Prevalence and antibiotics susceptibility patterns of carbapenem resistant Enterobacteriaceae

Abstract

*Enterobacteriaceae* is a family of Gram negative rods. However it natural habitat in the intestinal tract of humans and animals, but it has been implicated in many human diseases. The emergence of antimicrobial resistance among *Enterobacteriaceae* isolates has been increasingly reported worldwide and has become a major threat to the provision of healthcare. Carbapenems is beta-lactam antibiotics which is considered as a last line of therapy for multidrug resistant. The occurrence of carbapenem resistance among *Enterobacteriaceae* is a major health challenge which reduce the antibiotics choices that use to treat the infections which cause by these bacteria. This review was focused to increase our understanding about carbapenem resistance; and to display the size and extent of this problem base on up to day published works. The prevalence of carbapenem resistance *Enterobacteriaceae* (CRE) is slightly different among different countries, and their resistance rate for commonly uses antibiotics has been significantly detected. The use of combined antibiotics seem to be is only up to day known therapeuitic choice. The major worriesome, treatment of the infections causes by these multidrugs resistant organisms is extremely difficult which may results in high mortality rates and healthcare costs. We need to focus on continues searching for other highly effective and low cost alternatives therapies.

**Keywords:** antimicrobials resistant, carbapenemase producing Enterobacteriaceae, carbapenem resistant Enterobacteriaceae, clinical isolates, prevalence

Introduction

*Enterobacteriaceae* is a family of Gram negative rods, facultative anaerobes, ferment a wide range of carbohydrates, possess a complex antigenic structure, and produce a variety of toxins and other virulence factors. Natural habitat in the intestinal tract of humans and animals. It is more than 40 genera and 150 species. Only few genera were consider as true pathogens (*Escherichia*, *Salmonella*, *Shigella*, and *Yersinia*), and few are opportunistic pathogens (*Klebsiella*, *Citrobacter*, *Enterobacter*, *Proteus*, *Providencia*, *Morganella*, *Serratia*, and *Edwardsella*). Different members of *Enterobacteriaceae* has been known as a causatives of different intra-intestinal (as diarrhea) and extra-intestinal diseases includes wound infections, pneumonia, septicemia, bacteremia, and meningitis.

The emergence of antimicrobial resistance among *Enterobacteriaceae* has been increasingly reported worldwide and has become a major threat to the provision of healthcare. The resistance of carbapenems are increased dramatically worldwide and recently among members of *Enterobacteriaceae* family.

Carbapenems is beta-lactam antibiotics (includes imipenem, meropenem, erapenem and doripenem) which is considered as a last line of therapy for multidrug resistant (MDR). Carbapenem resistance has been detected and considered as a one of major health problem worldwide and limit the choice of selected antibiotics therapies to treat bacterial infections. Carbapenem resistance may result either from production of carbapenemase that breakdown carbapenem or production of beta-lactamase (ESBLs or Ampc) together with porin loss. Carbapenemase producing *enterobacteriaceae* (CPE) produce carbapenemase which is a main mechanism of carbapenem resistance. Carbapenemase was classified molecularly to three classes (A, B, and D). *K. pneumoniae* carbapenemase (KPC) which belong to molecular class A, OXA48 (class D), and New Delhi metallo beta-lactamase (class B) are the most common carbapenemases produce by *Enterobacteriaceae* family. These enzymes (K. pneumoniae carbapenemase, OXA48, and New Delhi metallo beta-lactamase) confer resistance to virtually all beta-lactam agents, including penicillins, cephalosporins, monobactams, and carbapenems. Detection of carbapenem resistance can be perform phenotypically or genotypically using molecular techniques. This review was focused to increase our understanding about carbapenem resistance; and to display the size and extent of this problem base on up to day published works.

Prevalence of CRE

Understanding the prevalence of CRE is necessary to provide information on the temporal, and geographic occurrence of carbapenem resistance; and the size of this problem in order to facilitate its prevention and control. Base on previously published researches, the prevalence’s of CRE among clinical samples were slightly different among different regions in the world.

