10.30699/ijmm.16.6.490

Iranian Journal of Medical Microbiology | ISSN:2345-4342

Prevalence of Extended-Spectrum Beta-Lactamase in Gram Negative Bacteria Isolated from Kermanshah Medical Centers: A Systematic Review and Meta-Analysis

Mosayeb Rostamian[1], Sepide Kadivarian[2], Sara Kooti[2], Shirin Dashtbin[3], Ramin Abiri[4], Amirhooshang Alvandi[5*]

1. *Infectious Diseases Research Center, Health Institute, Kermanshah University of Medical Sciences, Kermanshah, Iran*
2. *Department of Microbiology, School of Medicine, Kermanshah University of Medical Sciences, Kermanshah, Iran*
3. *Department of Microbiology, School of Medicine, Iran University of Medical Sciences, Tehran, Iran*
4. *Fertility and Infertility Research Center, Research Institute for Health Technology, Kermanshah University of Medical Sciences, Kermanshah, Iran*
5. *Medical Technology Research Center, Research Institute for Health Technology, Kermanshah University of Medical Sciences, Kermanshah, Iran*

ABSTRACT

Background and Aim: Nosocomial infections caused by gram-negative bacteria are among the most important health-threatening challenges of the current century, particularly following the emergence and spreading of antibiotic-resistance strains. Extended-spectrum beta-lactamase (ESBL), one of the most important antibiotic resistance mechanisms, is spreading worldwide. Surveillance and gathering data on the prevalence of antibiotic resistance and their associated encoding genes could assist in selecting treatment strategies and policies. This systematic review and meta-analysis was designed to assess the prevalence of ESBL-positive bacteria and their resistance genes in medical centers of Kermanshah city, west of Iran.

Materials and Methods: All studies published as original articles were retrieved by searching in EMBASE, Scopus, PubMed/Medline, Google Scholar, and Persian databases of SID and Magiran, using appropriate keywords All published studies in the field were included without time restriction until 30-Mar-2022. Comprehensive Meta-Analysis software was used to analyze the data.

Results: The prevalence of ESBL-positive and multidrug resistance (MDR) bacteria in Kermanshah medical centers were 34.8% and 56.1%, respectively. The highest and lowest prevalence of ESBL-positive bacteria was observed for *Enterobacter cloacae* (59.14%) and *Pseudomonas aeruginosa* (4.55%), respectively. The highest and lowest prevalence of the resistance genes were observed for *blaOXA-51* (99.3%) and *blaKPC* (0.6%), respectively. The highest resistance was estimated to mezlocillin antibiotic (92.2%).

Conclusion: This study showed that the prevalence of ESBL-positive and MDR bacteria is high in Kermanshah medical centers, and it provides significant information to health policymakers to implement appropriate strategies to reduce the prevalence of resistant bacteria.

Keywords: Extended-spectrum-beta-lactamase, Gram-negative bacteria, Antibiotic resistance, Prevalence, Meta-analysis

Received: 2022/03/06; **Accepted**: 2022/06/28; **Published Online:** 2022/09/09

Corresponding Information: **Amirhooshang Alvandi** , *Department of Microbiology, School of Medicine, Medical Technology Research Center, Research Institute for Health Technology, Kermanshah University of Medical Sciences, Kermanshah, Iran*
Email: ah_alvandi@kums.ac.ir

1. Introduction

Enterobacteriaceae and non-fermented gram-negative bacilli are the most important causes of nosocomial infections. Antimicrobial resistance among these bacteria is a serious global public health problem. One of the main reasons for treatment failure of nosocomial infections is the acquisition of antibiotic resistance genes and the development of the extended-spectrum beta-lactamase (ESBL) producing bacteria. *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Acinetobacter baumannii*, the most important ESBL-producing organisms, are responsible for the majority of nosocomial infections **(1, 2)**. These infectious agents become highly resistant to many antibiotics by producing the most common ESBL enzymes such as *blaCTX-M*, *blaTEM*, and *blaSHV* (They cause the spread of multidrug-resistant strains) **(3, 4)**. MDR resistance patterns of a bacteria are defined as follows: If a bacterium is insensitive to at least one agent in three or more antimicrobial groups, it is considered an MDR bacterium. Despite efforts that have been made to control nosocomial infections, the mortality rate associated with ESBL-producing is still high worldwide **(5)**. Many studies have been performed to determine the prevalence of ESBL-producing strains and genes in Iran. Therefore, due to the need for a comprehensive program and a complete registry, gathering published data as a meta-analysis could be helpful for a selection of antibiotic treatment strategies and policies **(6, 7)**. Since no systematic review and meta-analysis study has been performed previously in Kermanshah province, we aimed to collect and analyze the data from all published articles about the prevalence of ESBL-positive gram-negative bacteria and the frequency of different ESBL genes in Kermanshah medical centers. Because the prevalence of ESBLs-producing genes plays a key role in creating a different pattern of antibiotic resistance in bacteria, knowing the prevalence of genes and screening for ESBL-producing bacteria can help implement a plan to control and treat threatening infections in the future. This helps to prevent the transmission and spread of antibiotic resistance genes as much as possible.

2. Materials and Methods

Search strategy and selection criteria

The data of this systematic review and meta-analysis study were collected from international and local databases, including EMBASE, Scopus, PubMed/Medline, Google Scholar, SID, and Magiran. The related keywords were *extended-spectrum beta-lactamase*, *ESBL*, *β-lactams resistance*, *antibiotic resistance*, and *Kermanshah* alone or combined with "AND" and/or "OR" All published studies in the field were included without time restriction until 30-Mar-2022. To conduct the present study Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) checklist for diagnostic test accuracy was considered **(8)**.

Inclusion/exclusion criteria

Studies based on title, abstract, full text, and originality that corresponded to the study's purpose and had the study's desired characteristics were selected as eligible and entered into the study. Cohort studies, letters to editors, conferences, case reports, narrative or systematic reviews without proper data, and non-English articles were excluded.

Selection of studies and data gathering

The extracted data were checked as follows: name of the first author, year of publication, year of sample collection, medical center of sample collection, isolated bacteria, sample type, sample size, sample gender, phenotypic and genotypic methods, frequency of ESBL, multidrug resistance (MDR), Antibiotic resistance pattern, and frequency of ESBL genes.

Data statistical analysis

Using Comprehensive Meta-Analysis v2.2.064, meta-analysis and subgroup analysis were performed. The prevalence of ESBL positive cases, MDR cases, ESBL genes, and antibiotic resistance were presented with 95% confidence intervals (CIs) with the random-effects model. A subgroup analysis was performed based on the sampling years to assess the source of heterogeneity. I^2 statistics and the Cochrane Q test were used to measure the studies' heterogeneity. Regarding the asymmetrical data distribution, Egger's test was used to assess potential publication bias. The *P-value* equal to or less than 0.05 was considered the significance threshold.

3. Results

Literature search

In total, 925 relevant studies were collected by accurately searching databases using the appropriate keywords. Duplicate reports (182 articles) were removed, and the remaining 743 articles were reviewed. Based on the title/abstract, 322 articles were reviewed, and 53 relevant articles were evaluated by reading the full text. Finally, 23 studies were recognized as eligible for qualitative analysis and meta-analysis. PRISMA flow diagram of study selection is depicted in Figure 1 and the specifications extracted from the studies are shown in Table 1.

