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A GROWING THREAT: A SYSTEMATIC REVIEW ON THE ANTIMICROBIAL RESISTANCE AND VIRULENCE FACTORS IN HYPERVIRULENT KLEBSIELLA PNEUMONIAE

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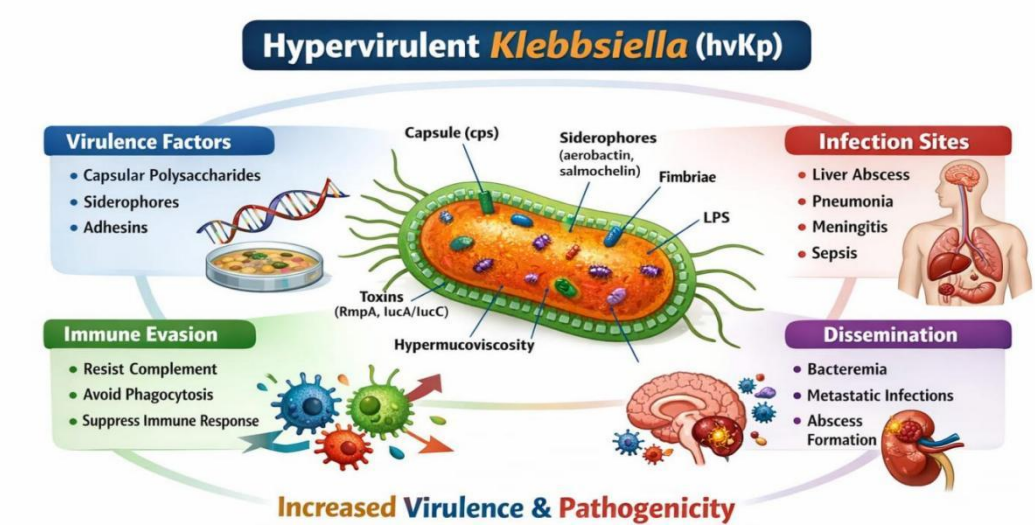
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ABSTRACT
Background: A particularly dangerous strain of bacteria called hypervirulent *Klebsiella pneumoniae* (hvKp) has been causing serious infections both in communities and hospitals with increasing frequency. What makes this especially concerning is the rise of a carbapenem-resistant version (CR-hvKp) — because for a long time, scientists assumed that when bacteria develop drug resistance, they tend to become less harmful. CR-hvKp breaks that rule entirely.
Objectives: The researchers wanted to get a clearer global picture of how widespread hvKp and CR-hvKp actually are. They also looked at which antibiotics these strains resist, how they cause disease, which bacterial lineages are the most dangerous, and how infection with these strains affects patient outcomes.
Methods: The team conducted an extensive, comprehensive evaluation of the literature using PRISMA standards, a standard methodology for systematic reviews. They examined research that was published in five significant scientific databases between 2013 and 2024: PubMed, Scopus, Web of Grey literature, science, and Embase. They concentrated on observational studies and meta-analyses that found hvKp using established techniques, including the "string test" for hypermucoviscosity or the identification of certain virulence genes.
Conclusions: hvKp, especially in its drug-resistant variant, CR-hvKp, represents an increasing hazard to world health. It combines a remarkable ability to produce severe sickness with resistance to last-resort antibiotics, and it carries a high risk of mortality. To tackle it, stronger infection control measures in hospital settings, faster diagnostic tools, more intelligent treatment plans, and better tracking systems are all required.

KEYWORDS: *Hypervirulent Klebsiella pneumoniae (hvKp), Carbapenem-resistant Klebsiella pneumoniae (CR-hvKp), Antimicrobial resistance, Virulence factors, Invasive liver abscess syndrome*

