Karbapeneneme Dirençli Gram-Negatif Çomak İnfeksiyonları

Epidemiyoloji

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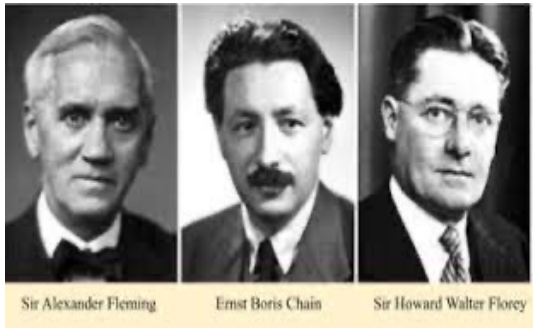
Sancaktepe Şehit Prof. Dr. İlhan Varank Eğitim ve Araştırma Hastanesi
İnfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği
31.Ocak. 2023

Antibiyotiklerin altın çağı



1976……Beta laktamaz inh.
1985…….İmipenem
1996 …….. Meropenem
2001 ……Ertapenem
2007 ……..Doripenem

Figure: 1 Timeline showing antibiotics reaching the clinic.

[The Timeline of Antibiotics - MDIS Blog]

Karbapenemler

ESBL pozitif Gram negatif

bakterilerden

kaynaklanan şiddetli

infeksiyonlarda hayat kurtarıcı **!!**

TABLE 2 | The first report of representative carbapenem-resistant *K. pneumoniae* (CRKP).

Strain	Year	Country	Ambler structural class	Molecular epidemiology	Reference
KPC-1-KP (1534)	1996	United States	A	Tn4401	Yigit et al., 2001
NDM-1-KP (05-506)	2008	India	B	N plasmids	Yong et al., 2009
OXA-48-KP (11978)	2001	Turkey	D	Tn1999	Poirel et al., 2004

Chang D, et al. Front Microbiol 2021;22 (12): 750662

Antibiyotiklerde direnç gelişimi

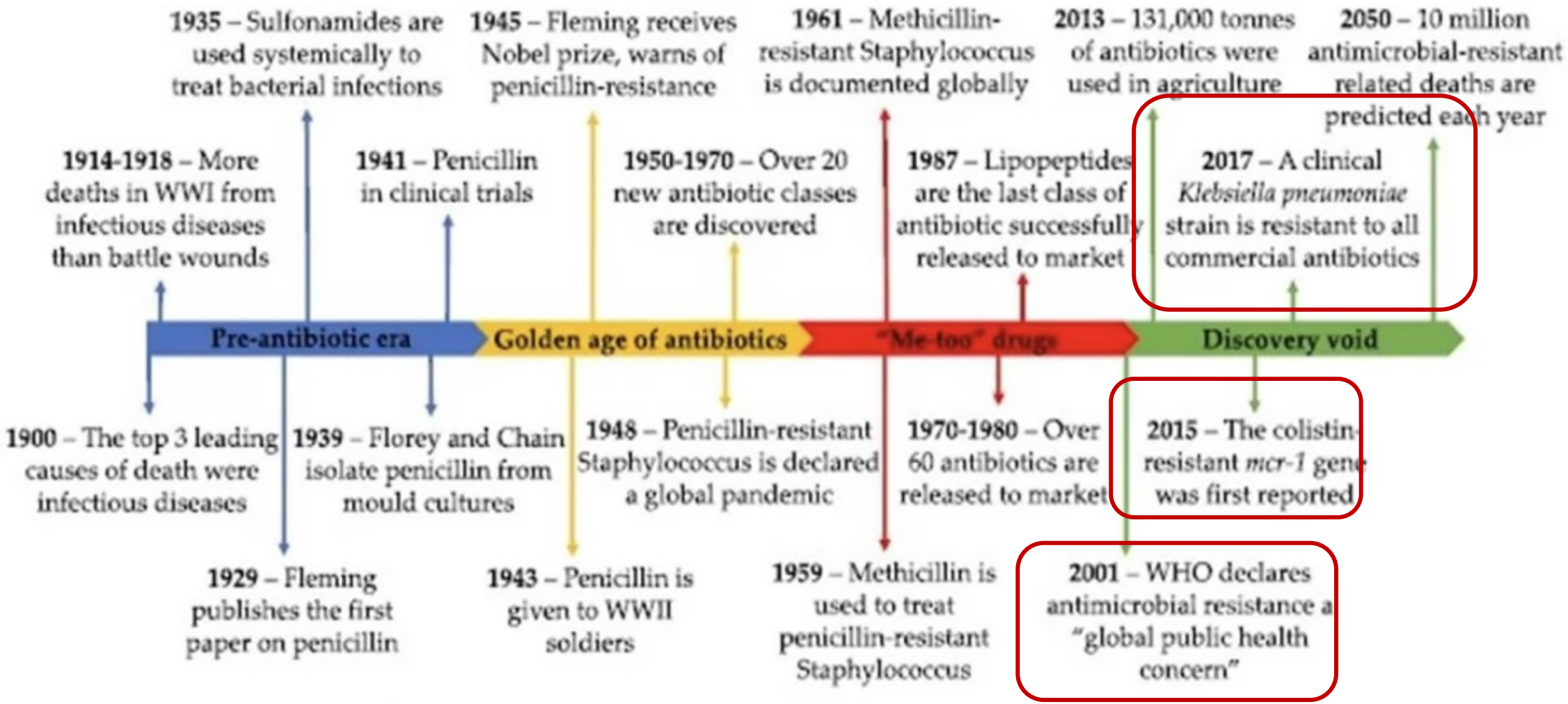


Figure: 2 Timeline showing antibiotic resistance (Browne, 2020)

(International Journal of Molecular Sciences)

[The Timeline of Antibiotics - MDIS Blog]

WHO priority pathogens list for R&D of new antibiotics

Priority 1: CRITICAL

- *Acinetobacter baumannii*, carbapenem-resistant
- *Pseudomonas aeruginosa*, carbapenem-resistant
- *Enterobacteriaceae*, carbapenem-resistant, ESBL-producing

Resistant germ	Threat Estimate, 2019 report	What CDC Counted, 2019 report	What CDC Did Not Count, 2019 report	Threat Estimate, 2013 report	New 2013 Threat Estimate, 2019 report	Can Data be Compared? 2013 vs 2019 reports	Year-to-Year Comparison Provided, 2019 report	Resistant Infection Increase/ Decrease, 2019 report
Carbapenem-resistant Enterobacteriaceae	13,100 cases & 1,100 deaths	Incident hospitalized positive clinical cultures, including hospital- & community-onset	Non-hospitalized cases	9,300 healthcare associated infections & 600 deaths	11,800 cases & 1,000 deaths (2012 estimates)	No	Cases over time from 2012-2017	Stable
Carbapenem-resistant *Acinetobacter* (formerly multidrug-resistant *Acinetobacter*)	8,500 cases & 700 deaths	Incident hospitalized positive clinical cultures, including hospital- & community-onset	Non-hospitalized cases	N/A—was listed as multidrug-resistant in 2013 report	11,700 cases & 1,000 deaths (2012 estimates)	No	Cases over time from 2012-2017	⬇ Decrease
Multidrug-resistant *Pseudomonas aeruginosa*	32,600 cases & 2,700 deaths	Incident hospitalized positive clinical cultures, including hospital- & community-onset	Non-hospitalized cases	6,700 healthcare associated infections & 440 deaths	46,000 cases & 3,900 deaths (2012 estimates)	No	Cases over time from 2012-2017	⬇ Decrease

Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2019

Karbapenem Dirençli Gram Negatif Bakteriler

- Tedavi seçenekleri sınırlı
- Mortalite oranları yüksek

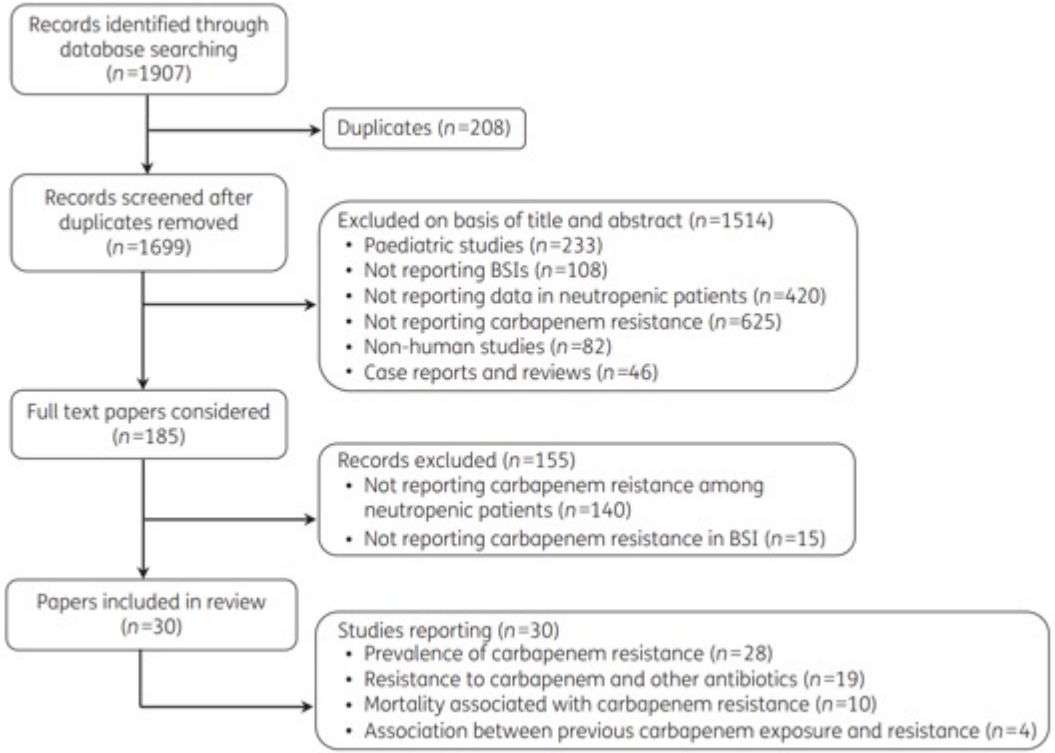
Sarah S, et al. Antimicrob Agents and Chemother 2021; 65(12): e01105-21.

J Antimicrob Chemother 2017; 72: 668–677
doi:10.1093/jac/dkw459 Advance Access publication 13 December 2016

Journal of Antimicrobial Chemotherapy

Global prevalence of carbapenem resistance in neutropenic patients and association with mortality and carbapenem use: systematic review and meta-analysis

Elda Righi[1,2]*, Anna Maria Peri[2,3], Patrick N. A. Harris[2], Alexander M. Wailan[2], Mariana Liborio[4], Steven W. Lane[5–7] and David L. Paterson[2]



- Karbapenem dirençli bakterilerden kaynaklanan infeksiyonlarda mortalite %33-71
- Karbapenem dirençli ise mortalite daha yüksek

Karbapenemlerde direnç mekanizmaları

- ❖ Karbapenemleri hidrolize eden β-laktamaz üretimi
- ❖ Permeabilitede azalma
- ❖ Efluks pompaları
- ❖ Bakteriyel hedef alanında değişiklik veya azalma

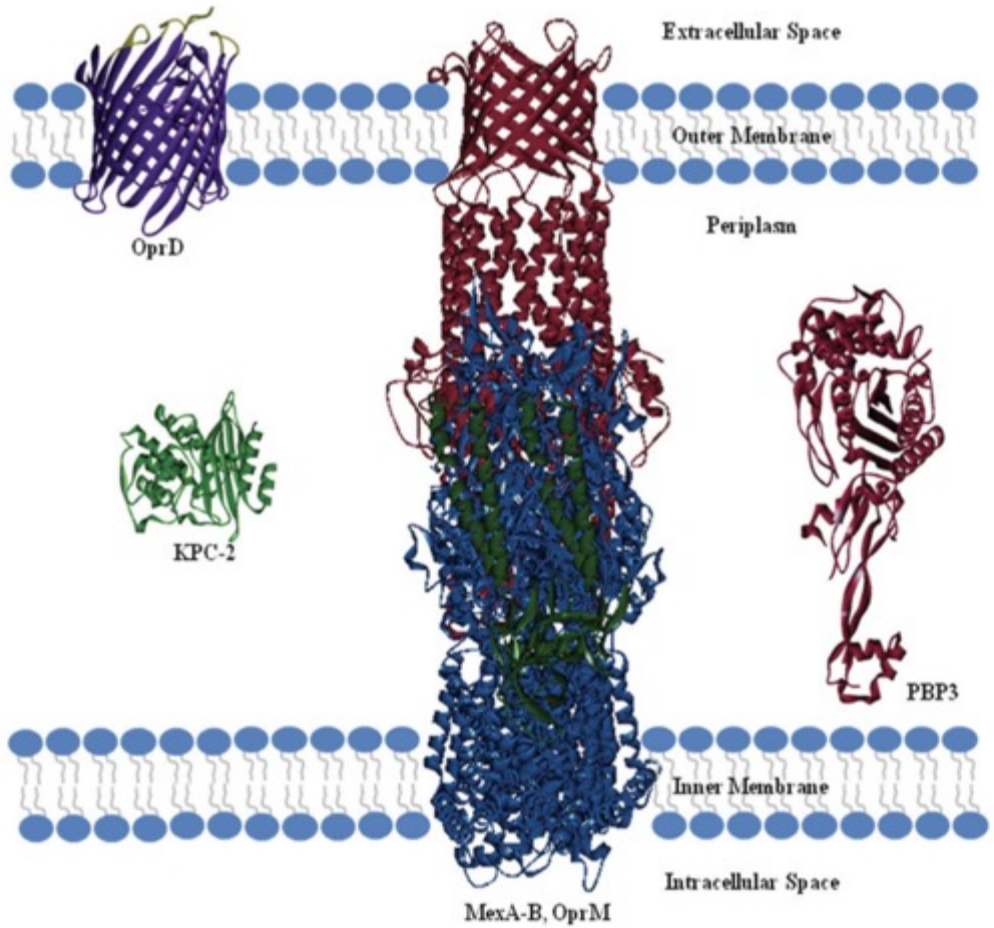


FIG. 4. Crystal structures of the carbapenemase, KPC-2 (Protein Data Bank [PDB] identifier 2OV5), present in the periplasm, *P. aeruginosa* porin, OprD (substrate binding loops highlighted in yellow) (PDB identifier 2ODJ) present in the outer membrane, *P. aeruginosa* efflux pump components, MexA, MexB, and OprM (PDB identifiers 1VF7, 2V50, and 3D5K), spanning the inner membrane and periplasmic and outer membranes, and *P. aeruginosa* PBP3 (PDB identifier 3PBN), anchored to the inner membrane.

Papp-Wallace KM, et al. Antimicrob Agents Chemother. 2011 Nov;55(11):4943-60

Karbapenemazlar

- Karbapenemazlar, yalnızca karbapenemleri değil, aynı zamanda geniş spektrumlu penisilinleri, oksimino-sefalosporinleri ve sefamisinleri de hidrolize edebilir

Ambler Classification of β-Lactamases

CLASS	ACTIVE SITE	ENZYME TYPE	SUBSTRATES	EXAMPLE
A	Serine	Penicillinases:		
		Broad-spectrum	Benzylpenicillin, aminopenicillins, carboxypenicillins, ureidopenicillins, narrow-spectrum cephalosporins	PC1 in *Staphylococcus aureus* TEM-1, SHV-1 in *Escherichia coli, Klebsiella pneumoniae,* other gram-negative bacteria
		Extended-spectrum (β-lactamase)	Substrates of broad-spectrum plus oxymino-β-lactams (cefotaxime, ceftazidime, ceftriaxone) and aztreonam	In Enterobacteriaceae: TEM-derived, SHV-derived, CTX-M–derived; PER-1, VEB-1, VEB-2, GES-1, GES-2, IBC-2 in *Pseudomonas aeruginosa*
		Carbapenemases	Substrates of extended-spectrum plus cephamycins and carbapenems	KPC-1, KPC-2, KPC-3 in *K. pneumoniae*; NMC/IMI, SME family
B	Metallo-β-lactamases (Zn^{2+})	Carbapenemases	Substrates of extended-spectrum plus cephamycins and carbapenems	NDM-1 in Enterobacteriaceae, IMP, VIM, GIM, SPM, SIM lineages in *P. aeruginosa, Acinetobacter* spp.
C	Serine	Cephalosporinases	Substrates of extended-spectrum plus cephamycins	AmpC-type enzymes in Enterobacteriaceae, *Acinetobacter* spp.
D	Serine	Oxacillinases:		
		Broad-spectrum	Aminopenicillins, ureidopenicillin, cloxacillin, methicillin, oxacillin, and some narrow-spectrum cephalosporins	OXA-family in *P. aeruginosa*
		Extended-spectrum	Substrates of broad-spectrum plus oxymino-β-lactams and monobactams	OXA-derived in *P. aeruginosa*
		Carbapenemases	Substrates of extended-spectrum plus cephamycins and carbapenems	OXA-derived in *Acinetobacter* spp.

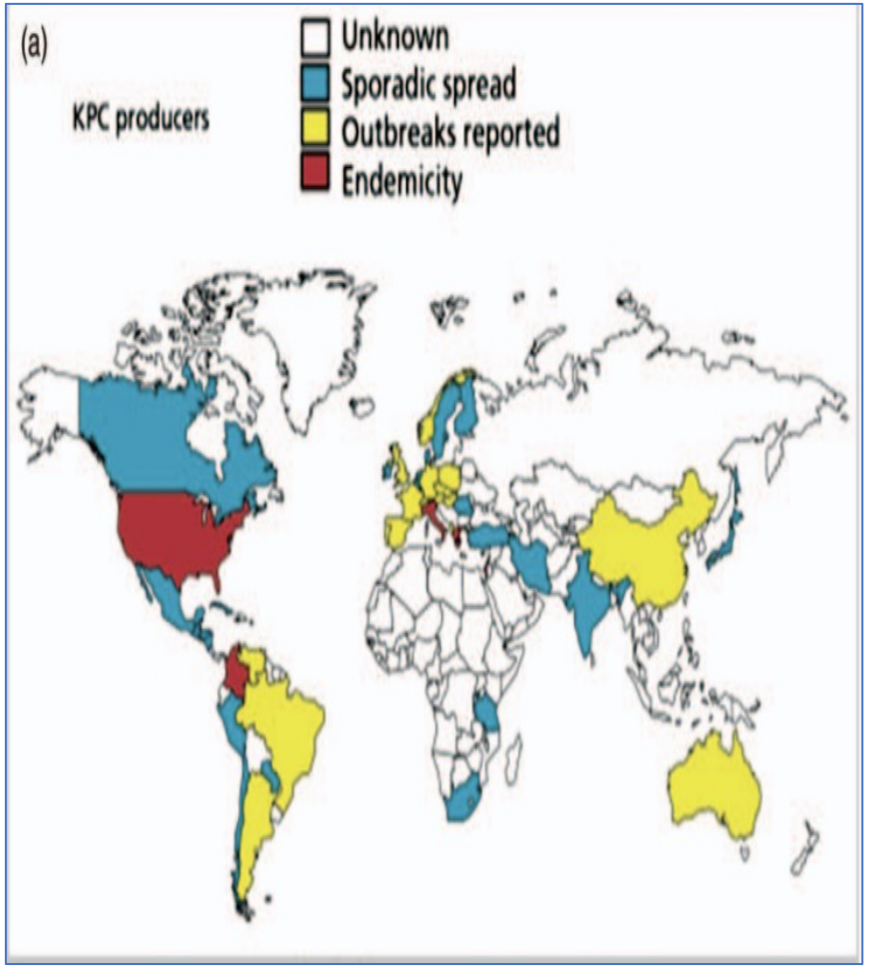
Ambler sınıf A karbapenemazlar

- KPC-1, KPC-2, KPC-3,

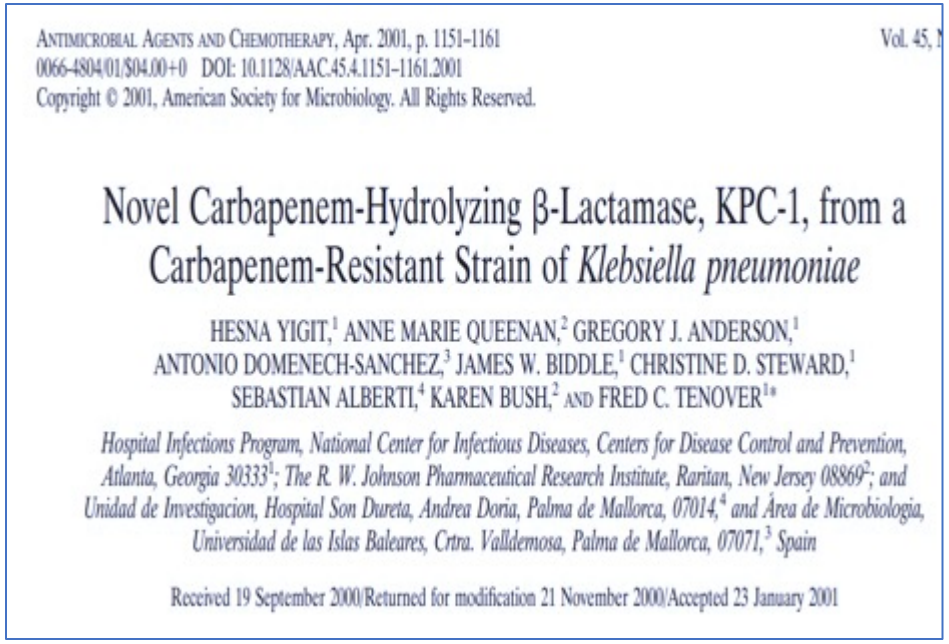
  NMC/IMI,

  SME

- En yaygın *K. pneumoniae* karbapenemaz **(KPC)**
- KPC*; E. coli, Citrobacter, Enterobacter, Salmonella, Serratia* ve nadiren *P. aeruginosa* (nadir)



