



HAL
open science

Is *Klebsiella pneumoniae* -associated bovine mastitis an emerging public health issue? A One Health perspective

Delphine Payros, Frédéric Auvray, Gilles Foucras, Eric Oswald

► To cite this version:

Delphine Payros, Frédéric Auvray, Gilles Foucras, Eric Oswald. Is *Klebsiella pneumoniae* -associated bovine mastitis an emerging public health issue? A One Health perspective. *ASM Animal Microbiology*, 2026, <10.1128/asmam.00023-25>. <hal-05598345>

HAL Id: hal-05598345

<https://hal.inrae.fr/hal-05598345v1>

Submitted on 21 Apr 2026

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons CC BY 4.0 - Attribution - International License



Is *Klebsiella pneumoniae*-associated bovine mastitis an emerging public health issue? A One Health perspective

Delphine Payros,¹ Frédéric Auvray,² Gilles Foucras,¹ Eric Oswald^{2,3}

AUTHOR AFFILIATIONS See affiliation list on p. 5.

ABSTRACT Bovine mastitis is a major driver of antimicrobial use and economic loss in dairy farming. Although long overshadowed by *Escherichia coli*, *Klebsiella pneumoniae* is now increasingly recognized as a key cause of moderate to severe clinical mastitis worldwide. Its persistence in farm environments, adaptation to dairy production systems, and intrinsic antimicrobial resistance contribute to poor therapeutic outcomes, high death rate, and substantial animal welfare impacts. Beyond veterinary relevance, *K. pneumoniae* is a leading human pathogen central to the global antimicrobial resistance crisis. Genomic analyses reveal a substantial overlap among environmental, animal, and human *Klebsiella* populations. Although hypervirulent lineages remain rare in cattle, their potential emergence warrants surveillance. This perspective highlights *K. pneumoniae* mastitis as an emerging One Health challenge requiring enhanced surveillance and targeted control strategies.

KEYWORDS One Health, hypervirulent *Klebsiella*, antimicrobial resistance, bovine mastitis, *Klebsiella pneumoniae*

Bovine mastitis is one of the most economically damaging and welfare-compromising diseases in the global dairy industry. It reduces milk yield and quality and remains as the leading driver of antimicrobial use on dairy farms worldwide (1, 2). While coliform mastitis has historically been dominated by *Escherichia coli*, the past decade has seen a clear increase in environmental mastitis associated with *Klebsiella* species, particularly *Klebsiella pneumoniae* and *K. oxytoca* (3–5). These opportunistic bacteria are now increasingly recognized as significant contributors to clinical mastitis, often associated with more severe clinical presentations (6, 7). The emergence of *K. pneumoniae* in dairy systems has implications that extend beyond milk production and udder health. *K. pneumoniae* is a well-established human pathogen and one of the highest-priority species in the global antimicrobial resistance (AMR) crisis. It may act as a shared reservoir of resistance determinants across animal, environmental, and human sectors (8–10). This perspective summarizes current knowledge on *K. pneumoniae* mastitis, assesses its significance within a One Health framework, and outlines research and policy priorities to address its potential emergence as a broader public health concern.

KLEBSIELLA MASTITIS: A RISING BURDEN IN DAIRY PRODUCTION?

Mastitis associated with *Klebsiella* spp. has become increasingly common in many dairy-producing regions (Table 1). A recent meta-analysis estimated a pooled global prevalence of *Klebsiella* spp. of 7.95% in milk samples from mastitis cases, with a marked increase from 3.85% during 2007–2012 to 12.16% during 2013–2020, and a higher prevalence reported in developing countries (5). Contributing factors include intensified dairy production systems, widespread use of organic bedding materials, such as sawdust, and climatic conditions favoring bacterial proliferation (11). However, this apparent emergence may also reflect historical underestimation, as infections were

Editor Jose A. Vazquez-Boland, The University of Edinburgh, Edinburgh, United Kingdom

Address correspondence to Delphine Payros, delphine.payros@inrae.fr.

Delphine Payros and Eric Oswald contributed equally to this article. The author order was determined by giving priority to the younger researcher for the first name and the senior researcher for the last name.

The authors declare no conflict of interest.

Published 12 February 2026

[This article was published on 12 February 2026 with errors in Table 1. The table was corrected in the current version, posted on 18 February 2026.]

Copyright © 2026 Payros et al. This is an open-access article distributed under the terms of the [Creative Commons Attribution 4.0 International license](https://creativecommons.org/licenses/by/4.0/).

TABLE 1 Worldwide prevalence of *Klebsiella* species associated with bovine mastitis