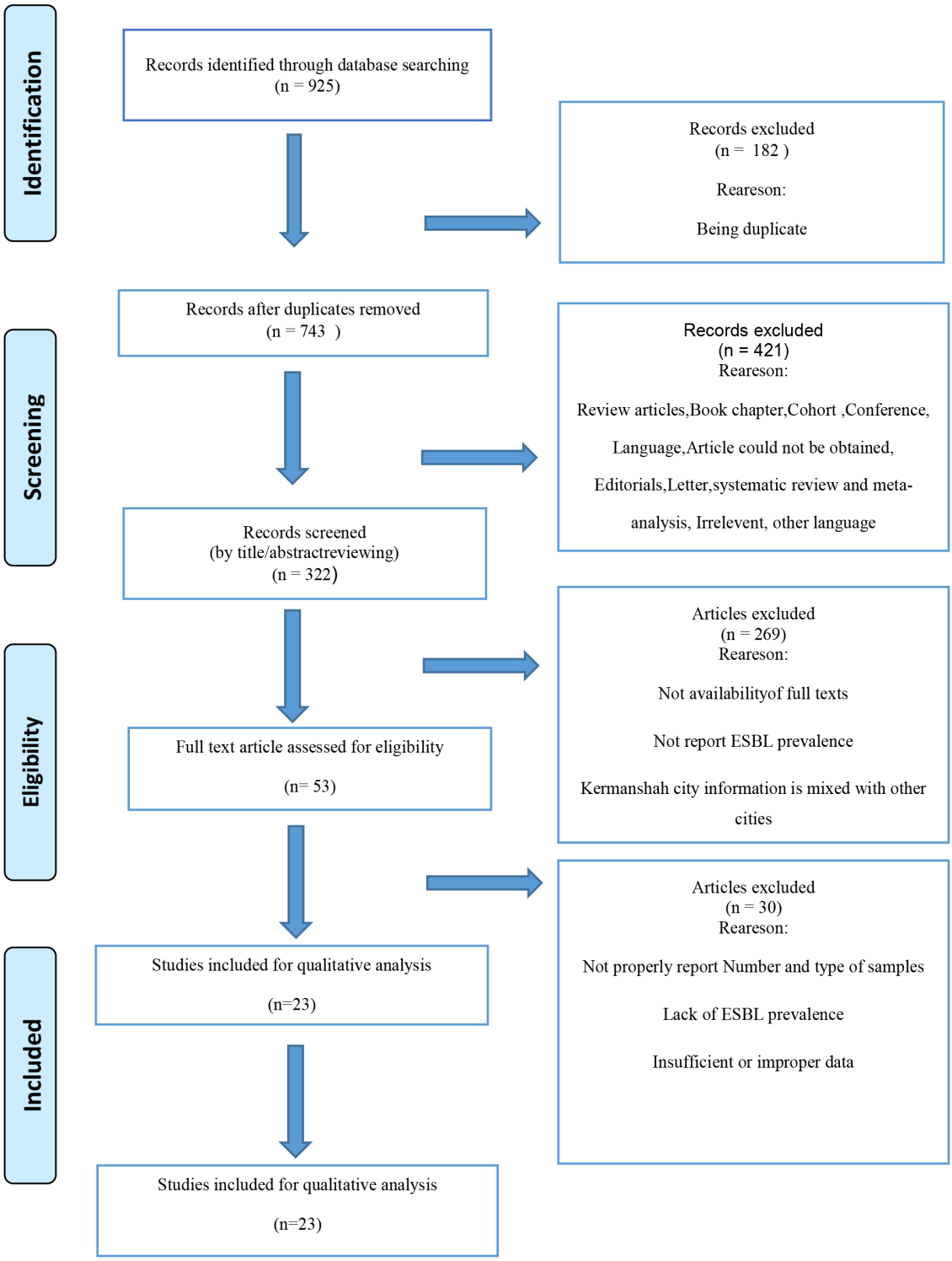

Figure 1. PRISMA flow diagram of study selection

Table 1. Studies characteristics

Authors	Published year	Sampling year	Sampling place	Sample type (bacteria)	Sample size	Samples include (No, %)	Male (No, %)	Female (No, %)	Phenotype method	Genotype method	Positive ESBL No.	MDR isolates No.	ESBL-producers MDR isolates No.	Reference
Akya et al.-1	2019	2014-2015	Clinic University of Medical Sciences, Central Laboratory	*E. coli*	240	Urine (n = 240, 100%)	25 (10.4 %)	215 (89.6%)	DDT, DDCT	PCR	67	96	N/A	(52)
Akya et al.-2	2018	2012-2013	Imam Khomeini hospital, Taleghani hospital, Imam Reza hospital	*K. pneumoniae*	100	Urine (n = 54, 54%), Burn (n = 15, 15%), Respiratory tract secretions (n = 15, 15%), Others (blood, wound, and ascetic fluid) (n = 16, 16%)	41 (41 %)	59 (59%)	DDT, DDCT	PCR	40	56	40	(53)
Akya et al.-3	2015	2013-2014	Imam Reza hospital	*C. freundii* *C. koseri* *C. braakii*	60 6 4	Urine (n = 39, 55.7%), Stool (n = 16, 22.9%), Sputum (n = 8, 11.4%), Wound (n = 5, 7.1%), Blood (n = 2, 2.9%)	28 (40 %)	42 (60%)	DDT, DDCT	PCR	5 0 0	N/A	N/A	(54)
Akya et al.-4	2017	2014-2015	Imam Khomeini hospital, Taleghani hospital, Imam Reza hospital, Central laboratory	*K. pneumoniae*	100	Urine (n = 58, 58%), Burn (n = 16, 16%), Tracheal (n = 14, 14%), Blood (n = 5, 5%), Ascites fluid (n = 3, 3%), Wound (n = 2, 2%), Burn dressing bed (n = 1, 1%), Cot (n = 1, 1%)	39 (39 %)	59 (59%)	DDT, DDCT	PCR	40	N/A	N/A	(55)
Azizi et al.	2017	2016	Imam Reza hospital	*A. baumannii*	80	Tracheal (n = 31, 38.75%), Urine (n = 13, 16.25%), Blood (n = 10, 12.5%), Sputum (n = 9, 11.25%), Catheter (n = 8, 10%), Wound (n = 5, 6.25%), CSF (n = 2, 2.5%), Pleural Fluid (n = 2, 2.5%)	43 (53.8%)	37 (46.2%)	DDT, DDCT	PCR	43	50	N/A	(56)
Davodian et al.-1	2015	2009-2011	Imam Khomeini hospital	*P. aeruginosa*	N/A	Wound (N/A)	N/A	N/A	DDT, DDCT	PCR	8	N/A	N/A	(57)
Davodian et al.-2	2016	2009-2011	N/A	*P. aeruginosa*	10	N/A	N/A	N/A	DDCT	PCR	0	N/A	N/A	(58)
Haidari et al.	2015	2013-2014	Imam Khomeini Taleghani Imam Reza	*P. aeruginosa*	60	Urine (n = 9, 15%), Burn (n = 32, 53.3%), Sputum (n= 10, 16.1%), Others (blood, wound, catheter and vaginal) (n= 9, 15%)	31 (51.7%)	29 (48.3%)	DDT	PCR	N/A	42	N/A	(59)
Hemmati et al.	2019	2017	N/A	*E. cloacae*	93	Urine (n= 31, 33.4%), Wound (n= 18, 19.3%), Blood (n= 16, 17.2%), Trachea	57 (61.3%)	36 (38.7%)	DDCT	PCR	55	65	N/A	(60)

Authors	Published year	Sampling year	Sampling place	Sample type (bacteria)	Sample size	Samples include (No, %)	Male (No, %)	Female (No, %)	Phenotype method	Genotype method	Positive ESBL No.	MDR isolates No.	ESBL-producers MDR isolates No.	Reference
						(n= 9, 9.7%), Sputum (n=7, 7.5%), CSF (n= 5, 5.4%), BAL (n= 4, 4.3%), Catheter (n= 3, 3.2%)								
Khodadoost et al.	2013	2011-2012	Clinic University of Medical Sciences	*E. coli*	140	Urine (n= 140, 100%)	15 (10.7%)	125 (89.3%)	DDT, DDCT	PCR	34	55	N/A	(61)
Mohajeri et al.-1	2014	2011-2013	N/A	*E. coli*	200	Urine (n=200, 100%)	N/A	N/A	DDT, DDCT	PCR	44	N/A	N/A	(62)
Mohajeri et al.-2	2018	2015-2016	Central laboratory	*K. pneumoniae*	50	Urine (n=50, 100%)	16 (32%)	34 (68%)	DDT, DDCT	PCR	17	35	13	(63)
Ranjbar et al.	2019	2016-2018	Imam Khomeini hospital	*A. baumannii*	35	Burn wound (n = 35, 100%)	N/A	N/A	DDT, DDST	PCR	19	N/A	N/A	(64)
Sarshar et al.	2016	2014	N/A	K. pneumoniae	60	Urine (n = 32, 53.3%), Burn (n = 8, 13.3%), Tracheal (n= 10, 16.6%), Blood (n = 5, 8.3%), Wound (n = 3, 5%), Bandage (n = 1, 1.6%), Cot (n = 1, 1.6%)	N/A	N/A	DDT, DDCT	PCR	27	27	N/A	(65)
Sarvazad et al.	2017	2016	N/A	*K. pneumoniae*	97	N/A	N/A	N/A	DDT	Multiplex-PCR	N/A	N/A	N/A	(66)
Vaziri et al.	2017	2016-2017	Imam Reza hospital	*K. pneumoniae*	57	Endotracheal tube (n= 384, 100%)	36 (63.2%)	21 (36.8%)	DDT, DDCT	PCR	22	N/A	N/A	(67)
Yousefi-Fatmesari et al.	2017	2016	Mohammad Kermanshahi hospital	*E. coli*	95	Urine (n = 95, 100%)	53 (55.8%)	42 (44.2%)	DDT, DDCT	PCR	24	N/A	N/A	(68)
Mohajeri et al.-3	2013	2010-2011	Imam Reza hospital, Taleghani hospital, Imam Khomeini hospital	*A. baumannii*	104	Sputum (n = 69, 66.3%), Blood (n = 32, 30.7%), Urine (n = 3, 2.8%)	N/A	N/A	DDT, DDST	PCR	N/A	N/A	34	(69)
Akya et al.-5	2015	2013	Imam Reza hospital	*C. freundii* *C. koseri* *C. braakii* CC *C. younga e*	77 13 9 1	N/A	N/A	N/A	DDT, MHT	PCR	N/A	N/A	N/A	(70)
Zare et al.	2015	2012-2013	Imam Khomeini hospital, Taleghani hospital, Imam Reza hospital, Central laboratory	*K. pneumoniae*	60	Urine (n = 38, 63.33%), Burn (n = 8, 13.33%), Respiratory tract secretions (n = 5, 8.33%), Blood (n = 3, 5%), Wound (n =4, 6.67%),	N/A	N/A	DDT, MHT	PCR	N/A	N/A	N/A	(71)