Brink AJ. Curr Opin Infect Dis 2019; 32: 609-16



ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Apr. 2001, p. 1151–1161 Vol. 45, N
0066-4804/01/$04.00+0 DOI: 10.1128/AAC.45.4.1151–1161.2001

Novel Carbapenem-Hydrolyzing β-Lactamase, KPC-1, from a Carbapenem-Resistant Strain of *Klebsiella pneumoniae*

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Received 19 September 2000/Returned for modification 21 November 2000/Accepted 23 January 2001

2001 yılında yayınlanan çalışma

Amerika'da ilk KPC-1

Journal of Hospital Infection 122 (2022) 217–219

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin

ELSEVIER

Healthcare Infection Society

Letter to the Editor

Outbreak of ceftazidime-avibactam resistant *Klebsiella pneumoniae carbapenemase (KPC)-producing Klebsiella pneumoniae* in a COVID-19 intensive care unit, Italy: urgent need for updated diagnostic protocols of surveillance cultures

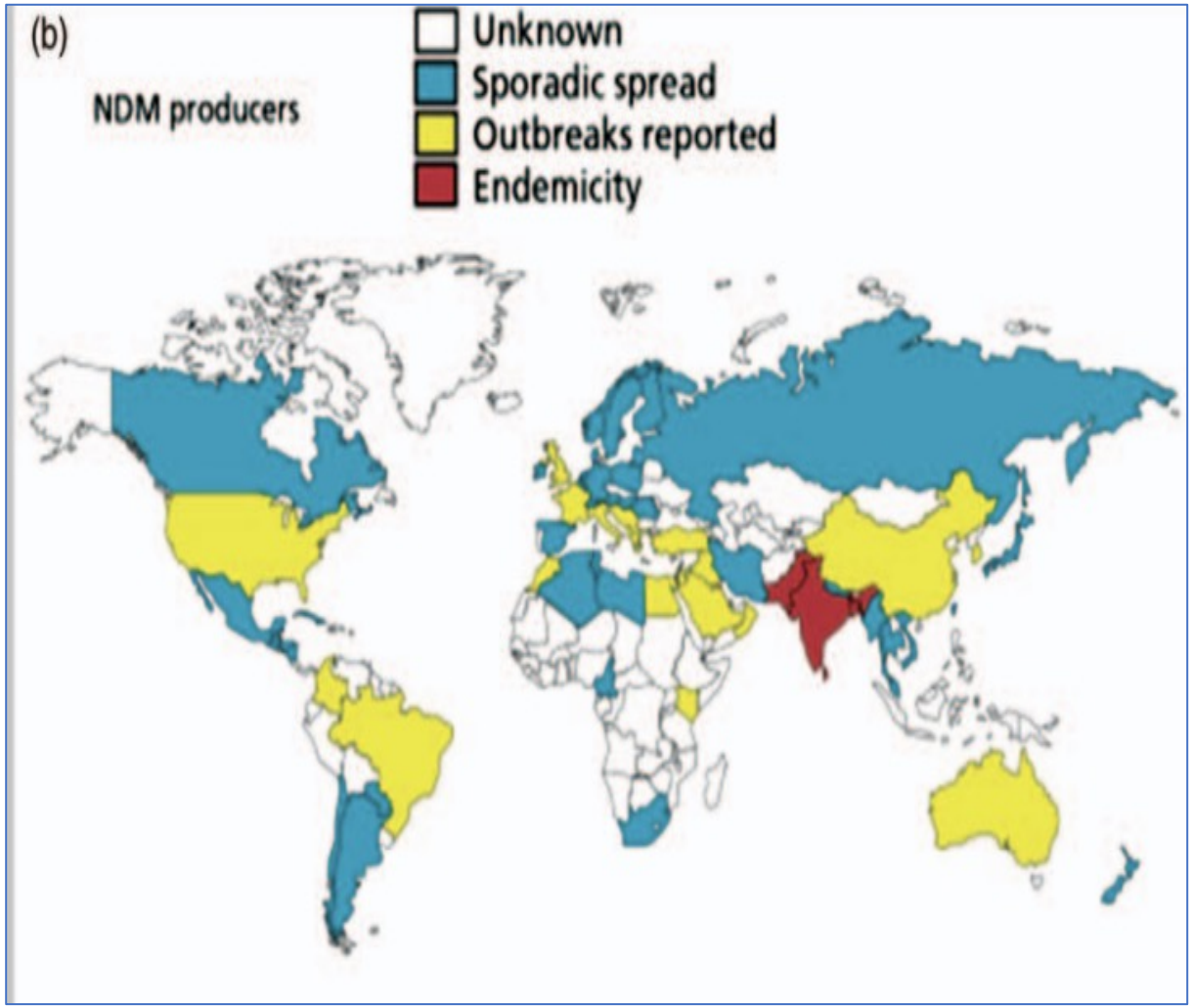
(Copan, Brescia, Italy), were inoculated on Brilliance CRE medium (Oxoid Ltd, Hampshire, UK) by automated direct plating using Wasp® instrument (Copan, Brescia, Italy). Bacterial species identification was performed on overnight colonies using matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) analysis (Bruker DALTONIK GmbH, Bremen, Germany) and carbapenemase production in EB isolates was investigated by the genotypic assay Xpert Carba-R on GeneXpert platform (Cepheid, Sunnyvale, CA, USA). KPC-EB isolates were tested for susceptibility to CZA by E-test method (BioMérieux, Marcy l'Étoile, France) whereas susceptibility to major antimicrobials was performed using a commercial microdilution system (Panel NMDR, Microscan WalkAway 96 Plus, Beckman Coulter, Switzerland). KPC-producing *Klebsiella pneumoniae* (KPC-Kp) was the predominant carbapenemase-producing EB identified by rectal

- 21 hasta seftazidim-avibaktam dirençli KPC suşu ile kolonize

Bianco G, et al. J Hosp Infect 2022;122:217-219.

Sınıf B karbapenemazlar

- NDM-1 (*Enterobacterales*)
- IMP, VIM, GIM, SPM, SIM
  (*Acinetobacter spp*. ve *P. aeruginosa*'da)



Brink AJ. Curr Opin Infect Dis 2019; 32: 609-16

Molecular Epidemiology of Carbapenem-resistant *Klebsiella pneumoniae* Isolates

Karbapeneme Dirençli *Klebsiella pneumoniae* Suşlarının Moleküler Epidemiyolojisi

Abstract

Aim: Carbapenem-resistant Klebsiella pneumoniae infection has become an important clinical problem with reduced therapeutic options. This study aimed to investigate the carbapenem resistance rates and responsible resistance genes in *K. pneumoniae* isolates derived from clinical samples collected in Istanbul.

Materials and Methods: This prospective study included a total of 1452 *K. pneumoniae* isolates from patients admitted to our hospital between July 2013 and July 2014. VITEK-2 (bioMérieux, Marcy-l'Ètoile, France) was used for microbial identification and antimicrobial susceptibility testing. The carbapenem-resistant isolates identified by VITEK-2 were also found to be resistant to ertapenem by the ertapenem gradient test. Resistance mechanisms of the carbapenem-resistant isolates were investigated using real time-polymerase chain reaction.

Results: Of the 1452 *K. pneumoniae* isolates, 45 (3.1%) were carbapenem-resistant. Of these, 32 (71.1%) were bla_{OXA-48}-positive, 9 (20%) bla_{NDM}-positive, and 1 (2.2%) bla_{VIM-1}-positive. None had the genes bla_{KPC} and $blaI_{MP-1}$. The greatest susceptibility by the isolated carbapenemase-producing *K. pneumoniae* was shown to the antimicrobials amikacin and gentamicin.

Discussion and Conclusion: In our hospital, there are several mechanisms causing carbapenem resistance, and the bla_{OXA-48} positivity rate of 71.1% is significant. This resistance may spread rapidly and, through enzymatic resistance gene transfer, lead to hospital epidemics difficult to manage. For this reason, accurate and rapid laboratory diagnosis is important in infection control. For faster results, molecular methods, as well as phenotypic methods, must be included in the hospital infrastructure.

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[1] Erzincan University, Mengücek Gazi Training and Research Hospital, Medical Microbiology Laboratory

[2] Haydarpaşa Numune Training and Research Hospital, Infectious Diseases and Clinical Microbiology

[3] Haydarpaşa Numune Training and Research Hospital, Medical Microbiology Laboratory

[4] İstanbul Medeniyet University, Faculty of Medicine, Department of Medical Microbiology

[5] Cerrahpaşa School of Medicine, Department of Medical Microbiology

- Klinik örneklerden izole edilen total 1452 *K. pneumoniae* suşu
- Suşlardan %3.1'inde karbapenem dirençli
- 45 suşun %71'inde bla_{OXA-48}, %20'sinde $_{blaNDM}$, %2.2'sinde bla_{VIM1} pozitif

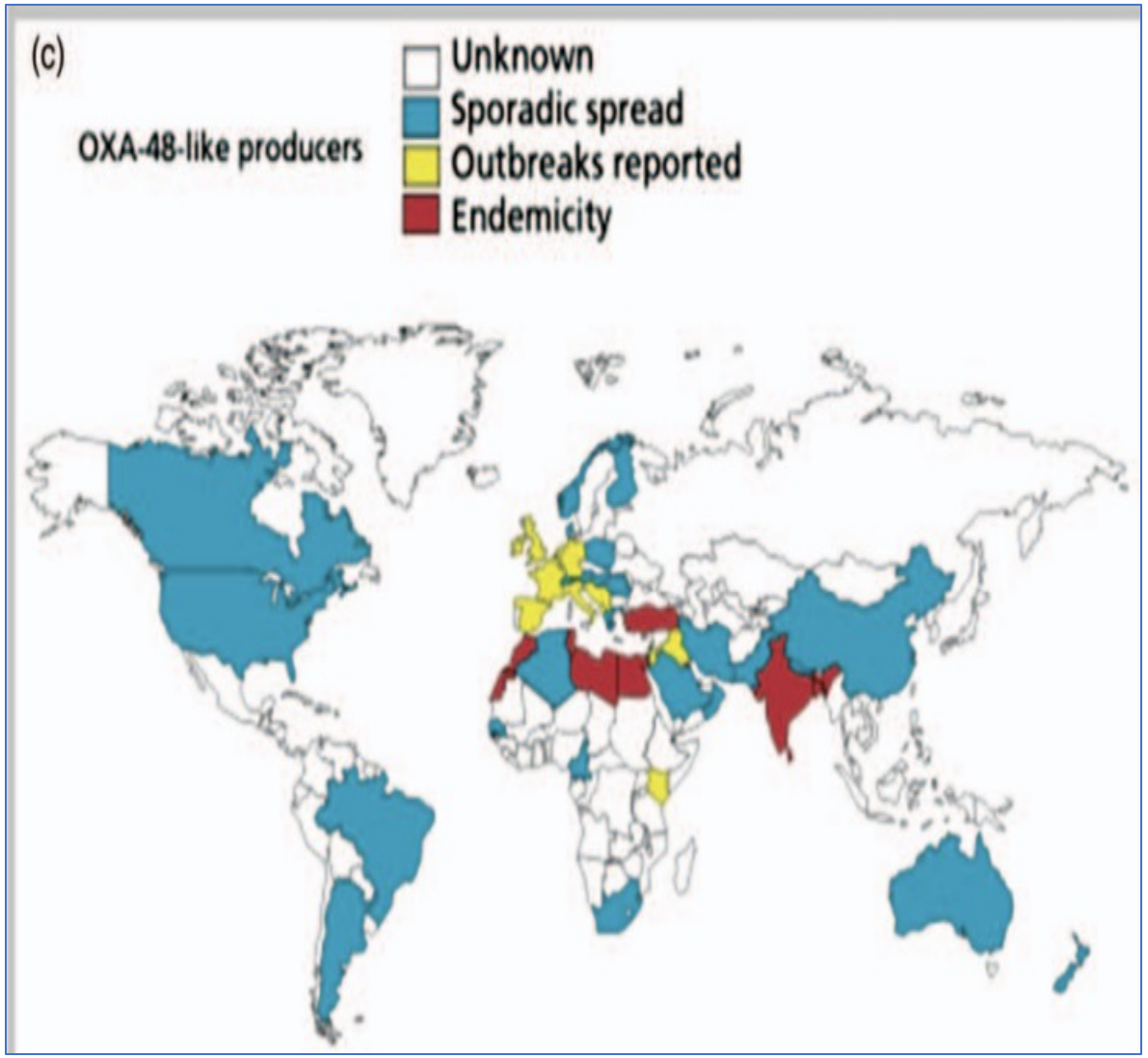
Davarci İ ve ark. Anatol Clin. 2019; 24(1)

Sınıf D karbapenemazlar

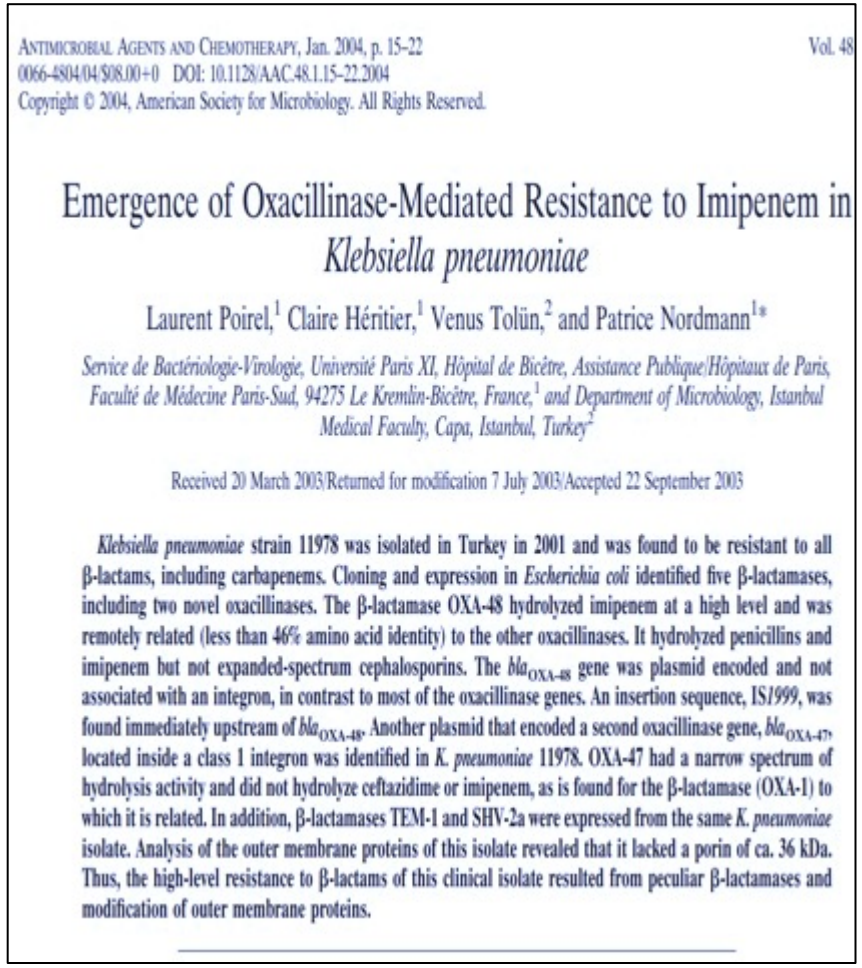
- OXA ailesi
- *Acinetobacter spp ve P. aeruginosa*

nadiren *Enterobacterales*'te

Codjoe F, et al. Med Sci (Basel). 2017 Dec 21;6(1):1.



