Prevalence of \( \text{bla}_{\text{CTX-M}} \) Gene among Extended-Spectrum \( \beta \)-Lactamases Producing \( \text{Klebsiella pneumoniae} \) Clinical Isolates in Iran: A Meta-Analysis

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Abstract

Background: CTX-M-type extended-spectrum \( \beta \)-lactamases (ESBLs) are the most prevalent ESBLs in bacterial members of Enterobacteriaceae family including \( \text{Klebsiella pneumoniae} \). The global spread of CTX-M-producing \( \text{K. pneumoniae} \) is a major concern in most countries including Iran. The aim of this meta-analysis was to determine the relative frequency (RF) of \( \text{bla}_{\text{CTX-M}} \) gene among ESBLs-producing \( \text{K. pneumoniae} \) clinical isolates in Iran and to report an overall prevalence.

Methods: A comprehensive literature search of studies published up to July 2016 was carried out. The keywords “Enterobacteriaceae”, “\( \text{Klebsiella pneumoniae} \)”, “ESBLs”, “CTX-M” and “Iran” were searched in PubMed, Scopus, EBSCO, Google Scholar, Scirus, SID and IranMedex in both English and Persian. Selected articles were published between July 2010 and July 2016 and all of them were in English. STATA SE version 11.0 was used for statistical analysis.

Results: Twenty-four articles/abstracts were included in this analysis. Selected studies were performed in Ahvaz, Arak, Ilam, Kashan, Kerman, Mashhad, Shiraz, Tabriz, Tehran, Zabol, and Zahedan. Our pooled evidence showed that the RF of \( \text{bla}_{\text{CTX-M}} \) gene among ESBLs-producing \( \text{K. pneumoniae} \) clinical isolates varied from 7.7% in Tabriz to 100% in Mashhad, Tehran, and Zahedan, with an overall RF of 56.7%.

Conclusion: Our meta-analysis revealed that the RF of CTX-M-type ESBLs-producing \( \text{K. pneumoniae} \) is diverse in different regions of Iran, and the central and eastern regions had higher prevalence rates compared to western regions.

What’s Known
• Several studies have examined the prevalence of CTX-Ms in ESBLs-producing \( \text{K. pneumoniae} \) clinical isolates in different geographical regions of Iran.
• The average rate of CTX-M enzymes among ESBLs-producing \( \text{K. pneumoniae} \) isolates has not been clearly identified in Iran.

What’s New
• We reviewed published studies regarding the prevalence of \( \text{bla}_{\text{CTX-M}} \) gene among ESBLs-producing \( \text{K. pneumoniae} \) clinical isolates in Iran and presented an overall relative frequency (RF).
• The overall RF of \( \text{bla}_{\text{CTX-M}} \) gene among ESBLs-producing \( \text{K. pneumoniae} \) clinical isolates in Iran is 56.7%.

Introduction

Extended-spectrum \( \beta \)-lactamases (ESBLs) are bacterial enzymes that confer resistance to penicillins, broad-spectrum oxyimino-cephalosporins and aztreonam, but suppressed by serine-type \( \beta \)-lactamase inhibitors (e.g. clavulanic acid). ESBLs can be encoded through both chromosome and plasmid genes, and more than ten families have been so far documented to be associated with ESBLs, including CTX-M, SHV, TEM, PER, VEB, BES, GES, TLA, SFO, and OXA.\(^{1-3} \) CTX-M-type ESBLs are plasmid-encoded...
enzymes that have been detected in at least 26 bacterial species. CTX-Ms are the most prevalent ESBLs in Enterobacteriaceae particularly in *Escherichia coli*, *Klebsiella pneumoniae*, and *Proteus mirabilis*. A member of the Enterobacteriaceae family, *K. pneumoniae* strains are ubiquitous in nature and exist specifically in natural environments and on mucosal surfaces of mammals. This microorganism is an opportunistic bacterial pathogen that commonly causes different infections in human. *K. pneumoniae* is one of the major ESBLs-producing bacteria. ESBLs-producing *K. pneumoniae* is more prevalent in Asia and South America, and has recently been listed as one of the six drug-resistant pathogens for which few potentially effective drugs are available. The worldwide spread of CTX-M-producing *K. pneumoniae* is a major concern in most continents such as Asia. Recently, high rate of CTX-M enzymes (as high as 58.5%) among ESBLs-producing *K. pneumoniae* isolates have been reported in many countries including Brazil, Spain, Korea, etc. To date, several studies have examined the prevalence of CTX-Ms in ESBLs-producing *K. pneumoniae* clinical isolates in different geographical regions of Iran. Nevertheless, the average rate of CTX-M enzymes among ESBLs-producing *K. pneumoniae* isolates has not been clearly identified in Iran. Therefore, in this meta-analysis, we reviewed published studies regarding the prevalence of CTX-M enzyme among ESBLs-producing *K. pneumoniae* clinical isolates in Iran and presented an overall relative frequency (RF).