Authors	Published year	Sampling year	Sampling place	Sample type (bacteria)	Sample size	Samples include (No, %)	Male (No, %)	Female (No, %)	Phenotype method	Genotype method	Positive ESBL No.	MDR isolates No.	ESBL-producers MDR isolates No.	Reference
						Sputum (n = 2, 3.33%)								
Norozi et al.	2014	2011-2013	N/A	*A. baumannii*	84	Sputum (n= 55, 65.48%), Blood (n= 27, 32.14%), Urine (n= 2, 2.38%)	N/A	N/A	DDT, DDST	PCR	34	40	N/A	(72)
Mohajeri et al.-4	2015	2010-2011	N/A	*A. baumannii*	42	Sputum (n= 36, 85.7%), Blood (n= 6, 14.3%)	29	13	DDT	PCR	N/A	42	N/A	(73)
Mohajeri et al.-5	2017	2011-2013	N/A	*A. baumannii*	75	N/A	N/A	N/A	DDT	PCR	N/A	37	N/A	(74)

*- The details of resistance genes and antibiotics susceptibility have been represented in Table 5.

Abbreviations: *E. coli*: *Escherichia coli*, *K. pneumoniae*: *Klebsiella pneumoniae*, *C. freundii*: *Citrobacter freundii*, *C. koseri*: *Citrobacter koseri*, *C. braakii*: *Citrobacter braakii*, *A. baumannii*: *Acinetobacter baumannii*, *P. aeruginosa*: *Pseudomonas aeruginosa*, *E. cloacae*: *Enterobacter cloacae*, CSF: Cerebrospinal fluid, BAL: Bronchoalveolar lavage, DDT: disk confirmatory test, DDCT: Double-disk confirmatory test, PCR: polymerase chain reaction, MDR: multidrug-resistant, N/A: not available

The prevalence of ESBL-positive bacteria in Kermanshah medical centers

To estimate the prevalence of ESBL-positive bacteria in Kermanshah medical centers, Iran, the proportion of ESBL-positive cases over sample size (*i.e.,* event rate) was applied as effect size. The calculated event rates were multiplied by 100 for easier representation of data in the tables and the text. Fifteen studies were applied for meta-analysis, in which the pooled prevalence of ESBL-positive bacteria in Kermanshah medical centers was 34.8 % (CI 95%: 28.0 – 42.3) (Figure 2). Since the CIs of the summary effect did not include zero, the null hypothesis was rejected, indicating a positive prevalence of ESBL-positive bacteria in Kermanshah medical centers. Also, the Q-value was significantly higher than the degrees of freedom (the number of studies minus 1) (*P*=0.000), showing significant between-studies heterogeneity. The I^2 test showed 85.44 % of true variances in the observed effects (Fig. 2).

Subgroup analysis of ESBL-positive bacteria prevalence based on the sampling year

To subgroup analysis of the ESBL-positive bacteria in Kermanshah medical centers based on the studies published year were divided into two subgroups, D1 (<2015) and D2 (2015≤). According to these subgroups, six and seven studies were categorized as D1 and D2, respectively. The prevalence of ESBL-positive bacteria was higher in D2, and there was significant heterogeneity between subgroups (Q-value: 6.347, *P*= 0.012) (Table 2). Table 2 shows that ESBL -positive bacteria prevalence in Kermanshah medical centers doubled after 2015.

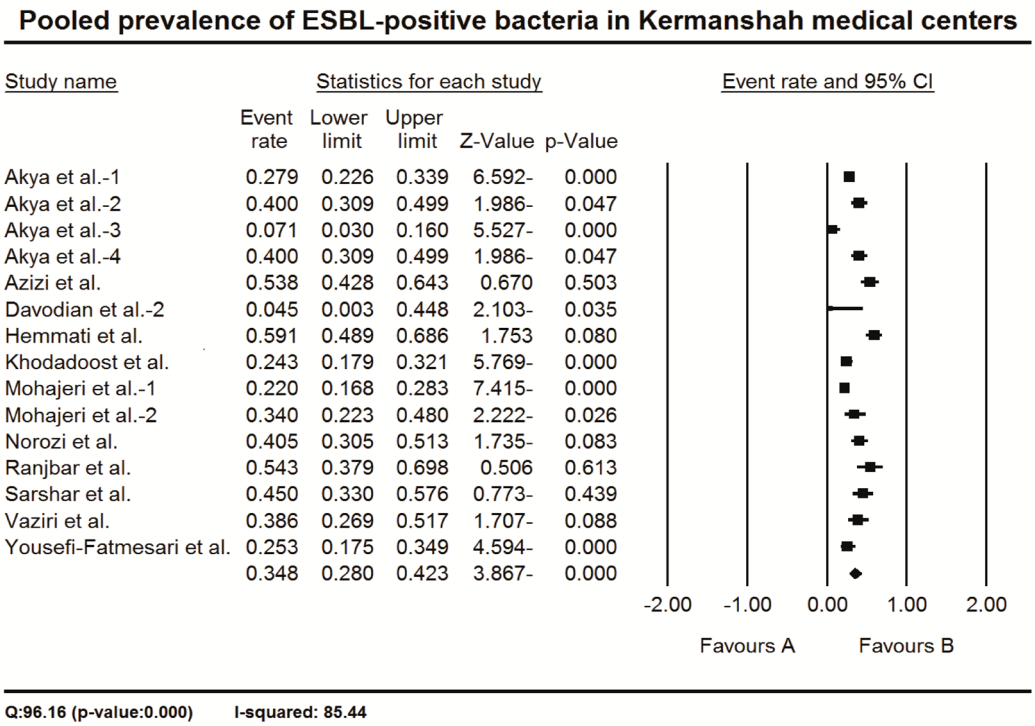

Figure 2. The pooled prevalence of ESBL-positive bacteria in Kermanshah medical center

Table 2. The prevalence of ESBL-positive bacteria in Kermanshah medical centers based on sampling years

Group name	Sampling year	Number of studies	Prevalence (%)	Lower limit	Upper limit	Z-value	*p*-value
D1	<2015	6	24.84	16.58	35.45	-4.27	0.000
D2	2015≤	7	43.93	33.56	54.86	-1.09	0.276
Overall	-	13	35.14	27.98	43.03	-3.62	0.000

Test of heterogeneity between subgroups: Q-value: 6.347, p-value: 0.012

Subgroup analysis of ESBL-positive prevalence based on the type of bacteria

Based on the type of bacteria, a subgroup analysis was done on the prevalence of ESBL-positive. The studies were divided into eight subgroups as follows: *A. baumannii* (3 records), *C. braakii* (1 study), *C. freundii* (1 study), *C. koseri* (1 study), *E. cloacae* (1 study), *E. coli* (4 studies), *K. pneumoniae* (5 studies), and *P. aeruginosa* (1 study). There was significant heterogeneity between subgroups (Q-value: 88.97, p-value: 0.000). The highest and lowest prevalence of ESBL-positive was observed for *E. cloacae* (59.14%) and *P. aeruginosa* (4.55%), respectively (Table 3).

