imipenem and meropenem was higher in the ESBL-positive group, and this differences were statistically significant (p<0.05). According to ESBL positivity no significant difference was found in amikacin and gentamicin resistance. For ciprofloxacin, resistance rate was quite high in the ESBL-positive group (88.9%). Because the automated identification system was used to identify a small number of isolates (13%), a concordance analysis between the automated system data and the DDST results could not be performed.

DISCUSSION

This study evaluated the antibiotic resistance profiles and ESBL production rates of *E.coli* and *Klebsiella spp*. strains isolated from various clinical specimens from a tertiary care hospital in relation to variables such as age, gender, clinical specimen and presentation. ESBL-producing Enterobacterales strains pose a serious threat in both hospital-acquired and community-acquired infections. The ESBL positivity rate in cultures obtained in ICU was found to be significantly higher. This may be related to the intensive use of antibiotics, the frequency of invasive procedures, and the closed environment conditions where resistant strains can easily spread. The high positivity rates obtained in this study demonstrate that empiric treatment options are narrowing and the risk of treatment failure is increasing, particularly in ICU.

In this study, 41% of 315 strains isolated from clinical samples were found to ESBL-positive. This rate is largely consistent with similar studies conducted in different regions of Turkiye. For example, Bursal et al. reported ESBL positivity in 41.4% of *E.coli* isolates and 53.2% of Klebsiella species in pediatric urinary tract infections.[9] In a study conducted by Duran et al. on ICU-acquired samples, these rates were 57.3% for E.coli and 46.3% for *K. pneumoniae*.[10] In other research, only *E.coli* isolates from urine were investigated and reported ESBL positivity as 34.2% in adult patients.[11]

In case of international results, systematic reviews by Ramatla and Olaitan at all. suggest that ESBL positivity is increasing worldwide, with regional variations. Global meta-analyses have reported ESBL positivity to be approximately 33% for *E. coli* and 32% for *K. pneumoniae*.12 The lower (20%) ESBL positivity found in studies conducted in

Table 2. Distribution of ESBL Results by Gender, Clinical Sample and Setting Type

	Total n	ESBL Positive n (%)*	ESBL Negative n (%)*	χ^2	p-value
Gender					
Female	218	81 (37.2)	137 (62.8)	4.220	0.040**
Male	97	48 (49.5)	49 (50.5)		
Clinical Sample					
Urine	228	85 (37.3)	143 (62.7)	8.055	0.045**
Blood	12	4 (33.3)	8 (66.7)		
ETA	57	28 (49.1)	29 (50.9)		
Wound	18	12 (66.7)	6 (33.3)		
Clinical Setting					
Outpatient Clinics	131	35 (27)	96 (73)	19.19	< 0.001**
Wards	34	19 (56)	15 (44)		
ICU	150	75 (50)	75 (50)		

* Row percentages **Pearson Chi-Square test

Table 3. Antibiotic Resistance Profiles of E. coli Isolates According to ESBL Results

Antibiotics	Total Resistance n (%)	ESBL+n (%)75	ESBL-n (%)138	p-value
Ampicillin	142 (66.7)	74 (98.7)	68 (49.3)	<0.001
Amoxicillin-clavulanate	94 (44.1)	61 (81.3)	33 (23.9)	<0.001
Piperacillin-tazobactam	27 (12.7)	19 (25.3)	8 (5.8)	<0.001
Trimethoprim-sulfamethoxazole	80 (37.6)	41 (54.6)	39 (28.3)	<0.001
Ciprofloxacin	82 (38.5)	56 (74.6)	26 (18.8)	<0.001
Gentamicin	39 (18.3)	21 (28.0)	18 (13.0)	0.012
Amikacin	15 (7.0)	12 (16.0)	3 (2.2)	<0.001
Imipenem	6 (2.8)	4 (5.3)	2(1.4)	0.186
Meropenem	12 (5.6)	7 (9.3)	5 (3.6)	0.118

Table 4. Antibiotic Resistance Profiles of Klebsiella spp. Isolates According to ESBL Results