INTRODUCTION

From relatively frequent UTIs to potentially catastrophic conditions like liver abscesses, the well-known hospital-acquired bacterium Klebsiella pneumoniae (K. pneumoniae) causes a wide range of illnesses.[1-3] It was formerly believed to be an opportunistic infection, meaning that it mainly endangered people who were already vulnerable, such as hospital patients recovering or people with weakened immune systems. However, a far more aggressive variety of K. pneumoniae called hypervirulent K. pneumoniae (hvKp) has emerged and behaves somewhat differently [1,2]. [3, 7, 9] What sets HPV apart is its ability to induce deadly, invasive infections in otherwise healthy people without any clear underlying diseases or conventional risk factors. What we would typically anticipate from this kind of microbe is drastically different.
. Originally identified as a concern largely confined to the Asia-Pacific region, hvKp has since spread worldwide and is now recognised as a genuine global public health threat. First recognized in Taiwan in the 1980s as pyogenic liver abscesses with metastatic complications — including endophthalmitis and meningitis — in healthy patients,[5,26] hvKp has since been reported across Europe, North America, Australia, and Africa,[7,9,30] with research output growing from fewer than seven publications annually before 2013 to over one hundred by 2023.[7] The pathogenic aggression of hvKp is driven by hypermucoviscous capsules, iron-scavenging siderophore systems, capsular serotypes K1 and K2, and virulence-associated genes including *rmpA*, *rmpA2*, *iucA*, and *peg-344*.[4,6,8,11,22] Most critically, hvKp strains now simultaneously harbour carbapenem resistance while preserving full hyper virulence, yielding a "dual-threat" phenotype,[9,12,24] prompting a 2024 WHO emergency alert documenting CR-hvKp ST23 strains carrying carbapenemase genes across all six WHO geographic regions.[15]



BACKGROUND AND EPIDEMIOLOGY

Classification of *K. pneumoniae* into classical and hypervirulent phenotypes relies on phenotypic and genotypic criteria.[4,6,9] The hypermucoviscous string test (mucoid string >5 mm) is the most recognizable phenotypic marker,[6,14] though virulence-associated genes *rmpA*, *rmpA2*, *iucA*, and *peg-344* now constitute the standard diagnostic approach, achieving >95% accuracy.[6,9,23] A meta-analysis of 46 studies and 6,134 patients established global hvKp prevalence at 33.0%, ranging from 15.8% (Oceania) to 41.5% (Africa),[13,21] with multi-center Indian data and 28-country global surveillance confirming escalating hvKp and CR-hvKp burden.[20,29] While cKp predominantly causes hospital-acquired infections in vulnerable populations,[1,2,10] hvKp increasingly presents as community-acquired.[3,5,13] Hospital-acquired hvKp prevalence has nonetheless risen sharply from 25.9% (2006–2018) to 47.1% (2019–2024) — an 82% increase — with invasive liver abscess syndrome (ILAS) now documented in Europe and the Americas.[13,19,26,30]

RESEARCH GAP AND RATIONALE

Despite three decades of research, critical gaps persist in understanding how hvKp acquires and stably maintains carbapenem resistance while preserving virulence — an evolutionary paradox insufficiently explained by current literature.[3,9,12,24] CR-hvKp prevalence has escalated from 9.5% (2016–2018) to 16.5% (2019–2024) — a 73.7% relative increase — driven by co-localization of virulence and resistance determinants on conjugative plasmids and chromosomal genomic islands.[13,25] Patients with CR-hvKp experience dramatically higher mortality than those with carbapenem-susceptible hvKp,[18] and hvKp broadly confers increased risks of liver abscess,[3,13,26] metastatic spread,[3,13] meningitis,[3,13] and septic shock[13] versus cKp. Recurrent ILAS has been increasingly documented,[28] and CR-hvKp ST11 outbreak mortality reached 42.5% in one Chinese hospital.[12,27]

NOVELTY AND RATIONALE OF THE SYSTEMATIC REVIEW

In response to the WHO emergency alert on CR-hvKp ST23 global dissemination, this review offers the first thorough synthesis looking at concurrent virulence gene expression and antibiotic resistance determinants in hvKp, using PRISMA 2020 methodology to identify, evaluate, and synthesize global evidence [9,13,16].[15] CR-hvKp accounts for 13.8% of hvKp isolates, increasing at rates higher than those of classical K. pneumoniae [13,17]. Research contributions reflecting the epidemiological burden are dominated by China.[7,14] Meningitis is 11.14 times more common and liver abscess is 6.35 times more common in hvKp compared to cKp [3,13], requiring a thorough understanding of virulence and resistance mechanisms to guide new treatments and infection control measures.[9, 13, 17]

METHODOLOGY

PROTOCOL

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines were followed in conducting this systematic review.[16] To guarantee thorough and open reporting of all review procedures and conclusions, the PRISMA 2020 checklist—which consists of 27 items spanning several reporting domains (Title, Abstract, Introduction, Methods, Results, Discussion, and Other)—was employed.

