Journal of Infection 90 (2025) 106493

Contents lists available at ScienceDirect

Journal of Infection

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

Letter to the Editor

Dynamic global variation in resistance and hypervirulence of carbapenem-resistant *Klebsiella pneumoniae* between 2010 and 2023

Dear Editor,

We read with great interest the article by Oskar Ljungquist et al.,[1] which provided critical insights into hypervirulent pandrug-resistant *Klebsiella pneumoniae* isolated from Ukrainian war victims. *K. pneumoniae*, a leading opportunistic pathogen of Gram-negative bacterial infections, including pneumonia, bacteremia and urinary tract infection, has been identified as the sixth most burdensome pathogen globally, according to the Global Burden of Disease study.[2] In 2024, carbapenem-resistant *K. pneumoniae* (CRKP) topped the WHO Bacterial Priority Pathogens List as the pathogen in the critical category.[3] Genomic characteristics of CRKP have been gradually elucidated in various global regions, especially in China, USA and Europe, contributing to both therapeutic strategies and controls targeting CRKP. However, the latest analyses of global genomic characteristics of CRKP, along with its dynamic variation, including resistance and virulence, remain scarce. This is particularly true when it comes to comparing the situation before and during the COVID-19 pandemic (2020–2023). To investigate dynamic changes of global CRKP, a total of 64,355 *K. pneumoniae* genomes were retrieved from NCBI Genbank, spanning the period from 1980 to Dec. 31, 2024. Among them, 26,713 qualified CRKP genomes with spatiotemporal metadata from 90 countries (2010–2023) were selected for further genomic analysis (Appendix Fig. 1).

Molecular characterization, including carbapenemase genes, multi-locus sequence typing (MLST), K-loci (KL), and virulence determinants, is detailed in the Appendix Tables 1–3. Before the COVID-19 pandemic (2010–2019), the number of CRKP presented a significant surge, however, a pronounced decline was observed during the COVID-19 pandemic (2020–2023) (Appendix Fig. 2). Notably, during the COVID-19 pandemic, CRKP isolates underwent significant epidemiological shifts: while ST11 and ST258 lineages exhibited decreasing trends, ST147 and ST15 clones experienced remarkable increases, highlighting the need for continuous monitoring (Appendix Fig. 2). In China, ST11-KL64 strains have surpassed ST11-KL47 strains as the predominant lineage since 2016, consistent to a previous study.[4] Conversely, in the USA, ST258-KL107 remained dominant over ST258-KL106 throughout the study period (Appendix Fig. 3). Global carbapenemase distribution analysis revealed that KPC-2 (45.3%), NDM-1 (11.5%), KPC-3 (11.4%), OXA-48 (8.5%), OXA-232 (4.8%), and NDM-5 (3.6%) were the six most prevalent enzymes (Appendix Table 1), similar to that reported previously.[5] Of particular concern is the rising prevalence of CRKP strains co-producing dual carbapenemases, with NDM/OXA and KPC/NDM emerging as the most frequently observed carbapenemases worldwide.

To investigate potential heterogeneity in molecular characteristics, as may differ both geographically and temporally, the carbapenemase distributions across the 20 countries with the highest prevalence rates from 2010 to 2023 were analyzed (Fig. 1). KPC-2 showed distinct ST-KL associations across different countries and regions: prominent in China (ST11-KL64, 52.3%; ST11-KL47, 31.2%), USA (ST258-KL106, 38.1%; ST307-KL102, 15.7%), Brazil (ST11-KL64: 27.5%; ST258-KL107: 17.8%), Germany (ST258-KL106: 80.3%), Australia (ST258-KL106: 87.2%), Greece (ST258-KL106: 69.6%), and Vietnam (ST15-KL10: 59.3%), respectively. Since 2016, the emergence of novel carbapenemase types has disrupted the previous dominance of KPC-2, fostering a polymicrobial landscape of CRKP; nevertheless, KPC-2 has still retained epidemiological prominence in China and Brazil. KPC-3 also demonstrated marked predominance within certain ST-KL, with particularly high prevalence rates observed in USA (ST258-KL107: 63.3%), Italy (ST512-KL107: 44.5%) and Canada (ST512-KL107: 38.3%). NDM-1, however, was predominant in Poland (36.8%) and Russia (43.0%) and has been gradually replaced by VIM-4 and OXA-48, respectively. OXA-48-like carbapenemases (OXA-48, OXA-232, OXA-181) dominated in Spain (68.0%), India (52.5), France (44.1%) and Saudi Arabia (58.6%), while IMP-1 prevailed in Japan (44.1%).