Table 3. The prevalence of ESBL-positive bacteria in Kermanshah medical centers is based on the type of bacteria

Group name	Number of records	Prevalence (%)	Lower limit	Upper limit	Z-value	*p*-value
A. baumannii	3	48.30	41.37	55.29	-0.48	0.634
C. braakii	1	10.00	0.59	67.36	-1.47	0.140
C. freundii	1	8.33	3.51	18.51	-5.13	0.000
C. koseri	1	7.14	0.43	57.72	-1.75	0.081
E. cloacae	1	59.14	48.91	68.64	1.75	0.080
E. coli	4	25.11	21.98	28.53	-12.28	0.000
K. pneumoniae	5	39.82	34.93	44.93	-3.86	0.000

P. aeruginosa	1	4.55	0.28	44.83	-2.10	0.035
Overall	17	34.72	32.17	37.37	-10.77	0.000

Test of heterogeneity between subgroups: Q-value: 88.97, p-value: 0.000

The prevalence of MDR bacteria and ESBL-producing MDR bacteria in Kermanshah medical centers

The proportion of MDR cases over sample size was used to estimate the prevalence of MDR bacteria in Kermanshah medical centers. The data of 11 studies were appropriate to be included in the meta-analysis, in which the pooled prevalence of MDR bacteria in Kermanshah medical centers was 56.1% (CI 95%: 47.5 – 64.4) (Fig 3). There was also significant heterogeneity between studies indicated by a Q-value higher than degrees of freedom (p-value= 0.000) and I^2 equal to 84.04% (Fig 3). The ESBL-producing MDR bacteria were only reported in three studies in which the pooled prevalence was 34.5% (CI 95%: 28.8 – 40.6), but there was no significant heterogeneity between studies (Q-value= 3.06 I^2 = 34.63%) (Fig 4).

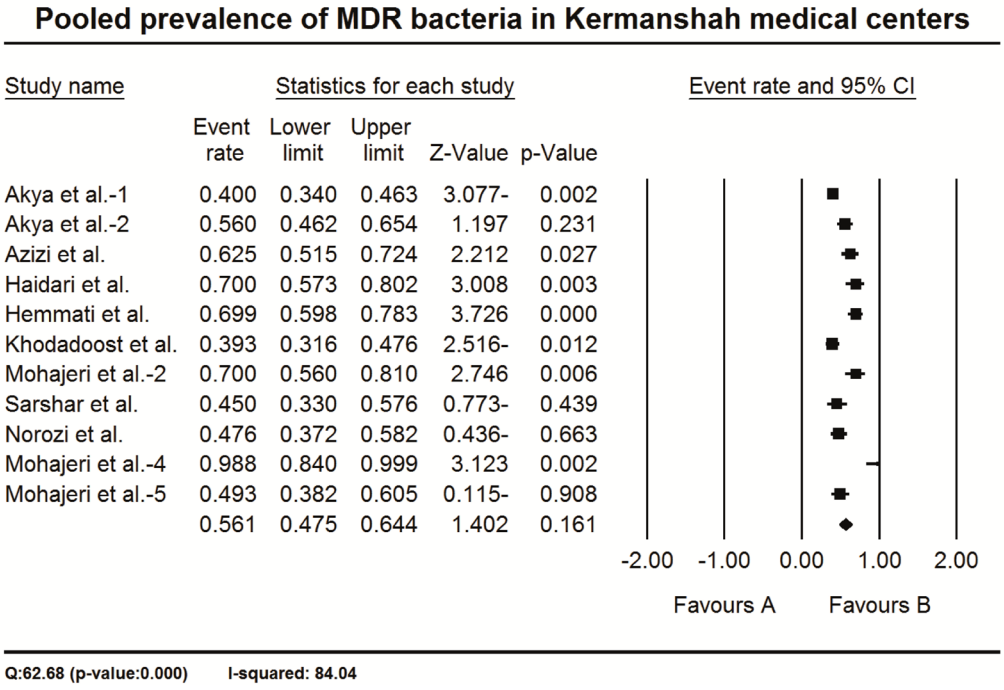

Figure 3. The pooled prevalence of MDR bacteria in Kermanshah medical centers

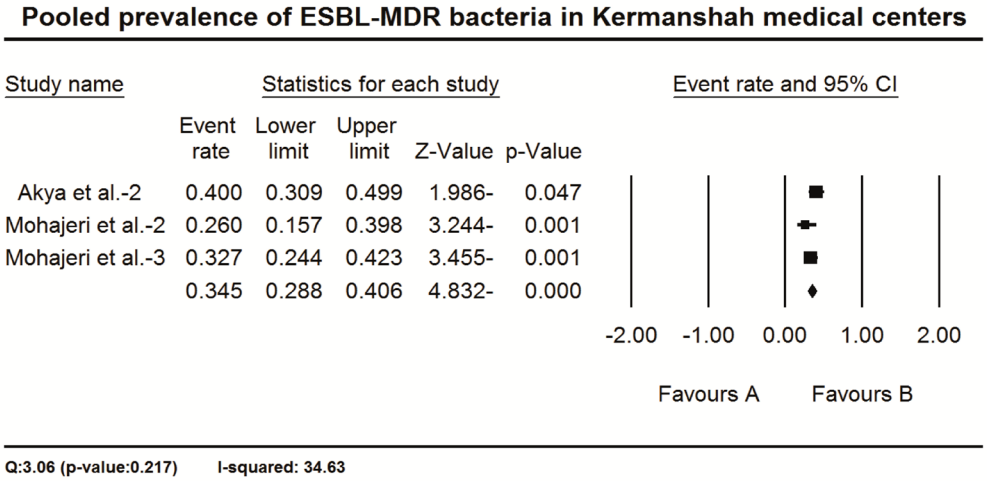

Figure 4. The pooled prevalence of ESBL-MDR bacteria in Kermanshah medical centers

The prevalence of ESBL genes in bacteria in Kermanshah medical centers

The ESBL genes evaluated in at least two studies were included in a random-effects model subgroup analysis. Nineteen genes (or gene groups) were included (Table 4), in which a significant heterogeneity existed between subgroups (Q-value: 132.42, p-value: 0.000), and the highest and lowest prevalence were observed for blaOXA-51 (99.3%) and KPC (0.6%), respectively (Table 4). The details of all genes studied have been shown in Table S1.

Table 4. The prevalence of ESBL genes in bacteria in Kermanshah medical centers based on bacteria

Gene	Number of records	Prevalence (%)	Lower limit	Upper limit	Z-value	P-value	I^2
blaCTX-M	13	20.2	13.5	29.1	-5.6	0.000	78.7
blaCTX-M-1	2	16.0	5.1	40.5	-2.6	0.011	91.7
blaCTX-M-2	2	1.4	0.3	6.9	-5.1	0.000	65.8
blaCTX-M-3	2	13.2	4.1	34.8	-2.9	0.003	88.2
blaOXA-23like	4	80.0	62.7	90.6	3.1	0.002	71.0
blaOXA-23like + blaOXA-24 like	2	20.7	7.2	46.7	-2.2	0.030	45.6
blaOXA-24 like	4	22.9	11.2	41.0	-2.8	0.005	9.7
blaOXA-51	3	99.3	95.8	99.9	5.3	0.000	0.0
blaOXA-58	3	0.7	0.1	4.2	-5.3	0.000	0.0
blaPER	2	4.2	0.9	17.9	-3.8	0.000	73.6
blaPER-1	2	23.4	6.1	58.8	-1.5	0.132	61.2
blaSHV	11	21.5	13.6	32.3	-4.6	0.000	95.3
blaTEM	11	15.1	9.6	23.0	-6.5	0.000	58.2
blaVEB-1	2	2.5	0.3	20.3	-3.1	0.002	0.0
KPC	2	0.6	0.1	5.8	-4.4	0.000	0.0
SHV+ TEM	3	18.7	7.6	38.9	-2.8	0.005	92.8
SHV+ TEM +blaCTX-M	3	17.6	7.0	37.8	-2.9	0.004	92.8
SHV+blaCTX-M	2	26.8	10.1	54.3	-1.7	0.095	0.0
TEM +blaCTX-M	4	14.8	6.5	30.4	-3.7	0.000	94.6
Overall	77	20.1	16.9	23.8	-12.6	0.000	91.6

Test of heterogeneity between subgroups: Q-value: 132.42, p-value: 0.000

The prevalence of antibiotic resistance in bacteria in Kermanshah medical centers

For a random-effects model meta-analysis, the antibiotics reported in at least two studies were included. These antibiotics were Ampicillin (AMP), Ceftriaxone (CRO), Cefotaxime (CTX), Ceftazidime (CAZ), Aztreonam (ATM), Imipenem (IMI), Piperacillin (PIP), Trimethoprim/sulfamethoxazole (SXT), Ciprofloxacin (CIP), Gentamicin (GEN), Amikacin (AMK), Nitrofurantoin (NIT), Meropenem (MEM), Rifampin (RIF), Tetracycline (TET), Gatifloxacin (GAT), Colistin (CST), Polymyxin B (Poly-B), Levofloxacin (LVX), Minocycline (MIN), Mezlocillin (MEZ), Tobramycin (TOB), Tigecycline (TIG), Cefepime (FEP), Cefpodoxime (CPD), AMP-Sulbactam (AMP-SUL), Nalidixic acid (NALA), Piperacillin /tazobactam (TZP), Cefazolin (CFZ), Ertapenem (ETP), Cefixime (CFM) (Table 5). The analysis showed significant between-subgroups heterogeneity (Q-value: 197.62, p-value: 0.000). The highest and lowest resistance was estimated to be MEZ (92.2%) and TIG (4.2%), respectively (Table 5).