Africa

The emergence of CRE has been observed and reported in many studies includes Oduyebo OO et al. (Nigeria), Legese MH et al.
Prevalence and antibiotics susceptibility patterns of carbapenem resistant Enterobacteriaceae

Almugadam BS, Ali NO, Ahmed AB, et al. Prevalence and antibiotics susceptibility patterns of carbapenem resistant Enterobacteriaceae. J Bacteriol Mycol Open Access. 2018;6(3):187-190. DOI: 10.15406/jbmoa.2018.06.00201

Prevalence and antibiotics susceptibility patterns of carbapenem resistant Enterobacteriaceae

(India) which reported the frequency of CRE were 13.95%, 69%, 5.1%, and 2.8% respectively.17-18

Asia

In Asia, the prevalence of CRE among clinical samples was determined in many studies includes Rao A et al.17 (India), Amjad A et al.18 (Pakistan), Jamal WY et al.19 (Kuwait), Li V et al.20 (China), Kandeel A et al.21 (Saudi Arabia), Nair PK et al.22 (India), Zaidah A et al.23 (Malaysia), Jan R et al.24 (South India) and Khare V et al.25 (India) which reported the prevalence of CRE were 13.95%, 69%, 8%, 18.1%, 1.77%, 12.26%, 5.76%, 8% and 37.9% respectively.17-25

Europe, Australia, and America (North and South)

The occurrence of CRE has been investigated in many studies includes Huang T et al.26 (Belgium), Baran I et al.27 (Turkey), Mathersa J et al.28 (USA), Pfaffer MA et al.29 (Latin America), Partina I et al.30 (Russia), Pfaffer MA et al.31 (Australia and New Zealand) and Logan LK et al.32 (USA) which reported the frequency of CRE were 3.46%, 2.8%, 5.7%, 6.6%, 11.6%, 0.1% and 0.08% respectively.26-32 Also Sader HS et al.33 study were found the occurrence of CRE in Poland, Italy, Greece and Romania were 17.3%, 7.5%, 7.4%, and 5.0% respectively.33

Antibiotics susceptibility patterns of CRE

All members of carbapenem resistance Enterobacteriaceae showed high resistant rate for all or most commonly uses penicillins, cephalosporins, monobactams, and quinolones as it reported by many studies.34-40 The antibiotics which has a good activity on most CRE isolates were fosfomycin, tigecycline, polymyxin, amikacin, gentamycin and colistin.31-41

Many studies suggests the use of combined therapies to treat CRE. Falagas ME et al.42 study suggests the use of combined antibiotics may offer a comparative advantage over monotherapy.43 Nabarro LB et al.44 Study conclude there is increasing evidence to support the use of combination therapy to treat infections that cause by CRE.45 Fredborg M et al.46 study conclude meropenem triple combinations with a polymyxin and rifampin exhibited highest synergistic activity against carbapenem producing Enterobacteriaceae.47

Discussion

Carbapenem is a one of antibiotics that offer broad spectrum activity and use as a last line therapy for multidrug resistant bacteria. The treatment of infections causes by drugs resistance bacteria is sometime impossible and may lead to unexpected or bad complications. Antimicrobial resistance increases the cost of health care, and possibility of complications. Without effective antimicrobials for prevention and treatment of CRE infections, medical procedures become very high risk. The major worrisome, treatment of the infections causes by these multidrug organisms is extremely difficult which may results in high mortality rates and healthcare costs.

In this review, we found carbapenem resistance has been emerged worldwide and is beginning to spread. This emergence might result from the absence of public health surveillance programs in most countries that hided this problem, so the public health surveillance programs must be establish in all countries to facilitate the discovery of problems as early as possible. Also new alternatives therapies need to be developed to encounter bacteria with this kind of resistance; and the hospitals need excellent infection treatment and control to prevent the morbidity and spread of CRE.

Also we found the prevalence of CRE in African countries are slightly low when compare with Asian countries; and in Australia and American countries is slightly low when compare with African countries. While the prevalence of CRE in European countries seem to be same in African. Also there is a marked reduction in the susceptibility of carbapenem resistance isolates to anther antibiotics. This differences in the prevalence of CRE and their susceptibility to antibiotics among the isolates of different world countries may arise from the different in geographical location and poor infection control in health care settings or the misuse and availability of non-prescribed therapies that describe by WHO as a accelerators of drugs resistant.

As we found the use of combined therapies up to day is only known appropriate and highly effective choice for treatment of CRE infections. But the use of combined therapies lead knock down the beneficial flora in the body and may associate with many serious diseases or unexpected complications. So the looking for anther alternatives therapies may be a one of the solutions for this problem.