Country	Sampling date	Prevalence (%)	<i>Klebsiella</i> species	Resistance gene detection	Reference
China	2022	6.1	<i>K. pneumoniae</i>	64.7% BlaTEM gene presence of EBSL strains	Cao et al. (15)
China	2000–2010	3.14	<i>K. pneumoniae</i>	Beta-lactam resistance	Liu et al. (16)
	2010–2020	7.45			
China	Unknown	36.3	<i>K. pneumoniae</i>	Not determined	Cheng et al. (17)
China	2021	26.5	<i>K. pneumoniae</i>	hvKP-blaTEM, blaSHV, blaNDM, blaCTX-M, blaDHA, and blaKPC	Wusiman et al. (18)
Niger	2019–2020	21.6	<i>K. pneumoniae</i>	blaTEM and blaCTX-M gene expression	Anueyiagu et al. (19)
		2.5	<i>K. oxytoca</i>		
		6.3	<i>K. aerogenes</i>		
Brazil	2010	98	<i>K. pneumoniae</i>	KPC-2 blaKPC-2 gene	Silva-Sanchez et al. (20)
Egypt	2018–2025	8	<i>K. pneumoniae</i>	No ESBL	Eissa et al. (21)
Pakistan	2022	11.8	<i>K. pneumoniae</i>	BlaTEM gene but remain sensitive to cefotaxime, ciprofloxacin	Sanam et al. (22)
Japan	2004–2014	38.8	<i>K. pneumoniae</i>	Not determined	Sugiyama et al. (6)
Japan	2012–2014	6.5	<i>K. pneumoniae</i>	ESBL-producer strains	Tsuka et al. (23)
		5.5	<i>K. oxytoca</i>		
Japan	2016–2017	12.3	<i>K. pneumoniae</i>	ESBL-producer strains TEM-116; CTX-2-M	Taniguchi et al. (24)
United States	Unknown	15.35	<i>K. pneumoniae</i>	ESBL strains <i>n</i> = 2/17	Gelalcha et al. (25)
Systemic review	2007–2012	3.85	<i>K. pneumoniae</i>	Not determined	Song et al. (5)
	2013–2020	12.16			
Belgium	2012–2013	0.8	<i>K. pneumoniae</i>		Supre et al. (26)
Scotland	2009–2010	Unknown	<i>K. pneumoniae</i>	4.7% ESBL	Pollock et al. (27)
Germany	2014	3.7	<i>K. pneumoniae</i>	No ESBL	Pirner et al. (28)
		5.37	<i>K. oxytoca</i>		
	2022	11.40	<i>K. pneumoniae</i>		
		5.11	<i>K. oxytoca</i>		
Germany	2021–2022	10.2	<i>K. pneumoniae</i>	Not determined	Krebs et al. (29)
		4.6			
		14.3			
		10.3			

frequently misclassified as coliform mastitis and attributed to *E. coli* in the absence of systematic microbiological identification. *K. pneumoniae* is ubiquitous in soil, feces, water, and bedding materials, facilitating repeated exposure of the teat canal (7, 12). Mastitis caused by *Klebsiella* spp. is most often associated with moderate to severe clinical forms, reflecting the strong acute inflammatory response triggered by these bacteria. In the literature, *Klebsiella* is frequently isolated from clinical mastitis cases characterized by fever, systemic illness, abnormal mammary secretions, and bacteremia. Acute systemic signs and irreversible udder damage are common and often lead to culling. Several studies report higher case-fatality rates and more severe clinical presentations for *Klebsiella* mastitis compared with coliform mastitis due to *E. coli* (4, 6). Consequently, the economic impact per case is substantial and usually greater. This is often due to pronounced and persistent reductions in milk yield (4, 13). Chronic infections, although less common than acute episodes, can be particularly problematic because *Klebsiella* demonstrates variable responses to antimicrobial therapy and may persist despite treatment (14).

PATHOGENESIS AND VIRULENCE FACTORS OF *K. PNEUMONIAE*

In humans, “classical” pathogenic *K. pneumoniae* (cKp) strains are responsible for a wide range of extra-intestinal infections, including pneumonia, sepsis, and urinary tract infections, particularly in hospitalized or immunocompromised individuals. These strains possess a diverse arsenal of virulence determinants that facilitate colonization, immune

evasion, and survival within host tissues, including capsular polysaccharides, lipopolysaccharides, siderophores, and adhesins (9). More than 160 capsular (K) serotypes have been described, with K1, K2, K5, K54, and K57 associated with enhanced invasiveness and increased resistance to phagocytic clearance. *K. pneumoniae* produces multiple siderophores, including enterobactin, salmochelin, yersiniabactin, and aerobactin, which play a critical role in iron acquisition and are central to invasive disease and severity (27). Lipopolysaccharide contributes to protection against complement and modulates inflammatory responses, while type 1 and 3 fimbriae mediate adhesion to mucosal and abiotic surfaces and contribute to biofilm formation. Some *K. pneumoniae* lineages carry the *pks* genomic island encoding the genotoxin colibactin, which has been implicated in enhanced virulence and potential links to carcinogenesis (30, 31). Collectively, these determinants—often carried on mobile genetic elements and subject to complex regulation—underlie the transition of *K. pneumoniae* from gut commensal to opportunistic and virulent pathogen (8, 32). Together, these determinants enable *K. pneumoniae* to induce prolonged inflammation and extensive tissue damage (9).

In bovine mastitis, the capsule impairs phagocytosis, while siderophore-mediated iron acquisition supports bacterial growth in the iron-limited environments, such as the mammary gland, potentially contributing to the severe systemic inflammatory responses frequently observed. Clinically, *K. pneumoniae* mastitis often presents as acute or hyperacute disease, resulting in systemic disease, agalactia, and high culling rates. Mortality can reach significant levels in cases of septicemia (33). Compared with *E. coli*, *K. pneumoniae* infections tend to cause more severe inflammatory responses, and specific genetic determinants likely contribute to infection severity and may account for the systemic “cytokine storm” observed in infected animals (6, 34, 35), as well as bacterial invasion beyond the mammary gland (36–38). Bovine *K. pneumoniae* isolates are enriched in gene clusters involved in ferric citrate, lactose, histidine, and arginine metabolism, likely reflecting positive selection within the nutrient environment of the mammary gland (39–42). They display marked genetic diversity, although predominant sequence types exist, including ST107, which has been identified worldwide (27, 40).