Antibiotics	Total Resistance n (%)	ESBL+n (%)75	ESBL-n (%)138	p-value
Ampicillin	100 (98.0)	53 (98.1)	47 (97.9)	>0.999
Amoxicillin-clavulanate	83 (81.4)	51 (94.4)	32 (66.7)	0.001
Piperacillin-tazobactam	69 (67.6)	46 (85.1)	23 (47.9)	<0.001
Trimethoprim-sulfamethoxazole	58 (56.9)	40 (74.0)	18 (37.5)	<0.001
Ciprofloxacin	75 (73.5)	48 (88.9)	27 (56.3)	<0.001
Gentamicin	37 (36.3)	21 (38.9)	16 (33.3)	0.707
Amikacin	30 (29.4)	14 (25.9)	16 (33.3)	0.588
Imipenem	57 (55.9)	36 (66.7)	21 (43.8)	0.043
Meropenem	61 (59.8)	41 (75.9)	20 (41.6)	0.001

Sub-Saharan Africa can be explained by the fact that resistance is also lower in places where access to antibiotics is less.[13] This variability in ESBL rates worldwide is attributed to many factors, including sample size, geographic conditions, antibiotic use policies, and laboratory diagnostic capabilities.[1,2,12] The 41% ESBL rate obtained in our study highlights the need for caution, particularly in empirical treatment planning, and the importance of incorporating local resistance data into treatment guidelines.

In our study, ESBL positivity was detected in 35% of *E.coli* strains and 53% of *Klebsiella spp*. strains. This suggests that Klebsiella species are genetically more prone to ESBL production and play a more dominant role in hospital-acquired infections. Studies in the literature also show higher positivity rates in *Klebsiella spp*. other than *E.coli*.[9,14,15] Furthermore, the majority of *E.coli* isolates in our study were obtained from outpatient patients and urine samples, while *Klebsiella* strains were obtained from invasive specimens from ICU as ETA. These different sample sources may explain the difference in observed resistance rates.

Lower ESBL positivity rates have also been reported in some studies. Of the 3899 enteric bacteria isolated from urine cultures, 17.9% (n: 699) were found to be ESBL-positive. ESBL positivity was significantly higher in the elderly and children. Resistance to parenterally available antibiotics such as piperacillin-tazobactam, aminoglycosides, and carbapenems was found to be low.[16] In another study examining bacteria isolated from urine cultures, 1443 *E.coli* and 255 *Klebsiella spp*. were evaluated, and the ESBL positivity rate was found to be 19.6% and 21.6%, respectively. [17]

We found ESBL positivity 49.5% in bacteria isolated from male patients and 37.2% in female patients. This difference is statistically significant, and similar findings are found in different studies. Similar results were reported a higher rate of antibiotic resistance in males. More frequent urinary tract disorders, catheterization, and long-term antibiotic use in male patients may be possible reasons for this difference. Furthermore, male patients' higher hospitalizations increase the risk of exposure to resistant bacteria.[9,11] In our study, ESBL positivity was most frequently detected in ETA and wound samples. The fact that these samples were mostly collected from ICU may increase the development of resistance due to the frequency of invasive procedures and long-term antibiotic use. Studies also show high ESBL rates in ICU and invasive samples.[10,14,15] This suggests that sample type and clinical unit are important factors to consider in resistance analysis.

The highest resistance rate among *E.coli* isolates was found to be against ampicillin (66%), followed by amoxicillin-clavulanate, quinolones, and trimethoprim-sulfamethoxazole in our study. Agents such as carbapenems and amikacin had the lowest resistance rates. These findings are consistent with the previous researchs.[16,18,19]

The highest resistance rate among *Klebsiella spp.* isolates was found to be against ampicillin (98%). High resistance rates were also found to be against amoxicillin-clavulanate, piperacillin-tazobactam, and quinolones. Meropenem resistance was found to be 75.9% and imipenem resistance was 66.7% in ESBL-positive Klebsiella strains. The high carbapenem resistance observed in our study has become a serious clinical problem, particularly in Klebsiella strains. The widespread use of carbapenems as first-line antibiotics is one of the factors that accelerate the development of resistance to this group. It is known that carbapenem resistance does not arise solely from carbapenem overuse; various mechanisms, including porin loss, efflux pump activation, and carbapenemase production, along with ESBL production, may also play a role in this resistance. However, our study only assessed ESBL at the phenotypic level; the presence of carbapenemases and other resistance mechanisms were not investigated. So, this is one of the limitations of the study.