Brink AJ. Curr Opin Infect Dis 2019; 32: 609-16



ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Jan. 2004, p. 15–22 Vol. 48
0066-4804/04/$08.00+0 DOI: 10.1128/AAC.48.1.15–22.2004

Emergence of Oxacillinase-Mediated Resistance to Imipenem in *Klebsiella pneumoniae*

Laurent Poirel,[1] Claire Héritier,[1] Venus Tolün,[2] and Patrice Nordmann[1]*

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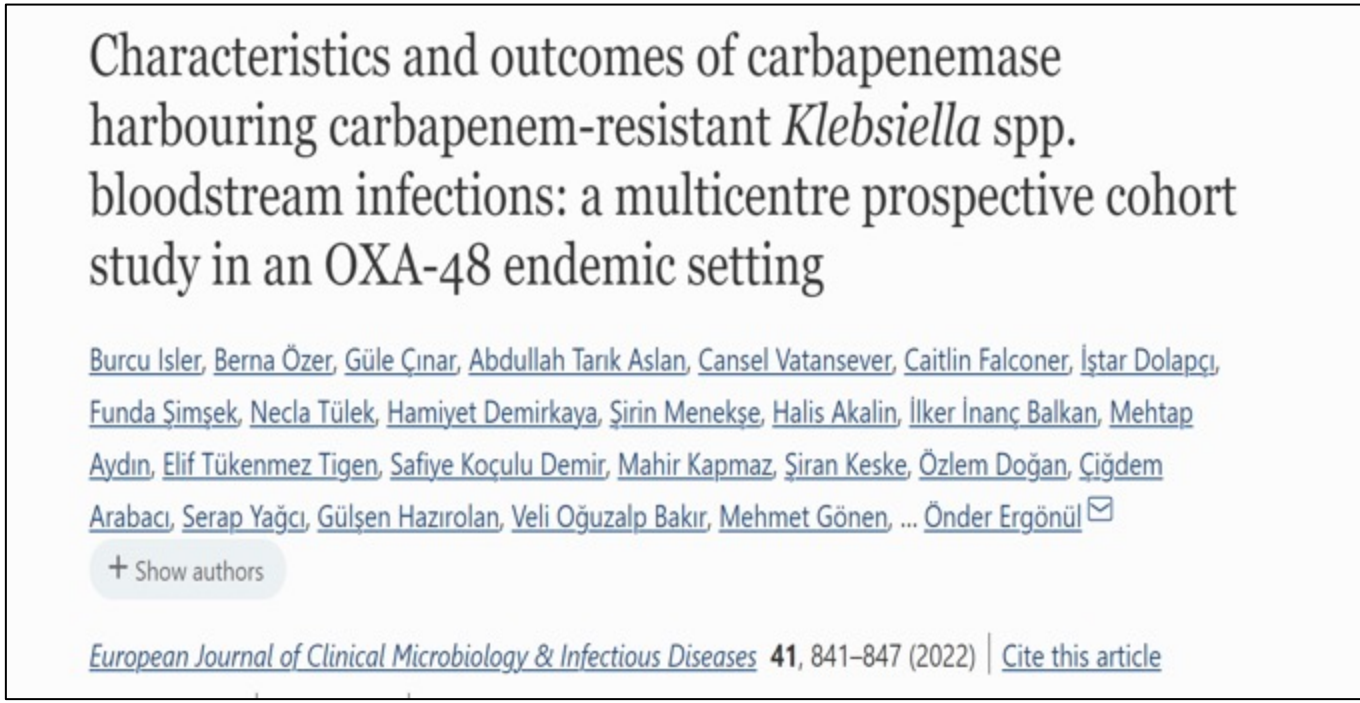
Received 20 March 2003/Returned for modification 7 July 2003/Accepted 22 September 2003

Klebsiella pneumoniae **strain 11978 was isolated in Turkey in 2001 and was found to be resistant to all β-lactams, including carbapenems. Cloning and expression in *Escherichia coli* identified five β-lactamases, including two novel oxacillinases. The β-lactamase OXA-48 hydrolyzed imipenem at a high level and was remotely related (less than 46% amino acid identity) to the other oxacillinases. It hydrolyzed penicillins and imipenem but not expanded-spectrum cephalosporins. The bla_{OXA-48} gene was plasmid encoded and not associated with an integron, in contrast to most of the oxacillinase genes. An insertion sequence, IS*1999*, was found immediately upstream of bla_{OXA-48}. Another plasmid that encoded a second oxacillinase gene, bla_{OXA-47}, located inside a class 1 integron was identified in *K. pneumoniae* 11978. OXA-47 had a narrow spectrum of hydrolysis activity and did not hydrolyze ceftazidime or imipenem, as is found for the β-lactamase (OXA-1) to which it is related. In addition, β-lactamases TEM-1 and SHV-2a were expressed from the same *K. pneumoniae* isolate. Analysis of the outer membrane proteins of this isolate revealed that it lacked a porin of ca. 36 kDa. Thus, the high-level resistance to β-lactams of this clinical isolate resulted from peculiar β-lactamases and modification of outer membrane proteins.**

- 2001 yılı İstanbul
- Karbapenem dahil tüm beta laktamlara dirençli *K. pneumoniae*



Characteristics and outcomes of carbapenemase harbouring carbapenem-resistant *Klebsiella* spp. bloodstream infections: a multicentre prospective cohort study in an OXA-48 endemic setting

Burcu Isler, Berna Özer, Güle Çınar, Abdullah Tarık Aslan, Cansel Vatansever, Caitlin Falconer, İştar Dolapçı, Funda Şimşek, Necla Tülek, Hamiyet Demirkaya, Şirin Menekşe, Halis Akalin, İlker İnanç Balkan, Mehtap Aydın, Elif Tükenmez Tigen, Safiye Koçulu Demir, Mahir Kapmaz, Şiran Keske, Özlem Doğan, Çiğdem Arabacı, Serap Yağcı, Gülşen Hazırolan, Veli Oğuzalp Bakır, Mehmet Gönen, ... Önder Ergönül

+ Show authors

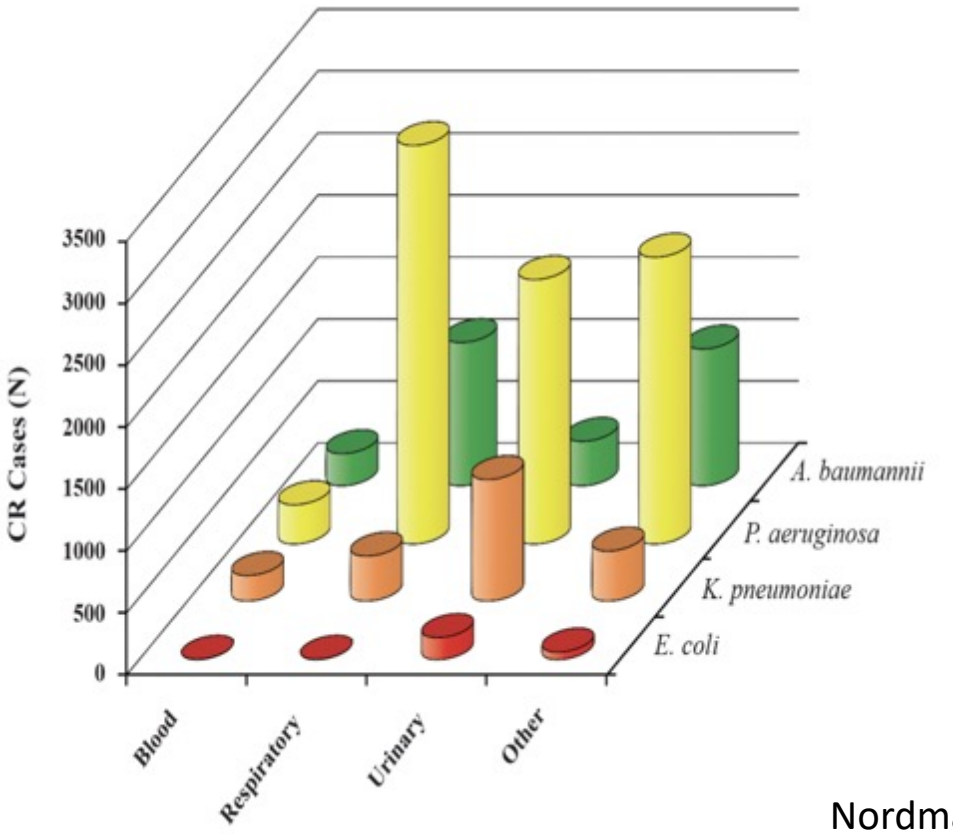
European Journal of Clinical Microbiology & Infectious Diseases **41**, 841–847 (2022) | Cite this article

- 2018- 2019 yılları arasında Türkiye'de yapılan çalışma
- 187 karbapenem dirençli *Klebsiella spp.*'den kaynaklanan kan dolaşımı infeksiyonu
- Prospektif, çok merkezli gözlemsel çalışma
- OXA-48 benzeri karbapenemaz oranı %75

Clinical Infectious Diseases
SUPPLEMENT ARTICLE

Epidemiology and Diagnostics of Carbapenem Resistance in Gram-negative Bacteria

Patrice Nordmann,[1,2,3,4] and Laurent Poirel[1,2,3]



- Karbapenem dirençli infeksiyonların, %82.3'ü *A. baumannii* veya *P. aeruginosa* %17.7'si *K. pneumoniae* veya *E. coli*
- Hem *P. aeruginosa* hem de *A. baumannii'den* kaynaklanan kan dolaşımı infeksiyonları solunum yolu infeksiyonlarından daha düşük oranda

Nordmann P and Laurent Poire L. Clin Infect Dis 2019:69 (Suppl 7) • S523

Enterobacterales

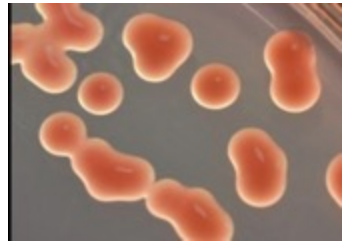


Table 2
Organism type, culture source, infection syndrome, and outcomes among Carbapenem-resistant Enterobacterales (CRE) cases at Emerging Infections Program sites, by epidemiological class, 2012-2015, n = 1499

	Number of cases (%)			*P* value
	All, n = 1499	CA, n = 149	HCA, n = 1350	
Organism type				
Klebsiella pneumoniae	800 (53.4)	28 (18.8)	772 (57.2)	.0008††
Escherichia coli	275 (18.3)	61 (40.9)	214 (15.9)	.1142
Enterobacter cloacae	208 (13.9)	27 (18.1)	181 (13.4)	<.0001
Klebsiella aerogenes	191 (12.7)	32 (21.5)	159 (11.8)	.5039
Klebsiella oxytoca	25 (1.7)	1 (0.7)	21 (1.8)	<.0001
Culture Source				
Urine	1305 (87.1)	146 (97.9)	1159 (85.9)	<.0001§
Blood*	162 (10.8)	3 (2.0)	159 (11.8)	
Other normally sterile site†	32 (2.1)	0 (0.0)	32 (2.4)	
Selected Infection Syndromes‡				
Urinary Tract Infection	1024 (63.7)	123 (82.6)	901 (66.7)	<.0001
Bacteremia/Sepsis	197 (13.1)	4 (2.7)	193 (14.3)	<.0001
Septic Shock	64 (4.3)	0 (0.0)	64 (4.7)	.0020
Pneumonia	34 (2.3)	0 (0.0)	34 (2.5)	.0425
Pyelonephritis	23 (1.5)	4 (2.7)	19 (1.4)	.2769
Vascular Graft Infection	1 (0.1)	1 (0.7)	0 (0.0)	.0994
No infection syndrome documented	218 (14.5)	19 (12.8)	199 (14.7)	.5134
Outcomes				
Hospitalized at the time of, or within 30 days after, the date of incident culture**	908/1490 (61.0)	29/149 (19.5)	879/1341 (65.6)	<.0001
Admission to an intensive care unit on the day of, or within 7 days after, initial culture	316/908 (34.8)	2/29 (6.9)	314/879 (35.7)	.0006
Died within 30 days of date of incident culture	167/1499 (11.1)	4/149 (2.7)	163/1350 (12.1)	.0002
Among cases with a sterile site culture	58/167 (34.7)	0/4 (0.0)	58/163 (35.6)	.2992
Among cases with a urine culture	109/167 (65.3)	4/4 (100.0)	105/163 (64.4)	

2012 ve 2015 yılları arasında yapılan 1.194 hastanın dahil edildiği çalışma

Enterobacterales içerisinde en sık etken *K. pneumoniae*

K. pneumoniae infeksiyonları genellikle sağlık bakım ilişkili

Table 4
Multilocus sequence types, beta-lactamase genes identified, and antimicrobial resistance profiles of community-associated Carbapenem-resistant Enterobacterales isolates that underwent whole genome sequencing analysis at CDC, 2012-2015, n = 12

Organism type*	Carbapenemase gene variants	MLST	Non-carbapenemase beta-lactamase gene variants	Antimicrobial resistance profile†
Enterobacter cloacae complex (n = 6)	None	Novel‡	ACT-70	AMC, AMP, ATM, CFZ, FOX, TZP
	None	108	ACT-55	AMP, ATM, CFZ, FOX, TZP§
	KPC-3	171	ACT-45, OXA-9, SHV-12, TEM-1A	AMC, AMP, ATM, CFZ, FEP, FOX, CIP, LVX, TZP, SXT, TOB
	None	45	TEM-1B	AMC, AMP, ATM, CFZ, FOX, CST, TZP, PMB, SXT
	None	365	None	AMC, AMP, ATM, CFZ, FOX, CST, TZP, PMB
	None	125	ACT-28	AMC, AMP, ATM, CFZ, FOX, CST, TZP, PMB
Escherichia coli (n = 3)	NDM-1	5498	TEM-1A	AMP, CFZ, FEP, FOX, CIP, GEN, LVX, TZP, TET, SXT, TOB§
	None	167	CTX-M-15, OXA-1	AMP, ATM, CFZ, FEP, FOX, CIP, GEN, LVX, TET, SXT
	None	131	CTX-M-15, OXA-1, TEM-1B	AMC, AMP, ATM, CFZ, FEP, FOX, CIP, LVX, TZP, SXT, TOB
Klebsiella pneumoniae (n = 3)	KPC-3	258	SHV-11	AMC, AMP, ATM, CFZ, CIP, LVX, TZP, SXT, TOB
	KPC-3	1737	LEN-17	AMC, AMP, ATM, CFZ, FEP, CIP, LVX, TZP, SXT, TOB
	KPC-3	485	SHV-27	AMC, AMP, ATM, CFZ, FEP, CIP, LVX, TZP, SXT

Enterobacterales karbapenem direnci

Table 3. Major mechanisms of carbapenem resistance in *Enterobacterales*

Mechanism	Acquisition	Determinant
β-lactamases:		
Class A. Serine carbapenemases	MGE	KPC[a] (*n* = 22 variants) IMI (-1,-2) SME[b] GES[b,c] NMC-A[b] FRI-1[b] IMI-1[b] SFC[b] SHV-38[b]
Class B. Metallo-beta-lactamases	MGE	VIM[a] (*n* = 46 variants) NDM[a] (*n* = 16 variants) IMP (*n* = 52 variants) GIM-1[b] SIM[b] SPM[b]
Class C. Cephalosporinase	MGE	CMY-10[b]
Class D. Oxacillinase-type	MGE	OXA-48-like[a] (*n* = 13 variants)
Impermeability (porin lesions)	CM	ompK35

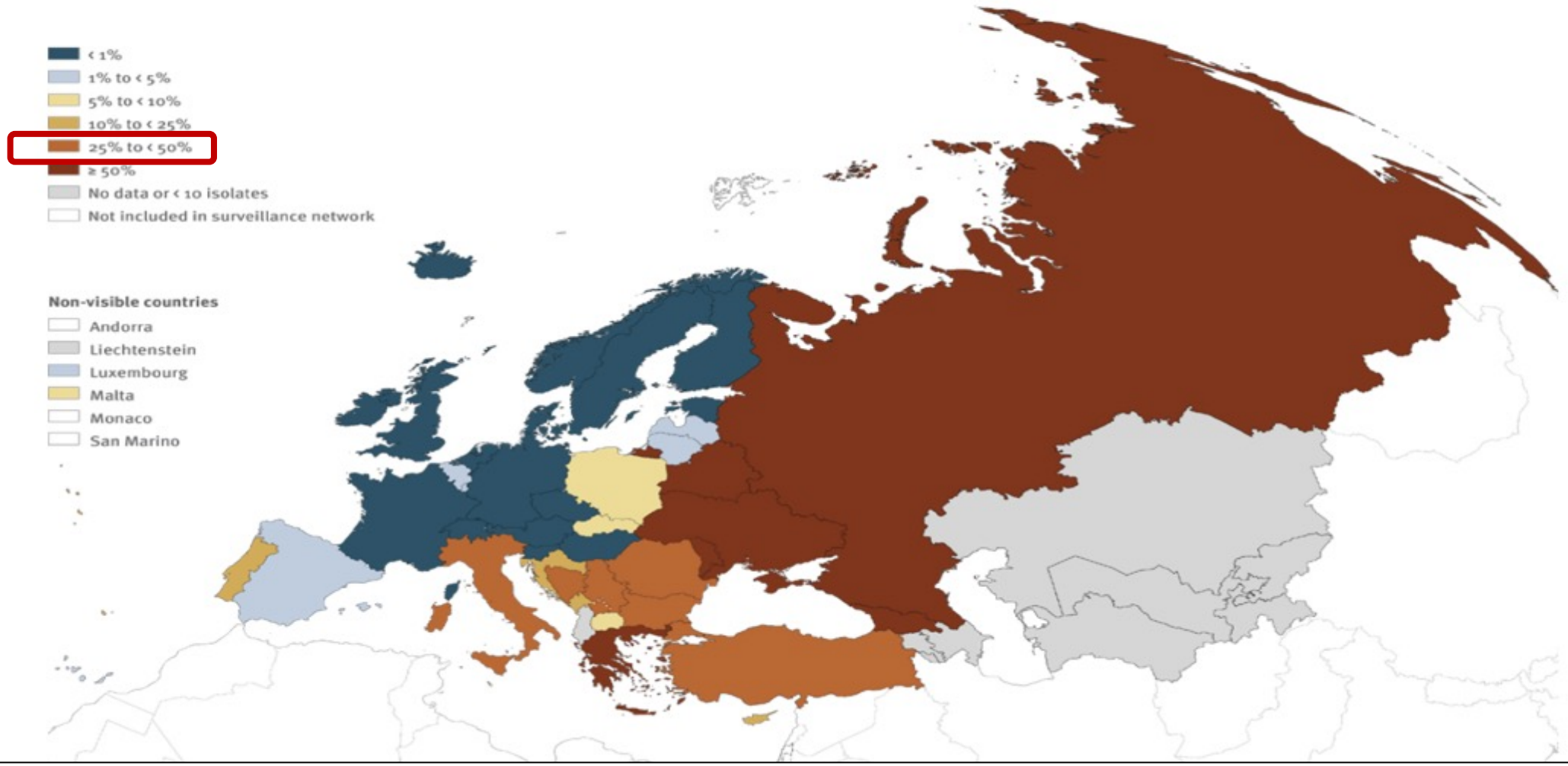
CM, chromosomal mutation; KPC, *Klebsiella* MGE, mobile genetic element; NDM, New D oxacillinase; VIM, Verona-integrated metallop
[a]Most common.
[b]Geographically variable but less common or
[c]Low-level carbapenem hydrolysis.

- Karbapenemazlar
- Porin kaybı
- Efluks pompaları

Species	Main mechanisms of resistance to carbapenems	
	Enzyme-mediated	Non-enzyme-mediated
CR-Enterobacterales	Various carbapenemases (Ambler class A, B, D) ± ESBL or AmpC β-lactamase(s)	Porin (OmpK35, OmpK36) loss (plus ESBL or AmpC β-lactamase [resistant to ertapenem, imipenem]) Multidrug-resistant efflux pump (e.g., AcrAB-TolC system)

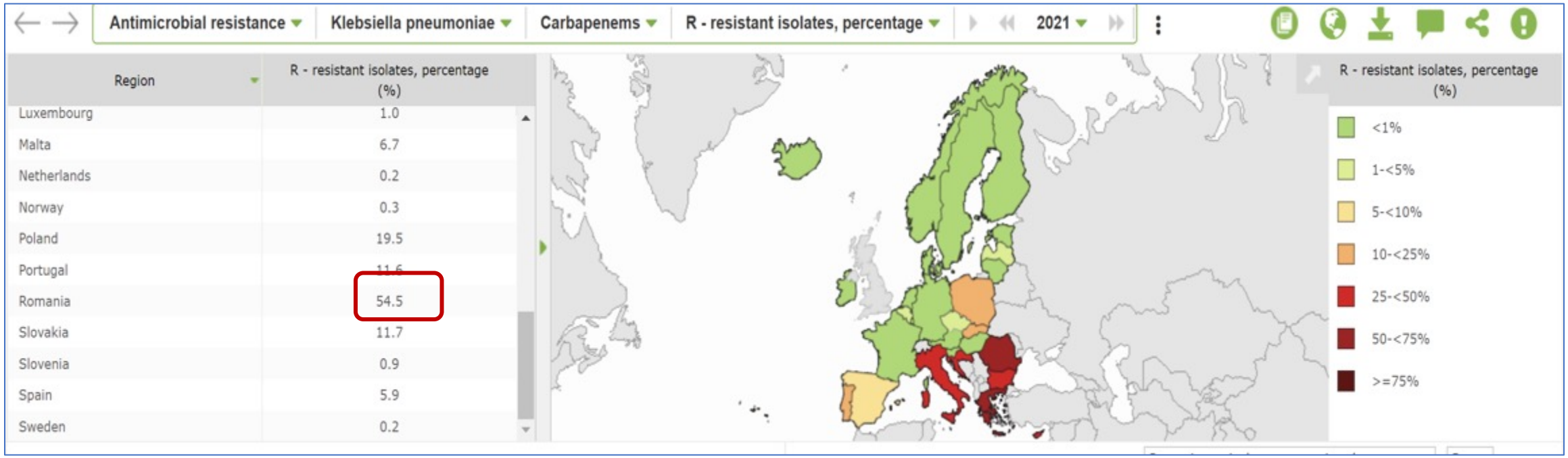
Brink AJ. Curr Opin Infect Dis 2019; 32: 609-16
Jean SS, et al. Front Cell Infect Microbiol. 2022: 15;12:823684

Fig. 5 *K. pneumoniae*: percentage of invasive isolates resistant to carbapenems (imipenem/meropenem), by country/area, WHO European Region, 2020



https://www.ecdc.europa.eu/sites/default/files/documents/Joint-WHO-ECDC-AMR-report-2022.pdf