Conclusion

The prevalence of CRE has been emerged worldwide. As we displayed there is a significant rate of carbapenem resistance among Enterobacteriaceae. Formulating an antimicrobial policy with its strict implementation and regular surveillance must be establish. Further studies need to focus on continues searching for a highly effective, low cost, and minimum side effect alternatives therapies.

Acknowledgements

None.

Competing interests

We declare that we have no competing interests.

References

1. Toolkit. Facility guidance for control of carbapenem-resistant enterobacteriaceae (CRE). CDE; 2015.
2. Koneman EW, Allen SO, Janda WM, et al. Colour atlas and textbook for diagnostic microbiology, Enterobacteriaceae. JB Lippincott Company, Philadelphia; 2006. p. 61-402.
3. Don JB, Noel RK, James TS. Bergey’s manual of systematic bacteriology. In: George MG, editor. The Gammaproteobacteria. Williams & Wilkins, New York: Springer; 2005. p. 1108.
4. Fouli M, Galani I, Antoniadou A, et al. An outbreak of infection due to beta-lactamase Klebsiella pneumoniae carbapenemase-2 producing K. pneumoniae in a Greek University Hospital: molecular characterization,epidemiology, and outcomes. Clin Infect Dis. 2010;50(3):364–373.
5. Hu F, Chen S, Xu X, et al. Emergence of carbapenem resistant clinical Enterobacteriaceae isolates from a teaching hospital in Shanghai, China. J Med Microbiol. 2012;61(Pt 1):132–136.
6. Sidjabat H, Nimmo GR, Walsh TR, et al. Carbapenem resistance in Klebsiella pneumoniae due to the New Delhi Metallo-β-lactamase. Clin Infect Dis. 2011;52(4):481–484.
7. Tzouvelekis L, Markogiannakis A, Psychogiou M, et al. Carbapenemases
in Klebsiella pneumoniae and Other Enterobacteriaceae. CMR. 2012;25(4):682–707.
8. Glasser C, Albigier B, Buist G, et al. European survey on carbapenemase-producing Enterobacteriaceae (EuSCAPE) working Group: carbapenemase-producing Enterobacteriaceae in Europe: a survey among national experts from 39 countries, February 2013. Euro Surveill. 2013;18(28):20525.
9. Van Dijk K, Voets GM, Scharringa J, et al. Disc diffusion assay for detection of class A, B and OXA-48 carbapenemases in Enterobacteriaceae using phenyl boronic acid, dipicolinic acid and temocillin. Clin Microbiol Infect. 2014;20(4):345–349.
10. Arend LN, Pilomeno M, Siebra CA, et al. Phenotypic and molecular characterization of 942 carbapenem-resistant Enterobacteriaceae (CRE) in southern Brazil. J Infect Chemother. 2015;21(4):316–318.
11. Oduyebo OO, Falayi O M, Oshun P, et al. Phenotypic determination of carbapenemase producing Enterobacteriaceae isolates from clinical specimens at a Tertiary Hospital in Lagos, Nigeria. Niger Postgrad Med J. 2015;22(4):223–227.
12. Legese MH, Weldearegay GM, Asrat D. Extended-spectrum beta-lactamase and carbapenem-producing Enterobacteriaceae among Ethiopian children. Infect Drug Resist. 2017;10:27–34.
13. Okoche D, Asimwe BB, Katabazi FA, et al. Prevalence and characterization of carbapenem-resistant Enterobacteriaceae isolated from Mulago National Referral Hospital, Uganda. PLoS One. 2015;10(8):e0135745.
14. Amer WH, Khalil HS, Abd El Wahab MAA. Risk factors, phenotypic and genotypic characterization of carbapenem resistant Enterobacteriaceae in Tanta University Hospitals, Egypt. Int J Infect Control. 2016;12:1.
15. Camara A, Mane MT, Ba-Diallo A, et al. Extended-spectrum beta-lactamase and carbapenemase-producing Enterobacteriaceae clinical isolates in a Senegalese teaching hospital: A cross sectional study. Afr J Microbiol Res. 2016;11(44):1600–1605.
16. Wartiti MA, Bahmani FZ, Elouennass M, et al. Prevalence of carbapenemase producing Enterobacteriaceae in a University Hospital in Rabat, Morocco: A19-months prospective study. The international arabic journal of antimicrobial agents. 2012;2(3):4.
17. Rao A, Indumathi VA. Detection of carbapenem resistant enterobacteriaceae from clinical isolates. Int J Curr Microbiol App Sci. 2016;5(5):864–869.
18. Anjaj A, Mirza IA, Abbasi SA, et al. Modifiable hodge protocol: A simple and effective tool for detection of carbapenemase production. Iran J Microbiol. 2011;3(4):189–193.
19. Jamal WV, Albert MJ, Rotimi VO. High prevalence of New Delhi Metallo-β-Lactamase- 1 (NDM-1) producers among carbapenem-resistant Enterobacteriaceae in Kuwait. PLoS One. 2016;11(3):e0152638.