Carbapenem-resistant Enterobacterales has been identified as one of the most critical threats on the WHO's

current pathogen list.[2] This resistance is directly associated with treatment failure, prolonged hospital stay, and increased costs. Studies demonstrated a strong correlation between ESBL positivity and carbapenem resistance.[12,16] Therefore, empiric treatment decisions require careful evaluation of local resistance data, controlled carbapenem use, and increased isolation precautions.

Klebsiella spp. antimicrobial resistance results were found in a study examining 507 Klebsiella isolates, 94.5% (n: 479) were identified as *K.pneumoniae* and 5.5% (n: 28) as K.oxytoca. Clinical samples were, in order of frequency, 41% (n: 208) as urine, 23.9% (n: 121) as blood, 16.4% (n: 83) as tracheal aspirates, 15% (n: 76) as wounds, and 3.7% (n: 19) as other clinical samples. ESBL production was detected in 65.1% (n: 330) of the Klebsiella isolates. The most effective antimicrobials in vitro for both ESBL-producing and non-ESBL-producing isolates were amikacin and imipenem. Among ESBL-producing *K.pneumoniae* isolates, resistance to amikacin was detected in 18% and imipenem in 23.5%.[14]

ESBL positivity was detected in 48% of *E. coli* strains and 67% of *K.pneumoniae* strains. The most effective antibiotics against the isolated strains were found to be carbapenems and amikacin for *E.coli* strains and amikacin, and ciprofloxacin for *K.pneumoniae* strains.[15]

In the study examining 1028 *E.coli* and 830 *Klebsiella spp*. isolated from blood cultures, the resistance rates were found to be 73.44%-100% for ampicillin, 0.97%-20.36% for meropenem, 2.14%-16.50% for amikacin, 19.16%-35.06% for gentamicin, 45.33%-41.44% for ciprofloxacin, 47.85%-50.48% for trimethoprim sulfamethoxazole, respectively.[19]

In a study evaluating more than three thousand *E.coli* strains grown in urine cultures from different patient groups, the antibiotics to which the isolates showed the highest susceptibility were carbapenems (>99%), and amikacin (94.2%), respectively. The highest resistance rates were detected for ampicillin (61.3%) and amoxicillin-clavulanate (37.5–45.7%). When age groups were compared, the highest resistance to all antibiotics except piperacillin-tazobactam, amikacin and ertapenem was seen in isolates from patients 65 years of age and older. When evaluated in terms of gender, strains isolated from male patients showed higher resistance rates to all antibiotics compared to female patients. Likewise, isolates from inpatients were found to be more resistant than outpatients. A similar distribution was observed in terms of ESBL production; the highest ESBL rate was detected in isolates from patients 65 years of age and older (34.2%). ESBL positivity rate was found in male patients (33.9%) compared to female patients (23.8%); It was found to be higher in inpatients (36.3%) than in outpatients (23.3%).[11]

Furthermore, in current study, ESBL-positive *E.coli* strains had significantly higher resistance rates to ampicillin (98.7% vs. 49.3%) and other antibiotics compared to ESBL-negative strains. This suggests that ESBL genes are carried in conjunction with multiple antibiotic resistance genes. Antibiotic resistance rates for ESBL-producing bacteria are 55.4% for quinolones and 12.3% for aminoglycosides. Resistance rates for bacteria that do not produce ESBL are 17.4% for quinolones and 9.7% for aminoglycosides.9 In another study, the highest resistance rate in E.coli strains isolated from urine cultures (n: 1844) was found to be ampicillin (67.22%), while the lowest resistance rate was found to be imipenem and meropenem (2.28%).[18]