The hypermucoviscous phenotype observed in some human isolates has led to the classification of “hypervirulent” *K. pneumoniae* (hvKP). hvKP is defined genetically as a *K. pneumoniae* lineage harboring the aerobactin siderophore locus (*iuc*) usually in combination with additional plasmid-encoded virulence determinants, such as *iroBCDN* (salmochelin) and *rmpA/rmpA2* (regulator of mucoid phenotype), which collectively distinguish it from cKp strains and confer enhanced invasive potential (43). hvKP emerged in East Asia in the 1980s–1990s as a major cause of community-acquired liver abscess in otherwise healthy individuals (31, 44) and has since been reported globally (45). Of particular concern is the emergence of carbapenem-resistant hvKP frequently belonging to high-risk clonal complexes, such as CC258, which has prompted international alerts and calls for enhanced surveillance (46). hvKP strains remain only sporadically reported in cattle, but their potential presence in dairy systems warrants surveillance (Table 1).

ANTIMICROBIAL RESISTANCE AND THERAPEUTIC CHALLENGES

Among gram-negative bacteria, severe *K. pneumoniae* mastitis is the type most likely to warrant antimicrobial treatment in contrast to non-severe cases, which no longer require systematic therapy (17, 47–49). Clinical outcomes are generally improved when antimicrobial treatment is administered (6), but therapeutic management is complicated by the intrinsic resistance of *K. pneumoniae* to several antimicrobials commonly used for mastitis therapy, including ampicillin and other narrow-spectrum β -lactams. Historically, treatment has relied on sulfonamides (sulfamethoxazole–trimethoprim) and, in more severe cases, on critically important antimicrobials, such as third- and fourth-generation cephalosporins (e.g., ceftiofur and cefquinome) and fluoroquinolones (e.g., marbofloxacin), guided by bacteriological identification and antimicrobial susceptibility testing. Increasing restrictions on the use of critically important antimicrobials under stewardship

frameworks have narrowed therapeutic options, emphasizing the need for judicious antimicrobial use and preventive control measures. The detection of extended-spectrum β -lactamase (ESBL)-producing *Klebsiella* in agricultural environments highlights the risk of resistance emergence and dissemination within dairy herds (25, 33, 50). Although carbapenem resistance remains rare in bovine isolates, the environmental detection of carbapenemase-encoding genes and sporadic reports of carbapenemase-producing strains raise concerns regarding interspecies transmission (51). Cure rates for *Klebsiella* mastitis are lower than those reported for *E. coli* mastitis (4), and supportive therapy, including fluid administration and nonsteroidal anti-inflammatory drugs, is essential in severe cases. These challenges underscore the need for improved diagnostics, strengthened antimicrobial stewardship, and alternative interventions, including vaccination and enhanced environmental management (11, 52–55).

ONE HEALTH IMPLICATIONS

Within a One Health framework, *Klebsiella* spp. and their mobile genetic elements circulate among interconnected animal, human, and environmental reservoirs (25, 56). The dairy farm represents a complex ecosystem in which humans, animals, and environmental microbes co-evolve (57). *K. pneumoniae* persists in manure, bedding materials, water troughs, and biofilms on milking equipment, creating conditions favorable for environmental persistence, horizontal gene transfer, and cross-species exposure (10). *Klebsiella* spp. are major reservoirs and exchange hubs for AMR in human medicine. Although direct zoonotic transmission of mastitis-associated strains has not been conclusively demonstrated, overlapping genomic signatures among isolates from humans, animals, and environmental sources warrant caution (58–60). Their presence in dairy environments may facilitate dissemination of ESBLs, carbapenemase genes, and other mobile resistance determinants or plasmids among environmental, commensal, and pathogenic bacteria (51, 60). These plasmids may encode antimicrobial resistance determinants, virulence factors, or both. While non-conjugative plasmids tend to remain lineage-restricted, self-transmissible plasmids facilitate horizontal dissemination of adaptive traits within and across *Klebsiella* populations (61). This dynamic is illustrated by the recent identification of hybrid IncFIB–IncFIIk plasmids carrying both multidrug resistance and virulence genes in hvKP isolates from cattle and humans, highlighting the role of livestock in the emergence and amplification of high-risk plasmid lineages (62). Genomic similarity between certain human and bovine isolates suggests potential interspecies transmission, highlighting livestock as a possible reservoir of antimicrobial-resistant *Klebsiella* and emphasizing the importance of genomic epidemiology to clarify transmission pathways (27, 63–65). While pasteurization effectively eliminates *Klebsiella* from milk, risks may persist through raw milk consumption, occupational exposure, and environmental dissemination via manure and wastewater (57, 66). The potential emergence of hvKP in dairy environments is of particular concern, as these strains harbor an expanded repertoire of virulence factors compared with classical isolates. hvKP resistant to critically important antimicrobials has not been reported in cattle from high-income countries. However, contrasting recent epidemiological patterns may emerge between high- and low- or middle-income countries and regions, as described for ESBL-producing *E. coli* and *K. pneumoniae* (58, 67). These differences underscore the need for region-specific AMR control strategies (68). Contrasting epidemiological patterns highlight the need for region-specific control strategies, prioritizing the limitation of human-to-human transmission in high-income countries while strengthening sanitation, biosecurity, and environmental measures in low- and middle-income countries.