Table 5. The prevalence of antibiotic resistance in bacteria in Kermanshah medical centers

Antibiotics	Number of records	Prevalence (%)	Lower limit	Upper limit	Z-value	P-value	I^2
AMK	9	67.5	51.0	80.6	2.1	0.038	88.9
AMP	9	86.0	73.9	93.0	4.6	0.000	90.6
AMP-SUL	4	39.4	19.0	64.3	-0.8	0.409	90.6
ATM	8	39.3	24.0	56.9	-1.2	0.232	91.0
CAZ	16	60.6	47.7	72.1	1.6	0.107	94.1
CFM	2	68.3	34.2	90.0	1.1	0.289	0.0
CFZ	4	85.7	66.7	94.8	3.2	0.001	89.3
CIP	13	57.5	43.1	70.7	1.0	0.306	93.7
CPD	9	67.6	50.6	80.9	2.0	0.042	91.3
CRO	13	64.2	49.3	76.8	1.9	0.061	93.7
CST	6	17.7	7.9	35.3	-3.2	0.001	91.5
CTX	14	67.4	54.0	78.5	2.5	0.012	94.6
ETP	4	5.4	1.7	15.7	-4.7	0.000	65.2
FEP	8	72.7	55.7	84.9	2.6	0.011	90.3
GAT	4	63.3	38.3	82.7	1.0	0.296	76.1
GEN	13	45.6	32.1	59.7	-0.6	0.541	95.2
IMI	15	37.0	24.7	51.2	-1.8	0.072	96.3
LVX	6	77.3	59.6	88.8	2.9	0.004	57.2
MEM	10	51.0	34.2	67.6	0.1	0.908	95.6
MEZ	4	92.2	79.0	97.4	4.2	0.000	60.8
MIN	4	26.3	11.4	49.7	-2.0	0.048	0.0
NALA	3	65.7	37.3	86.1	1.1	0.276	82.9
NIT	3	39.3	16.6	67.8	-0.7	0.469	95.5
PIP	5	84.4	67.0	93.5	3.4	0.001	79.8
Poly-B	5	15.3	6.7	31.4	-3.6	0.000	0.0
RIF	3	91.4	75.1	97.4	3.7	0.000	0.0
SXT	11	56.1	41.0	70.2	0.8	0.428	87.4
TET	6	73.4	54.3	86.5	2.4	0.018	82.1
TIG	4	4.2	1.4	12.1	-5.3	0.000	0.0
TOB	10	44.0	29.3	59.8	-0.7	0.457	90.3
TZP	6	34.1	18.0	54.8	-1.5	0.129	94.8
Overall	231	55.6	52.2	59.0	3.2	0.002	94.2

Test of heterogeneity between subgroups: Q-value: 197.62, p-value: 0.000

Abbreviations: Ampicillin (AMP), Ceftriaxone (CRO), Cefotaxime (CTX), Ceftazidime (CAZ), Aztreonam (ATM), Imipenem (IMI), Piperacillin (PIP), Trimethoprim/sulfamethoxazole (SXT), Ciprofloxacin (CIP), Gentamicin (GEN), Amikacine (AMK), Nitrofurantoin (NIT), Meropenem (MEM), Rifampin (RIF), Tetracycline (TET), Gatifloxacin (GAT), Colistin (CST), Polymyxin B (Poly-B), Levofloxacin (LVX), Minocycline (MIN), Mezlocillin (MEZ), Tobramycin (TOB), Tigecycline (TIG), Cefepime (FEP), Cefpodoxime (CPD), AMP-Sulbactam (AMP-SUL), Nalidixic acid (NALA), Piperacillin/tazobactam (TZP), Cefazolin (CFZ), Ertapenem (ETP), Cefixime (CFM)

Publication bias

The prevalence of ESBL-positive bacteria was applied for Egger's test to evaluate the potential publication bias. The test indicated no bias in the reports on the prevalence of ESBL-positive bacteria in Kermanshah medical centers (p-value=0.464).

4. Discussion

Despite many studies on the prevalence of ESBL-producing bacteria in various clinical specimens worldwide, the growing global trend of ESBL-producing bacteria indicates a lack of regular monitoring and implementation of appropriate control programs by health care systems **(9-11)**. The first step in controlling resistant pathogens is identifying their prevalence and characteristics. In this regard, systematic review and meta-analysis studies will assist in estimating these parameters by collecting all relevant studies in this field. The present study was the first systematic review and meta-analysis of ESBL-producing gram-negative bacteria in various medical centers in Kermanshah. As our results showed, the pooled prevalence of ESBL-positive gram-negative bacteria in medical centers Kermanshah medical centers was 34.8 %, which is between the range reported for the global prevalence of ESBL-positive gram-negative bacteria (1.9% and 53%) **(12)**. A systematic review and meta-analysis study estimated the prevalence of ESBL in gram-negative bacteria worldwide at 25% **(13)**. The prevalence of ESBL has been reported from 45% in Africa to 3% in North America **(13)**. As compared to other regions of Iran, the pooled prevalence of ESBL-positive gram-negative bacteria in Kermanshah medical centers was higher than the global level **(13)** and lower than in China **(14)**, Nigeria **(15),** and Ethiopia **(16)**.

Compared to other regions of the world, the pooled prevalence of ESBL-positive gram-negative bacteria in our study was lower than that was reported for Pakistan **(17)**, Afghanistan **(18)**, China **(14)**, South-East Asia, and the African area **(19)**, with the frequency of 40%, 51.9%, 46%, 37%, and 76% respectively. At the same time, it was higher than that was reported for Europe, the Americas, and the Eastern Mediterranean **(19)** with the frequency of 10.19%, 2%, and 5%. The differential in ESBL incidence in these studies might be explained by several factors, including differences in geographic location and socioeconomic condition **(20)**, differences in the diagnostic methods, procedures, and performance **(17)**, the studies aim **(11)**, the availability of medications, and type of infection, species, and hospital/ward.

Our results also showed that the prevalence of ESBL-producing gram-negative bacteria in Kermanshah medical centers has been increasing in recent years, which is similar to the findings of meta-analysis studies in Ethiopia **(19)**, Tunisia **(21-24)**, and India **(25)**. The increasing prevalence of these resistant strains is a cause for concern and emphasizes the need to pay more attention to care and control systems.

The appearance of ESBL-producing *E. cloacae* in clinical isolates poses a significant challenge to nosocomial infection treatment **(26)**. Our study, the highest prevalence of ESBL-positive bacteria was observed for *E. cloacae*. In our study, Ali et al., found a high frequency of 79 % ESBL-producing *E. cloacae* among clinical isolates obtained from the Military Hospital in Rawalpindi **(27)**. Similarly, according to a study done at the Aga Khan University Hospital in Karachi, Pakistan, 50% of *E. cloacae* strains were positive for ESBL **(28)**. Also, the frequency of *A. baumannii*, *K. pneumoniae*, and *E. coli* producing ESBL was high in our study, which is consistent with previous studies done in Iran **(29, 30)**. In a comprehensive study in Iran, the prevalence of ESBL-positive *E. coli* was 89.8% **(29)**. In a meta-analysis in Iran, the prevalence of ESBL-positive *K. pneumoniae* was estimated at 43.5% **(31)**. Similarly, in some other parts of the world, including Ethiopia **(32)**, Saudi Arabia **(33)**, the United Arab Emirates **(34)**, and Tunisia **(35),** the prevalence of ESBL-positive *K. pneumoniae* was higher than that was estimated in our study. The increasing prevalence of ESBL-producing *K. pneumoniae* and *E. coli* strains is worrying and requires implementing policies and regional/global efforts to reduce this ascending prevalence.

Multidrug resistance (MDR) bacteria were found in 56.1 % of Kermanshah medical institutions (34.5% in ESBL-positive strains). In Iran, according to a meta-analysis study, the prevalence of MDR ranged from 32.8% in *K. pneumoniae* strains to 58% **(32)** in *P. aeruginosa* strains (36). In other regions of the world, the prevalence of MDR varies in a European study; it ranged from 0% in Estonia and Iceland to 49.4% in Romania **(37)**. In Ethiopia, the total prevalence of MDR was 69.9% **(38)**. The main reason for increasing and disseminating MDR strains is the unnecessary and excessive use of antibiotics that may lead to the acquisition of drug-resistance elements **(39-41)**.