High resistance rates were observed in ESBL-positive strains not only to β-lactam antibiotics but also to aminoglycosides and quinolones. This is because plasmids carrying ESBL genes often also carry aminoglycoside resistance genes.[20] However, it is emphasized that these antibiotics may still be effective in urinary tract infections but should not be preferred alone for empirical treatment.[21] Although quinolones are antibiotics unaffected by β-lactamases, high ciprofloxacin resistance rates are also observed in ESBL-positive bacteria. The quinolone resistance develops

due to both chromosomal mutations and plasmid-borne mechanisms and has a high potential for co-transmission with ESBL. These two types of resistance are frequently observed together, particularly under increasing antibiotic pressure in the hospital environment.[22,23] So, careful use of antibiotics and regular monitoring of antibiotic resistance profiles are also essential.

The strengths of our study include the following: It was conducted using clinical samples collected from different clinics of a tertiary hospital; it evaluated the antibiotic resistance profiles and ESBL production of two important pathogens, *E.coli* and *Klebsiella spp.*; and it correlated with demographic factors such as age and gender; and the patient's presentation. Our limitations include the fact that the study was based on a single center, our sample size was low, molecular analysis was not performed, the presence of carbapenemases was not investigated, clinical data about the patients (antibiotic use, length of hospital stay, comorbidities, etc.) were not used, and the distribution of adult and pediatric patients was unbalanced.

CONCLUSION

This study evaluated the antibiotic resistance profiles and ESBL production of *E.coli* and *Klebsiella spp*. isolates from various clinical specimens. The findings indicate that antibiotic resistance and ESBL positivity were significantly higher, particularly in older age groups, males, and inpatients. Our results suggest that demographic and clinical factors play a significant role in the risk of developing resistant bacterial infections. It is vital to restrict the unnecessary use of broad-spectrum cephalosporins and fluoroquinolones. Reducing antibiotic pressure will also limit the spread of ESBL-producing clones and plasmids carrying these genes. In light of these findings, it is suggested that both empirical treatment approaches and infection control measures should be tailored to each patient group.

Ethics Approval

The study was approved by the Lokman Hekim University Non-Interventional Clinical Research Ethics Committee on 12.05.2022 (Decision No: 2022/77).

Peer-review

Externally and internally peer-reviewed.

Conflicts of Interest

None declared.