K. pneumoniae karbapenem direnci



http://atlas.ecdc.europa.eu/public/index.aspx

K. pneumoniae karbapenem direnci

Table 1. Reported Carbapenem Nonsusceptibility or Resistance Rates by Region

Species	Nonsusceptibility or Resistance Rate									
	Asia-Pacific	Ref.	India, Nepal, Pakistan, Vietnam	Ref.	Europe	Ref.	North America	Ref.	Latin America	Ref.
Klebsiella pneumoniae	5%–25%	[50][b]	0%–52%	[26][d]	0.2%–33.4%	[41][b]	3.1%–4.9%	[3][c]	1.3%–28.6%	[56][a]
	1.6%–19.1%	[49][c]	…	…	31.7%–58.6%	[21][c]	12.9%	[55][c]	16.0%	[57][a]
	3.8%	[57][a]	…	…	15.7%	[57][a]	6.0%	[57][a]	…	…
Escherichia coli	0%–3%	[50][b]	0%–34%	[26][d]	0%–7.0%	[41][b]	0.2%–0.4%	[3][c]	0.4%–9.0%	[56][a]
	1.6%–7.1%	[49][c]	…	…	…	…	4.3%	[55][c]	…	…
Enterobacteriaceae (other)	0%	[50][b]	2.7%–21.3%	[26][d]	…	…	2.10%	[55][c]	…	…
	2.4%–32.1%	[49][c]	…	…	…	…	…	…	…	…
	0.4%–12.5%	[48][b]	…	…	…	…	…	…	…	…

Nordmann P and Laurent Poire L. Clin Infect Dis 2019:69 (Suppl 7) • S523

246 Karbapenem dirençli *K. pneumoniae* (CRKp) %13'ünde kolistin de dirençli

Clinical Infectious Diseases

MAJOR ARTICLE

Colistin Resistance in Carbapenem-Resistant *Klebsiella pneumoniae*: Laboratory Detection and Impact on Mortality

Laura J. Rojas,[1,2,3] Madiha Salim,[4] Eric Cober,[5] Sandra S. Richter,[6] Federico Perez,[3,7] Robert A. Salata,[7] Robert C. Kalayjian,[8] Richard R. Watkins,[9,10] Steve Marshall,[3] Susan D. Rudin,[1,3] T. Nicholas Domitrovic,[1,3] Andrea M. Hujer,[1,3] Kristine M. Hujer,[1,3] Yohei Doi,[11] Keith S. Kaye,[4] Scott Evans,[12] Vance G. Fowler Jr,[13,14] Robert A. Bonomo,[1,2,3,7,15,16] and David van Duin[17]; for the Antibacterial Resistance Leadership Group

[1]Department of Medicine, and [2]Department of Molecular Biology and Microbiology, Case Western Reserve University School of Medicine, and [3]Research Service, Louis Stokes Cleveland Department of Veterans Affairs Medical Center, Cleveland, Ohio; [4]Division of Infectious Diseases, Detroit Medical Center, Wayne State University, Michigan; [5]Department of Infectious Diseases, and [6]Department of Laboratory Medicine, Cleveland Clinic, [7]Division of Infectious Diseases and HIV Medicine, Department of Medicine, Case Western Reserve University School of Medicine, and [8]Department of Medicine, MetroHealth Medical Center, Cleveland, Ohio; [9]Department of Internal Medicine, Northeast Ohio Medical University, Rootstown, and [10]Division of Infectious Diseases, Cleveland Clinic Akron General, Akron, Ohio; [11]Division of Infectious Diseases, University of Pittsburgh School of Medicine, Pennsylvania; [12]Department of Biostatistics and the Center for Biostatistics in AIDS Research, Harvard School of Public Health, Boston, Massachusetts; [13]Division of Infectious Diseases, and [14]Duke Clinical Research Institute, Duke University, Durham, North Carolina; [15]Department of Molecular Biology and Microbiology, and [16]Department of Pharmacology, Case Western Reserve University School of Medicine, Cleveland, Ohio; and [17]Division of Infectious Diseases, University of North Carolina, Chapel Hill

Background. Polymyxins including colistin are an important "last-line" treatment for infections caused by carbapenem-resistant *Klebsiella pneumoniae* (CRKp). Increasing use of colistin has led to resistance to this cationic antimicrobial peptide.

Methods. A cohort nested within the Consortium on Resistance against Carbapenems in *Klebsiella pneumoniae* (CRACKLE) was constructed of patients with infection, or colonization with CRKp isolates tested for colistin susceptibility during the study period of December, 2011 to October, 2014. Reference colistin resistance determination as performed by broth macrodilution was compared to results from clinical microbiology laboratories (Etest) and to polymyxin resistance testing. Each patient was included once, at the time of their first colistin-tested CRKp positive culture. Time to 30-day in-hospital all-cause mortality was evaluated by Kaplan-Meier curves and Cox proportional hazard modeling.

Results. In 246 patients with CRKp, 13% possessed ColR CRKp. ColR was underestimated by Etest (very major error rate = 35%, major error rate = 0.4%). A variety of rep-PCR strain types were encountered in both the ColS and the ColR groups. Carbapenem resistance was mediated primarily by bla_{KPC-2} (46%) and bla_{KPC-3} (50%). ColR was associated with increased hazard for in-hospital mortality (aHR 3.48; 95% confidence interval, 1.73-6.57; $P < .001$). The plasmid-associated ColR genes, *mcr-1* and *mcr-2* were not detected in any of the ColR CRKp.

Conclusions. In this cohort, 13% of patients with CRKp presented with ColR CRKp. The apparent polyclonal nature of the isolates suggests *de novo* emergence of ColR in this cohort as the primary factor driving ColR. Importantly, mortality was increased in patients with ColR isolates.

K. pneumoniae kolistin direnci

International Journal of Antimicrobial Agents ■■ (2016) ■■–■■

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International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag

Epidemiology of infections caused by polymyxin-resistant pathogens

Helen Giamarellou [a,b,*]

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- İtalya……2011'de %27.5 ve 2013-2014 yıllarında %43
- Güney Kore ……%6.8
- 31 merkezin sonucu……%5.4-%9.7

2013 EARS-Net verisi: Tüm suşlarda direnç %8.8

karbapenemaz pozitif suşlarda kolistin direnci %32

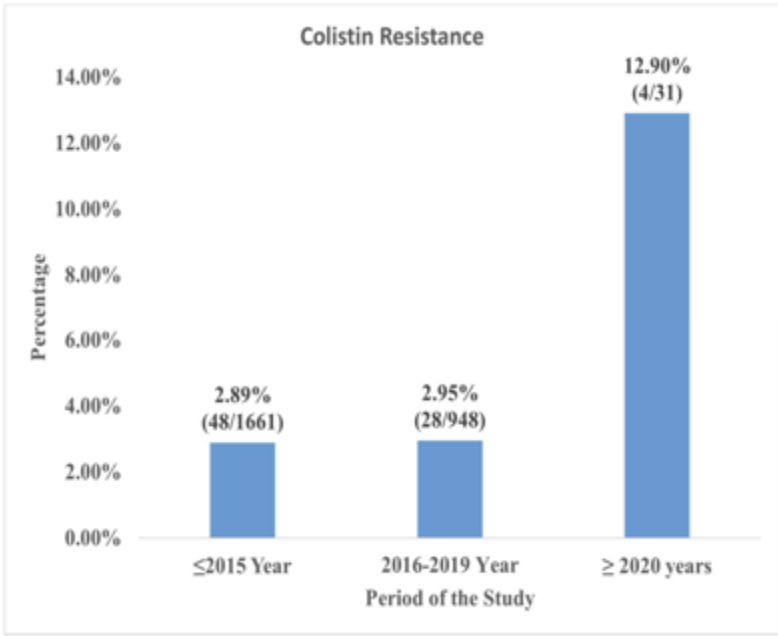
pathogens

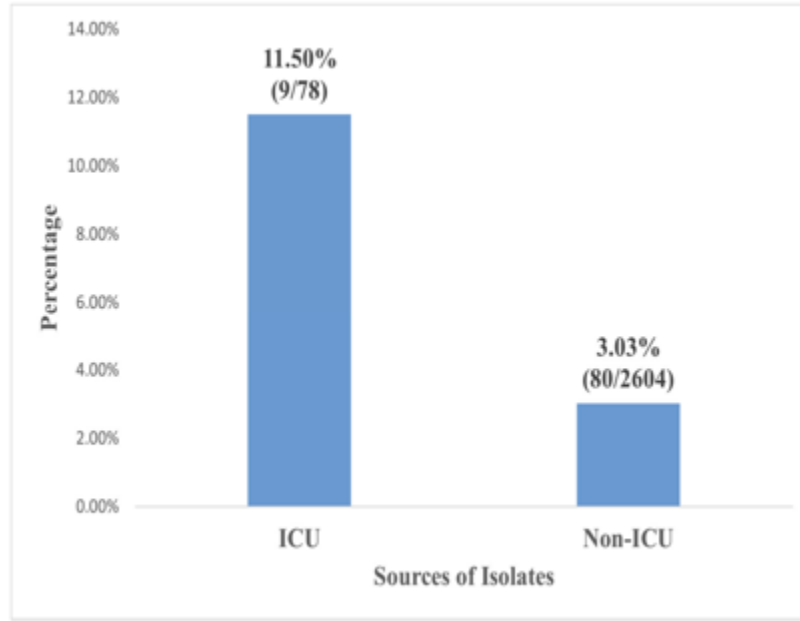
MDPI

Systematic Review

Global Prevalence of Colistin Resistance in *Klebsiella pneumoniae* from Bloodstream Infection: A Systematic Review and Meta-Analysis

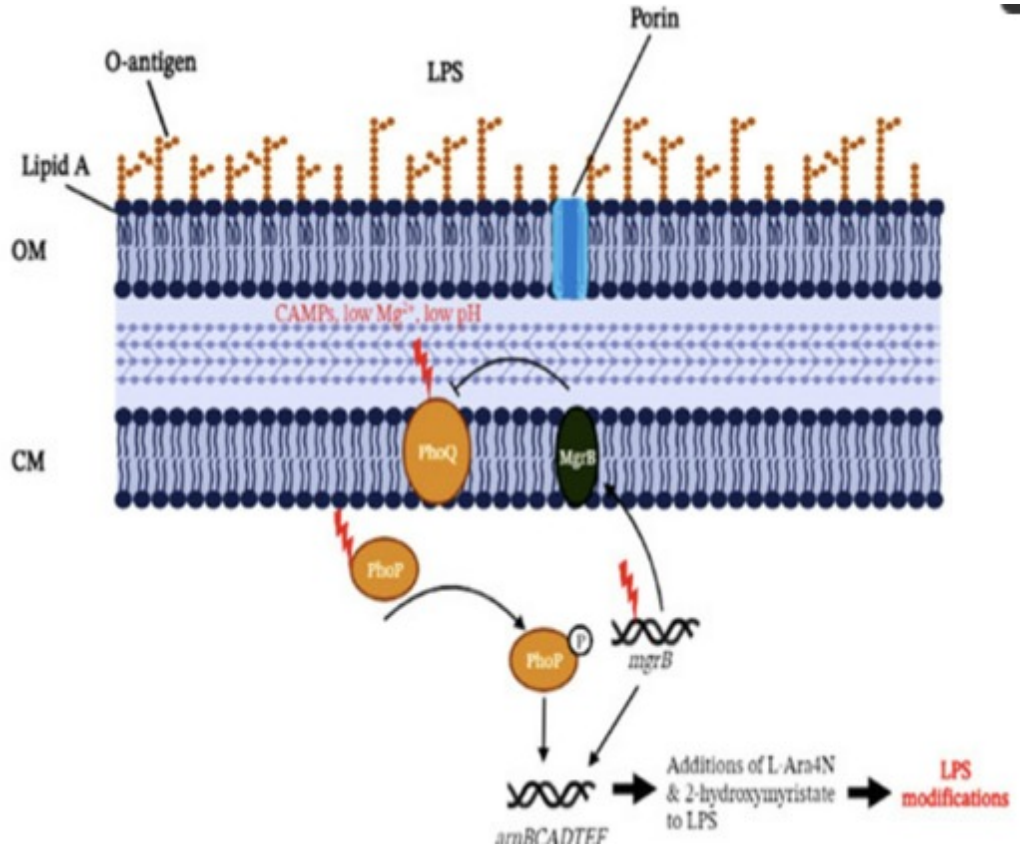
Leonard Ighodalo Uzairue [1,2,*], Ali A. Rabaan [3,4,5], Fumilayo Ajoke Adewumi [6], Obiageli Jovita Okolie [7], Jamiu Bello Folorunso [8], Muhammed A. Bakhrebah [9], Mohammed Garout [10], Wadha A. Alfouzan [11,12], Muhammad A. Halwani [13], Aref A. Alamri [14], Shaima A. Halawani [14], Fatimah S. Alshahrani [15], Abdulkarim Hasan [16,17], Abbas Al Mutair [18,19,20,21], Saad Alhumaid [22], Johnson Etafo [23], Idorenyin Utip [24], Ikenna Maximillian Odoh [25] and Nkolika S. Uwaezuoke [26]





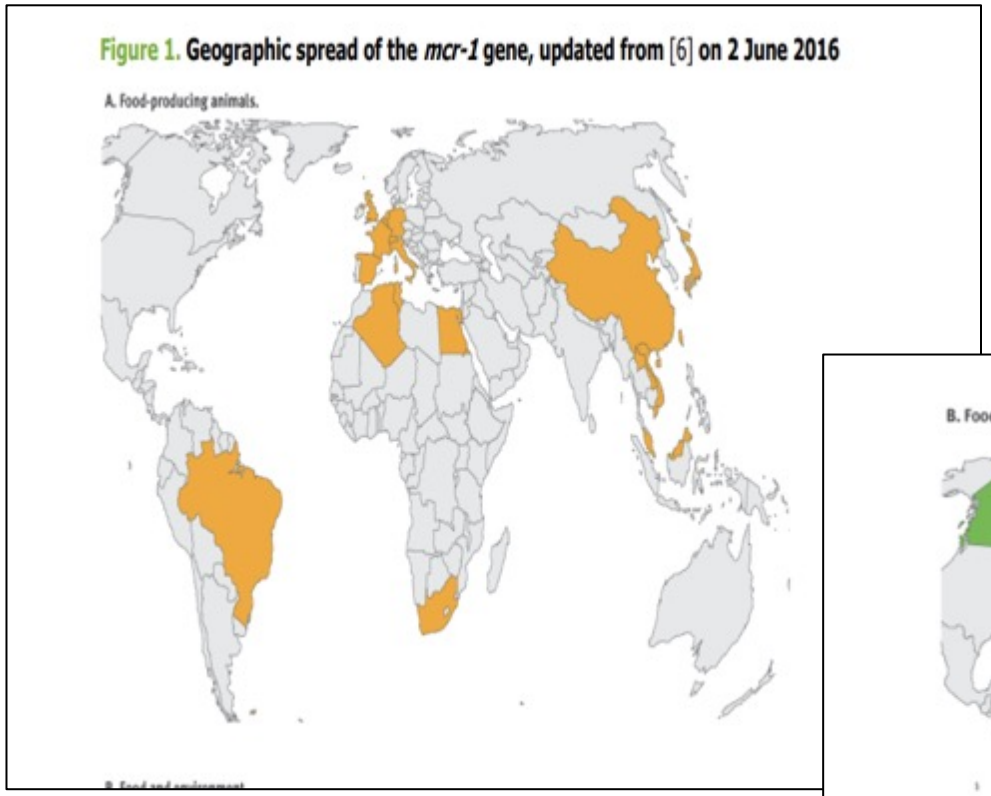
Kolistin direnci

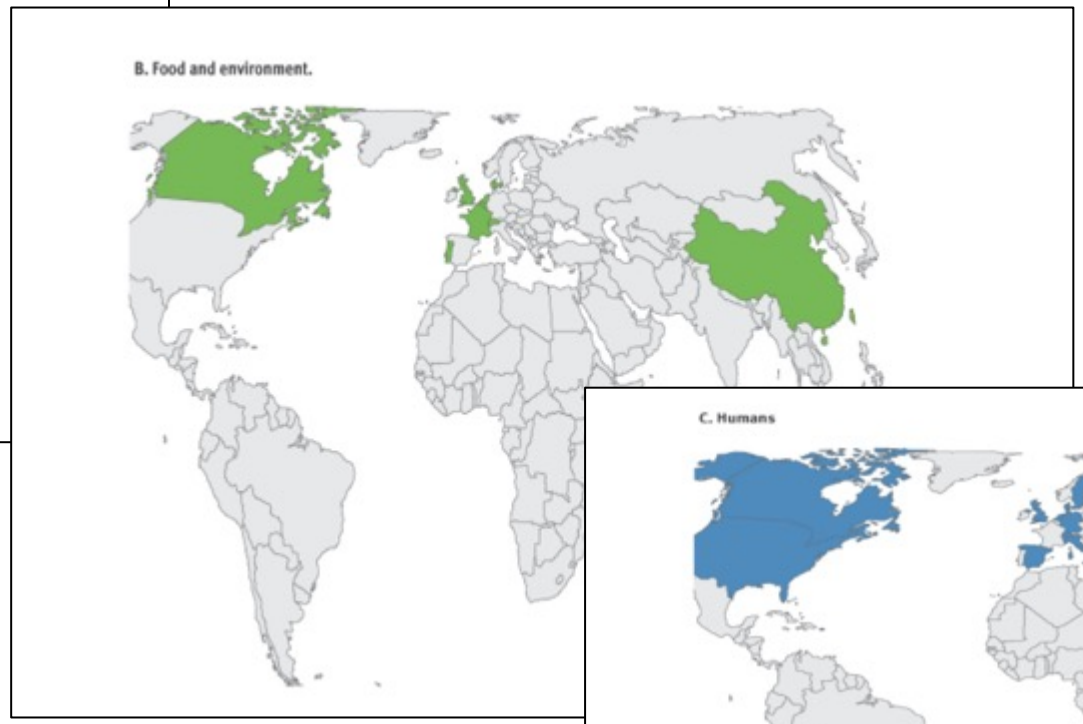
- **Lipid A'nın negatif yüklü fosfat grubunun pozitif yüklü L-Ara4-N ve pEtN ile modifikasyonu**
- LPS biyosentezinde mutasyonlar
- Efluks pompa sistemlerinde aşırı ekspresyonu
- Dış membran porinlerinde modifikasyon

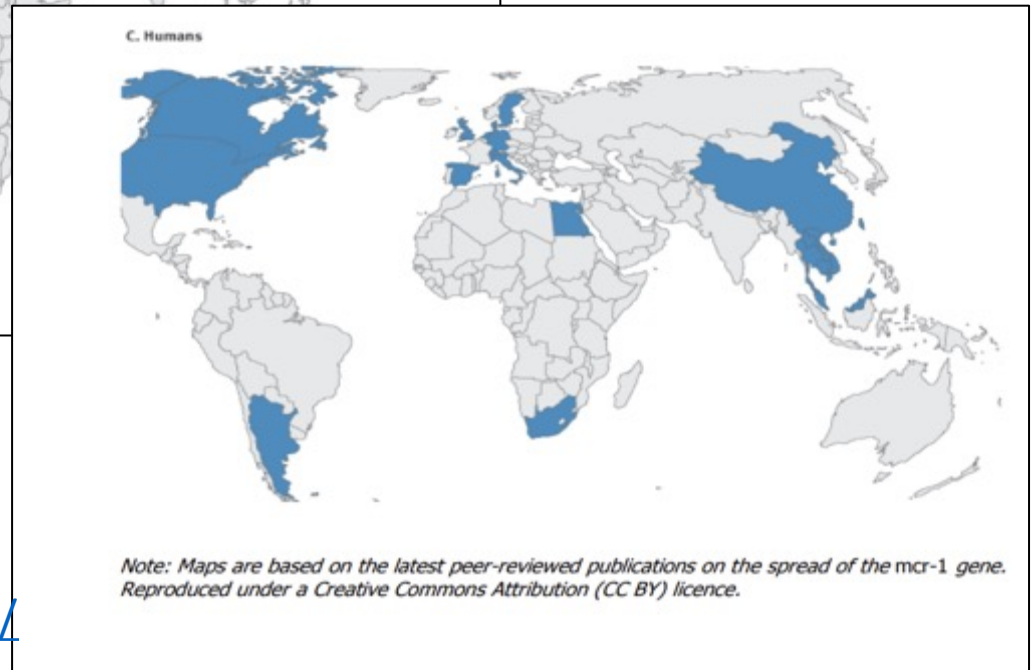


Cells. 2022 Sep 26;11(19):2995.