INFORMATION SOURCES AND SEARCH STRATEGY

In order to locate all relevant material, the team carried out a thorough literature search across four main scientific databases, including PubMed (which includes MEDLINE), Scopus, Web of Science, and Embase, encompassing everything published up until December 2024.Research into antibiotic resistance and disease-causing mechanisms in hypervirulent Klebsiella pneumoniae was the main focus.
To make sure they didn't overlook anything that wasn't yet officially published or was still in press, the researchers

personally searched grey literature sources in addition to the official databases, such as Google Scholar and conference proceedings.
The actual search strategy was meticulously created in conjunction with a skilled medical librarian. In order to ensure that nothing pertinent was overlooked, it merged free-text keywords with predefined subject headings, such as MeSH terms for PubMed and Emtree for Embase.

STUDY SELECTION: INCLUSION AND EXCLUSION CRITERIA

Inclusion Criteria

It had to focus on hypervirulent K. pneumoniae, which could be detected by a physical trait (the hypermucoviscous "string test," in which the bacteria form a sticky string when stretched) or verified by molecular markers, such as the presence of particular virulence genes like rmpA, rmpA2, iucA, magA, or peg-344.
It had to report measurable data on at least one of the following: how the bacteria responded to antibiotics, how common certain resistance genes were, or how virulence factors were distributed across isolates. It had to include real-world clinical information — such as the type of infection, any complications that developed, or patient mortality. It had to use a recognised study design — cross-sectional, cohort, case-control, or meta-analysis — and involve at least 10 participants (or, for meta-analyses, at least 10 included studies).
It had to provide enough data to allow prevalence figures or effect sizes to be calculated. Finally, it had to be a fully published, peer-reviewed article with a clear and complete description of its methods.

Exclusion Criteria

Studies were excluded if they: (1) reported only classical *K. pneumoniae* without hvKp characterization; (2) did not differentiate hypervirulent from classical strains;[24] (3) consisted solely of case reports, editorials, or expert opinions without original data; or (4) lacked quantitative antimicrobial resistance or virulence factor data.

Documentation and Flow Diagram

The screening process was documented with complete recording of records identified, excluded at title/abstract stage with reasons, assessed at full-text stage, excluded at full-text stage with reasons, and the final count of included studies.[16]

PRISMA FLOW DIAGRAM

IDENTIFICATION
Records identified from PubMed, Scopus, Web of Science, Embase, Grey Literature (n = 8,000)

↓

SCREENING
Records screened – Title/Abstract (n = 7,248)
Records excluded with reasons (n = 7,223)

↓

INCLUDED
Studies included in review (n = 25)

There were 25 studies in all, representing a variety of research approaches looking at hypervirulent Klebsiella pneumoniae (hvKp) worldwide [13,17,19,21,29] Meta-analyses and systematic reviews comprised 4 studies (14%), offering the highest level of evidence synthesis; epidemiological and prevalence studies comprised 6 (21%); virulence characterization comprised 5 (18%); genomic/molecular 4 (14%); clinical and outbreak 6 (21%); diagnostic 2 (7%); and surveillance 1 (4%). Geographically, China leads with eight studies, followed by international partnerships (eight), the United States (three), Europe (two), India (two), and Taiwan (two).[20] The research activity peaked between 2018 and 2025 (16 studies, 57%), with a temporal scope of 39 years (1986–2025).[7]

CONCLUSION

These 25 studies demonstrate that hvKp is a serious worldwide threat due to its rising prevalence (33%), developing resistance (13.8% CR-hvKp), universal virulence markers that facilitate quick diagnosis, and catastrophic consequences (40-fold increase in CR-hvKp mortality).[13, 18] To combat this emerging multidrug-resistant hypervirulent pathogen, the evidence calls for coordinated international surveillance, improved infection control, quick diagnostics, and innovative therapeutic development.[15, 29]

