ECCMID 2023 | Poster #P0384

VITEK2 Advanced Expert System β-Lactam Resistance Phenotyping Compared to Whole Genome Sequencing in Enterobacterales Isolates from European Medical Centres

Cecilia Carvalhaes, Paul Rhomberg, Nabina Gurung, Nathan Veeder, Mariana Castanheira
JMI Laboratories, North Liberty, Iowa, USA

Introduction

- The rapid detection of β-lactam resistant phenotypes such as transferable AmpC (tAmpC), ESBL, and carbapenemase are important for appropriate antimicrobial therapy administration and infection control.
- The VITEK2 Advanced Expert System (AES) provides interpretations of β-lactam resistance phenotypes based on an extensive database of MIC distributions and prevalent resistance mechanisms in Enterobacterales isolates.
- In this study, the AES β-lactam resistance phenotypes were compared to whole genome sequencing results from 572 European Enterobacterales isolates.

Materials and Methods

- Isolates were collected from 39 medical centres in 19 European countries as part of the SENTRY Antimicrobial Surveillance Program during 2017–2020 (Figure 1).
- A total of 251 *Klebsiella pneumoniae*, 174 *Escherichia coli*, 48 *Enterobacter cloacae* species complex, and 99 other Enterobacterales isolates were tested (Figure 2A).
- Antimicrobial susceptibility testing was performed by VITEK2 AES v9.02 under Global European + Phenotypic mode, using the N388 and XN11 susceptibility cards (Iberic cards) and these results were compared to reference broth microdilution outcomes.
- The following β-lactam and β-lactam/β-lactamase inhibitor combination agents were tested:
  - Amoxicillin/clavulanate, ampicillin, cefepime, cefixime, cefotaxime, cefoxitin, ceftazidime, ceftazidime/avibactam, ceftolozane/tazobactam, ceftriaxone, cefuroxime, ertapenem, imipenem, and mecillinam.
- EUCAST breakpoints were applied, except for compounds where AES criteria were not compatible with most recent EUCAST criteria.
- Discordant results were repeated by both methods using the same bacterial inoculum.
- Whole genome sequencing (WGS) was performed on isolates that met the following criteria by BMD:
  - *E. coli* and *K. pneumoniae* isolates displaying MIC values ≥2 mg/L for at least 2 of the following β-lactams: aztreonam, cefepime, ceftazidime, or ceftriaxone; and/or
  - Enterobacterales isolates displaying meropenem and/or imipenem MIC values >1 mg/L.
- Enterobacterales isolates that did not meet the criteria for molecular characterization were considered wildtype.
- The accuracy, sensitivity, and specificity of AES reports for β-lactam resistant phenotypes were compared to resistant genotypes confirmed by WGS.

Results

- Figure 2B shows the distribution of the 572 Enterobacterales isolates displaying carbapenemase, ESBL, tAmpC-encoding genes and wildtype genotypes.
- AES provided phenotypic reports for 564 (98.6%) isolates, including isolates harbouring carbapenemase (212; 37.6%), extended-spectrum β-lactamase (ESBL; 161; 28.5%), and transferable AmpC (tAmpC; 51; 9.0%) genes as well as wild-type (WT; 140; 24.8%) isolates.
- Eight of 572 isolates (1.4%) failed to report an AES phenotype due to technical error or because the organism expressed a phenotype that was not present in the AES knowledge base.
- Overall, the AES report was accurate for 551/564 isolates (97.7%; Table 1).
- AES accurately reported carbapenemase, ESBL, and tAmpC phenotypes for 96.5%, 98.6%, and 97.9% of isolates, respectively.
- All but 1 (99.8%) WT isolate was correctly categorized by AES, including when isolates displayed intrinsic resistance or an acquired penicillinase.
- AES sensitivity/specificity rates were 99.5%/94.6%, 97.5%/99.0%, 84.3%/99.2%, and 100%/99.8% for reporting carbapenemase, ESBL, tAmpC genes, and WT isolates, respectively (Table 1).
- Table 2 displays the discrepancies between the AES phenotype and genotype, including 8 isolates carrying tAmpC, 1 carbapenemase, and 4 ESBL genes by WGS.
- Additionally, 4 isolates harbouring ESBL were reported as AmpC, and 1 VIM-1–producing *E. coli* isolate was misreported as displaying an ESBL phenotype.

Table 1. VITEK2 AES β-lactam resistance phenotypes compared to whole genome sequencing genotypes.