Plazmid kaynaklı mcr-1 geni







Hayvanlarda insanlardan 600 kat fazla kolistin tüketimi !!

https://www.ecdc.europa.eu/sites/default/files/media/en/publications/

> Epidemiol Mikrobiol Imunol. 2022 Summer;71(2):86-92.

Colistin resistance and heteroresistance in Klebsiella pneumoniae & Escherichia coli clinical isolates from intensive care units

M A Meheissen, S M Hendawy, F S Shabaan, A M Elmenshawy, R A Harfoush

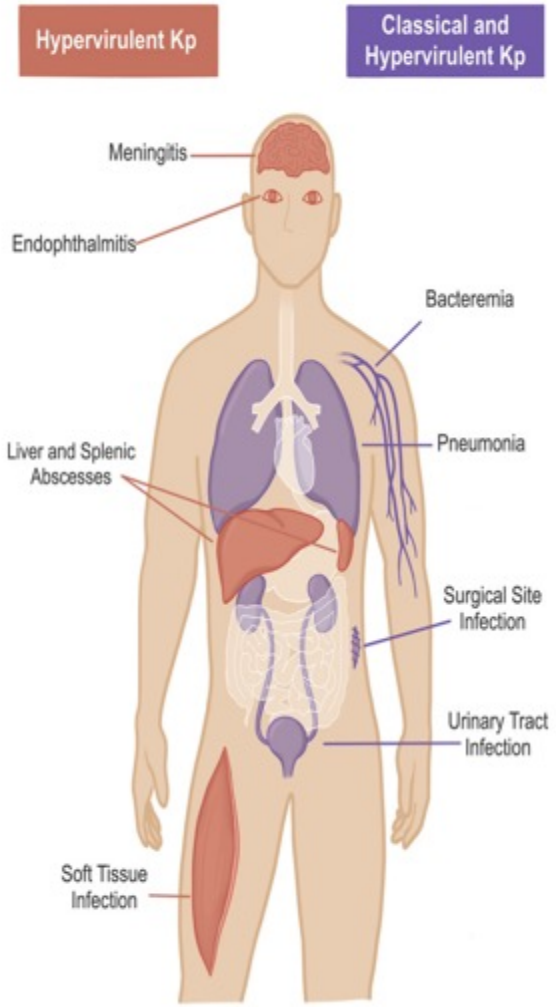
PMID: 35940862

- 70 kolistin dirençli, 30 kolistin duyarlı *K. pneumoniae* ve *E. coli* suşu
- Kolistin duyarlı *K. pneumoniae* suşlarının %23.3'ü kolistin için heteroresistan

- Standart test yöntemleriyle **duyarlı** olarak belirlenir
- Ancak **dirençli subpopulasyon** varlığı

Hipervirulan *K. pneumoniae*

- İlk olarak 1980'lerin sonlarında Tayvan'da karaciğer apsesi olan hastada saptanmış
- Genellikle genç ve sağlıklı bireylerde karaciğer apsesi, pnömoni, menenjit ve endoftalmi etkeni
- Toplum ve hastane kaynaklı infeksiyonlara yola açar
- Morbidite ve mortalite oranı yüksek



Xuemei Yang, et el. Emerg Microbes Infect. 2022 Dec;11(1):841-849.

Gonzalez-Ferrer S et al.Infect Immun. 2021 Mar 17;89(4):e00693-20.

Hipervirulan *K. pneumoniae*

- ‘String test’ sonucu pozitif, hipermukoviskoz fenotip (rmpA ve rmpA2 genleri)
- Sideroforlar aracılığıyla artmış demir absorbsiyonu (aerobaktin, enterobaktin, yersiniabactin, salmochelin)

Huang Y et al.J Hosp Infect . 2023 Jan;131:70-80.

Kumabe A, et al. QJM. 2014;107(12):1053.

Hipervirulan *K. pneumoniae*

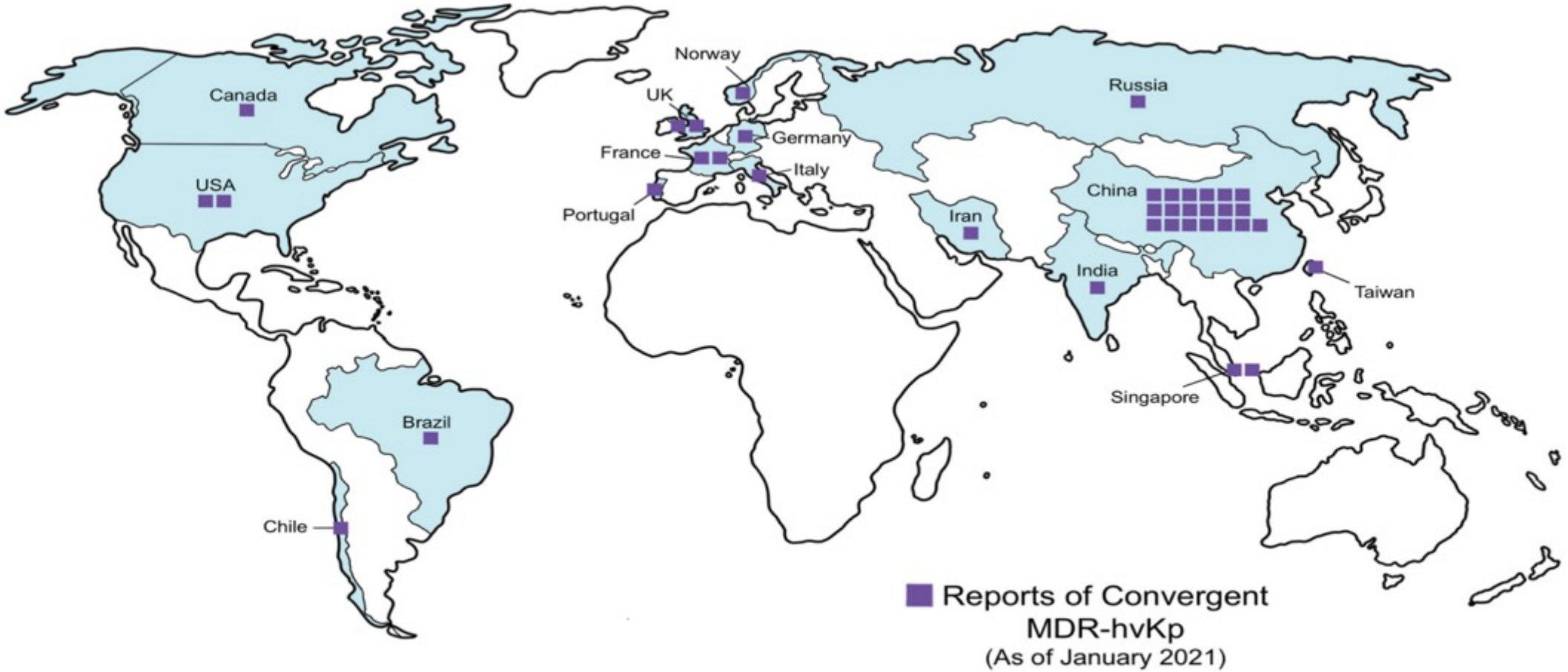


FIG 2 Global reports of infections with multidrug-resistant and hypervirulent *K. pneumoniae* (MDR-hvKp). Countries where convergent MDR-hvKp infections have been reported are shaded blue, and the number of reports from each country is indicated with purple squares. Reports represented are current as of January 2021.

Gonzalez-Ferrer S et al.Infect Immun. 2021;89(4):e00693-20.

Özgün Çalışma/Original Article Mikrobiyol Bul 2023;57(1):30-44/doi: 10.5578/mb.20239903

Geliş Tarihi (Received): 04.07.2022 • Kabul Ediliş Tarihi (Accepted): 15.10.2022

Klebsiella pneumoniae Hipervirülan Kapsül Genotiplerinin Antibiyotik Duyarlılığı ve Beta-Laktamaz Genleri ile İlişkisi

Relationship of Hypervirulent Capsular Genotypes of *Klebsiella pneumoniae* with Antibiotic Susceptibility and Beta-Lactamase Genes

Duygu DALĞIÇ(ID), Tülay KANDEMİR(ID), Ali ÜÇKAYABAŞI(ID), Toğrul NAĞIYEV(ID)

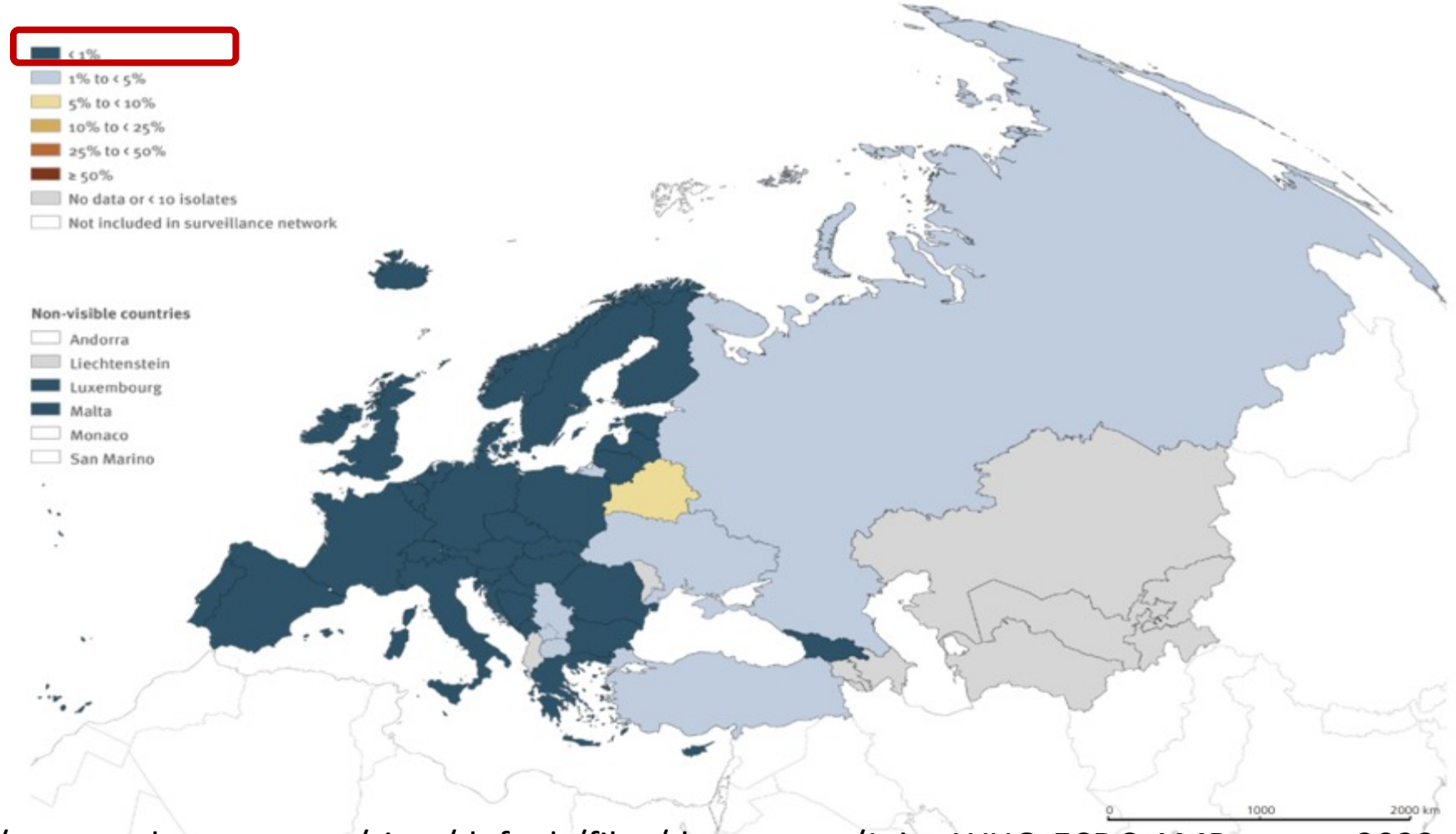
Çukurova Üniversitesi Tıp Fakültesi, Tıbbi Mikrobiyoloji Anabilim Dalı, Adana.

Çukurova University Faculty of Medicine, Department of Medical Microbiology, Adana, Türkiye.

- Adana Şehir Hastanesi Mikrobiyoloji Laboratuvarı'nda elde edilen 180 *K. pneumoniae* suşu
- 11 (%6.1)'i hipervirülan kapsül genotiplerine (K1, K2, K5, K20, K54 ve K57) sahip

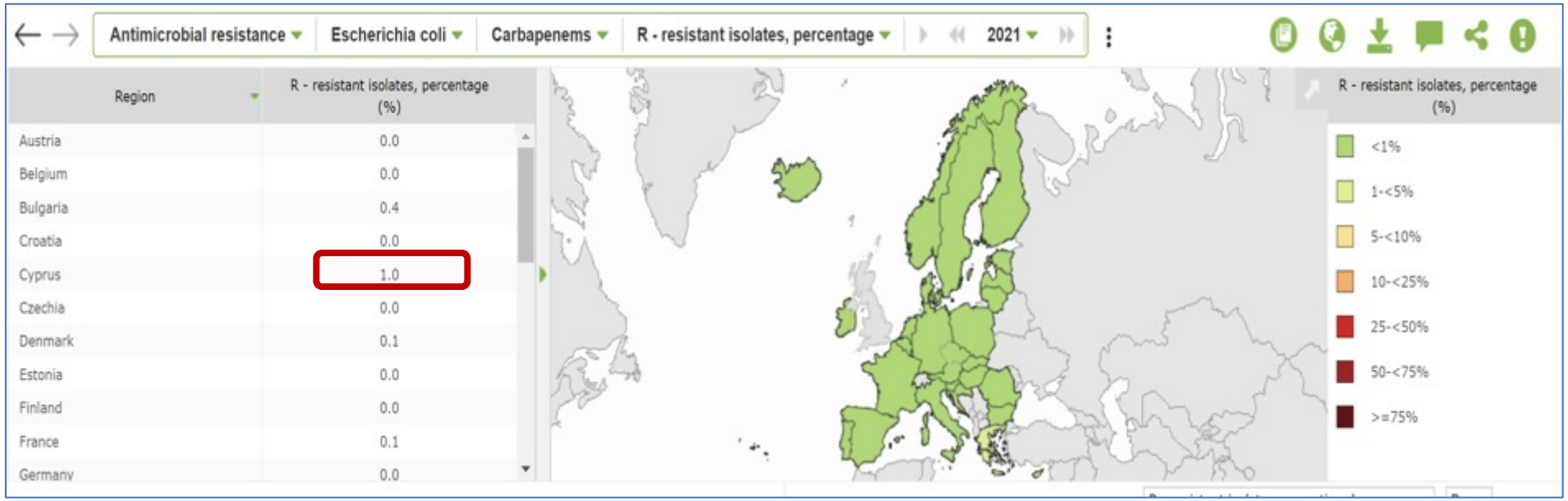
E. coli karbapenem direnci

Fig. 3 *E. coli*: percentage of invasive isolates resistant to carbapenems (imipenem/meropenem), by country/area, WHO European Region, 2020



https://www.ecdc.europa.eu/sites/default/files/documents/Joint-WHO-ECDC-AMR-report-2022.pdf

E. coli karbapenem direnci



http://atlas.ecdc.europa.eu/public/index.aspx

Original Article
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DOI: https://doi.org/10.1590/fst.82321

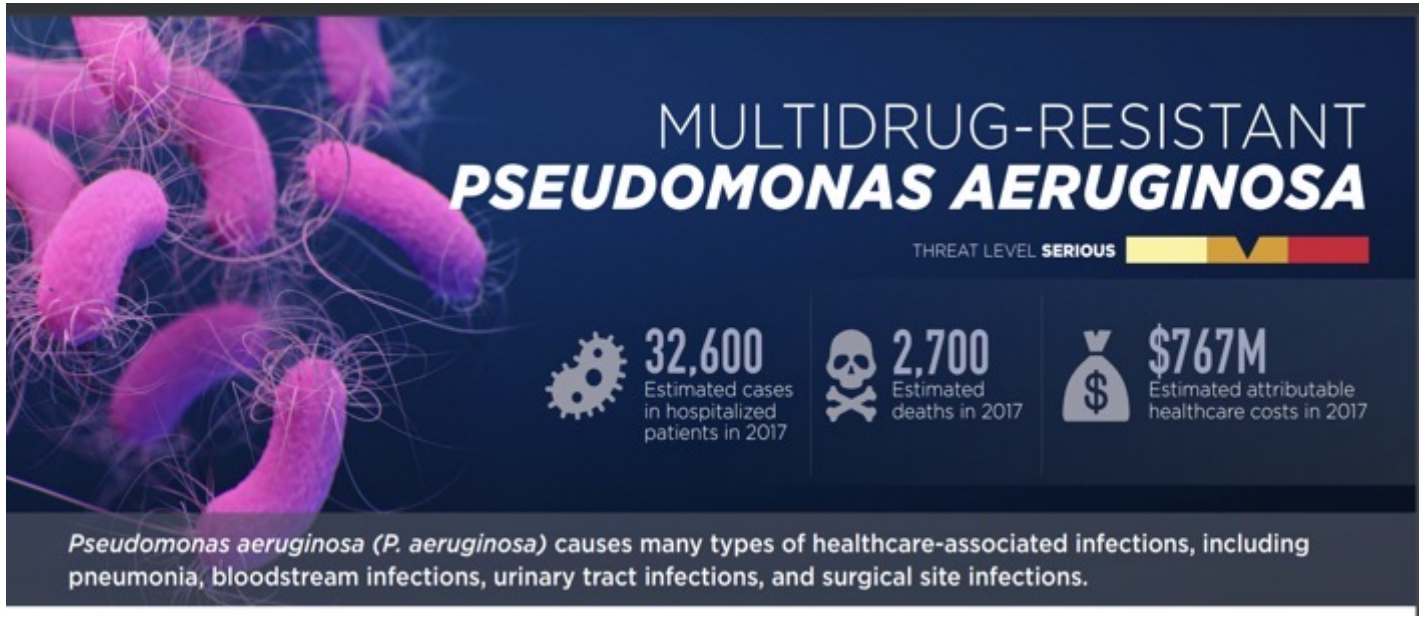
Study on molecular mechanism of carbapenem- and colistin-resistance in *Escherichia coli*

Na LV[1], Xiumei JIA[2], Weijuan YU[1]*

Table 1 Presence of colistin resistant *E. coli* isolates from 2016 to 2018.