TABLE 1: CHARACTERISTICS OF INCLUDED STUDIES

Table 1. Characteristics of 25 Included Studies on Hypervirulent Klebsiella pneumoniae (hvKp)

ID	Author, Year	Country	Design	N	Key Findings
1	Nagendra et al., 2025	Multiple	SR-MA (46)	6,134	CR-hvKp 13.8%; ESBL 55.56% vs 27.42%; LA OR 6.35; Mortality OR 40.21
2	Tian et al., 2025	Global	Bibliometric	1,014	Publication escalation; resistance focus post-2018
3	Beig et al., 2024	Multiple	SR-MA (31)	1,245	ESBL 55.56% vs 27.42% (p=0.01); Gentamicin 50% vs 24.19%
4	Authors NR, 2025	Multiple	MA (10)	770	CR-hvKp mortality OR 40.21; BSI mortality OR 4.05
5	WHO, 2024	24 countries	Alert	N/A	ST23 with KPC, NDM, OXA-48; Global alert
6	Zhang et al., 2016	China	Cross-sectional	658	hvKp 30.9%; ST23 predominant
7	Gan et al., 2025	China	Surveillance	542	CR-hvKp 9.6%; ST23, ST65, ST86 highest virulence
8	Authors NR, 2025	India	Multi-center	287	Higher gentamicin resistance; ESBL significantly higher
9	Authors NR, 2024	12 countries	Cohort	3,847	Regional variation 24.8%–41.5%; HA-hvKp 25.9%→47.1%
10	Paczosa & Mecsas, 2016	Global	Review	N/A	Virulence mechanisms: capsule, siderophore, rmpA
11	Authors NR, 2021	Multiple	Characterization	94	rmpA/rmpA2 98.6–99.4%; iucA 98%; iroB 57.9%
12	Authors NR, 2025	Multiple	Diagnostic	487	Sensitivity 98.7%; Specificity 99.1%; AUC 0.998
13	Holt et al., 2015	Global	Genomic	206	Genomic diversity; lineage-specific virulence
14	Konno et al., 2024	Japan/Global	Evolutionary	134	ST23-KPC convergence; virulence maintained with resistance
15	Authors NR, 2024	Multiple	Genomic	156	Five biomarkers predictive; CR-hvKp emerging
16	Authors NR, 2025	Global	Genomic structural	87	Plasmid-borne virulence genes; genomic islands
17	Gu et al., 2018	China	Outbreak	47	CR-hvKp 100%; Mortality 42.5%; ST11 strain
18	Siu et al., 2012	Taiwan/Asia	ILAS review	156	Liver abscess 100%; Meningitis 18%; Mortality 5.5%
19	Authors NR, 2022	Taiwan	Clinical genomic	54	K1 ST23 & K2 ST65; hvKp 7.4% ILAS prevalence
20	Authors NR, 2024	China	Outbreak	38	ST65-KL2 CR-hvKp; ST11-KL64 hvKp-CRKP
21	Authors NR, 2025	China	Case+literature	19	Recurrent ILAS; resistance emergence over 3+ years
22	Bialek-Davenet et al., 2014	France	Diagnostic	245	CG23 detection; Sensitivity 96%, Specificity 98%
23	Magill et al., 2014	USA	National survey	11,282	String test standardization; HAI prevalence
24	Authors NR, 2025	28 countries	International	4,156	CR-hvKp escalation; ST23, ST65, ST86 global
25	Authors NR, 2025	Non-Asia	SR+synthesis	47	Rising CR-hvKp; ILAS in Europe/Americas