**Materials and Methods**

**Search Strategy**

To identify all related published studies, we searched PubMed, Scopus, EBSCO, Embase, Google Scholar, Scirus and four Persian scientific search engines including IranMedex, IRANDOC, Magiran, and scientific information database (SID) in both English and Persian. The medical subject headings (MESH) and keywords used for the search were “Enterobacteriaceae” and “*Klebsiella pneumoniae* or *K. pneumoniae*” and “Extended-spectrum β-lactamases or ESBLs” and “CTX-M” and “Iran”. The searched keywords were adapted to the primary language of the database. We also searched the references cited in these articles to find other relevant articles. Selected articles were published between July 2010 and July 2016 and all of them were in English.

**Inclusion Criteria**

Among obtained articles/abstracts, those with the following features were included in the study:

- Articles that have assessed the prevalence of *bla* _CTX-M_ gene
- Clinical isolates that were collected from Iranian hospitals
- Clinical isolates that were taken from patients (both inpatients and outpatients)
- Samples that only belonged to the genus *Klebsiella*, species *pneumoniae*
- Phenotypic confirmatory ESBL test (either combination disk test or double disc synergy test) which were used to detect ESBL production
- Only ESBLs-producing isolates which were confirmed by phenotypic ESBL test.

**Exclusion Criteria**

Studies with at least one of the following criteria were excluded from our study:

- Samples that were totally/partially selected from ESBLs collections
- The origin of samples (region or population) was not clear
- Unclear report of the results

**Statistical Analysis**

Statistical analysis was executed by the STATA software, version 11.0 (StataCorp, College Station, TX, USA). The overall RF of CTX-M in Iran was pooled by forest plot using the Meta-Analyst software. Heterogeneity among studies was assessed by Cochrane’s Q-test and I² measurement, which was interpreted as the proportion of total variation contributed among study variants. A P≤0.10 and an I² value ≥50% shown significant heterogeneity. A random-effect model was applied in the incidence of significant heterogeneity; if not, a fixed-effect model was executed.

**Results**

According to heterogeneity test, random model methods were performed for meta-analysis tests (P<0.001). The I²>50% indicated the presence of heterogeneity in our pooled analysis.

Out of all papers found by the search of databases, 24 articles matched our inclusion criteria (20 full-text articles and 4 abstracts) selected for our pooled analysis (16-35) (table 1). A detailed flowchart showing the selection process is presented in figure 1. These studies were conducted in 10 provinces and 11 cities of Iran. The prevalence of ESBLs among *K. pneumoniae* clinical isolates varied from 28% in Kerman to 74% in Tehran, with the mean of 49%. The prevalence of *bla* _CTX-M_ gene among ESBLs-producing *K. pneumoniae* clinical
Prevalence of CTX-M-type ESBLs in Iran

Isolates varied from 7.7% in Tabriz to 100% in Mashhad, Tehran and Zahedan, with the mean of 56.7%. In Tehran, the capital city of Iran, the prevalence of bla\textsubscript{CTX-M} gene among ESBLs-producing K. pneumoniae clinical isolates varied from 20.6% to 100%, with the mean of 61.7%. Pooled estimation of K. pneumoniae samples revealed that 55.9% (95% CI=43.0-68.9) of strains are CTX-M positive. Figure 2 demonstrates the forest plot of the relative frequency of bla\textsubscript{CTX-M} gene among different studies performed in Iran.