Understanding the diversity of ESBL-producing genes is important to identify the genes responsible for multi-resistance patterns **(42)**. Our results showed that Ambler class D genes (*blaOXA* genes) were the most common ESBL genes, followed by Ambler class A gene. Similar to our results, Oliveira et al. found that the majority of isolates (96.5 %) were positive for blaOXA-51 in their investigation from two general hospitals in Brazil **[26]**. However, in contrast to our results, in some studies, *blaTEM*, *blaCTX-M*, and *blaSHV* (but not *blaOXA*) genes have been identified as the most common genes encoding ESBL **(30, 43-46)**.

The lowest prevalence was observed for *KPC* genes in our study (0.6%), similar to that reported by Yang et al., in a Chinese hospital that found a low prevalence of 2.9% for KPC-positive *K. pneumonia* **(47)**. Differences in ESBL genes may be due to the differences in socioeconomic status, geographical areas, and the quality of diagnostic methods **(48)**.

In our study, the highest resistance was estimated to be MEZ (92.2%). Following our study, the high resistance rates to MEZ (50%) were reported by Ozer et al. (49). Also, several more studies have revealed the high prevalence of resistance to MEZ in recent years **(50, 51)**. This indicates that MEZ should be less used, and other alternative antibiotics should be used to treat the infections caused by ESBL-positive bacteria.

A limitation of our study is the low number of studies included, so only 15 studies were qualified to be included in which only three studies reported ESBL-producing MDR bacteria. In addition, ESBL genotypes were reported in only two studies. In the future, more studies are recommended to ensure the prevalence of ESBL-producing bacteria in Kermanshah.

5. Conclusion

Altogether, this systematic review and meta-analysis showed that the prevalence of ESBL-positive and MDR bacteria is high in Kermanshah medical centers. It provides significant information to health policymakers to implement appropriate strategies to reduce the prevalence of resistant bacteria.

Acknowledgment

The authors of this article express their gratitude and appreciation to the Vice Chancellor for Research and Technology of the Kermanshah University of Medical Science.

Conflict of Interest

Nothing to declare.

Funding

No funding.

Ethics approval and consent to participate

The study was done under the supervision of the Ethical Committee of Kermanshah University of Medical Sciences (ethical code IR. KUMS. REC.1400.021).

Reference

1. Breijyeh Z, Jubeh B, Karaman R. Resistance of gram-negative bacteria to current antibacterial agents and approaches to resolve it. Molecules. 2020;25(6):1340. [PMID] [PMCID] [DOI:10.3390/molecules25061340]
2. Mehrad B, Clark NM, Zhanel GG, Lynch III JP. Antimicrobial resistance in hospital-acquired gram-negative bacterial infections. Chest. 2015;147(5):1413-21. [DOI:10.1378/chest.14-2171] [PMID] [PMCID]
3. Peymani A, Naserpour-Farivar T, Zare E, Azarhoosh K. Distribution of blaTEM, blaSHV, and blaCTX-M genes among ESBL-producing P. aeruginosa isolated from Qazvin and Tehran hospitals, Iran. J Prev Med Hyg. 2017;58(2):E155.
4. Pishtiwan AH, Khadija KM. Prevalence of blaTEM, blaSHV, and blaCTX-M genes among ESBL-producing Klebsiella pneumoniae and Escherichia coli isolated from thalassemia patients in Erbil, Iraq. Mediterr J Hematol Infect Dis. 2019;11(1). [DOI:10.4084/mjhid.2019.041] [PMID] [PMCID]
5. Pana ZD, Zaoutis T. Treatment of extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBLs) infections: what have we learned until now? F1000Research. 2018;7. [DOI:10.12688/f1000research.14822.1] [PMID] [PMCID]
6. Pormohammad A, Nasiri MJ, Azimi T. Prevalence of antibiotic resistance in Escherichia coli strains simultaneously isolated from humans, animals, food, and the environment: a systematic review and meta-analysis. Infect Drug Resist. 2019;12: 1181. [DOI:10.2147/IDR.S201324] [PMID] [PMCID]
7. Barzegar S, Arzanlou M, Teimourpour A, Esmaelizad M, Yousefipour M, MohammadShahi J, et al. Prevalence of the Integrons and ESBL Genes in Multidrug-Resistant Strains of Escherichia coli Isolated from Urinary Tract Infections, Ardabil, Iran. Int J Med Microbiol. 2022;16(1):56-65. [DOI:10.30699/ijmm.16.1.56]
8. McInnes MD, Moher D, Thombs BD, McGrath TA, Bossuyt PM, Clifford T, et al. Preferred reporting items for a systematic review and meta-analysis of diagnostic test accuracy studies: the PRISMA-DTA statement. JAMA. 2018;319(4):388-96. [DOI:10.1001/jama.2017.19163] [PMID]
9. Flokas ME, Karanika S, Alevizakos M, Mylonakis E. Prevalence of ESBL-producing Enteroba-

cteriaceae in pediatric bloodstream infections: a systematic review and meta-analysis. PloS one. 2017;12(1):e0171216. [PMID] [PMCID] [DOI:10.1371/journal.pone.0171216]

10. Storberg V. ESBL-producing Enterobacteriaceae in Africa-a non-systematic literature review of research published 2008-2012. Infect Ecol Epidemiology. 2014;4(1):20342. [DOI:10.3402/iee.v4.20342] [PMID] [PMCID]
11. Flokas ME, Alevizakos M, Shehadeh F, Andreatos N, Mylonakis E. ESBL-producing Enterobacteriaceae Colonization in Long-Term Care Facilities (LTCFs): A Systematic Review and Metaâ analysis. Int J Antimicrob Agents. 2017. [DOI:10.1016/j.ijantimicag.2017.08.003] [PMID]
12. Irek EO, Amupitan AA, Aboderin AO, Obadare TO. A systematic review of healthcare-associated infections in Africa: An antimicrobial resistance perspective. Afr J Lab Med. 2018;7(2):1-9. [DOI:10.4102/ajlm.v7i2.796] [PMID] [PMCID]
13. Mansouri F, Sheibani H, Javedani Masroor M, Afsharian M. Extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae and urinary tract infections in pregnant/postpartum women: A systematic review and meta-analysis. Int J Clin Pract. 2019;73(12):e13422. [DOI:10.1111/ijcp.13422] [PMID]
14. Zhang J, Zheng B, Zhao L, Wei Z, Ji J, Li L, et al. Nationwide high prevalence of CTX-M and an increase of CTX-M-55 in Escherichia coli isolated from patients with community-onset infections in Chinese county hospitals. BMC Infect Dis. 2014;14(1):1-10. [DOI:10.1186/s12879-014-0659-0] [PMID] [PMCID]
15. Tanko N, Bolaji RO, Olayinka AT, Olayinka BO. A systematic review on the prevalence of extended-spectrum beta lactamase-producing Gram-negative bacteria in Nigeria. J Glob Antimicrob Resist. 2020;22:488-96. [DOI:10.1016/j.jgar.2020.04.010] [PMID]
16. Tufa TB, Fuchs A, Tufa TB, Stötter L, Kaasch AJ, Feldt T, et al. High rate of extended-spectrum beta-lactamase-producing gram-negative infections and associated mortality in Ethiopia: a systematic review and meta-analysis. Antimicrob Resist Infect Control. 2020;9(1):1-10. [PMCID] [DOI:10.1186/s13756-020-00782-x] [PMID]
17. Abrar S, Hussain S, Khan RA, Ul Ain N, Haider H, Riaz S. Prevalence of extended-spectrum-β-lactamase-producing Enterobacteriaceae: first systematic meta-analysis report from Pakistan. Antimicrob Resist Infect Control. 2018;7(1):1-11. [DOI:10.1186/s13756-018-0309-1] [PMID] [PMCID]
18. Tariq TM. Bacteriologic profile and antibiogram of blood culture isolates from a children's hospital in Kabul. J Coll Physicians Surg Pak. 2014;24(6):396-9.
19. Kiros T, Workineh L, Tiruneh T, Eyayu T, Damtie S, Belete D. Prevalence of Extended-Spectrum β-Lactamase-Producing Enterobacteriaceae in Ethiopia: A Systematic Review and Meta-Analysis. Int J Microbiol. 2021;2021. [DOI:10.1155/2021/6669778] [PMID] [PMCID]
20. Livermore DM, Canton R, Gniadkowski M, Nordmann P, Rossolini GM, Arlet G, et al. CTX-M: changing the face of ESBLs in Europe. J Antimicrob Chemother. 2007;59(2):165-74. [DOI:10.1093/jac/dkl483] [PMID]
21. Ben Sallem R, Ben Slama K, Estepa V, Jouini A, Gharsa H, Klibi N, et al. Prevalence and characterisation of extended-spectrum beta-lactamase (ESBL)-producing Escherichia coli isolates in healthy volunteers in Tunisia. Eur J Clin Microbiol Infect Dis. 2012;31(7):1511-6. [DOI:10.1007/s10096-011-1471-z] [PMID]
22. Abbassi MS, Torres C, Achour W, Vinué L, Sáenz Y, Costa D, et al. Genetic characterisation of CTX-M-15-producing Klebsiella pneumoniae and Escherichia coli strains isolated from stem cell transplant patients in Tunisia. Int J Antimicrob Agents. 2008;32(4):308-14. [DOI:10.1016/j.ijantimicag.2008.04.009] [PMID]
23. Dahmen S, Bettaieb D, Mansour W, Boujaafar N, Bouallegue O, Arlet G. Characterization and molecular epidemiology of extended-spectrum β-lactamases in clinical isolates of Enterobacteriaceae in a Tunisian University hospital. Microb Drug Resist. 2010;16(2):163-70. [DOI:10.1089/mdr.2009.0108] [PMID]
24. Elhani D, Bakir L, Aouni M, Passet V, Arlet G, Brisse S, et al. Molecular epidemiology of extended-spectrum β-lactamase-producing Klebsiella pneumoniae strains in a university hospital in Tunis, Tunisia, 1999-2005. Clin Microbiol Infect. 2010;16(2):157-64. [DOI:10.1111/j.1469-0691.2009.03057.x] [PMID]
25. Datta S, Wattal C, Goel N, Oberoi JK, Raveendran R, Prasad K. A ten year analysis of multidrug resistant blood stream infections caused by Escherichia coli & Klebsiella pneumoniae in a tertiary care hospital. Indian J Med Res. 2012;135(6):907.
26. Amin H, Zafar A, Ejaz H, Jameel N-u-A. Phenotypic characterization of ESBL producing

