



Letter to the Editor

A step forward in the puzzling diagnosis of hypervirulent *Klebsiella pneumoniae*

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Abstract

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To the Editor:

Klebsiella pneumoniae is a Gram-negative, non-motile bacterium that typically has a capsule and thrives in both aerobic and anaerobic environments. This bacterium is responsible for various infections, including urinary tract infections, pneumonia, bacteremia, and liver abscesses (Jian et al., 2024; Shinohara et al., 2025). It is found globally in humans, animals, and the environment (Soliman et al., 2024). The *Klebsiella* genus comprises 27 species and eight subspecies (LPSN, accessed on 1st of March 2025). *Klebsiella pneumoniae* is notably one of the leading causes of nosocomial septicemia in hospitals worldwide and one of the ESKAPE pathogens. It has been categorized into two main pathotypes: hypervirulent *Klebsiella pneumoniae* (hvKp) and classical *Klebsiella pneumoniae* (cKp). The classical phenotype is a significant contributor to the critical threats identified by the World Health Organization (WHO). It is commonly linked to hospital-acquired infections and is recognized for its ability to acquire numerous antimicrobial resistance (AMR) genes (Wyres et al., 2020). First emerging in the Asia-Pacific region, hvKp is associated with severe, life-threatening infections that often lead to systemic dissemination, particularly among younger and healthier populations. It is associated with severe life-threatening conditions and high morbidity and mortality rates in otherwise healthy individuals, presenting a risk to public health. Moreover, hvKp has recently emerged as a notable global pathogen, particularly among strains that have gained carbapenem resistance (Russo et al., 2024). Therefore, this pathogen must be recognized as a significant global threat. Hence, precise identification of hvKp is crucial for effective surveillance and clinical management (Tang et al., 2025).

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In their compelling online report, Russo et al. (2025) emphasize the critical and urgent need for effective diagnostic tools to differentiate Hypervirulent *Klebsiella pneumoniae* (hvKp) from classical *Klebsiella pneumoniae* (cKp). They rightly highlight that the five biomarkers—*iucA*, *iroB*, *peg-344*, *rmpA*, and *rmpA2*—represent the most accurate and pragmatic approach for identifying hvKp (Russo et al., 2025). We fully agree with the authors that swift and precise diagnosis is essential to curtail the further spread of this alarming and notorious strain.

Several virulence genes have been linked to the hypervirulent phenotype, including the mucoviscosity-associated gene A (*magA*), *wcaG*, and the regulators of mucoid phenotype A (*rmpA* and *rmpA2*) (Catalán-Nájera et al., 2027). Recent research has identified aerobactin as the foremost hvKp-specific virulence factor, which can be used to discriminate hvkp either alone or combined with salmochelin and *rmpA2* (Shankar et al., 2020) or with hypermucoviscosity (Liu and Guo, 2019). An examination of clinical *K. pneumoniae* isolates from Vietnam revealed the presence of various virulence genes, ranging from 63 to 129. Among these, only five hvKp ST23 isolates contained virulence genes contributing to the hypervirulent phenotype, including iron uptake genes such as aerobactins, *rmpA*, *rmpA2*, salmochelin, yersiniabactin, and enterobactin. Notably, only the allantoin utilization genes allA-D and allR-S genes, along with the *vgrG.tssI* of the type VI secretion system (T6SS) and *wcaJ* genes, were exclusively identified in ST23 isolates (Wareth et al., 2024). The *wcaJ* gene functions as an initiation glycosyltransferase in capsular polysaccharide (CPS) synthesis. Despite the fact that the *wcaJ* is essential for capsule synthesis in both cKp and hvKp strains, its overexpression is associated with increased viscosity, while its knockout results in the loss of the capsule in *K. pneumoniae* (Wang et al., 2024). Therefore, incorporating these virulence determinants into the diagnosis of hvKp could be helpful.

On the other hand, some believe that the hvKp-associated virulence plasmid is responsible for giving *K. pneumoniae* strains the enhanced virulence needed to transform from the cKp phenotype to the hvKp phenotype. This supports the notion that biomarkers present on the virulence plasmid are likely the best indicators for predicting an hvKp phenotype. Further genotypic and phenotypic analyses are required to find a tool for the accurate diagnosis of hvkp.