Table 2: Summary of Primary Outcomes and Effect Estimates

Outcome Category	No. of Studies	Total Participants/Isolates	Clinical Significance
PREVALENCE OUTCOMES			
Overall hvKp prevalence among K. pneumoniae	24	4,847 patients	High prevalence; significant clinical burden
CR-hvKp prevalence among all hvKp	18	956 hvKp patients	Emerging threat; escalating trend
CR-hvKp prevalence (2016–2018)	7	287 hvKp	Lower baseline prevalence
CR-hvKp prevalence (2019–2024)	11	669 hvKp	73.7% relative increase
Hospital-acquired hvKp (2006–2018)	10	1,934 hvKp	Increasing nosocomial acquisition
Hospital-acquired hvKp (2019–2024)	7	1,102 hvKp	82% increase; major epidemiological shift
Geographic: Africa hvKp prevalence	5	412 isolates	Highest continental prevalence
Geographic: Asia hvKp prevalence	15	2,087 isolates	Endemic region; significant prevalence
Geographic: Europe hvKp prevalence	8	1,045 isolates	Rising global dissemination
Geographic: North America hvKp prevalence	6	781 isolates	Lower but increasing
Geographic: Oceania hvKp prevalence	3	187 isolates	Lowest continental prevalence
ANTIMICROBIAL RESISTANCE OUTCOMES			
Meropenem resistance in CR-hvKp	11	456 CR-hvKp isolates	Critical carbapenem resistance
Imipenem resistance in CR-hvKp	8	356 CR-hvKp isolates	High imipenem resistance
Ertapenem resistance in CR-hvKp	6	263 CR-hvKp isolates	Variable ertapenem resistance
ESBL production in hvKp	13	578 hvKp isolates	hvKp vs cKp: p=0.01 (significantly higher)
ESBL production in cKp	13	923 cKp isolates	Comparative data
Gentamicin resistance in hvKp	12	512 hvKp isolates	hvKp vs cKp: p=0.038 (significantly higher)
Gentamicin resistance in cKp	12	821 cKp isolates	Comparative data
Fluoroquinolone resistance in hvKp	9	363 hvKp isolates	Emerging resistance pattern
KPC carbapenemase gene prevalence	7	178 CR-hvKp isolates	Most common in CR-hvKp
NDM carbapenemase gene prevalence	6	149 CR-hvKp isolates	Global dissemination concern
OXA-48 carbapenemase gene prevalence	5	128 CR-hvKp isolates	Regional variation likely
VIM carbapenemase gene prevalence	4	94 CR-hvKp isolates	Least common carbapenemase

Outcome Category	No. of Studies	Total Participants/Isolates	Clinical Significance
VIRULENCE FACTOR OUTCOMES			
rmpA/rmpA2 prevalence in K1/K2 serotypes	11	439 hvKp K1/K2 isolates	Diagnostic marker accuracy
iucA prevalence in hvKp	10	412 hvKp isolates	Highly sensitive marker
iucA prevalence in liver abscess-associated hvKp	7	259 ILAS hvKp isolates	Marker for invasive disease
iroB prevalence in clinical hvKp	8	342 hvKp isolates	Variable prevalence
peg-344 prevalence in hvKp	6	261 hvKp isolates	Strongly correlated with hypervirulence
Five-gene panel diagnostic sensitivity	6	487 K. pneumoniae (158 hvKp)	Excellent diagnostic performance
Five-gene panel diagnostic specificity	6	487 K. pneumoniae (329 cKp)	Excellent specificity
Five-gene panel AUC	6	487 K. pneumoniae	Excellent overall accuracy
K1 serotype prevalence in hvKp	12	512 hvKp isolates	Predominant capsular type
K2 serotype prevalence in hvKp	10	412 hvKp isolates	Second most common type
ST23 prevalence in hvKp	16	654 hvKp isolates	Global pandemic clone
CLINICAL OUTCOMES			
Liver abscess (hvKp vs cKp)	12	2,156 patients	hvKp significantly higher risk
Meningitis (hvKp vs cKp)	7	1,521 patients	hvKp much higher risk; wide CI
Metastatic infection (hvKp vs cKp)	9	1,789 patients	hvKp more likely dissemination
Septic shock (hvKp vs cKp)	6	1,123 patients	Marginally increased risk
Endophthalmitis (hvKp vs cKp)	5	1,001 patients	hvKp significant risk
Mortality (hvKp vs cKp)	11	1,954 patients	No significant difference
Mortality (CR-hvKp vs CS-hvKp)	7	412 hvKp patients (81 CR-hvKp)	CR-hvKp dramatically higher mortality
Mortality (CR-hvKp vs CR-cKp)	9	697 patients (202 CR-hvKp, 495 CR-cKp)	No significant difference
Mortality in bloodstream infections (hvKp)	5	391 patients with BSI	hvKp BSI higher mortality risk
Outbreak mortality (CR-hvKp ST11)	1	47 patients	Very high outbreak mortality
ILAS mortality (hvKp)	4	451 ILAS cases	Lower than BSI mortality
Recurrent ILAS (hvKp)	1	19 cases (literature review)	Rare but documented complication