Year	No. of strains tested	No. of positive strains	Positive rate(%)
2016	298	1	0.34%
2017	351	1	0.28%
2018	379	2	0.53%

2016 ve2018 yılları arasında Çin'de 1028 *E. coli* suşu ile yapılan çalışma



U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

- *P. aeruginosa* özellikle hastanelerde ve immun sistem baskılandığında infeksiyon yapar
- Pnömoni, kan dolaşım sistemi infeksiyonları, üriner sistem ve cerrahi alan infeksiyonlarına neden olur
- Karbapenem direnci özellikle karbapenemaz yapan mobil genetik elemanlar ile taşınır
- Mobil genetik elenmanlar hastane ortamında bakterinin kolayca yayılmasını sağlar

P. aeruginosa karbapenem direnci

Table 1. Major mechanisms of carbapenem resistance in *Pseudomonas aeruginosa*

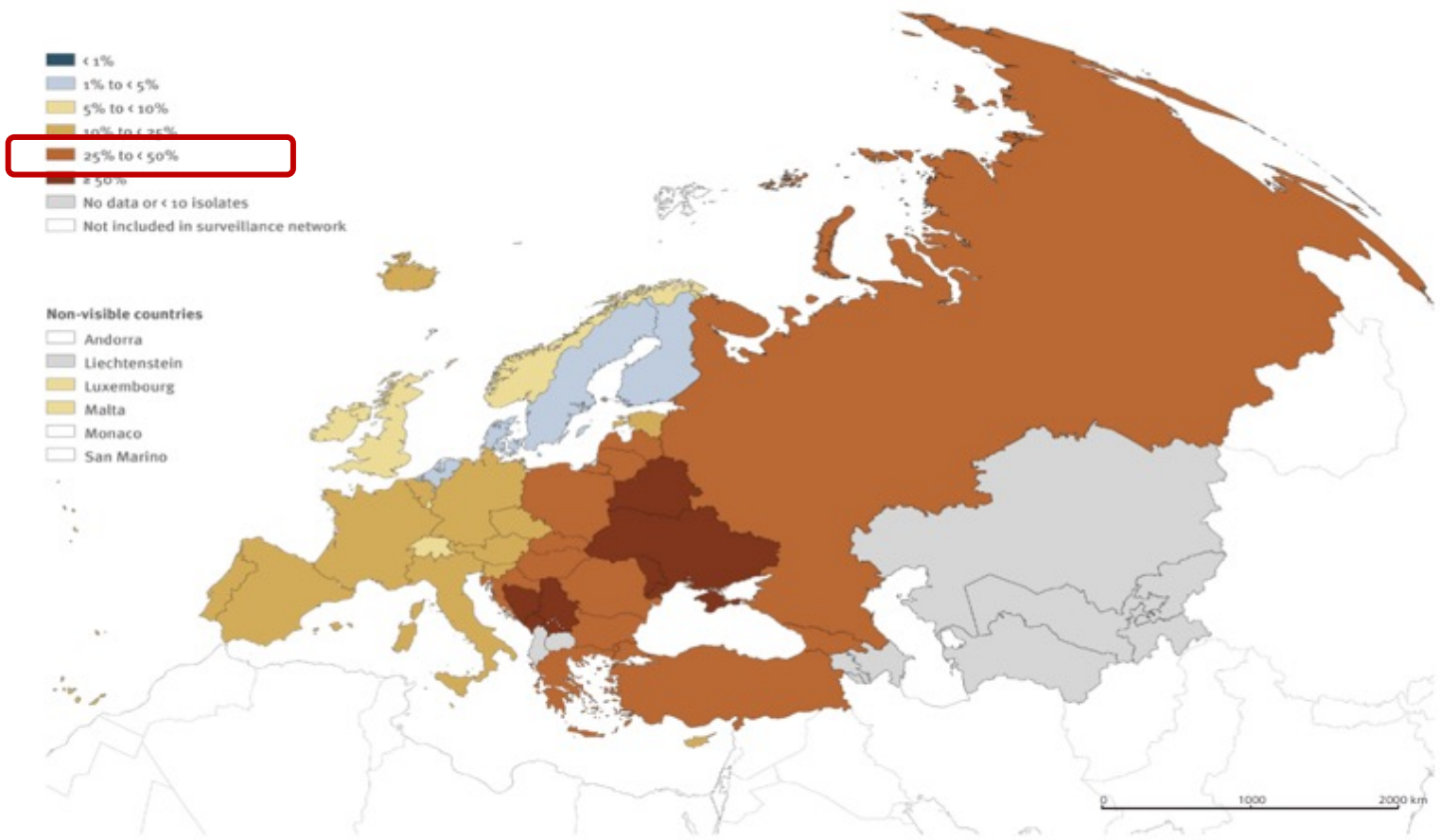
Mechanism	Genetic event	Determinant
β-lactamases:		
Class A. Serine carbapenemases	MGE	KPC[a]
Class B. Metallo-β-lactamase	MGE	VIM[b] ($n = 24$ variants) IMP[b] ($n = 33$ variants) SIM[a] GIM[a] KHM[a] SPM[a] AIM[a] SMB[a] TMB[a] FIM[a] SIM[a] DIM[a] NDM[a]
Class D. Oxacillinase-type	MGE	OXA-40[a] OXA-198[a]
Impermeability	CM	Loss of OprD
Efflux pumps	CM	MexAB-OprM MexEF-OprN MexCD-OprJ

CM, chromosomal mutation; KPC, *Klebsiella pneumoniae* carbapenemase; MGE, mobile genetic element; NDM, New Delhi metallo-β-lactamase; OXA, oxacillinase; VIM, Verona-integrated metalloprotease.
[a]Geographically variable but less common or rare and sporadic.
[b]Most common.

- β-laktamaz üretimi
- Permeabilitede azalma
- Efluks pompaları

Brink AJ. Curr Opin Infect Dis 2019; 32: 609-16
Codjoe F, et al. Med Sci (Basel). 2017 Dec 21;6(1):1.

Fig. 6 *P. aeruginosa*: percentage of invasive isolates with resistance to carbapenems (imipenem/meropenem), by country/area, WHO European Region, 2020

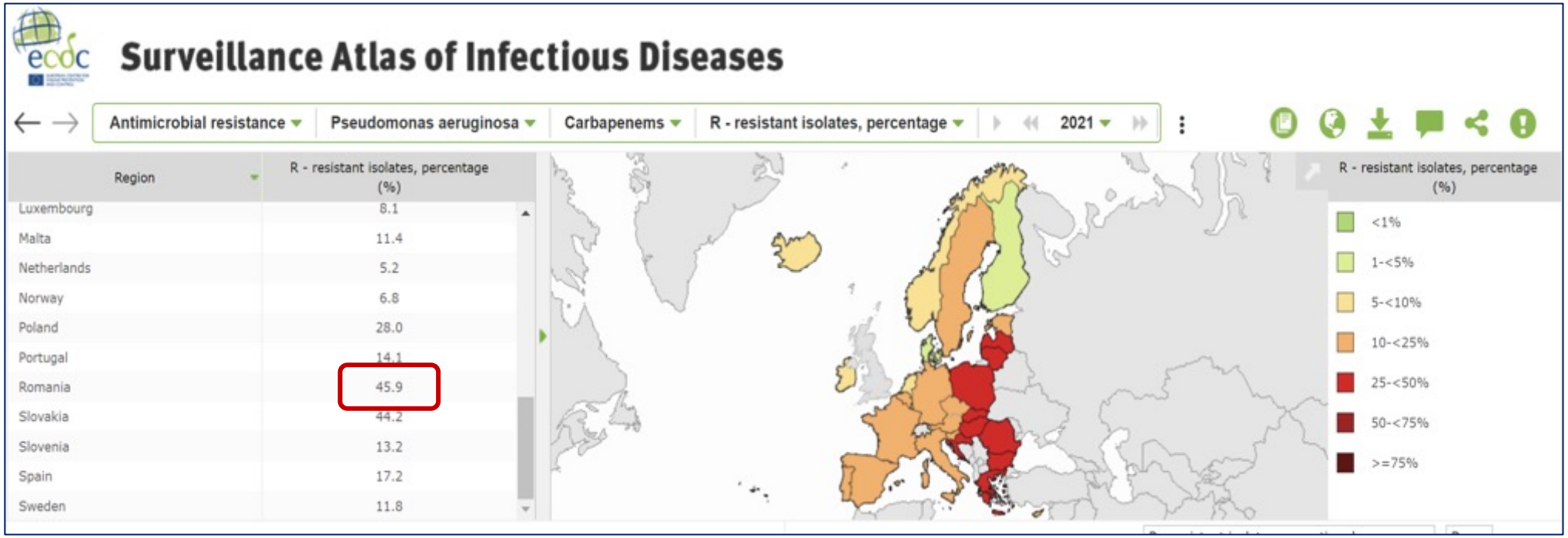


Note: data for Serbia and Kosovo (All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999)) were combined for this map. Data for the United Kingdom for 2020 do not include Scotland and Wales.

Data sources: 2020 data from the Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR, ©WHO 2021. All rights reserved.) and 2020 data from the European Antimicrobial Resistance Surveillance Network (EARS–Net, ©ECDC 2021).
Map production: ©WHO.

https://www.ecdc.europa.eu/sites/default/files/documents/Joint-WHO-ECDC-AMR-report-2022.pdf

P. aeruginosa karbapenem direnci



P. aeruginosa karbapenem direnci

Table 1. Reported Carbapenem Nonsusceptibility or Resistance Rates by Region

	Nonsusceptibility or Resistance Rate									
Species	Asia-Pacific	Ref.	India, Nepal, Pakistan, Vietnam	Ref.	Europe	Ref.	North America	Ref.	Latin America	Ref.
Pseudomonas aeruginosa	17%–50%	[50][b]	…	…	0%–35.6%	[41][b]	10.3%–19.4%	[3][c]	64.6%	[51][c]
	25.4%–34.6%	[49][c]	…	…	24.2%–56.4%	[21][c]	58.5%	[55][c]	14%–57%	[52][d]
	10.3%–46.7%	[48][b]	…	…	14.4%	[57][a]	26.1%	[57][a]	38.1%–45.8%	[56][a]
	16.8%	[57][a]	…	…						

Nordmann P and Laurent Poire L. Clin Infect Dis 2019:69 (Suppl 7) • S523

P. aeruginosa'da imipenem direnç oranları

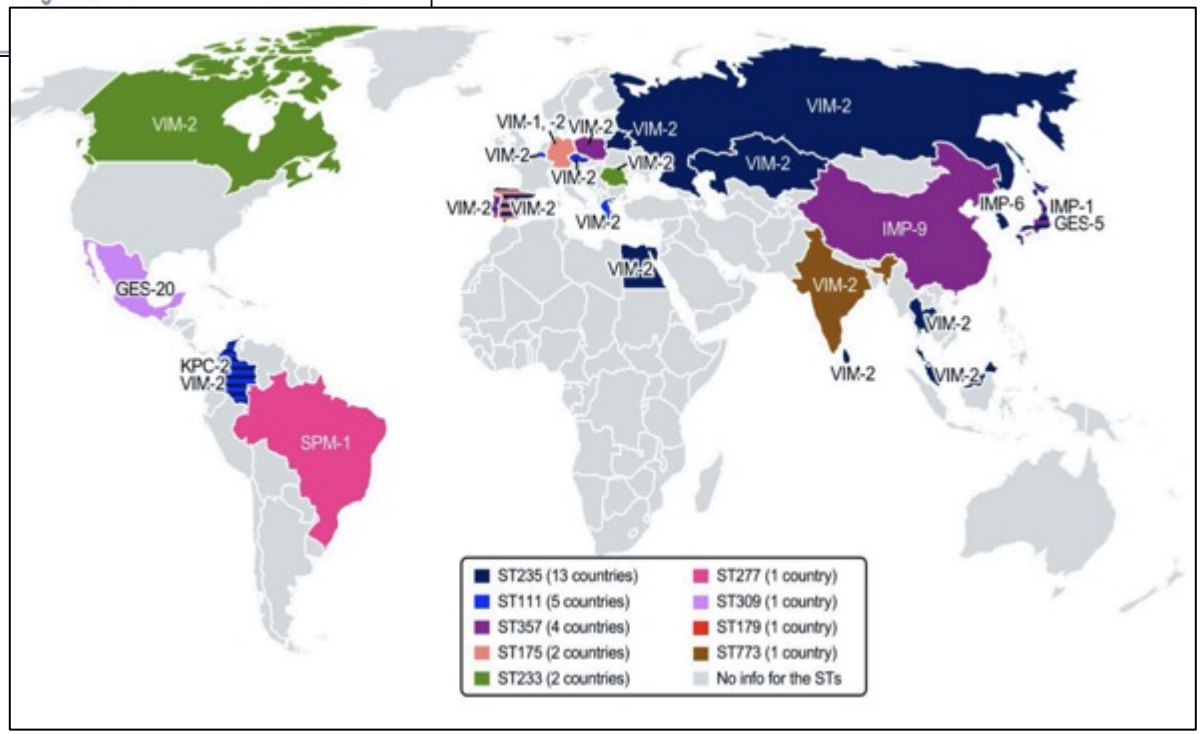
Yoon E_J, et al. Front Microbiol. 2021; 12: 614058.

P. aeruginosa karbapenem direnci

TABLE 1 | Rates of gene(s) encoding carbapenemases among isolates of carbapenem-resistant (CR) Enterobacterales, CR- *Pseudomonas aeruginosa* and CR-*Acinetobacter baumannii* complex in different surveillances.

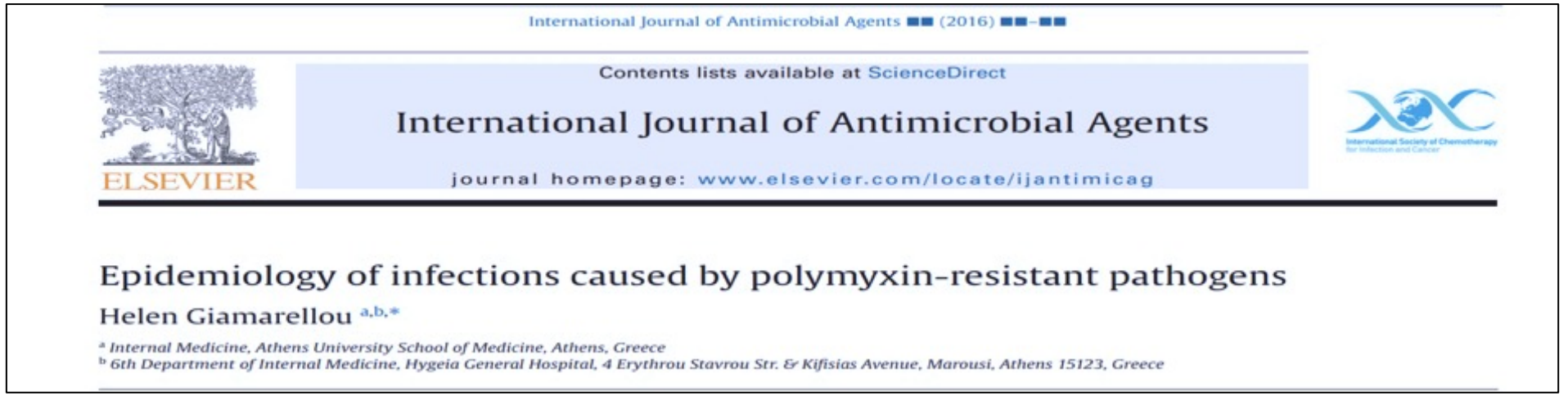
Surveillance	Rates (%) of gene(s) encoding carbapenemase(s)	Main carbapenemase(s)	Country	Study period
CR-*P. aeruginosa*				
Wang et al., 2010	8.5	IMP-9, VIM-2	China	2006–2007
Kao et al., 2016	6.4	VIM-3, VIM-2, OXA-10	Taiwan	2000–2010
McCracken et al., 2019	4.3	GES-5, VIM-2, VIM-4	Canada	2007–2016
Schäfer et al., 2019	30.6	VIM-2	German	2015–2017
Kateete et al., 2016	32	VIM	Uganda	2007–2009
Moubareck et al., 2019	32	VIM		

Jean SS, et al. Front Cell Infect Microbiol. 2022: 15;12:823684



Yoon E_J, et al. Front Microbiol. 2021; 12: 614058.

P. aeruginosa kolistin direnci



International Journal of Antimicrobial Agents ■■ (2016) ■■–■■

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Epidemiology of infections caused by polymyxin-resistant pathogens

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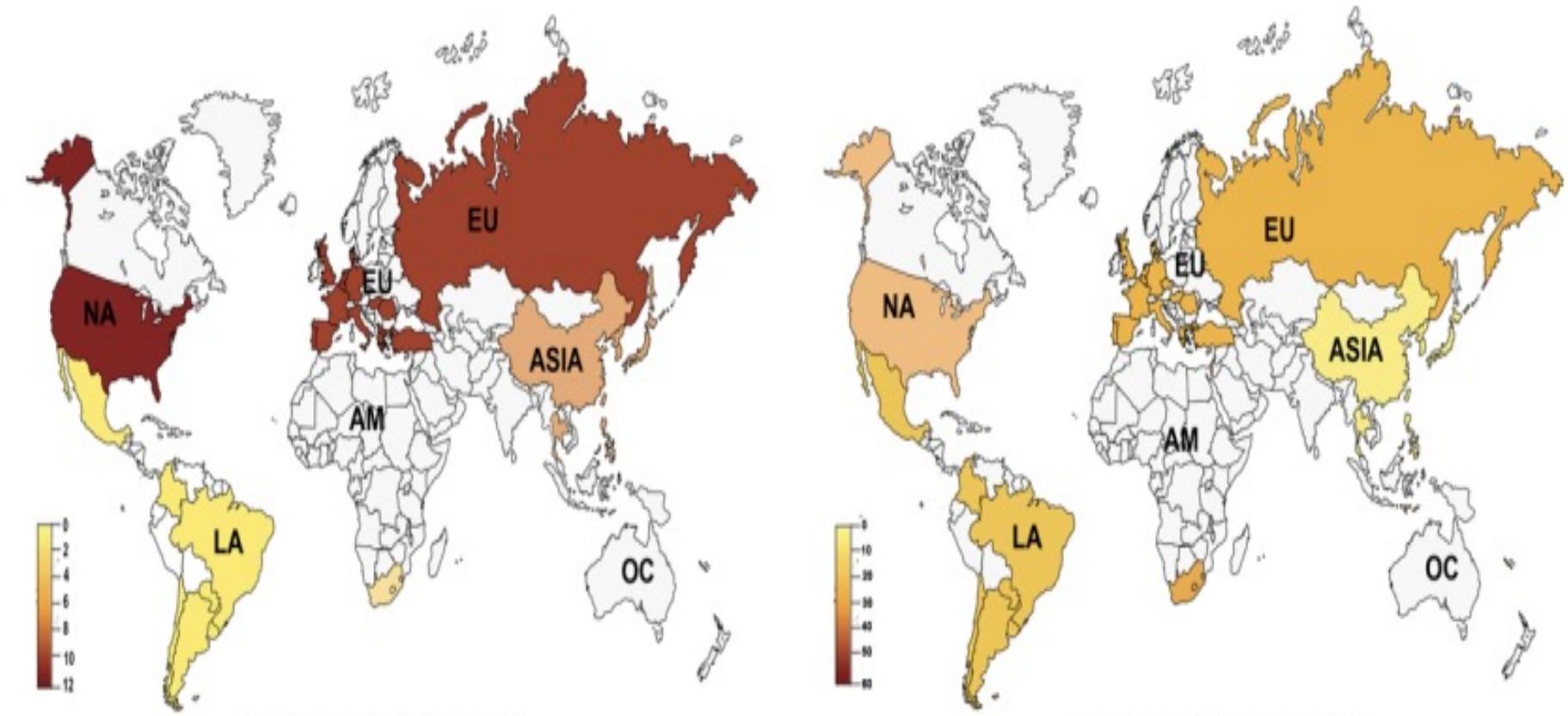
[b] 6th Department of Internal Medicine, Hygeia General Hospital, 4 Erythrou Stavrou Str. & Kifisias Avenue, Marousi, Athens 15123, Greece

- İran……2012-2013 yılları 352 suşta direnç %3.8
- Yunanistan…… 2011-2012 yılları 881 suşta direnç %6.3
- 31 merkez…… 2011-2012 yılları 2191 suşta direnç %0.2

Global trends of antimicrobial susceptibility to ceftaroline and ceftazidime–avibactam: a surveillance study from the ATLAS program (2012–2016)



Seftazidime–avibaktam duyarlılığında azalma !