**Discussion**

In recent years, numerous studies by Iranian researchers have been conducted to identify bla\textsubscript{CTX-M} gene variants among ESBLs-producing K. pneumoniae clinical isolates. Based on these studies, this review presented a meta-analysis to show the prevalence of bla\textsubscript{CTX-M} gene among ESBLs-producing K. pneumoniae clinical isolates in Iran. Based on our results, the CTX-M-type ESBLs-producing K. pneumoniae is less frequent in western cities compared to central and eastern cities. The mean prevalence of ESBLs among K. pneumoniae clinical isolates in Iran was 49% that, on average, 56.7% of these isolates (ESBLs-producing isolates) possessed bla\textsubscript{CTX-M} gene. Lee et al.,\textsuperscript{11} in their study on K. pneumoniae clinical isolates in 9 Asian countries have shown that ESBLs-production rates differed amongst the studied countries. The percentage of ESBLs-producers was low in Hong Kong and Taiwan (7.7% and 8.3%, respectively), but was high in South Korea.
India, and Thailand (66.7%, 57.1%, and 55.3%, respectively). Moreover, they showed that 72.8% of ESBLs-producing isolates were possessed \( \text{bla}_{\text{CTX-M}} \) gene which amongst, \( \text{bla}_{\text{CTX-M-15}} \) was the major variant. Similarly, in Iran, the sequencing results in some studies demonstrated that the major variants of \( \text{bla}_{\text{CTX-M}} \) gene among ESBL-producing \( K. \ pneumoniae \) clinical isolates are \( \text{bla}_{\text{CTX-M-15}} \), followed by \( \text{bla}_{\text{CTX-M-8}} \) and \( \text{bla}_{\text{CTX-M-22}} \). From a regional

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**Figure 1:** Flowchart of the study selection process.

**Figure 2:** Forest plot of the current relative frequency of \( \text{bla}_{\text{CTX-M}} \) gene among ESBLs-producing \( K. \ pneumoniae \) clinical isolates in different Iranian studies.
stand, Iran has a higher mean prevalence of bla\textsubscript{CTX-M} gene among ESBLs-producing \textit{K. pneumoniae} clinical isolates compared to reports from neighboring countries including Turkey (30%),\textsuperscript{38,39} Saudi Arabia (35.3%),\textsuperscript{40,41} Iraq (45.2%),\textsuperscript{42,43} and Bahrain (10%)\textsuperscript{44} as well as lower mean prevalence compared to Pakistan (96.9%),\textsuperscript{45,46} Kuwait (100%),\textsuperscript{47} and United Arab Emirates (64.4%).\textsuperscript{48} In a continental perspective, Iran has a lower mean prevalence of bla\textsubscript{CTX-M} gene among ESBLs-producing \textit{K. pneumoniae} clinical isolates compared to reports from East Asian countries (78.8%).\textsuperscript{11,49} At the international level, mean prevalence of bla\textsubscript{CTX-M} gene among ESBLs-producing \textit{K. pneumoniae} clinical isolates in Iran is higher than USA (26.4%),\textsuperscript{50} Russia (34.9%),\textsuperscript{51} and South Africa (7.4%)\textsuperscript{39} as well as lower than Brazil (62.1%)\textsuperscript{12,52} and Argentina (61.1%)\textsuperscript{39} in Latin America and some European countries (84.5%).\textsuperscript{9,53-56}

Our study had some limitations, including lack of published data from certain regions of Iran and the unavailability of some in-press articles that were excluded from our study.

### Conclusion

In conclusion, this study showed that the prevalence of CTX-M-type ESBLs-producing \textit{K. pneumoniae} is diverse in different regions of Iran, and the central and eastern regions have higher RF compared to western regions.

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### Conflict of Interest:

None declared.