20. Li Y, Shen Y, Zhang Y, et al. Rapid increase in prevalence of carbapenem-resistant Enterobacteriaceae (CRE) and emergence of colistin resistance gene mcr-1 in CRE in a hospital in Henan, China. J Clin Microbiol. 2018;56(4):1932–1937.
21. Kandeel A. Epidemiology of carbapenemase producing Enterobacteriaceae in a general hospital. J Microbiol Infect Dis. 2015;5(2):57–62.
22. Nair PK, Vaz MS. Prevalence of carbapenem resistant Enterobacteriaceae from a tertiary care hospital in Mumbai, India. JMMID. 2013;3(4):207–210.
23. Zaidah A, Mohammad N, Suraiya S, et al. High burden of carbapenem-resistant Enterobacteriaceae (CRE) fecal carriage at a teaching hospital: costeffectiveness of screening in low-resource setting. Antimicrobial Resistance & Infection Control. 2017;6:42.
24. Jan R, George N, Mathew M, et al. Prevalence of carbapenem resistant enterobacteriaceae in a tertiary care referral centre: Kerala, South India. International Journal of Current Research. 2016;8(12):44353–44355.
25. Khare V, Gupta P, Haider F, et al. Study on MICs of tigecycline in clinical isolates of carbapenem resistant Enterobacteriaceae (CRE) at a tertiary care centre in North India. J Clin Diagn Res. 2017;11(3):DC18-DC21.
26. Te-Din H, Catherine B, Pierre B, et al. Prevalence and mechanisms of resistance to carbapenems in Enterobacteriaceae isolates from 24 hospitals in Belgium. J Antimicrob Chemother. 2013;68(8):1832–1837.
27. Baran I, Aksu N. Phenotypic and genotypic characteristics of carbapenem-resistant Enterobacteriaceae in a tertiary-level referral hospital in Turkey. Ann Clin Microbiol Antimicrob. 2016;15:20.
28. Mathersa J, Coxa HL, Kitchell B, et al. Molecular dissection of an outbreak of carbapenem-resistant enterobacteriaceae reveals intergenus KPC carbapenemase transmission through a promiscuous plasmid. mBio. 2011;2(6):e00204–e00211.
29. Pfaller MA, Shortridge D, Sader HS, et al. Ceftolozane-tazobactam activity against drug-resistant Enterobacteriaceae and Pseudomonas aeruginosa causing healthcare-associated infections in Latin America: report from an antimicrobial surveillance program (2013-2015). Braz J Infect Dis. 2017;21(6):627–637.
30. Partina I, Kalinogorskaya O, Kojima S, et al. Surveillance of antimicrobial susceptibility of Enterobacteriaceae pathogens isolated from intensive care units and surgical units in Russia. Jpn J Antibiot. 2016;69(1):41–51.
31. Pfaller MA, Shortridge D, Sader HS, et al. Ceftolozane-tazobactam activity against drug-resistant Enterobacteriaceae and Pseudomonas aeruginosa causing healthcare-associated infections in Australia and New Zealand: Report from an Antimicrobial Surveillance Program (2013–2015). J Glob Antimicrob Resist. 2017:186–194.
32. Logan IK, Renschler JP, Gandra S, et al. Carbapenem Resistant Enterobacteriaceae in Children, United States, 1999–2012. Emerg Infect Dis. 2015;21(11):2014–2021.
33. Sader HS, Castanheira M, Flamm RK, et al. Tigecycline activity tested against carbapenem-resistant Enterobacteriaceae from 18 European nations: results from the SENTRY surveillance program (2010-2013). Diagn Microbiol Infect Dis. 2015;83(2):183–186.
34. Almugadam BS, Elbala AS, Elkheir AS, et al. Carbapenem Resistance Enterobacteriaceae in Children. Enterobacteriaceae Among Wound Isolates, Kosti City, Sudan. Clin Microbiol. 2018;7:1.
35. Bouamri M, Arsalane L, Kamouni Y, et al. Antimicrobial susceptibility of urinary Klebsiella pneumoniae and the emergence of carbapenem-resistant strains: A retrospective study from a university hospital in Morocco, North Africa. African Journal of Urology. 2015;21(1):36–40.
36. Zhao Z, Lan F, Liu M, et al. Evaluation of automated systems for aminoglycosides and fluoroquinolones susceptibility testing for Carbapenem-resistant Enterobacteriaceae. Antimicrobial Resistance & Infection Control. 2017;6:77.
37. Christophy R, Osman M, Miall M, et al. Prevalence, antibiotic susceptibility and characterization of antibiotic resistant genes among carbapenem-resistant Gram-negative bacilli and yeast in intestinal flora of cancer patients in North Lebanon. J Infect and Public Health. 2017;10(6):716–720.
38. Almugadam BS, Mohamed HA, Hamid HO, et al. Frequency of Carbapenem Resistance Enterobacteriaceae among Urinary Isolates in Kosti City, Sudan 2017. World J Biol Med Science. 2017;4(4):23–28.
39. Nordmann P, Gniadkowski M, Giske CG, et al. Identification and screening of carbapenemase-producing Enterobacteriaceae. Clin Microbiol Infect. 2012;18(5):432–438.