KNOWLEDGE GAPS AND RESEARCH PRIORITIES

Link virulence to host adaptation

Determine whether bovine-adapted *K. pneumoniae* lineages (if any) can acquire hypervirulence determinants and assess their impact on mastitis severity and outcomes.

Identify and quantify environmental reservoirs

Clarify the role of bedding, manure, water, soil, and farm infrastructure in the persistence and transmission of *Klebsiella* spp. within dairy systems.

Resolve One Health transmission pathways

Define the directionality and frequency of animal–human and human–animal transmission using high-resolution genomic epidemiology.

Understand plasmid-driven risk emergence

Elucidate the role of resistance–virulence plasmids, particularly IncF-type hybrids, in the emergence and spread of high-risk *Klebsiella* clones.

CONCLUSIONS

The contribution of *K. pneumoniae* to bovine mastitis has likely been historically underestimated, in part due to diagnostic limitations. Whether its apparent emergence reflects improved detection or a genuine epidemiological shift, *K. pneumoniae* mastitis now represents a significant and growing challenge in modern dairy systems. Coordinated efforts across veterinary, environmental, and public health sectors are therefore essential to mitigate its impact on dairy production, antimicrobial stewardship, and the broader antimicrobial resistance crisis (20, 69, 70). Proactive genomic surveillance, improved environmental control measures, and targeted intervention strategies will be critical to safeguarding both animal and human health against the escalating threat posed by *K. pneumoniae*.

ACKNOWLEDGMENTS

Artificial intelligence tools, such as Microsoft Copilot, ChatGPT, and DeepL, were used to assist with the English editing.

AUTHOR AFFILIATIONS

¹Univ Toulouse, ENVT, INRAE, IHAP, Toulouse, France

²Univ Toulouse, ENVT, INRAE, INSERM, IRSD, Toulouse, France

³CHU de Toulouse, Hôpital Purpan, Toulouse, France

AUTHOR ORCIDs

Delphine Payros  <http://orcid.org/0000-0003-4820-7986>

Frédéric Auvray  <http://orcid.org/0000-0001-5532-1045>

Gilles Foucras  <https://orcid.org/0000-0002-0363-0337>

Eric Oswald  <http://orcid.org/0000-0002-3017-0081>

AUTHOR CONTRIBUTIONS

Delphine Payros, Conceptualization, Formal analysis, Supervision, Writing – original draft, Writing – review and editing | Frédéric Auvray, Writing – original draft, Writing – review and editing | Gilles Foucras, Writing – original draft | Eric Oswald, Conceptualization, Formal analysis, Supervision, Writing – original draft, Writing – review and editing