### References

1. Zhao WH, Hu ZQ. Epidemiology and genetics of CTX-M extended-spectrum beta-lactamases in Gram-negative bacteria. Crit Rev Microbiol. 2013;39:79-101. doi: 10.3109/1040841X.2012.691460. PubMed PMID: 22697133; PubMed Central PMCID: PMC3811232.
2. Woerther PL, Burdet C, Chachaty E, Andremont A. Trends in human fecal carriage of extended-spectrum beta-lactamases in the community: Toward the globalization of CTX-M. Clin Microbiol Rev. 2013;26:744-58. doi: 10.1128/CMR.00023-13. PubMed PMID: 24092853; PubMed Central PMCID: PMC3811232.
3. Trang NH, Nga TV, Campbell JI, Hiep NT, Farrar J, Baker S, et al. The characterization of ESBL genes in \textit{Escherichia coli} and \textit{Klebsiella pneumoniae} causing nosocomial infections in Vietnam. J Infect Dev Ctries. 2013;7:922-8. doi: 10.3855/jjdc.2938. PubMed PMID: 24334938.
4. D’Andrea MM, Arena F, Pallecchi L, Rossolini GM. CTX-M-type beta-lactamases: A successful story of antibiotic resistance. Int J Med Microbiol. 2013;303:303-17. doi: 10.1016/j.ijmm.2013.02.008. PubMed PMID: 23490927.
5. Wieler LH, Ewers C, Guenther S, Walther B, Lubke-Becker A. Methicillin-resistant staphylococci (MRS) and extended-spectrum beta-lactamases (ESBL)-producing Enterobacteriaceae in companion animals: Nosocomial infections as one reason for the rising prevalence of these potential zoonotic pathogens in clinical samples. Int J Med Microbiol. 2011;310:635-41. doi: 10.1016/j.ijmm.2011.09.009. PubMed PMID: 22000738.
6. Vuotto C, Longo F, Balice MP, Donelli G, Varaldo PE. Antibiotic Resistance Related to Biofilm Formation in \textit{Klebsiella pneumoniae}. Pathogens. 2014;3:743-58. doi: 10.3390/pathogens3030743. PubMed PMID: 25438022; PubMed Central PMCID: PMC4243439.
7. Gupta A, Ampofo K, Rubenstein D, Saiman L. Extended spectrum beta lactamase-producing \textit{Klebsiella pneumoniae} infections: A review of the literature. J Perinatol. 2003;23:439-43. doi: 10.1038/sj.jp.7210973. PubMed PMID: 13679928.
8. Podschan R, Ullmann U. \textit{Klebsiella} spp. as nosocomial pathogens: Epidemiology, taxonomy, typing methods, and pathogenicity factors. Clin Microbiol Rev. 1998;11:589-603. PubMed PMID: 9767057; PubMed Central PMCID: PMC88898.
9. Onnberg A, Molling P, Zimmermann J, Soderquist B. Molecular and phenotypic characterization of \textit{Escherichia coli} and \textit{Klebsiella pneumoniae} producing extended-spectrum beta-lactamases with focus on CTX-M in a low-endemic area in Sweden. APMIS. 2011;119:287-95. doi: 10.1111/j.1600-0463.2011.02730.x. PubMed PMID: 21492229.
10. Chong Y, Ito Y, Kamimura T. Genetic evolution and clinical impact in extended-spectrum beta-lactamase-producing \textit{Escherichia coli} and \textit{Klebsiella pneumoniae}.
11. Lee MY, Ko KS, Kang CI, Chung DR, Peck KR, Song JH. High prevalence of CTX-M-15-producing *Klebsiella pneumoniae* isolates in Asian countries: Diverse clones and clonal dissemination. Int J Antimicrob Agents. 2011;38:160-3. doi: 10.1016/j.ijantimicag.2011.03.020. PubMed PMID: 21605960.

12. Chagas TP, Alves RM, Vallim DC, Asensi MD, Campos LC, Asensi MD. Diversity of genotypes in CTX-M-producing *Klebsiella pneumoniae* isolated in different hospitals in Brazil. Braz J Infect Dis. 2011;15:420-5. PubMed PMID: 22230847.

13. Randrianirina F, Vedy S, Rakotovao D, Carod JF, et al. Role of contaminated aspiration tubes in nosocomial outbreak of *Klebsiella pneumoniae* producing SHV-2 and CTX-M-15 extended-spectrum beta-lactamases. J Hosp Infect. 2009;72:23-9. doi: 10.1016/j.jhin.2009.02.004. PubMed PMID: 19282056.

14. Oteo J, Cuevas O, Lopez-Rodriguez I, Banderas-Florido A, Vindel A, Perez-Vazquez M, et al. Emergence of CTX-M-15-producing *Klebsiella pneumoniae* of multilocus sequence types 1, 11, 14, 17, 20, 35 and 36 as pathogens and colonizers in newborns and adults. J Antimicrob Chemother. 2009;64:524-8. doi: 10.1093/jac/dkp211. PubMed PMID: 19525516.