Hypervirulent CRKP (hvCRKP) poses a global public health threat and has a high potential to cause difficult-to-treat infections.[6] In this study, the rate of hvCRKP demonstrated a marked upward from 0.3% to 31.8% before 2019 (Fig. 2). During the COVID-19 pandemic (2020–2023), hvCRKP stably maintained a high epidemic. Among hvCRKP strains, KL64 (58.9%), KL47 (12.8%), and KL112 (8.0%) were predominant, warranting heightened surveillance (Appendix Table 3). Notably, in China, 94.4% (374/396) of OXA-232-producing ST15-KL112 strains were hypervirulent. However, hypervirulence defined by virulence determinants should be used more prudently owing to lacking a standardized definition of hypervirulence.[7]

CRKP isolates were primarily recovered from blood (13.7%), respiratory samples (12.0%), urine (11.8%), and rectal swabs (6.2%), respectively. Moreover, ST11, ST258, ST147, ST15, ST307 and ST16 strains displayed significant source-specific distribution patterns (Chi-square test, $P < 0.001$, Appendix Table 4). Notably, 1.9% of isolates were derived from hospital wastewater, underscoring the importance of One Health-driven surveillance.[8]

Genomic characteristics of global CRKP exhibit divergent trends in resistance and hypervirulence between before and during the COVID-19 pandemic. Substantial interregional molecular heterogeneity was found, and understanding the dynamic characteristics of carbapenemases, ST-KL lineages, carbapenemase genes, and virulence determinants is crucial to the development of effective prevention and treatment. Integrating One Health principles into surveillance strategies is critical for managing the global spread of these pathogens.

https://doi.org/10.1016/j.jinf.2025.106493

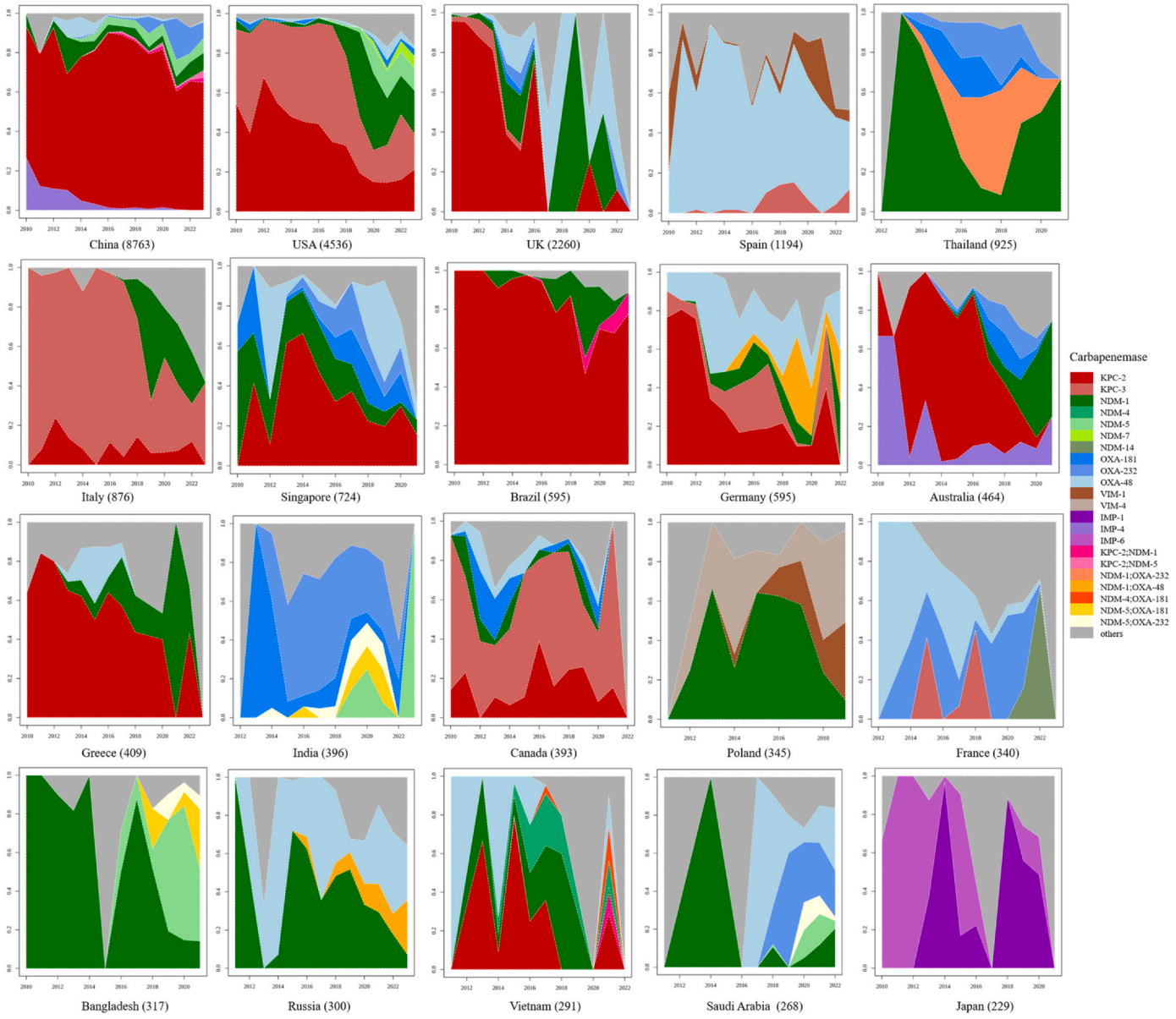

Fig. 1. Temporal variation of carbapenemases across twenty high-prevalence nations. X-axis represents year, and Y-axis represents the proportion of different carbapenemases.