REFERENCES

- Deng Z, Koop G, Lam TJGM, van der Lans IA, Vernooij JCM, Hogeveen H. 2019. Farm-level risk factors for bovine mastitis in Dutch automatic milking dairy herds. *J Dairy Sci* 102:4522–4535. <https://doi.org/10.3168/jds.2018-15327>
- Stevens M, Piepers S, De Vliegher S. 2016. Mastitis prevention and control practices and mastitis treatment strategies associated with the consumption of (critically important) antimicrobials on dairy herds in Flanders, Belgium. *J Dairy Sci* 99:2896–2903. <https://doi.org/10.3168/jds.2015-10496>
- Panchal J, Patel A, Patel S, Goswami D. 2024. Understanding mastitis: microbiome, control strategies, and prevalence - A comprehensive review. *Microb Pathog* 187:106533. <https://doi.org/10.1016/j.micpath.2023.106533>
- Ruegg PL. 2017. A 100-year review : mastitis detection, management and prevention. *J Dairy Sci* 100:10381–10397. <https://doi.org/10.3168/jds.2017-13023>
- Song J, Xiang W, Wang Q, Yin J, Tian T, Yang Q, Zhang M, Ge G, Li J, Diao N, Liu F, Shi K, Cai R, Du R, Gong Q. 2023. Prevalence and risk factors of *Klebsiella* spp. in milk samples from dairy cows with mastitis—a global systematic review. *Front Vet Sci* 10:1143257. <https://doi.org/10.3389/fvet.2023.1143257>
- Sugiyama M, Watanabe M, Sonobe T, Kibe R, Koyama S, Kataoka Y. 2022. Efficacy of antimicrobial therapy for bovine acute *Klebsiella pneumoniae* mastitis. *J Vet Med Sci* 84:1023–1028. <https://doi.org/10.1292/jvms.21-0617>
- Zadoks RN, Griffiths HM, Munoz MA, Ahlstrom C, Bennett GJ, Thomas E, Schukken YH. 2011. Sources of *Klebsiella* and *Raoultella* species on dairy farms: be careful where you walk. *J Dairy Sci* 94:1045–1051. <https://doi.org/10.3168/jds.2010-3603>
- Martin RM, Bachman MA. 2018. Colonization, infection, and the accessory genome of *Klebsiella pneumoniae*. *Front Cell Infect Microbiol* 8:4. <https://doi.org/10.3389/fcimb.2018.00004>
- Paczosa MK, Meccas J. 2016. *Klebsiella pneumoniae*: going on the offense with a strong defense. *Microbiol Mol Biol Rev* 80:629–661. <https://doi.org/10.1128/MMBR.00078-15>
- Wyres KL, Holt KE. 2018. *Klebsiella pneumoniae* as a key trafficker of drug resistance genes from environmental to clinically important bacteria. *Curr Opin Microbiol* 45:131–139. <https://doi.org/10.1016/j.mib.2018.04.04>
- Hogan J, Smith KL. 2012. Managing environmental mastitis. *Vet Clin North Am Food Anim Pract* 28:217–224. <https://doi.org/10.1016/j.cvfa.2012.03.009>
- Munoz MA, Ahlström C, Rauch BJ, Zadoks RN. 2006. Fecal shedding of *Klebsiella pneumoniae* by dairy cows. *J Dairy Sci* 89:3425–3430. [https://doi.org/10.3168/jds.S0022-0302\(06\)72379-7](https://doi.org/10.3168/jds.S0022-0302(06)72379-7)
- Gröhn YT, Wilson DJ, González RN, Hertl JA, Schulte H, Bennett G, Schukken YH. 2004. Effect of pathogen-specific clinical mastitis on milk yield in dairy cows. *J Dairy Sci* 87:3358–3374. [https://doi.org/10.3168/jds.S0022-0302\(04\)73472-4](https://doi.org/10.3168/jds.S0022-0302(04)73472-4)
- Roberson JR. 2012. Treatment of clinical mastitis. *Vet Clin North Am Food Anim Pract* 28:271–288. <https://doi.org/10.1016/j.cvfa.2012.03.011>
- Cao W, Xu Y, Huang Y, Xu T. 2023. Isolation of pathogenic bacteria from dairy cow mastitis and correlation of biofilm formation and drug resistance of *Klebsiella pneumoniae* in Jiangsu, China. *Agriculture* 13:1984. <https://doi.org/10.3390/agriculture13101984>
- Liu K, Zhang L, Gu X, Qu W. 2022. The prevalence of *Klebsiella* spp. associated with bovine mastitis in China and its antimicrobial resistance rate: a meta-analysis. *Front Vet Sci* 9:757504. <https://doi.org/10.3389/fvet.2022.757504>
- Cheng J, Zhou M, Nobrega DB, Cao Z, Yang J, Zhu C, Han B, Gao J. 2021. Virulence profiles of *Klebsiella pneumoniae* isolated from 2 large dairy farms in China. *J Dairy Sci* 104:9027–9036. <https://doi.org/10.3168/jds.2020-20042>
- Wusiman M, Zuo J, Yu Y, Lv Z, Wang M, Nie L, Zhang X, Wu J, Wu Z, Jiang W, Pan Z, Zhang W, Yin H, Huang C, Chen Z, Miao J, Chen W, Han X. 2024. Molecular characterization of *Klebsiella pneumoniae* in clinical bovine mastitis in 14 provinces in China. *Vet Res Commun* 49:18. <https://doi.org/10.1007/s11259-024-10598-4>
- Anueyiagu KN, Agusi ER, Kabantiyok D, Ayanbimpe GM, Ikeh EI. 2025. Zoonotic potential of ESBL-producing coliforms in pastorally managed ruminants with subclinical mastitis in Plateau State, Nigeria. *Front Antibiot* 4:1632264. <https://doi.org/10.3389/frabi.2025.1632264>