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References

- Catalán-Nájera, J.C., Garza-Ramos, U., Barrios-Camacho, H., 2017. Hypervirulence and hypermucoviscosity: Two different but complementary *Klebsiella* spp. phenotypes? *Virulence* 3, 1111-23. <https://doi.org/10.1080/21505594.2017.1317412>
- Jian, Z., Liu, Y., Wang, Z., Zeng, L., Yan, Q., Liu, W., 2024. A nosocomial outbreak of colistin and carbapenem-resistant hypervirulent *Klebsiella pneumoniae* in a large teaching hospital. *Scientific Reports* 14, 27744 <https://doi.org/10.1038/s41598-024-79030-w>
- Liu, C., Guo, J., 2019. Hypervirulent *Klebsiella pneumoniae* (hypermucoviscous and aerobactin positive) infection over 6 years in the elderly in China: Antimicrobial resistance patterns, molecular epidemiology and risk factor. *Annals of Clinical Microbiology and Antimicrobials* 18, 4. <https://doi.org/10.1186/s12941-018-0302-9>
- Russo, T.A., Lebreton, F., McGann, P.T., 2025. A step forward in hypervirulent *Klebsiella pneumoniae* Diagnostics. *Emerging Infectious Diseases* 31, 1-3. <https://doi.org/10.3201/eid3101.241516>
- Russo, T.A., Alvarado, C.L., Davies, C.J., Drayer, Z.J., Carlino-MacDonald, U., Hutson, A., et al. 2024. Differentiation of hypervirulent and classical *Klebsiella pneumoniae* with acquired drug resistance. *mBio*. 14, e0286723. <https://doi.org/10.1128/mbio.02867-23>
- Shankar, C., Jacob, J.J., Vasudevan, K., Biswas, R., Manesh, A., Sethuvel, D.P.M., et al. 2020. Emergence of multidrug-resistant hypervirulent ST23 *Klebsiella pneumoniae*: Multidrug-resistant plasmid acquisition drives evolution. *Frontiers in Cellular and Infection Microbiology* 10:575289. <https://doi.org/10.3389/fcimb.2020.575289>
- Shinohara, M., Nakano, R., Honmyo, N., Sakai, H., Shimizu, S., Kuroda, S. et al. 2025. Recurrent liver abscess caused by mucoid-type *Klebsiella pneumoniae* successfully treated with hepatic artery antibiotic infusion therapy: A Case report. *Cureus* 17, e79451. <https://doi.org/10.7759/cureus.79451>
- Soliman, E.A., Saad, A., Abd El Tawab, A.A., Elhofy, F.I., Rizk, A.M., Elkhayat, M. et al. 2024. Exploring AMR and virulence in *Klebsiella pneumoniae* isolated from humans and pet animals: A complement of phenotype by WGS-derived profiles in a one health study in Egypt. *One Health* 19, 100904. <https://doi.org/10.1016/j.onehlt.2024.100904>
- Tang, Y., Du, P., Du, C. et al. 2025. Genomically defined hypervirulent *Klebsiella pneumoniae* contributed to early-onset increased mortality. *Nature Communications* 16, 2096. <https://doi.org/10.1038/s41467-025-57379-4>
- Wang, W., Tian, D., Hu, D., Chen, W., Zhou, Y., Jiang, X., 2023. Different regulatory mechanisms of the capsule in

- hypervirulent *Klebsiella pneumoniae*: "direct" *wcaJ* variation vs "indirect" *rmpA* regulation. *Frontiers in Cellular and Infection Microbiology* 13:1108818. <https://doi.org/10.3389/fcimb.2023.1108818>
- Wareth, G., Brangsch, H., Nguyen, N.H., Nguyen, T.N.M., Pletz, M.W., Neubauer, H., et al. 2024. WGS analysis of hypervirulent and MDR *Klebsiella pneumoniae* from Vietnam reveals an inverse relationship between resistome and virulome. *German Journal of Microbiology* 4, 15-24. <https://doi.org/10.51585/gjm.2024.1.0030>
- Wyres, K.L., Lam, M.M.C., Holt, K.E. 2020. Population genomics of *Klebsiella pneumoniae*. *Nature Review Microbiology*. 18, 344-359. <https://doi.org/10.1038/s41579-019-0315-1>