β-lactam resistance genotype (No. of isolates)	AES phenotypic report		
	Accuracy	Sensitivity	Specificity
Carbapenemase (212)	96.5%	99.5%	94.6%
ESBL (161)	98.6%	97.5%	99.0%
tAmpC (51)	97.9%	84.3%	99.2%
WT (140)	99.8%	100.0%	99.8%

Abbreviations: ESBL, extended-spectrum β-lactamase; tAmpC, transferrable AmpC; WT, wildtype.

Table 2. List of discordances between VITEK2 AES phenotype and WGS genotype

WGS genotype	AES phenotype	No. of occurrences
Carbapenemase	ESBL	1
ESBL	AmpC	4
tAmpC	Carbapenemase	4
	ESBL	3
	WT	1

Abbreviations: ESBL, extended-spectrum β-lactamase; tAmpC, transferrable AmpC; WT, wildtype.

Figure 1. Distribution of the 572 Enterobacterales isolates included in this study stratified by country.

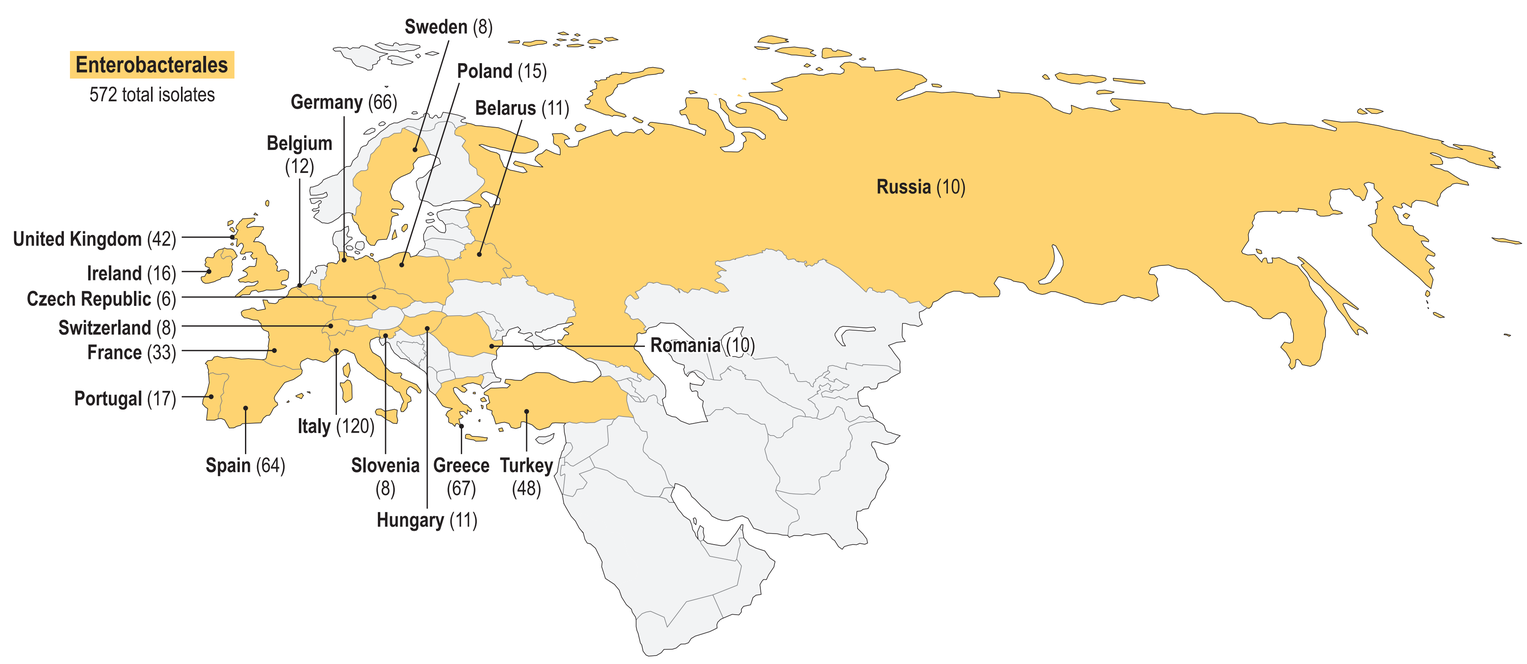
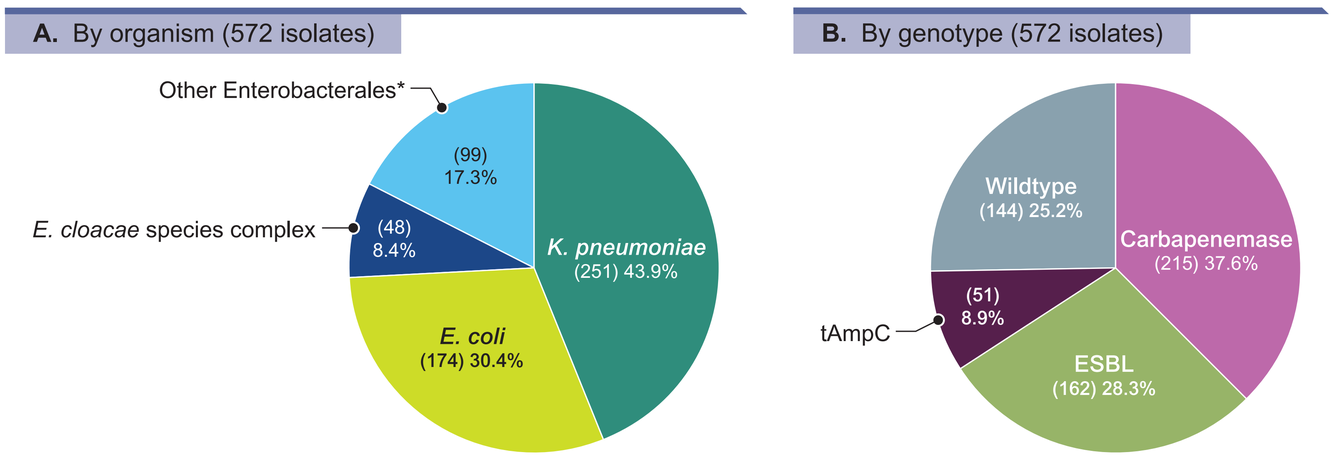