- Silva-Sanchez J, Barrios-Camacho H, Hernández-Rodríguez E, Duran-Bedolla J, Sanchez-Perez A, Martínez-Chavarría LC, Xicohtencatl-Cortes J, Hernández-Castro R, Garza-Ramos U. 2021. Molecular characterization of KPC-2-producing *Klebsiella pneumoniae* ST258 isolated from bovine mastitis. *Braz J Microbiol* 52:1029–1036. <https://doi.org/10.1007/s42770-021-00445-y>
- Eissa N, Salman MB, Younes AM, Mohamed ESA, Abu-Seida AM, Abdulkarim A, Zin Eldin AI. 2025. One Health approach on zoonotic multidrug-resistant *Klebsiella pneumoniae* isolated from Egyptian cattle, horses, and humans. *Open Vet J* 15:4219–4234. <https://doi.org/10.5455/OVJ.2025.v15.i9.28>
- Sanam, Haq IU, Kamal M, Khan S, Khattak I, Khan NU, Ali T, Riaz S, Massa S, Usman T. 2025. Prevalence and antimicrobial resistance of *Klebsiella pneumoniae* isolated from subclinical mastitis in selected pure dairy cattle breeds in Pakistan. *Curr Microbiol* 82:548. <https://doi.org/10.1007/s00284-025-04550-1>
- Tsuka T, Ozaki H, Saito D, Murase T, Okamoto Y, Azuma K, Osaki T, Ito N, Murahata Y, Imagawa T. 2021. Genetic characterization of CTX-M-2-producing *Klebsiella pneumoniae* and *Klebsiella oxytoca* associated with bovine mastitis in Japan. *Front Vet Sci* 8:659222. <https://doi.org/10.3389/fvets.2021.659222>
- Taniguchi T, Latt KM, Tarigan E, Yano F, Sato H, Minamino T, Misawa N. 2021. A 1-year investigation of extended-spectrum beta-lactamase-producing *Escherichia coli* and *Klebsiella pneumoniae* isolated from bovine mastitis at a large-scale dairy farm in Japan. *Microb Drug Resist* 27:1450–1454. <https://doi.org/10.1089/mdr.2020.0481>
- Gelalcha BD, Mohammed RI, Gelgie AE, Kerro Dego O. 2023. Molecular epidemiology and pathogenomics of extended-spectrum beta-lactamase producing- *Escherichia coli* and - *Klebsiella pneumoniae* isolates from bulk tank milk in Tennessee, USA. *Front Microbiol* 14:1283165. <https://doi.org/10.3389/fmicb.2023.1283165>
- Supré K, Lommelen K, De Meulemeester L. 2014. Antimicrobial susceptibility and distribution of inhibition zone diameters of bovine mastitis pathogens in Flanders, Belgium. *Vet Microbiol* 171:374–381. <https://doi.org/10.1016/j.vetmic.2014.02.045>
- Pollock J, Foster G, Henderson K, Bell J, Hutchings MR, Paterson GK. 2025. Antimicrobial resistance profiles and molecular epidemiology of *Klebsiella pneumoniae* isolates from Scottish bovine mastitis cases. *Epidemiol Infect* 153:e15. <https://doi.org/10.1017/S0950268824001754>
- Pirner LH, Petzl W, Gangl A, Huber-Schlenstedt R, Sorge US. 2024. *In vitro* antimicrobial resistance of *Escherichia coli*, *Serratia marcescens*, *Klebsiella oxytoca*, and *Klebsiella pneumoniae* on Bavarian dairy farms between 2014 and 2022. *J Dairy Sci* 107:8402–8412. <https://doi.org/10.3168/jds.2023-24536>
- Krebs I, Zhang Y, Wente N, Leimbach S, Krömker V. 2023. Severity of clinical mastitis and bacterial shedding. *Pathogens* 12:1098. <https://doi.org/10.3390/pathogens12091098>
- Nougayrède J-P, Homburg S, Taieb F, Boury M, Brzuszkiewicz E, Gottschalk G, Buchrieser C, Hacker J, Dobrindt U, Oswald E. 2006. *Escherichia coli* induces DNA double-strand breaks in eukaryotic cells. *Science* 313:848–851. <https://doi.org/10.1126/science.1127059>
- Zhu J, Wang T, Chen L, Du H. 2021. Virulence factors in hypervirulent *Klebsiella pneumoniae*. *Front Microbiol* 12:642484. <https://doi.org/10.3389/fmicb.2021.642484>
- Nguyen TNT, Howells G, Short FL. 2025. How *Klebsiella pneumoniae* controls its virulence. *PLoS Pathog* 21:e1013499. <https://doi.org/10.1371/journal.ppat.1013499>
- Risetti RM, de Paula CL, Yamada AY, Bertani AM de J, Costa ABN, Sacchi CT, Campos KR, Guerra ST, Guimarães FF, Joaquim SF, Langoni H, Rall VLM, Bertolini AB, Paz PJ de L, Bello TS, Filho MFA, Panegossi LC, Reznik AU, Ribeiro MG, Camargo CH. 2025. Detection of multiple clones and extended-spectrum β -lactamase production among *Klebsiella pneumoniae* complex isolates from the milk of cows with different severity scores of clinical mastitis. *Lett Appl Microbiol* 78:ovaf118. <https://doi.org/10.1093/lambio/ovaf118>
- Bannerman DD, Paape MJ, Hare WR, Hope JC. 2004. Characterization of the bovine innate immune response to intramammary infection with *Klebsiella pneumoniae*. *J Dairy Sci* 87:2420–2432. [https://doi.org/10.3168/jds.S0022-0302\(04\)73365-2](https://doi.org/10.3168/jds.S0022-0302(04)73365-2)
- Hisaeda K, Arima H, Sonobe T, Nasu M, Hagiwara K, Kirisawa R, Takahashi T, Kikuchi N, Nagahata H. 2011. Changes in acute-phase proteins and cytokines in serum and milk whey from dairy cows with naturally