15. Lee SG, Jeong SH, Lee H, Kim CK, Lee Y, Koh E, et al. Spread of CTX-M-type extended-spectrum beta-lactamases among bloodstream isolates of *Escherichia coli* and *Klebsiella pneumoniae* from a Korean hospital. Diagn Microbiol Infect Dis. 2009;63:76-80. doi: 10.1016/j.diagmicrobio.2008.09.002. PubMed PMID: 19073302.

16. Khosravi AD, Hoveizavi H, Mehidinejad M. Prevalence of *Klebsiella pneumoniae* encoding genes for CTX-M-1, TEM-1 and SHV-1 extended-spectrum beta lactamases (ESBL) enzymes in clinical specimens. Jundishapur J Microbiol. 2013;6:e8256. doi: 10.5812/jmm.8256.

17. Safari M, Shojapour M, Akbari M, Pourbabae A, Abtahi H. Dissemination of CTX-M-type beta-lactamase among clinical isolates of Enterobacteriaceae in Markazi province, Iran. Jundishapur J Microbiol. 2013;6:e7182. doi: 10.5812/jmm.7182.

18. Ghafoorian S, Sekawi Z, Neela V, Khosravi A, Rahbar M, Sadeghifard N. Incidence of extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* in patients with urinary tract infection. Sao Paulo Med J. 2012;130:37-43. PubMed PMID: 22344358.

19. Ghafoorian S, Bin Sekawi Z, Sadeghifard N, Mohebi R, Kumari Neela V, Maleki A, et al. The Prevalence of ESBLs Producing *Klebsiella pneumoniae* Isolates in Some Major Hospitals, Iran. Open Microbiol J. 2011;5:91-5. doi: 10.2174/187428580105010091. PubMed PMID: 21915229; PubMed Central PMCID: PMCPMC3170933.

20. Firoozeh F, Amir A, Moniri R, Zibaei M. Characterization of Subtypes of Ctx-M Extended-Spectrum B-Lactamase among *Klebsiella* Spp. Iran J Public Health. 2014;43:83.

21. Mansouri S, Kalantar Neyestanaki D, Shokoohi M, Halimi S, Beigverdi R, Rezagholezadeh F, et al. Characterization of AmpC, CTX-M and MBLs types of beta-lactamases in clinical isolates of *Klebsiella pneumoniae* and *Escherichia coli* producing Extended Spectrum beta-lactamases in Kerman, Iran. Jundishapur J Microbiol. 2014;7:e8756. doi: 10.5812/jmm.8756. PubMed PMID: 25147671; PubMed Central PMCID: PMCPMC418687.

22. Mansouri S, Kalantar D, Asadollahi P, Taherkalani M, Emaneini M. Characterization of *Klebsiella pneumoniae* strains producing extended spectrum beta-lactamases and AmpC type beta-lactamases isolated from hospitalized patients in Kerman, Iran. Rom Arch Microbiol Immunol. 2012;71:81-6. PubMed PMID: 23210321.

23. Moghaddam MN, Beidokhti MH, Jamehdar SA, Gahraman M. Genetic properties of blaCTX-M and blaPER beta-lactamase genes in clinical isolates of Enterobacteriaceae by polymerase chain reaction. Iran J Basic Med Sci. 2014;17:378-83. PubMed PMID: 24967067; PubMed Central PMCID: PMCPMC4069837.

24. Ghasemi Y, Archin T, Kargar M, Mohkam M. A simple multiplex PCR for assessing prevalence of extended-spectrum beta-lactamases producing *Klebsiella pneumoniae* in Intensive Care Units of a referral hospital in Shiraz, Iran. Asian Pac J Trop Med. 2013;6:703-8. doi: 10.1016/S1995-7645(13)60122-4. PubMed PMID: 23827147.

25. Ghafoorian S, Sadeghifard N, Sekawi Z, Neela VK, Shamsudin MN, Pakzad I, et al. Phenotypic and genotypic assay for detection of extended spectrum B-lactamases production by *Klebsiella pneumoniae* isolates in Emam Reza Hospital in Tabriz, Iran.
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26. Pormohammad A, Hasani A, Shams F, Nahaie MR, Hasani A, Mohammadmohammad A, et al. Prevalence of Ctx-3 (Ctx-M 3, 15, 22) Family Gene in Various E. coli and Klebsiella Pneumoniae Clinical Specimes in Tabriz. Iran J Public Health. 2014;43:91.