Karbapenem direçli *K. pneumoniae'da* (%88.4–81.6)

Karbapenem dirençli *P. aeruginosa*'da (%89.6–72.7)

Zhang et al. Antimicrob Resist Infect Control (2020) 9:166

Acinetobacter baumanii

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

- Karbapenem dirençli *A. baumanii* infeksiyonları sıklıkla yoğun bakım ünitelerinde ortaya çıkar
- Pnömoni, yara yeri infeksiyonu, kan dolaşımı ve üriner sistem infeksiyonlarına neden olur

A. baumanii karbapenem direnci

Table 2. Major mechanisms of carbapenem resistance in *Acinetobacter baumannii*

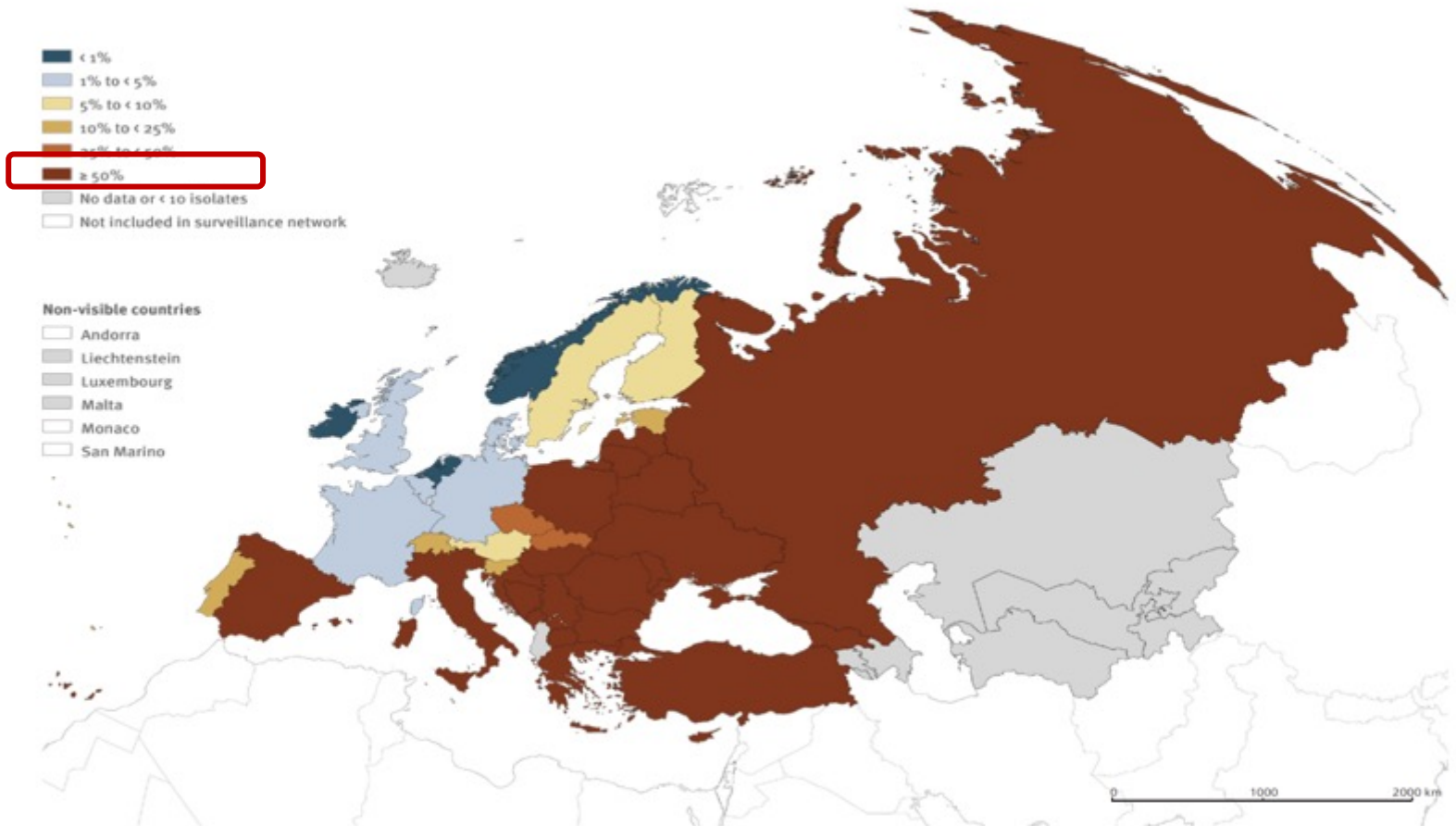
Mechanism	Acquisition	Determinant
β-lactamase:		
Class A. Serine carbapenemases	MGE	KPC[a]
Class B. Metallo-β-lactamases	MGE	VIM (-1, -2, -3, -4, and -11) SIM-1 IMP (-1, -2, -4, -5, -6, -8, -10, -11, and -19) NDM (-1, -2)
Class D. Oxacillinase-type	MGE	OXA-23 cluster: (OXA-23, -27 and -49) OXA-24/40 cluster (OXA-25, -26, -40 and -72) OXA-58 OXA-51 cluster ($n = 14$ variants) OXA-48[a] OXA-235
	CM	High-level OXA-51
Impermeability	CM	Functional loss of porins CarO, Omp 33–36 and OprD homolog
Efflux pumps	CM	AdeABC
Altered penicillin-binding proteins	CM	Variable binding

CM, chromosomal mutation; KPC, *Klebsiella pneumoniae* carbapenemase; MGE, mobile genetic element; NDM, New Delhi metallo-β-lactamase; OXA, oxacillinase; VIM, Verona-integrated metalloprotease.
[a]Rare.

- Karbapenemaz (Ambler sınıf B, D) yapımı ve sınıf C sefalosporinazın aşırı üretimi
- Permeabilitede bozulma
- Efluks pompaları (AdeABC,..gibi)
- PBP'lerde değişiklik

Brink AJ. Curr Opin Infect Dis 2019; 32: 609-16
Jean SS, et al. Front Cell Infect Microbiol. 2022: 15;12:823684

Fig. 7 *Acinetobacter* spp.: percentage of invasive isolates with resistance to carbapenems (imipenem/meropenem), by country/area, WHO European Region, 2020

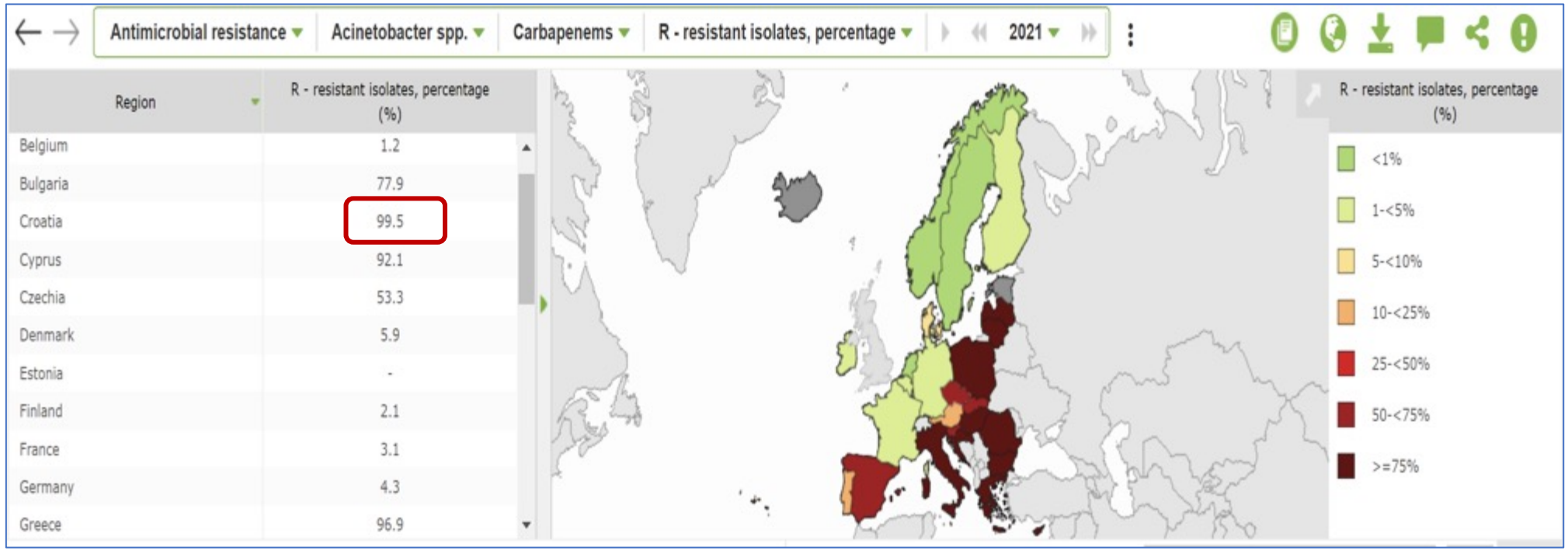


Note: data for Serbia and Kosovo (All references to Kosovo in this document should be understood to be in the context of the United Nations Security Council resolution 1244 (1999)) were combined for this map. Data for the United Kingdom for 2020 do not include Scotland and Wales.

Data sources: 2020 data from the Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR, ©WHO 2021. All rights reserved.) and 2020 data from the European Antimicrobial Resistance Surveillance Network (EARS–Net, ©ECDC 2021).
Map production: ©WHO.

https://www.ecdc.europa.eu/sites/default/files/documents/Joint-WHO-ECDC-AMR-report-2022.pdf

A. baumanii karbapenem direnci



http://atlas.ecdc.europa.eu/public/index.aspx

A. baumanii karbapenem direnci

Table 1. Reported Carbapenem Nonsusceptibility or Resistance Rates by Region

	Nonsusceptibility or Resistance Rate									
Species	Asia-Pacific	Ref.	India, Nepal, Pakistan, Vietnam	Ref.	Europe	Ref.	North America	Ref.	Latin America	Ref.
Acinetobacter baumannii	55.7%–56.2%	[53][a]	0%–100%	[26][d]	58.1%–60.5%	[53][a]	32.0%–36.5%	[53][a]	53.1%–54.6%	[53][a]
	78.4%–79.00%	[53][a]	…	…	76.3%–77.8%	[53][a]	42.3%–45.1%	[53][a]	85.6%–86.3%	[53][a]
	71.4%–71.9%	[49][c]	…	…	2.5%–81.5%	[41][b]	40.1%–50.4%	[3][c]	57.5%	[51][c]
	25.0%–90.5%	[48][b]	…	…	65.8%–84.6%	[21][c]	11.4%	[55][c]	21%–90%	[52][d]
	…	…	…	…	90.7%–100%	[54][c]	…	…	79.3%–89.2%	[56][a]

Nordmann P and Laurent Poire L. Clin Infect Dis 2019:69 (7) • S523

A. baumanii kolistin direnci

- *A. baumanii*'de kolistin direnci ilk kez 1999 yılında bildirildi.
- Bulgaristan'da 2005 yılında %16.7
- İspanya'da 2006 yılında %19
- Kore'de 2007 yılında %30.6
- Yunanistan'da 2014 yılında karbapenem dirençli suşlarda %21.1

Giamarellou H. Int J Antimicrob Agents. 2016 Dec;48(6):614-621.

A. baumanii mcr gen dağılımı

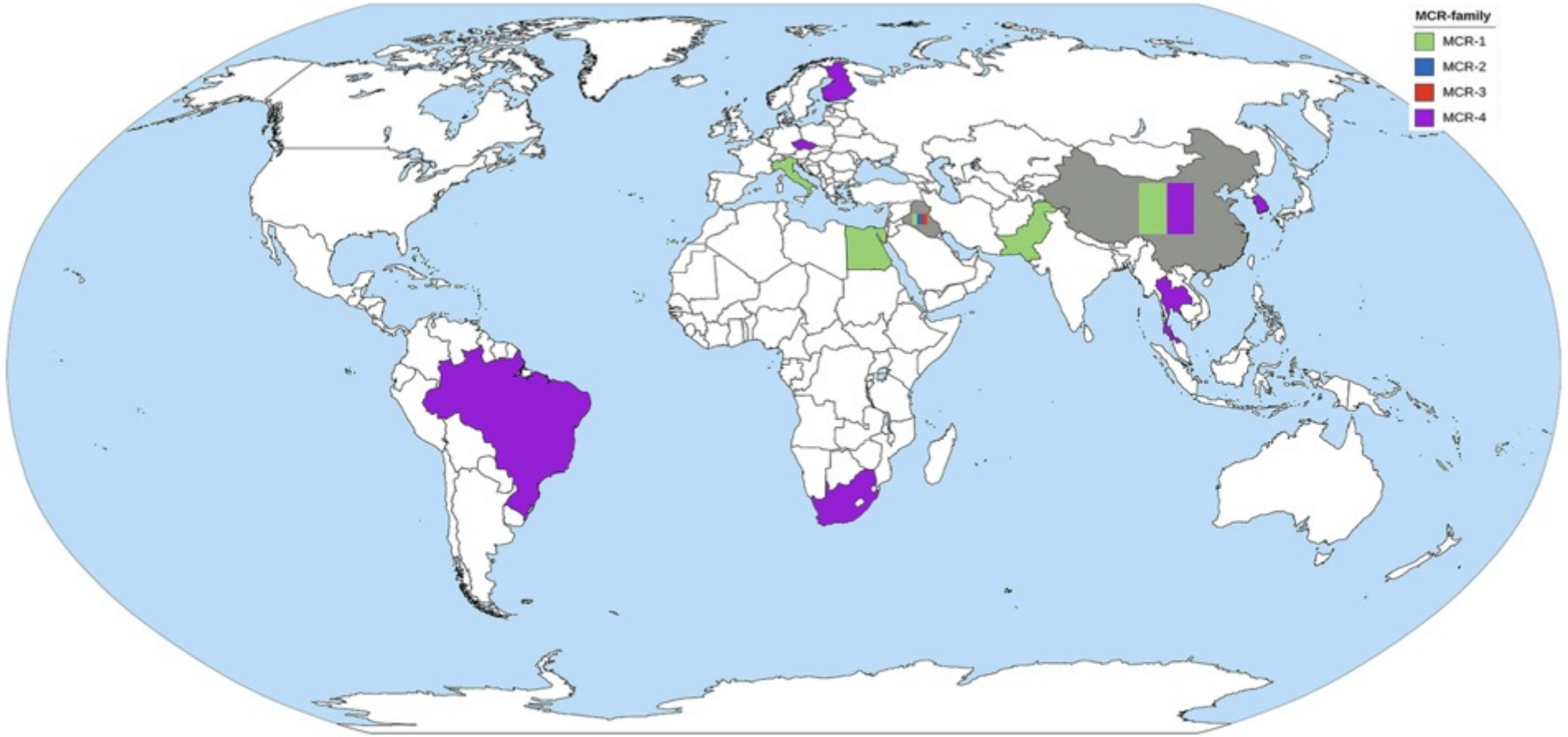


FIGURE 4 | The worldwide dissemination of the *mcr* gene in *Acinetobacter* spp. Countries that reported only one type of *mcr* gene were colored to represent the *mcr* gene. Countries that reported more than one type of *mcr* gene were filled with gray background containing color bands of the reported *mcr* gene.

Front Cell Infect Microbiol. 2022; 12: 882236.

Open Forum Infectious Diseases

SUPPLEMENT ARTICLE

Antimicrobial Susceptibility of *Acinetobacter calcoaceticus–Acinetobacter baumannii* Complex and *Stenotrophomonas maltophilia* Clinical Isolates: Results From the SENTRY Antimicrobial Surveillance Program (1997–2016)

Ana C. Gales,[1] Harald Seifert,[2,3] Deniz Gur,[4] Mariana Castanheira,[5] Ronald N. Jones,[5] and Helio S. Sader[5]

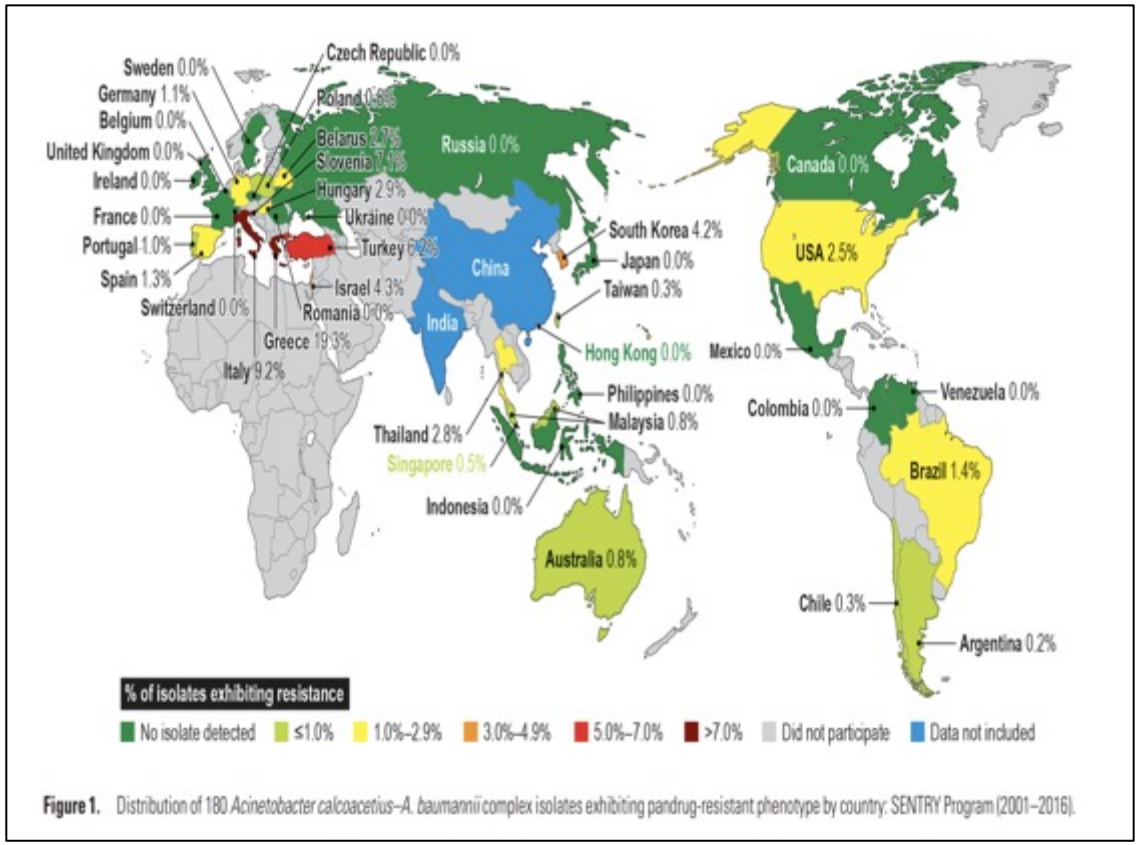


Figure 1. Distribution of 180 *Acinetobacter calcoacetius–A. baumannii* complex isolates exhibiting pandrug-resistant phenotype by country: SENTRY Program (2001–2016).

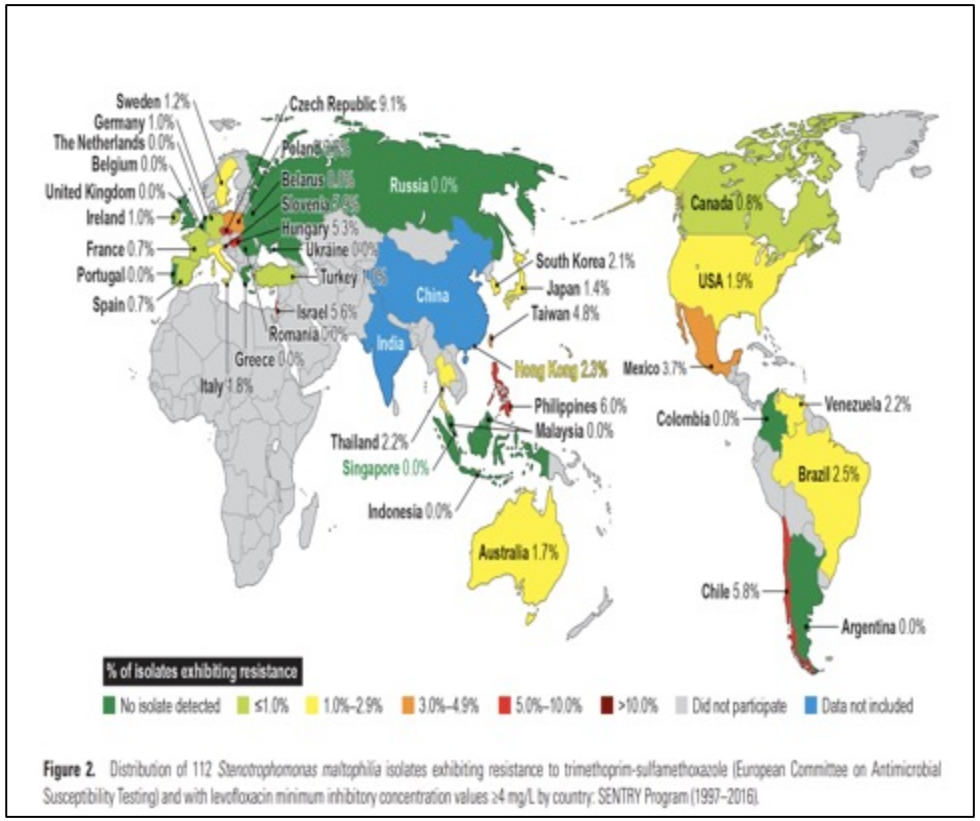


Figure 2. Distribution of 112 *Stenotrophomonas maltophilia* isolates exhibiting resistance to trimethoprim-sulfamethoxazole (European Committee on Antimicrobial Susceptibility Testing) and with levofloxacin minimum inhibitory concentration values ≥4 mg/L by country: SENTRY Program (1997–2016).