Enterobacter cloacae among children. Pak J Med Sci. 2013;29(1):144. [DOI:10.12669/pjms.291.2385] [PMID] [PMCID]

27. Ali A, Rafi S, Qureshi A. Frequency of extended spectrum beta lactamase producing gram negative bacilli among clinical isolates at clinical laboratories of Army Medical College, Rawalpindi. Rawalpindi PRO. 2004;2:25-9.
28. Jabeen K, Zafar A, Hasan R. Frequency and sensitivity pattern of extended spectrum beta lactamase producing isolates in a tertiary care hospital laboratory of Pakistan. J Pak Med Assoc. 2005;55(10):436.
29. Leylabadlo HE, Pourlak T, Aghazadeh M, Asgharzadeh M, Kafil HS. Extended-spectrum beta-lactamase producing gram negative bacteria In Iran: A review. Afr J Infect Dis. 2017;11(2):39-53. [DOI:10.21010/ajid.v11i2.6] [PMID] [PMCID]
30. Ghaderi RS, Yaghoubi A, Amirfakhrian R, Hashemy SI, Ghazvini K. The prevalence of genes encoding ESBL among clinical isolates of Escherichia coli in Iran: A systematic review and meta-analysis. Gene Reports. 2020;18:100562. [DOI:10.1016/j.genrep.2019.100562]
31. Beigverdi R, Jabalameli L, Jabalameli F, Emaneini M. Prevalence of extended-spectrum β-lactamase-producing Klebsiella pneumoniae: First systematic review and meta-analysis from Iran. J Glob Antimicrob Resist. 2019;18:12-21. [DOI:10.1016/j.jgar.2019.01.020] [PMID]
32. Mohd Asri NA, Ahmad S, Mohamud R, Mohd Hanafi N, Mohd Zaidi NF, Irekeola AA, et al. Global prevalence of nosocomial multidrug-resistant Klebsiella pneumoniae: a systematic review and meta-analysis. Antibiotics. 2021;10(12):1508. [PMID] [PMCID] [DOI:10.3390/antibiotics10121508]
33. Al-Agamy MH, Shibl AM, Tawfik AF. Prevalence and molecular characterization of extended-spectrum β-lactamase-producing Klebsiella pneumoniae in Riyadh, Saudi Arabia. Ann Saudi Med. 2009;29(4):253-7. [DOI:10.4103/0256-4947.55306] [PMID] [PMCID]
34. Alfaresi MS, Elkoush AA, Alshehhi HM, Abdulsalam AI. Molecular characterization and epidemiology of extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae isolates in the United Arab Emirates. Med Princ Pract. 2011;20(2):177-80. [DOI:10.1159/000319912] [PMID]
35. Dziri O, Dziri R, Maraoub A, Chouchani C. First report of SHV-148-Type ESBL and CMY-42-type AmpC β-lactamase in klebsiella pneumoniae clinical isolates in Tunisia. Microb Drug Resist. 2018;24(10):1483-8. [DOI:10.1089/mdr.2018.0073] [PMID]
36. Vaez H, Salehi-Abargouei A, Ghalehnoo ZR, Khademi F. Multidrug resistant Pseudomonas aeruginosa in Iran: A systematic review and metaanalysis. J Glob Infect Dis. 2018;10(4):212. [DOI:10.4103/jgid.jgid_113_17] [PMID] [PMCID]
37. Heuer O, Gunell M, Economopoulou A, Blomquist A, Brown D, Walton C, et al. European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2010. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net) Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net) OH ed pp 30-31 Stockholm 2011 European Centre for Disease Prevention. 2010:30-1.
38. Moges F, Endris M, Belyhun Y, Worku W. Isolation and characterization of multiple drug resistance bacterial pathogens from waste water in hospital and non-hospital environments, Northwest Ethiopia. BMC Res Notes. 2014;7(1):1-6. [DOI:10.1186/1756-0500-7-215] [PMID] [PMCID]
39. Alp E, Leblebicioglu H, Doganay M, Voss A. Infection control practice in countries with limited resources. Ann Clin Microbiol Antimicrob. 2011;10(1):1-4. [DOI:10.1186/1476-0711-10-36] [PMID] [PMCID]
40. Ayari K, Bourouis A, Chihi H, Mahrouki S, Naas T, Belhadj O. Dissemination and genetic support of broad-spectrum beta-lactam-resistant Escherichia coli strain isolated from two Tunisian hospitals during 2004-2012. Afr Health Sci. 2017; 17(2):346-55. [DOI:10.4314/ahs.v17i2.8] [PMID] [PMCID]
41. Alp E, Damani N. Healthcare-associated infections in intensive care units: epidemiology and infection control in low-to-middle income countries. J Infect Dev Ctries. 2015;9(10). [DOI:10.3855/jidc.6832] [PMID]
42. Karanika S, Karantanos T, Arvanitis M, Grigoras C, Mylonakis E. Fecal colonization with extended-spectrum beta-lactamase-producing Enterobacteriaceae and risk factors among healthy individuals: a systematic review and metaanalysis. Rev infect dis. 2016;63(3):310-8. [DOI:10.1093/cid/ciw283] [PMID]
43. Arsalane L, Zerouali K, Katfy K, Zouhair S. Molecular characterization of extended

spectrum β-lactamase-producing Escherichia coli in a university hospital in Morocco, North Africa. Afr J Urol. 2015;21(3):161-6. [DOI:10.1016/j.afju.2015.02.005]