Figure 2. Characterization of Enterobacterales isolates included in the study.



*Organisms included: *Proteus* spp. (25 isolates), *Citrobacter* spp. (24), *Serratia marcescens* (15), *Klebsiella aerogenes* (11), *Klebsiella oxytoca* (9), *Providencia* spp. (6), and *Morganella morganii* (3).

Conclusions

- VITEK2 AES provided β-lactam resistance phenotypes for 98.6% (564/572) of isolates from a large and challenging collection of Enterobacterales from Europe.
- AES β-lactam resistance phenotypes were correctly reported for 97.7% (551/564) of Enterobacterales isolates harbouring a variety of β-lactamase genes, including 96.5%, 98.6%, and 97.9% of carbapenemase, ESBL, and tAmpC, respectively.
- The AES phenotypic report could significantly aid antimicrobial stewardship initiatives and improve patient care if it was used in clinical laboratories as a rapid tool for the detection of resistance mechanisms among Enterobacterales from Europe.

Acknowledgements

This project was supported by bioMérieux. CG Carvalhaes, PR Rhomberg, N Gurung, N Veeder, and M Castanheira are employees of JMI Laboratories, which was a paid consultant to bioMérieux in connection with the development of this poster.

References

Carvalhaes CG, Shortridge D, Woosley LN, Gurung N, Castanheira M. Performance of the Vitek 2 Advanced Expert System (AES) as a Rapid Tool for Reporting Antimicrobial Susceptibility Testing (AST) in Enterobacterales from North and Latin America. Microbiol Spectr. 2023 Jan 16:e0467322. doi: 10.1128/spectrum.04673-22. Epub ahead of print.

Sanders CC, Peyret M, Moland ES, Shubert C, Thomson KS, Boeufgras JM, Sanders WE Jr. Ability of the VITEK2 advanced expert system to identify β-lactam phenotypes in isolates of Enterobacterales and Pseudomonas aeruginosa. J Clin Microbiol. 2000 Feb;38(2):570-4.

CLSI. M07Ed11. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically. Wayne, PA, Clinical and Laboratory Standards Institute, 2018.

EUCAST. The European Committee on Antimicrobial Susceptibility Testing. Breakpoint tables for interpretation of MICs and zone diameters. Version 12.0, 2022.

Jacoby GA. AmpC β-lactamases. Clin Microbiol Rev. 2009 Jan;22(1):161-82.

Contact

Cecilia Carvalhaes, MD, PhD, D(ABMM)
JMI Laboratories
345 Beaver Kreek Centre, Suite A
North Liberty, IA 52317
Phone: (319) 665-3370
Fax: (319) 665-3371
Email: cecilia-carvalhaes@jmilabs.com

SCAN ME

To obtain a PDF of this poster:
Scan the QR code or visit https://www.jmilabs.com/data/posters/ECCMID2023_VITEK2.pdf