Table 4. Frequency of Extensively Drug-Resistant *Acinetobacter calcoaceticus–A. baumannii* Complex Isolates Over 4-Year Intervals According to the Geographic Region and Period of Time (SENTRY Program, 1997–2016)

	Frequency (%) of XDR Isolates[a] by Time Period (No. Tested)					
Geographic Region (No. of XDR Isolates)	1997–2000 (1833)	2001–2004 (1775)	2005–2008 (2698)	2009–2012 (3748)	2013–2016 (3698)	Overall (13 752)
Asia-Pacific (1324)	9.6	24.3	62.8	80.3	72.7	56.9
Europe (3007)	43.1	43.5	64.5	71.3	79.0	66.4
Latin America (2072)	17.0	36.2	67.1	77.3	86.6	61.5
North America (1369)	10.0	26.9	46.2	54.4	40.8	38.8
Total (7772)	21.6	33.6	61.3	71.0	66.6	56.5

Abbreviation: XDR, extensively drug-resistant.
[a]Organisms include *A. baumannii* (6), *A. calcoaceticus-A. baumannii* complex (7756), *A. nosocomialis*

A. baumanii …..direnç %38.8-66.4

Table 8. Trimethoprim-Sulfamethoxazole Susceptibility Rates of 6453 *Stenotrophomonas maltophilia* Isolates by Geographic Region and 4-Year Periods

	Number of Isolates (% Susceptible by Time Period)[a]					
Geographic Region	1997–2000	2001–2004	2005–2008	2009–2012	2013–2016	Overall
Asia-Pacific	135 (91.9)	100 (96.0)	123 (91.9)	147 (97.3)	107 (93.5)	612 (94.1)
Europe	246 (91.1)	355 (97.5)	336 (98.5)	409 (96.3)	687 (96.5)	2033 (96.3)
Latin America	97 (96.9)	223 (94.6)	172 (96.5)	115 (93.0)	94 (91.5)	701 (94.7)
North America	632 (96.2)	440 (98.6)	380 (97.4)	556 (98.4)	1099 (95.8)	3107 (96.9)
Total	1110 (94.6)	1118 (97.2)	1011 (96.9)	1227 (97.1)	1987 (95.7)	6453 (96.2)

[a]Susceptible according to criteria published by European Committee on Antimic

Stenotrophomonas…..TMP-SMX duyarlılığı %94.1-96.9

Gales AC, et al. Open Forum Infect Dis. 2019 Mar; 6(1): S34–S46.

Multicenter Study > J Hosp Infect. 2018 Mar;98(3):260-263. doi: 10.1016/j.jhin.2017.11.014.
Epub 2017 Dec 15.

Rapid emergence of colistin resistance and its impact on fatality among healthcare-associated infections

M Aydın [1], Ö Ergönül [2], A Azap [3], H Bilgin [4], G Aydın [5], S A Çavuş [6], Y Z Demiroğlu [7], H E Alışkan [8], O Memikoğlu [3], Ş Menekşe [9], Ş Kaya [10], N A Demir [11], I Karaoğlan [12], S Başaran [13], Ç Hatipoğlu [14], Ş Erdinç [14], E Yılmaz [15], A Tümtürk [16], Y Tezer [16], H Demirkaya [17], Ş E Çakar [18], Ş Keske [2], S Tekin [2], C Yardımcı [19], Ç Karakoç [20], P Ergen [21], Ö Azap [17], L Mülazımoğlu [4], O Ural [11], F Can [22], H Akalın [15];
Turkish Society of Clinical Microbiology and Infectious Diseases, Healthcare-related Infections Study Group, Turkey

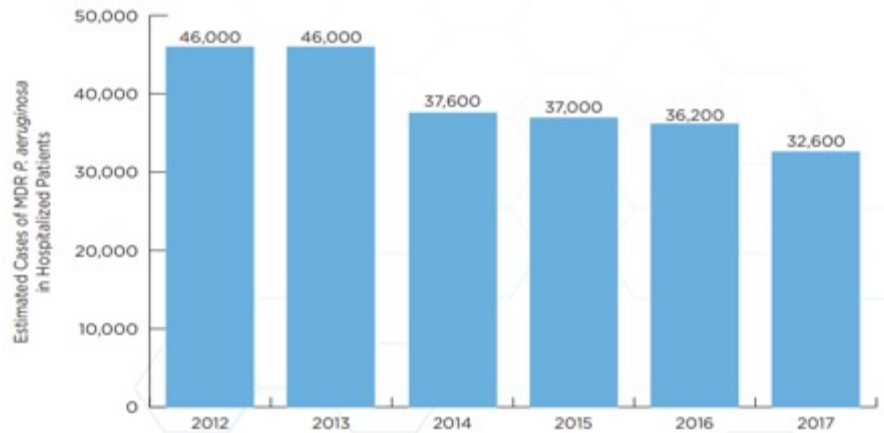
- Sağlık bakımıyla ilişkili 1556 Gram negatif bakteri infeksiyonu
- Retrospektif çok merkezli çalışma
- Mortalite oranları *A. baumanii'de* %58 , *P. aeruginosa'da* %45 , *K. pneumoniae* %41
- *A. baumanii* karbapenem direnci %91.8; kolistin direnci %2.1
- *K. pneumonia* karbapenem direnci %51.9; kolistin direnci %16.1
- *P. aeruginosa* karbapenem direnci %42.9, kolistin direnci %8.8
- *E. cloaca* karbapenem direnci %23.3,kolistin direnci %5.7

ULUSAL SAĞLIK HİZMETİ İLİŞKİLİ İNFEKSİYONLAR SÜRVEYANS AĞI (USHİESA) ÖZET RAPORU 2021

ANTİMİKROBİYAL DİRENÇLİ PATOJEN	Antimikrobiyal Direnç Oranları				PERSENTİL				
	Hastane Sayısı†	Toplam Etken Sayısı	Dirençli Etken Sayısı	Ağırlıklı Genel Ortalama	% 10	% 25	% 50 (Ortanca)	% 75	% 90
TÜRKİYE GENELİ									
Vankomisin dirençli *E. faecium*	208(45)	2132	427	20.03	0.00	8.33	18.75	28.62	48.57
Vankomisin dirençli *E. faecalis*	209(37)	1547	62	4.01	0.00	0.00	1.16	7.84	12.41
MRSA	302(58)	2382	1148	48.19	19.09	33.33	41.67	60.00	76.92
MRKNS	282(75)	2620	2253	85.99	68.72	82.37	90.91	94.25	100.00
E. coli Suşlarında ESBL	359(92)	3743	2041	54.53	21.54	40.63	60.00	73.68	82.97
Klebsiella pneumoniae Suşlarında ESBL	378(154)	7594	5012	66.00	8.84	48.27	77.42	90.00	95.82
Karbapenem dirençli *Acinetobacter baumannii*	336(169)	8314	7575	91.11	75.84	90.91	96.30	100.00	100.00
Karbapenem dirençli *Pseudomonas aeruginosa*	315(89)	3477	2234	64.25	34.16	47.72	66.67	84.92	93.80
Karbapenem dirençli *Klebsiella pneumoniae*	375(165)	8548	5434	63.57	37.31	51.89	67.03	81.61	90.00
Kolistin dirençli *Acinetobacter baumannii*	340(151)	6824	748	10.96	0.00	1.48	6.12	17.23	30.77
Kolistin dirençli *Klebsiella pneumoniae*	348(140)	5879	1877	31.93	5.41	15.15	27.27	44.19	58.82

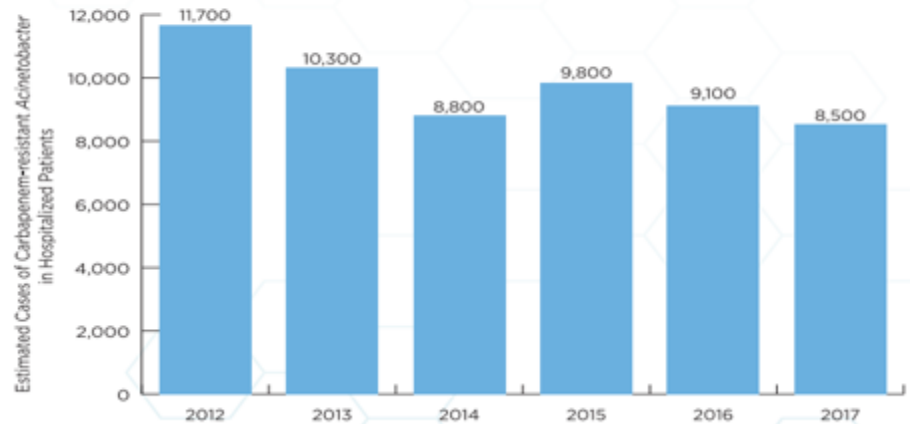
CASES OVER TIME

Continued infection control and appropriate antibiotic use are important to maintain decreases in MDR *P. aeruginosa* infections.



CASES OVER TIME

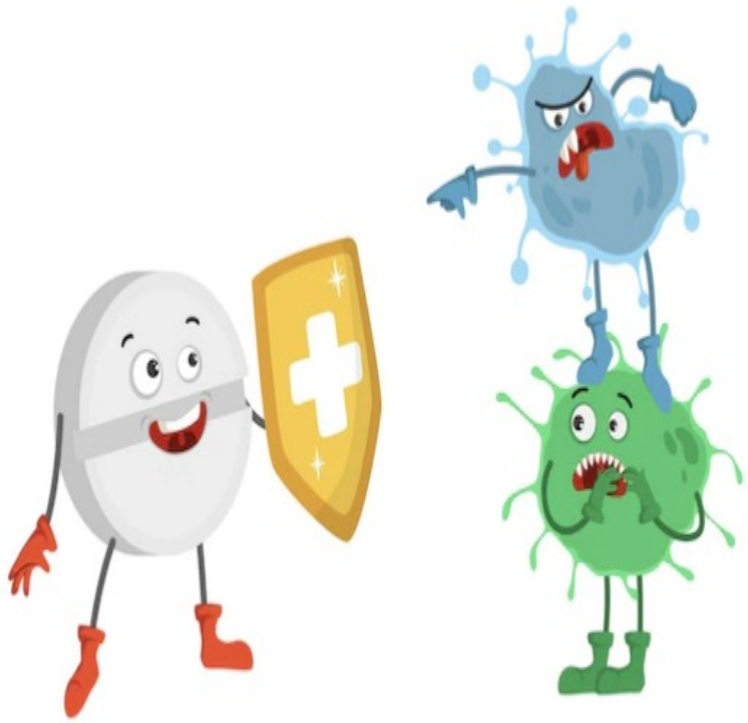
Continued infection control and appropriate antibiotic use are important to maintain decreases in carbapenem-resistant *Acinetobacter* infections.



U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

Karbapenem dirençli Gram negatif çomaklardan kaynaklanan infeksiyonlar ile mücadele edebilmek için

- Antibiyotikleri uygun kullanımı
- Direncin erken tanımlanması
- Kolonize ve enfekte hastaların izolasyonu
- İnfeksiyon kontrol önlemlerine uyum



Food and Agriculture Organization of the United Nations

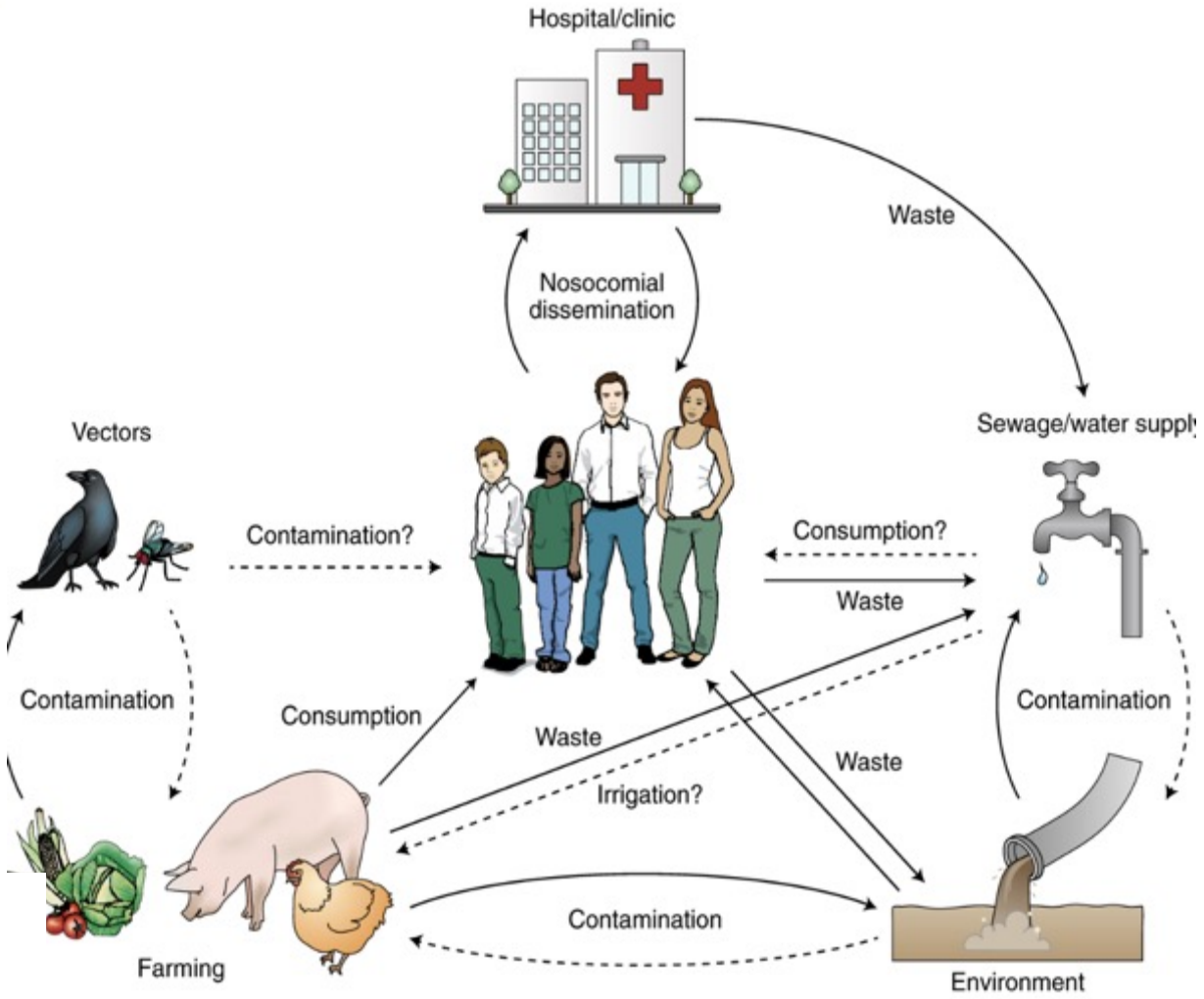
WORLD ORGANISATION FOR ANIMAL HEALTH

World Health Organization

UN environment

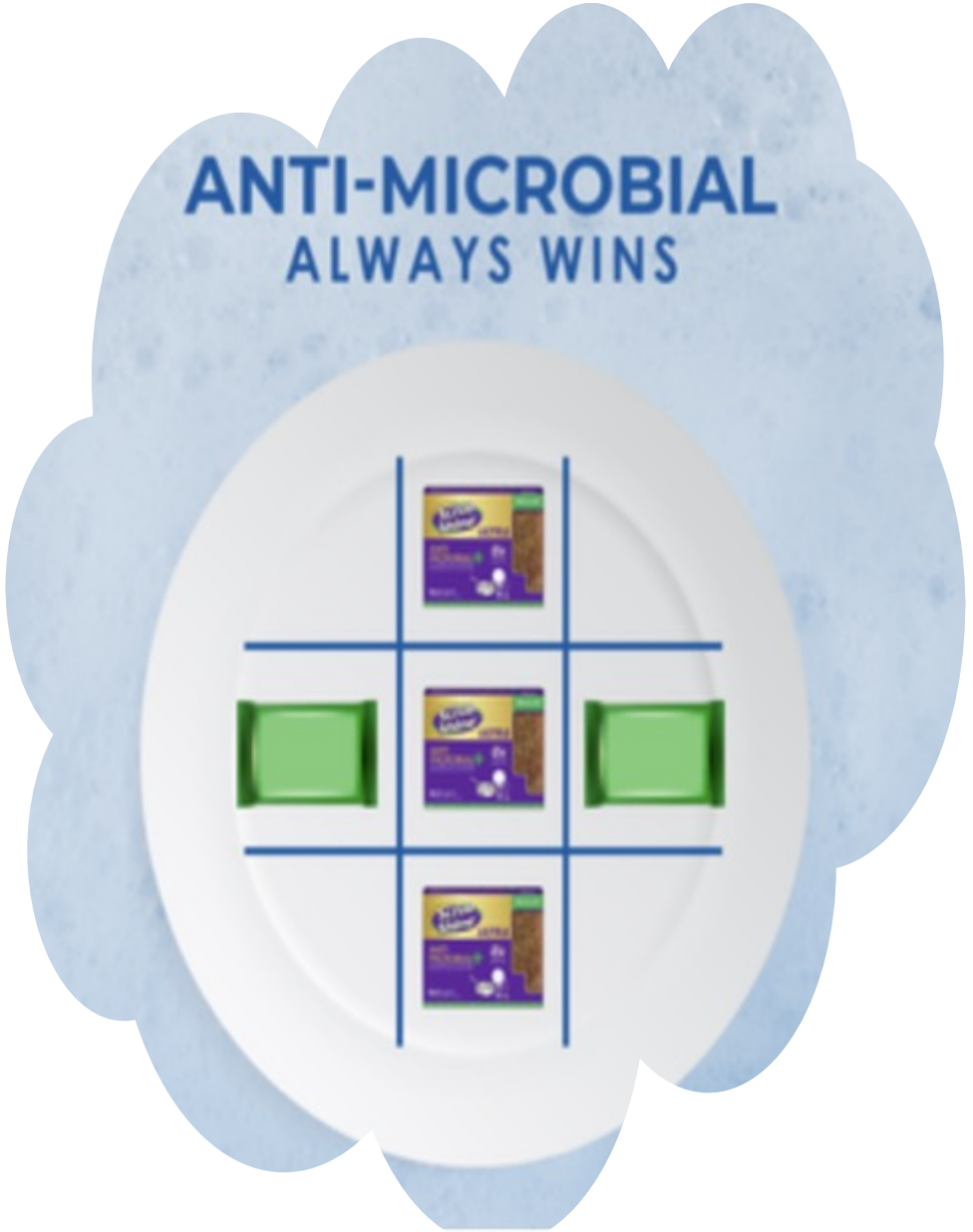
Jointly advancing the response to Antimicrobial Resistance (AMR) through a One Health approach

- Tek başına tıp alanında yapılan çabalar yetersiz
- Uluslararası ve çok sektörlü bir yaklaşım gerekir
- İnsan sağlığı, hayvan sağlığı ve çevre sağlığı arasındaki bağlantılara odaklanıp sorunlar bir bütün olarak değerlendirilmeli



Walsh TR. Nature Microbiology.2018:3;854-855 T

Yıldız SS ve ark. Mikrobiyol Cemiy Derg 2021;51(4):341-7



İlginiz için teşekkürler