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References

1. Prestinaci F, Pezzotti P, Pantosti A. Antimicrobial resistance: A global multifaceted phenomenon. Pathog Glob Health. 2015;109(7):309–318.
2. WHO Bacterial Priority Pathogens List, 2024: Bacterial pathogens of public health importance to guide research, development and strategies to prevent and control antimicrobial resistance. https://www.who.int/publications/i/item/9789240093461 Date accessed: June 30, 2025
3. Paterson DL. Resistance in Gram-negative bacteria: Enterobacteriaceae. Am J Infect Control. 2006;34(5 Suppl 1):S20–S28.
4. Bradford PA. Extended-spectrum beta-lactamases in the 21st century: Characterization, epidemiology, and detection. Clin Microbiol Rev. 2001;14(4):933–951.
5. Yassara S, Zeouk I, Jaouhar S, et al. Extended-spectrum beta-lactamases: definition, history, an update on their genetic environment and detection methods. J Med Microbiol. 2025;74(6):002033.
6. Rawat D, Nair D. Extended-spectrum beta-lactamases in Gram-negative bacteria. J Glob Infect Dis. 2010;2(3):263–274.
7. Schwaber MJ, Carmeli Y. Mortality and delay in effective therapy associated with ESBL production in Enterobacteriaceae bacteremia: A systematic review. J Antimicrob Chemother. 2007;60(5):913–920.
8. European Committee on Antimicrobial Susceptibility Testing (EUCAST). Breakpoint tables for interpretation of MICs and zone diameters Version 11.0. Available from: https://www.eucast.org. Accessed September 24, 2022.
9. Bursal B, Özdemir AA, Topal N, et al. Çocuklarda genişlemiş spektrumlu beta-laktamaz üreten bakteriler ile ilişkili üriner sistem enfeksiyonlarına dair bulgular: Tek merkez deneyimi. J Pediatr Inf 2025;19(1):13-23.
10. Duran H, Çeken N, Atik B. Escherichia Coli ve Klebsiella Pneumoniae Türlerinde Antibiyotik Direnci ne Durumda? Yoğun Bakım Ünitesinden Beş Yıllık Analiz. Fırat Tıp Dergisi 2022: 27(2): 116-120.
11. Mirza HC, Sancak B. Comparison of antimicrobial susceptibilities of Escherichia coli isolated from urinary cultures of different patient groups: A university hospital experience. Klimik Derg. 2020; 33(3): 270-6.
12. Ramatla T, Mafokwane T, Lekota K, et al. "One Health" perspective on prevalence of co-existing extended-spectrum β-lactamase (ESBL)-producing Escherichia coli and Klebsiella pneumoniae: a comprehensive systematic review and meta-analysis. Ann Clin Microbiol Antimicrob. 2023;22(1):88. doi:10.1186/s12941-023-00638-3
13. Olaitan MO, Orababa OQ, Shittu RB, et al. Prevalence of ESBL-producing Escherichia coli in sub-Saharan Africa: A meta-analysis using a One Health approach. One Health. 2025;20:101090. doi:10.1016/j.onehlt.2025.101090
14. Temiz, H., Özbek, E., Vural, D. G., & Özekinci, T. Klebsiella izolatlarının antimikrobiyal direnç oranlarının değerlendirilmesi. Türk Mikrobiyol Cem Derg, 2015: 45(2), 68-74.
15. Parlak M, Çıkman A, Bektaş A, et al. Escherichia coli ve Klebsiella pneumoniae suşlarında genişlemiş spektrumlu beta-laktamaz üretimi ve antibiyotiklere direnç: Beş yıllık izlem. Sakarya Med J 2012; 2:11-5.
16. Karamanlıoğlu D, Yıldız PA, Kaya M, Sarı N. İdrar kültürlerinden izole edilen enterik bakterilerde genişlemiş spektrumlu β-laktamaz oluşturma sıklığı ve antibiyotik duyarlılıkları. Klimik Derg. 2019; 32: 233-9.
17. Avcıküçük H, Altın N. Evaluation of the distribution and antibiotic resistance profile of strains isolated from urine specimens. Klimik Derg. 2022;35(2):95-102.
18. Çalışkan A, Öner SZ, Demir M, et al. Antimicrobial Resistance of E. coli Strains Isolated from Urine Cultures. Anatolian Journal of Pharmaceutical Sciences. 2024:3(2), 212–219.
19. Tanrıverdi Çaycı Y., Bıyık İ., Çınar C., Yuoser M., Birinci A. Antimicrobial Susceptibility Prole of Enterobacterales Isolated from Blood Cultures Between 2016-2021. J Biotechnol and Strategic Health Res. 2025;9(1):25-30.
20. Alyamani EJ, Khiyami AM, et al. The occurrence of ESBL-producing Escherichia coli carrying aminoglycoside resistance genes in urinary tract infections in Saudi Arabia. Ann Clin Microbiol Antimicrob. 2017;16(1):1.
21. Karaiskos I, Lagou S, Pontikis K, et al. The "Old" and the "New" Antibiotics for MDR Gram-Negative Pathogens: For Whom, When, and How. Front Public Health. 2019;7:151.
22. Salah FD, Soubeiga ST, Ouattara AK, et al. Distribution of quinolone resistance gene (qnr) in ESBL-producing Escherichia coli and Klebsiella spp. in Lomé, Togo. Antimicrob Resist Infect Control. 2019;8:104.
23. Rodríguez-Martínez JM, Machuca J, Cano ME, et al. Plasmid-mediated quinolone resistance: Two decades on. Drug Resist Updat. 2016;29:13-29.