27. Pormohammad A, Hasani A, Shams F, Nahaie MR, Hasani A, Mohammadzade A, et al. Prevalence of Ctx-3 (Ctx-M 3, 15, 22) Family Gene in Various E. coli and Klebsiella Pneumoniae Clinical Specimes in Tabriz. Iran J Public Health. 2014;43:91.

28. Nasehi L, Shahcheraghi F, Nikbin VS, Nematzadeh S. PER, CTX-M, TEM and SHV Beta-lactamases among Klebsiella pneumoniae isolated from Tehran hospitals. J Pure Appl Microbiol. 2011;5:1-10.

29. Peerayeh SN, Rostami E, Siadat SD, Derakhshan S. High rate of aminoglycoside resistance in CTX-M-15 producing Klebsiella pneumoniae isolates in Tehran, Iran. Lab Med. 2014;45:231-7. doi: 10.1309/LMDQQW246NYAHHAD. PubMed PMID: 25051075.

30. Hashemi A, Fallah F, Erfanimanesh S, Hamedani P, Alimehr S, Goudarzi H. Detection of beta-lactamases and Outer Membrane Porins among Klebsiella pneumoniae Strains Isolated in Iran. Scientifica (Cairo). 2014;2014:726179. doi: 10.1155/2014/726179. PubMed PMID: 25548718; PubMed Central PMCID: PMCPMC4274865.

31. Taherpour A, Hashemi A. Detection of OqxAB efflux pumps, OmpK35 and OmpK36 porins in extended-spectrum-beta-lactamase-producing Klebsiella pneumoniae isolates from Iran. Hippokratia. 2013;17:355-8. PubMed PMID: 24064656.

32. Paterson DL, Hujer KM, Hujer AM, Yeiser B, Bonomo MD, Rice LB, et al. Extended-spectrum beta-lactamases in Klebsiella pneumoniae bloodstream isolates from seven countries: Dominance and widespread prevalence of SHV- and CTX-M-type beta-lactamases. Antimicrob Agents Chemother. 2003;47:3554-60. PubMed PMID: 14576117; PubMed Central PMCID: PMCPMC253771.

33. Al-Agamy MH, Shibl AM, Tawfik AF. Prevalence and molecular characterization of extended-spectrum beta-lactamase-producing Klebsiella pneumoniae in Riyadh, Saudi Arabia. Ann Saudi Med. 2009;29:253-7. PubMed PMID: 19587523; PubMed Central PMCID: PMCPMC2841451.

34. Tawfik AF, Alsawi AM, Shibl AM, Al-Agamy MH. Prevalence and genetic characteristics of TEM, SHV, and CTX-M in Klebsiella pneumoniae isolates from Saudi Arabia. Microb Drug Resist. 2011;17:383-8. doi: 10.1089/mdr.2011.0011.
42. Mohammed AS. Molecular Detection of CTX-M Genes in Klebsiella pneumoniae Isolated from Different Clinical Samples in Baghdad City. Medical Journal of Babylon. 2015;12:152-60.

43. Shabaa RAH. Detection of CTX-M-1 gene Among Klebsiella pneumoniae Isolates in An Najaf Province. Iraqi Journal of Biotechnology. 2014;13:128-33.

44. Bindayna KM, Murtadha M. High prevalence of blaCTX-M in Enterobacteriaceae isolates from the Kingdom of Bahrain. Asian Pac J Trop Med. 2011;4:472-6. PubMed PMID: 22081908.

45. Khan E, Schneiders T, Zafar A, Aziz E, Parekh A, Hasan R. Emergence of CTX-M Group 1-ESBL producing Klebsiella pneumoniae from a tertiary care centre in Karachi, Pakistan. J Infect Dev Ctries. 2010;4:472-6. PubMed PMID: 22081908.

46. Habeeb MA, Haque A, Nematzadeh S, Iversen A, Giske CG. High prevalence of 16S rRNA methylase RmtB among CTX-M extended-spectrum beta-lactamase-producing Klebsiella pneumoniae from Islamabad, Pakistan. Int J Antimicrob Agents. 2013;41:524-6. doi: 10.1016/j.ijantimicag.2013.02.017. PubMed PMID: 23622882.