- occurring peracute mastitis caused by *Klebsiella pneumoniae* and the relationship to clinical outcome. *J Vet Med Sci* 73:1399–1404. <https://doi.org/10.1292/jvms.10-0403>
36. Gao J, Li S, Zhang J, Zhou Y, Xu S, Barkema HW, Nobrega DB, Zhu C, Han B. 2019. Prevalence of potential virulence genes in *Klebsiella* spp. isolated from cows with clinical mastitis on large Chinese dairy farms. *Foodborne Pathog Dis* 16:856–863. <https://doi.org/10.1089/fpd.2019.2657>
 37. Ribeiro MG, Motta RG, Paes AC, Allendorf SD, Salerno T, Siqueira AK, Fernandes MC, Lara GHB. 2008. Peracute bovine mastitis caused by *Klebsiella pneumoniae*. *Arq Bras Med Vet Zootec* 60:485–488. <https://doi.org/10.1590/S0102-09352008000200031>
 38. Tong X, Barkema HW, Nobrega DB, Xu C, Han B, Zhang C, Yang J, Li X, Gao J. 2025. Virulence of bacteria causing mastitis in dairy cows : a literature review. *Microorganisms* 13:167. <https://doi.org/10.3390/microorganisms13010167>
 39. Holt KE, Wertheim H, Zadoks RN, Baker S, Whitehouse CA, Dance D, Jenney A, Connor TR, Hsu LY, Severin J, et al. 2015. Genomic analysis of diversity, population structure, virulence, and antimicrobial resistance in *Klebsiella pneumoniae*, an urgent threat to public health. *Proc Natl Acad Sci USA* 112:E3574–E3581. <https://doi.org/10.1073/pnas.1501049112>
 40. Zheng Z, Gorden PJ, Xia X, Zheng Y, Li G. 2022. Whole-genome analysis of *Klebsiella pneumoniae* from bovine mastitis milk in the U.S. *Environ Microbiol* 24:1183–1199. <https://doi.org/10.1111/1462-2920.15721>
 41. Biggel M, Nüesch-Inderbinen M, Logean M, Corti S, Kelbert L, Stephan R. 2025. Genomic characterization of *Klebsiella* spp. from bovine mastitis: dissemination of a conserved, highly transmissible *lac_{acc}⁺ fec⁺* plasmid drives burden of disease. *Appl Environ Microbiol* 91:e01162-25. <https://doi.org/10.1128/aem.01162-25>
 42. O'Brien B, Yushchenko A, Suh J, Jung D, Cai Z, Nguyen NS, Semret M, Dufour S, Fanning S, Ronholm J. 2025. Subtle genomic differences in *Klebsiella pneumoniae sensu stricto* isolates indicate host adaptation. *One Health* 20:100970. <https://doi.org/10.1016/j.onehlt.2025.100970>
 43. Tang Y, Du P, Du C, Yang P, Shen N, Russo TA, Liu C. 2025. Genomically defined hypervirulent *Klebsiella pneumoniae* contributed to early-onset increased mortality. *Nat Commun* 16:2096. <https://doi.org/10.1038/s41467-025-57379-4>
 44. Russo TA, Marr CM. 2019. Hypervirulent *Klebsiella pneumoniae*. *Clin Microbiol Rev* 32:e00001-19. <https://doi.org/10.1128/CMR.00001-19>
 45. Das M. 2024. Global update on hypervirulent *Klebsiella pneumoniae*. *Lancet Infect Dis* 24:e621. [https://doi.org/10.1016/S1473-3099\(24\)00610-8](https://doi.org/10.1016/S1473-3099(24)00610-8)
 46. European Centre for Disease Prevention and Control. 2024. Emergence of hypervirulent *Klebsiella pneumoniae* ST23 carrying carbapenemase genes in EU/EEA countries, first update Event background Whole-genome sequencing and epidemiological analysis. <https://doi.org/10.2900/993023>
 47. Fuenzalida MJ, Ruegg PL. 2019. Negatively controlled, randomized clinical trial to evaluate intramammary treatment of nonsevere, Gram-negative clinical mastitis. *J Dairy Sci* 102:5438–5457. <https://doi.org/10.3168/jds.2018-16156>
 48. Ruegg PL. 2021. What is success ? A narrative review of research evaluating outcomes of antibiotics used for treatment of clinical mastitis. *Front Vet Sci* 8:639641. <https://doi.org/10.3389/fvets.2021.639641>
 49. de Jong E, McCubbin KD, Speksnijder D, Dufour S, Middleton JR, Ruegg PL, Lam TJGM, Kelton DF, McDougall S, Godden SM, Lago A, Rajala-Schultz PJ, Orsel K, De Vlieghe S, Krömker V, Nobrega DB, Kastelic JP, Barkema HW. 2023. Invited review: selective treatment of clinical mastitis in dairy cattle. *J Dairy Sci* 106:3761–3778. <https://doi.org/10.3168/jds.2022-22826>
 50. Bonardi S, Cabassi CS, Fiaccadori E, Cavirani S, Parisi A, Bacci C, Lamperti L, Rega M, Conter M, Marra F, Crippa C, Gambi L, Spadini C, Iannarelli M, Paladini C, Filippin N, Pasquali F. 2023. Detection of carbapenemase- and ESBL-producing *Klebsiella pneumoniae* from bovine bulk milk and comparison with clinical human isolates in Italy. *Int J Food Microbiol* 387:110049. <https://doi.org/10.1016/j.jiffoodmicro.2022.110049>
 51. Cantón R, Akóva M, Carmeli Y, Giske CG, Glupczynski Y, Gniadkowski M, Livermore DM, Miriagou V, Naas T, Rossolini GM, Samuelsen Ø, Seifert H, Woodford N, Nordmann P. 2012. Rapid evolution and spread of carbapenemases among Enterobacteriaceae in Europe. *Clin Microbiol Infect* 18:413–431. <https://doi.org/10.1111/j.1469-0691.2012.03821.x>
 52. Dego OK. 2021. Control and prevention of mastitis: part two. *IntechOpen*. <https://doi.org/10.5772/intechopen.93484>
 53. Li X, Xu C, Liang B, Kastelic JP, Han B, Tong X, Gao J. 2023. Alternatives to antibiotics for treatment of mastitis in dairy cows. *Front Vet Sci* 10:1160350. <https://doi.org/10.3389/fvets.2023.1160350>