Citation: Almugadam BS, Ali NO, Ahmed AB, et al. Prevalence and antibiotics susceptibility patterns of carbapenem resistant Enterobacteriaceae. J Bacteriol Mycol Open Access. 2018;6(3):187–190. DOI: 10.15406/jpmona.2018.06.00201

Prevalence and antibiotics susceptibility patterns of carbapenem resistant Enterobacteriaceae.

Copyright: ©2018 Almugadam et al.
40. Kim S, Shin J, Shin S, et al. Characteristics of carbapenem-resistant Enterobacteriaceae isolates from Korea. Diagn Microbiol Infect Dis. 2013;76(4):486–490.
41. Falagas ME, Kastoris AC, Kapaskelis AM, et al. Fosfomycin for the treatment of multidrug-resistant, including extended-spectrum beta-lactamase producing, Enterobacteriaceae infections: A systematic review. The Lancet Infectious Diseases. 2010;10(1):43–50.
42. Petrosillo N, Giannella M, Lewis R, et al. Treatment of carbapenem-resistant Klebsiella pneumoniae: the state of the art. Expert Rev Anti Infect Ther. 2013;11(2):159–177.
43. Tzouvelekis LS, Markogiannakis A, Piperaki E, et al. Treating infections caused by carbapenemase-producing Enterobacteriaceae. Clin Microbiol Infect. 2014;20(9):862–872.
44. van Duin D, Kaye KS, Neuner EA, et al. Carbapenem-resistant Enterobacteriaceae: a review of treatment and outcomes. Diagn Microbiol Infect Dis. 2013;75(2):115–120.
45. Jiang X, Poirel L, Nordmann P. Lack of polymyxin resistance among carbapenemase-producing Enterobacteriaceae in a university hospital in China. Infect Dis. 2017;40(7):556–557.
46. Kelesidis T, Karageorgopoulos DE, Kelesidis I, et al. Tigecycline for the treatment of multidrug-resistant Enterobacteriaceae: a systematic review of the evidence from microbiological and clinical studies. J Antimicrob Chemother. 2008;62(5):895–904.
47. Zhan L, Wang S, Guo Y, et al. Outbreak by Hypermucoviscous Klebsiella pneumoniae ST11 Isolates with Carbapenem Resistance in a Tertiary Hospital in China. Front Cell Infect Microbiol. 2017;7:182.
48. Falagas ME, Lourida P, Poulakakos P, et al. Antibiotic treatment of infections due to Carbapenem-Resistant Enterobacteriaceae: Systematic Evaluation of the Available Evidence. Antimicrob. Agents Chemother. 2014;58(2):654–663.
49. Nabarro LB, Veeraraghavan B. Combination therapy for carbapenem-resistant Enterobacteriaceae: increasing evidence, unanswered questions, potential solutions. Eur J Clin Microbiol Infect Dis. 2015;34(12):2307–2311.
50. Fredborg M, Sondergaard TE, Wang M. Synergistic activities of meropenem double and triple combinations against carbapenemase-producing Enterobacteriaceae. Diagn Microbiol Infect Dis. 2017;88(4):355–360.