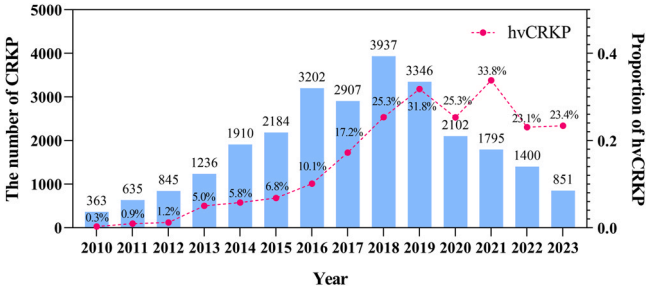

Fig. 2. Dynamic changes of the proportion of hvCRKP in CRKP.

Ethics

The Ethics Committee of the China-Japan Friendship Hospital (CJFH) approved this study (2022-KY-054).

Funding

This work was supported by the CAMS Innovation Fund for Medical Sciences (CIFMS; No.2021-I2M-1-030).

CRediT authorship contribution statement

Zhang Feilong: Writing – review & editing, Methodology, Software, Data curation. Yang Wenting: Methodology. Lu Binghuai: Writing – review & editing, Visualization, Funding acquisition. Cao Bin: Writing – review & editing, Visualization.

Declaration of Competing Interest

We declare no competing interests.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jinf.2025.106493.

References

1. Ljungquist O, Magda M, Giske CG, Tellapragada C, Nazarchuk O, Dmytriiev D, et al. *Pandrug-resistant Klebsiella pneumoniae isolated from Ukrainian war victims are hypervirulent. J Infect* 2024 Dec;**89**(6):106312. PubMed PMID: 39396555. Epub 2024/10/14.
2. IPC Group. *Global burden associated with 85 pathogens in 2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet Infect Dis* 2024 Aug;**24**(8):868–95. PubMed PMID: 38640940. Epub 2024/04/20.
3. World Health Organization. *WHO bacterial priority pathogens list, 2024: Bacterial pathogens of public health importance to guide research, development and strategies to prevent and control antimicrobial resistance*. World Health Organization, 9, 2024, 17 May. ISBN: 978-92-4-009346-1:72. https://wwwwhoint/publications/i/item/9789240093461.
4. Wang Q, Wang R, Wang S, Zhang A, Duan Q, Sun S, et al. *Expansion and transmission dynamics of high risk carbapenem-resistant Klebsiella pneumoniae subclones in China: An epidemiological, spatial, genomic analysis. Drug Resist Updat* 2024 May;**74**:101083. PubMed PMID: 38593500. Epub 2024/04/10.
5. Karlowsky JA, Lob SH, Kazmierczak KM, Badal RE, Young K, Motyl MR, et al. *In vitro activity of imipenem against carbapenemase-positive Enterobacteriaceae isolates collected by the SMART Global Surveillance Program from 2008 to 2014. J Clin Microbiol* 2017 Jun;**55**(6):1638–49. PubMed PMID: 28298454. Pubmed Central PMCID: PMC5442520. Epub 2017/03/17.
6. Lei TY, Liao BB, Yang LR, Wang Y, Chen XB. *Hypervirulent and carbapenem-resistant Klebsiella pneumoniae: A global public health threat. Microbiol Res* 2024 Nov;**288**:127839. PubMed PMID: 39141971. Epub 2024/08/14 22:51.
7. Yang Y, McNally A, Zong Z. *Call for prudent use of the term hypervirulence in carbapenem-resistant Klebsiella pneumoniae. Lancet Microbe* 2025 Feb 21:101090. PubMed PMID: 39993405. Epub 2025/02/25.
8. Zou H, Zhou Z, Berglund B, Zheng B, Meng M, Zhao L, et al. *Persistent transmission of carbapenem-resistant, hypervirulent Klebsiella pneumoniae between a hospital and urban aquatic environments. Water Res* 2023 Aug 15;**242**:120263. PubMed PMID: 37390655. Epub 2023/07/01.

Zhang Feilong
Peking Union Medical College, Chinese Academy of Medical Sciences, China-Japan Friendship Hospital, Beijing, China

Yang Wenting
Peking University China-Japan Friendship School of Clinical Medicine, Beijing, China

Lu Binghuai *
Peking Union Medical College, Chinese Academy of Medical Sciences, China-Japan Friendship Hospital, Beijing, China
Peking University China-Japan Friendship School of Clinical Medicine, Beijing, China

Cao Bin **
Peking Union Medical College, Chinese Academy of Medical Sciences, China-Japan Friendship Hospital, Beijing, China

*Correspondence to: Peking Union Medical College, Chinese Academy of Medical Sciences, China-Japan Friendship Hospital, No. 2 East Yinghua Street, Chaoyang District, Beijing 100029, China.

**Correspondence to: Peking Union Medical College, Chinese Academy of Medical Sciences, China-Japan Friendship Hospital, No. 2 East Yinghua Street, Chaoyang District, Beijing 100029, China.
E-mail addresses: zs25041@126.com (L. Binghuai), caobin_ben@163.com (C. Bin).