 54. Rainard P, Gilbert FB, Martins RP, Germon P, Foucras G. 2022. Progress towards the elusive mastitis vaccines. *Vaccines (Basel)* 10:296. <https://doi.org/10.3390/vaccines10020296>
 55. Touza-Otero L, Landin M, Diaz-Rodriguez P. 2024. Fighting antibiotic resistance in the local management of bovine mastitis. *Biomed Pharmacother* 170:115967. <https://doi.org/10.1016/j.biopha.2023.115967>
 56. Ludden C, Moradigaravand D, Jamrozy D, Gouliouris T, Blane B, Naydenova P, Hernandez-Garcia J, Wood P, Hadjirin N, Radakovic M, Crawley C, Brown NM, Holmes M, Parkhill J, Peacock SJ. 2020. A One Health study of the genetic relatedness of *Klebsiella pneumoniae* and their mobile elements in the East of England. *Clin Infect Dis* 70:219–226. <https://doi.org/10.1093/cid/ciz174>
 57. Robinson TP, Bu DP, Carrique-Mas J, Fèvre EM, Gilbert M, Grace D, Hay SI, Jiwakanon J, Kakkar M, Kariuki S, Laxminarayan R, Lubroth J, Magnusson U, Thi Ngoc P, Van Boeckel TP, Woolhouse MEJ. 2016. Antibiotic resistance is the quintessential One Health issue. *Trans R Soc Trop Med Hyg* 110:377–380. <https://doi.org/10.1093/trstmh/trw048>
 58. Dereeper A, Gruel G, Pot M, Couvin D, Barbier E, Bastian S, Bambou J-C, Gelu-Simeon M, Ferdinand S, Guyomard-Rabenirina S, Passet V, Martino F, Piveteau P, Reynaud Y, Rodrigues C, Roger P-M, Roy X, Talarmin A, Tressieres B, Valette M, Brisse S, Breurec S. 2022. Limited transmission of *Klebsiella pneumoniae* among humans, animals, and the environment in a Caribbean Island, Guadeloupe (French West Indies). *Microbiol Spectr* 10:e01242-22. <https://doi.org/10.1128/spectrum.01242-22>
 59. Nery Garcia BL, Dantas STA, da Silva Barbosa K, Mendes Mitsunaga T, Butters A, Camargo CH, Nobrega DB. 2024. Extended-spectrum beta-lactamase-producing *Escherichia coli* and other antimicrobial-resistant Gram-negative pathogens isolated from bovine mastitis: a One Health perspective. *Antibiotics (Basel)* 13:391. <https://doi.org/10.3390/antibiotics13050391>
 60. Huang X, Yao X, Hou Y, Zhang D, Xie R, Shi C, Shang Y, Bi H, Song W, Hua L, Li C, Chen H, Wu B, Peng Z. 2025. Global trends of antimicrobial resistance and virulence of *Klebsiella pneumoniae* from different host sources. *Commun Med* 5:383. <https://doi.org/10.1038/s43856-025-01112-1>
 61. Yang X, Liu X, Xu Y, Yang C, Chan EW-C, Shum H, Chen S. 2022. Genetic and functional characterization of a conjugative KpVP-2-Type virulence plasmid from a clinical *Klebsiella pneumoniae* strain. *Front Microbiol* 13:914884. <https://doi.org/10.3389/fmicb.2022.914884>
 62. Wang J, Ji X, Garcia P, Li J, Zhang L, Wang H, Wang R, He T. 2025. Evolution and transmission potential of iuc3-positive virulence plasmids in hypervirulent *Klebsiella pneumoniae*. *Microbiol Res* 299:128242. <https://doi.org/10.1016/j.micres.2025.128242>
 63. Lopes BS, Altayb HN, Mahdy K, Ei Sakka N. 2025. Molecular epidemiology of extended-spectrum beta-lactamase-producing *Klebsiella pneumoniae* bloodstream infections from Aberdeen, Scotland, and their comparison to isolates from England. *Microb Genom* 11:001413. <https://doi.org/10.1099/mgen.0.001413>
 64. Naranjo-Lucena A, Slowey R. 2023. Invited review: Antimicrobial resistance in bovine mastitis pathogens: a review of genetic determinants and prevalence of resistance in European countries. *J Dairy Sci* 106:1–23. <https://doi.org/10.3168/jds.2022-22267>
 65. Wareth G, Neubauer H. 2021. The animal-foods-environment interface of *Klebsiella pneumoniae* in Germany: an observational study on pathogenicity, resistance development and the current situation. *Vet Res* 52:16. <https://doi.org/10.1186/s13567-020-00875-w>
 66. Rahman MH, Akther S, Ahmed S, Shahadat MN, Munsif MN, Siddique AB. 2025. Epidemiological factors associated with the prevalence of mobile genetic elements, and antimicrobial resistance patterns in *Klebsiella pneumoniae* of farm environments in Bangladesh. *BMC Med Genomics* 18:114. <https://doi.org/10.1186/s12920-025-02181-w>
 67. Miltgen G, Berti V, Milenkov M, Schmitt H, Wagenaar JA, Armand-Lefevre L. 2025. Circulation of extended-spectrum β -lactamase and plasmid-borne cephalosporinase-producing *Escherichia coli* from a One Health perspective: a narrative review. *Clin Microbiol Infect*:S1198-743X(25)00610-X. <https://doi.org/10.1016/j.cmi.2025.12.003>
 68. Khamisse E, Bertrand X, Bouchard D, Collineau L, Fortineau O, Haenni M, Madec J-Y, Saegerman C, Giraud E, Oswald E. 2025. Rethinking the role

- of animals in antimicrobial resistance. *Lancet Microbe* 101248:101248. <https://doi.org/10.1016/j.lanmic.2025.101248>
69. Christaki E, Marcou M, Tofarides A. 2020. Antimicrobial resistance in bacteria: mechanisms, evolution, and persistence. *J Mol Evol* 88:26–40. <https://doi.org/10.1007/s00239-019-09914-3>
70. Navon-Venezia S, Kondratyeva K, Carattoli A. 2017. *Klebsiella pneumoniae*: a major worldwide source and shuttle for antibiotic resistance. *FEMS Microbiol Rev* 41:252–275. <https://doi.org/10.1093/femsre/fux013>