44. To KK, Lo W-U, Chan JF, Tse H, Cheng VC, Ho P-L. Clinical outcome of extended-spectrum beta-lactamase-producing Escherichia coli bacteremia in an area with high endemicity. Int J Infect Dis. 2013;17(2):e120-e4. [DOI:10.1016/j.ijid.2012.09.008] [PMID]
45. Ouedraogo A-S, Sanou M, Kissou A, Sanou S, Solaré H, Kaboré F, et al. High prevalence of extended-spectrum ß-lactamase producing enterobacteriaceae among clinical isolates in Burkina Faso. BMC Infect Dis. 2016;16(1):1-9. [DOI:10.1186/s12879-016-1655-3] [PMID] [PMCID]
46. Lukac PJ, Bonomo RA, Logan LK. Extended-spectrum β-lactamase-producing Enterobacteriaceae in children: old foe, emerging threat. Clin Infect Dis. 2015;60(9): 1389-97. [DOI:10.1093/cid/civ020] [PMID] [PMCID]
47. Yang J, Ye L, Guo L, Zhao Q, Chen R, Luo Y, et al. A nosocomial outbreak of KPC-2-producing Klebsiella pneumoniae in a Chinese hospital: dissemination of ST11 and emergence of ST37, ST392 and ST395. Clin Microbiol Infect. 2013;19(11):E509-E15. [DOI:10.1111/1469-0691.12275] [PMID]
48. Diriba K, Awulachew E, Gemede A, Anja A. The magnitude of extended-spectrum beta-lactamase-producing Enterobacteriaceae from clinical samples in Ethiopia: a systematic review and meta-analysis. Access Microbiology. 2021;3(3). [DOI:10.1099/acmi.0.000195] [PMID] [PMCID]
49. Ozer B, Duran N, Onlen Y, Savas L. Efflux pump genes and antimicrobial resistance of Pseudomonas aeruginosa strains isolated from lower respiratory tract infections acquired in an intensive care unit. J Antibiot. 2012;65(1):9-13. [DOI:10.1038/ja.2011.102] [PMID]
50. Fozouni L, Yaghoobpour M, Ahani Azari A. Probiotics in goat milk: a promising solution for management of drug-resistant Acinetobacter baumannii. J Biomed J. 2019;7(2):31-8.
51. Pourshafie MR, Mousavi SF, Parzadeh M. Ribotipagem e perfil de resistência a antibióticos de Pseudomonas aeruginosa isolada no Irã. Braz J Microbiol. 2007;38:435-9. [DOI:10.1590/S1517-83822007000300010]
52. Akya A, Ahmadi M, Khodamoradi S, Rezaei MR, Karani N, Elahi A, et al. Prevalence of bla CTX-M, bla CTX-M-2, bla CTX-M-8, bla CTX-M-25 and bla CTX-M-3 Genes in Escherichia coli Isolated from Urinary Tract Infection in Kermanshah City, Iran. J Clin Diagnostic Res. 2019;13(8).
53. Akya A, Elahi A, Chegenelorestani R, Rezaee M. Dissemination of multidrug-resistant, class I and II integrons and molecular typing of CTX-M-producing Klebsiella pneumoniae. Int j appl basic med res. 2018;8(2):100. [PMID] [PMCID] [DOI:10.4103/ijabmr.IJABMR_333_16]
54. Akya A, Jafari S, Ahmadi K, Elahi A. Frequency of blaCTX-M, blaTEM and blaSHV genes in Citrobacters isolated from Imam Reza Hospital in Kermanshah. J Maz Univ Med Sci. 2015;25(127): 65-73.
55. Rezaei M. Phenotypic and Genotypic Assessment of ESBL Production in Klebsiella pneumoniae Isolates from Kermanshah Medical Centers (Iran). Qom Univ Med Sc J. 2017;11(9):61-9.
56. Azizi M, Mortazavi SH, Etemadimajed M, Gheini S, Vaziri S, Alvandi A, et al. Prevalence of extended-spectrum β-Lactamases and antibiotic resistance patterns in Acinetobacter baumannii isolated from clinical samples in Kermanshah, Iran. Jundishapur J Microbiol. 2017;10(12):1-7. [DOI:10.5812/jjm.61522]
57. Davodian E, Sadeghifard N, Ghasemian A, Noorbakhsh S. Molecular detection of blaveb-1 beta-lactamase encoding gene among extended spectrum b-lactamase positive wound isolates of Pseudomonas aeruginosa. Arch Pediatr Infect Dis. 2015;3(4). [DOI:10.5812/pedinfect.26362]
58. Davodian E, Sadeghifard N, Ghasemian A, Noorbakhsh S. Presence of blaPER-1 and blaVEB-1 beta-lactamase genes among isolates of Pseudomonas aeruginosa from South West of Iran. J Epidemiol Glob Health. 2016;6(3):211-3. [DOI:10.1016/j.jegh.2016.02.002] [PMID] [PMCID]
59. Erfan H, Alisha A. The frequency of broad-spectrum beta-lactamase CTX-M genotypes in Pseudomonas aeruginosa isolated from Kermanshah hospitals (2013-14). J Kermanshah Univ Medical Sci. 2015;19(4):207-14.
60. Hemmati M, Vaziri S, Afsharian M, Mansouri F, Zamanian MH, Fereshteh S, et al. Molecular Investigation of Extended-Spectrum β-Lactamase and Patterns of Antibiotic Resistance in Enterobacter cloacae Isolates from Teaching Hospitals in Kermanshah, Iran. J Clin Diagnostic

Res. 2019;13(9). [DOI:10.7860/JCDR/2019/41823.13116]

61. Khodadoost M, Akya A, Ale Taha SM, Adabagher S. The frequency of antibiotic resistance and ctx-m gene in Escherichia coli isolated. Studies in Medical Sciences. 2013;24(5):318-28.
62. Mohajeri P, Rostami Z, Farahani A, Norozi B. Distribution of ESBL producing Uropathogenic Escherichia coli and carriage of selected [beta]-lactamase genes in Hospital and community isolates in west of Iran. Ann Trop Med Public Health. 2014;7(5):219. [DOI:10.4103/1755-6783.154823]
63. Mohajeri P, Kavosi S, Esmailzadeh T, Farahani A, Dastranj M. Molecular characteristics of extended-spectrum-beta-lactamase-producing Klebsiella pneumoniae isolates in the West of Iran. Advances in Human Biology. 2018;8(3):175. [DOI:10.4103/AIHB.AIHB_20_18]
64. Ranjbar R, Farahani A. Study of genetic diversity, biofilm formation, and detection of Carbapenemase, MBL, ESBL, and tetracycline resistance genes in multidrug-resistant Acinetobacter baumannii isolated from burn wound infections in Iran. Antimicrob Resist Infect Control. 2019;8(1):1-11. [DOI:10.1186/s13756-019-0612-5] [PMID] [PMCID]
65. Sarshar MHF, Akya A. The frequency of extended spectrum β-lactamase genes of SHV-2a, SHV-5 and SHV-12 in clinical isolates of klebsiella pneumoniae isolated from Kermanshah medical centers in 2014. Arak Med Univ J. 2016;19(2):59-67.
66. Sarvazad H, Darbouy M. Correlation of Antibiotic Resistance with SHV, CTX-M and TEM Extended-Spectrum Beta Lactamases Genes among Klebsiella pneumoniae Isolates from Patients in Kermanshah Hospitals. J Ardabil Univ Medical Sci. 2017;17(3):353-62.
67. Vaziri S, Mansouri F, Abiri R, Alvandi A, Mortazavi SH, Ahmadi K, et al. Prevalence study of extended spectrum beta-lactamase in klebsiella pneumonia isolated from patients with ventilator-associated pneumonia in Kermanshah City, Iran. J Isfahan Med Sch. 2017;35(444):1113-9.
68. Yousefi-Fatmesari G, Hemmati M, Mortazavi S, Mansouri F, Azizi M, Etemadimajed M, et al. Frequency of blaCTX-M, blaTEM, and blaSHV genes in Escherichia coli isolated from urine samples of children in Kermanshah city, Iran. J Isfahan Med Sch. 2017;35(430):551-7.
69. Mohajeri P, Farahani A, Feizabadi MM, Ketabi H, Abiri R, Najafi F. Antimicrobial susceptibility profiling and genomic diversity of Acinetobacter baumannii isolates: A study in western Iran. Iran J Microbiol. 2013;5(3):195.
70. Akya A, Jafari S, Ahmadi K, Elahi A. The Frequency of Carbapenemase Genes in Citrobacter Frundii and Citrobacter Koseri Isolated from Clinical Specimens in Imam Reza Hospital, Kermanshah, Iran. J Kerman Univ Medical Sci. 2015;22(6):629-38.
71. Zare A, Akya A, Nejat P. The frequency of blaVIM, blaIMP, blaKPC and blaNDM Carbapenemase genes in clinical isolates of Klebsiella Pneumoniae in Kermanshah medical centers. 2015.
72. Norozi B, Farahani A, Mohajeri P, Davoodabadi A. Molecular epidemiology of hospital acquired OXA-carbapenemase-producing Acinetobacter baumannii in Western Iran. Asian Pacific J Trop Dis. 2014;4:S803-S7. [DOI:10.1016/S2222-1808(14)60731-3]
73. Mohajeri P, Farahani A, Feizabadi M, Norozi B. Clonal evolution multidrug resistant Acinetobacter baumannii by pulsed-field gel electrophoresis. Indian J Med Microbiol. 2015;33 (1):87-91. [DOI:10.4103/0255-0857.148390] [PMID]
74. Mohajeri P, Farahani A, Mehrabzadeh RS. Molecular characterization of multidrug resistant strains of Acinetobacter baumannii isolated from intensive care units in west of Iran. J Clin Diagnostic Res. 2017;11(2):DC20. [PMID] [DOI:10.7860/JCDR/2017/21156.9397] [PMCID]