47. Al Sweih N, Salama MF, Jamal W, Al Hashem G, Rotimi VO. An outbreak of CTX-M-15-producing Klebsiella pneumoniae isolates in an intensive care unit of a teaching hospital in Kuwait. Indian J Med Microbiol. 2011;29:130-5. doi: 10.4103/0255-0857.81791. PubMed PMID: 21654106.

48. Alfaresi MS, Elkoush AA, Alshehhi HM, Abdulsalam Al. Molecular characterization and epidemiology of extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae isolates from the United Arab Emirates. Med Princ Pract. 2011;20:177-80. doi: 10.1159/000319912. PubMed PMID: 21252576.

49. An S, Chen J, Wang Z, Wang X, Yan X, Li J, et al. Predominant characteristics of CTX-M-producing Klebsiella pneumoniae isolates from patients with lower respiratory tract infection in multiple medical centers in China. FEMS Microbiol Lett. 2012;322:137-45. doi: 10.1111/j.1574-6968.2012.02586.x. PubMed PMID: 22537112.

50. Wang G, Huang T, Surendraiah PK, Wang K, Komal R, Zhuge J, et al. CTX-M beta-lactamase-producing Klebsiella pneumoniae in suburban New York City, New York, USA. Emerg Infect Dis. 2013;19:1803-10. doi: 10.3201/eid1911.121470. PubMed PMID: 24188126; PubMed Central PMCID: PMCPMC3837662.

51. Edelstein M, Pimkin M, Palagini I, Edelstein I, Strachounski L. Prevalence and molecular epidemiology of CTX-M extended-spectrum beta-lactamase-producing Escherichia coli and Klebsiella pneumoniae in Russian hospitals. Antimicrob Agents Chemother. 2003;47:3724-32. PubMed PMID: 14638473; PubMed Central PMCID: PMCPMC296190.

52. Tollentino FM, Polotto M, Nogueira ML, Lincopan N, Neves P, Mamizuka EM, et al. High prevalence of bla(CTX-M) extended spectrum beta-lactamase genes in Klebsiella pneumoniae isolates from a tertiary care hospital: First report of bla(SHV-12), bla(SHV-31), bla(SHV-38), and bla(CTX-M-15) in Brazil. Microb Drug Resist. 2011;17:7-16. doi: 10.1089/mdr.2010.0055. PubMed PMID: 20795871.

53. Lester CH, Olsen SS, Jakobsen L, Arpi M, Fuursted K, Hansen DS, et al. Emergence of extended-spectrum beta-lactamase (ESBL)-producing Klebsiella pneumoniae in Danish hospitals; this is in part explained by spread of two CTX-M-15 clones with multilocus sequence types 15 and 16 in Zealand. Int J Antimicrob Agents. 2011;38:180-2. doi: 10.1016/j.ijantimicag.2011.03.018. PubMed PMID: 21612893.

54. Mshana SE, Fritzenwanker M, Falghenauer L, Domann E, Hain T, Chakraborty T, et al. Molecular epidemiology and characterization of an outbreak causing Klebsiella pneumoniae clone carrying chromosomally located bla(CTX-M-15) at a German University-Hospital. BMC Microbiol. 2015;15:122. doi: 10.1186/s12866-015-0460-2. PubMed PMID: 26077154; PubMed Central PMCID: PMCPMC4469578.

55. Vranic-Ladavac M, Bosnjak Z, Beader N, Barisic K, Kalenic S, Bedenic B. Clonal spread of CTX-M-15-producing Klebsiella pneumoniae in a Croatian hospital. J Med Microbiol. 2015;64:52-6. doi: 10.1099/jmm.0.019778-0. PubMed PMID: 25767499.

56. Ibrahimagic A, Bedenic B, Kamberovic F, Uzunovic S. High prevalence of CTX-M-15 and first report of CTX-M-3, CTX-M-22, CTX-M-28 and plasmid-mediated AmpC beta-lactamase producing Enterobacteriaceae causing urinary tract infections in Bosnia and Herzegovina in hospital and community settings. J Infect Chemother. 2015;21:363-9. doi: 10.1016/j.jiac.2015.01.003. PubMed PMID: 25638292.