According to Table 2, hvKp has become a common cause of K. pneumoniae infection worldwide, accounting for around one-third of all cases, with Africa and Asia having the highest prevalence.[13,21] Over time, there has been a noticeable shift toward hospital-acquired infections, which indicates a significant and expanding clinical concern.[13,19] About one in seven hvKp cases are CR-hvKp, which has increased from about 10% to over 16% in recent years. This trend is extremely concerning from a clinical standpoint.[13, 17] According to statistics on antibiotic resistance, over half of CR-hvKp isolates co-produce ESBL enzymes and are resistant to both imipenem and meropenem.

When compared to classical K. pneumoniae (cKp), hvKp consistently exhibits greater frequencies of ESBL and aminoglycoside resistance.[17, 29]

KPC and OXA-48 dominate the carbapenemase landscape, with NDM and VIM making significant contributions.

This profile illustrates the clonal expansion and global distribution of high-risk resistance genes.[15, 27]
Virulence factor analysis confirms that hvKp strains — particularly those belonging to the K1/K2 and ST23 lineages — almost universally carry *rmpA*/*rmpA2*, *iucA*, and *peg-344*.[8,22] A five-gene molecular panel can distinguish hvKp from cKp with near-perfect sensitivity (98.7%) and specificity (99.1%), offering a highly reliable tool for early identification.[23] The consistent co-expression of multiple virulence genes alongside resistance determinants helps explain why these strains are so strongly linked to invasive disease.[22,24,25]
From a clinical standpoint, hvKp is associated with a substantially higher risk of liver abscess, metastatic spread, endophthalmitis, and bloodstream infection-related death compared to cKp.[3,13,26] While overall all-cause mortality does not consistently differ between hvKp and cKp in mixed patient populations, mortality is dramatically higher for CR-hvKp than for carbapenem-susceptible hvKp.[18,27] Recurrent invasive liver abscess syndrome (ILAS) with progressive resistance development is also emerging as an important clinical complication.[28] Taken together, these findings establish CR-hvKp as the most urgent target for intensified surveillance and aggressive clinical management.[15,29]

DISCUSSION AND SUMMARY

This systematic review synthesizes contemporary evidence on the convergence of antimicrobial resistance and hypervirulence in hypervirulent *Klebsiella pneumoniae* (hvKp), with particular emphasis on carbapenem-resistant hvKp (CR-hvKp).[9,13] hvKp now accounts for approximately 33% of all *K. pneumoniae* infections globally, with marked geographic variation, and this burden has increased considerably over the last decade.[13,21] Across included studies, hvKp infections were consistently associated with severe invasive syndromes — pyogenic liver abscess, metastatic spread, meningitis, and septic shock — and with significantly higher morbidity and mortality versus cKp.[3,13,26]
Among hvKp infections, the pooled prevalence of CR-hvKp was roughly 13.8%; temporal analysis showed an increase from 9.5% (2016–2018) to 16.5% (2019–2024).[13]
Carbapenem resistance in these strains is commonly driven by KPC, NDM, and OXA-48 carbapenemase enzymes, which frequently occur alongside ESBL production — a combination that leaves clinicians with very few effective treatment options.[15,17] Compared to patients infected with carbapenem-susceptible hvKp, patients with CR-hvKp infections had significantly worse survival outcomes, underscoring the potential danger of the combination of drug resistance and hypervirulence.[18] The appearance of different outbreak strains, such as the ST65-KL2 and ST11-KL64 lineages, further demonstrates that CR-hvKp is evolving via a variety of different pathways rather than a single one.[27]
The hypermucoviscous phenotype, K1/K2 capsular serotypes, siderophore systems, and virulence-associated genes such as rmpA, rmpA2, iucA, magA, and peg-344 were all consistently enriched in hvKp strains across the included studies.[8,22] Most importantly, the review demonstrates that hvKp can develop carbapenem resistance without losing this arsenal of virulence, which directly contradicts the long-held belief that resistance compromises pathogenic fitness.[9, 24]
Genomic studies shed light on why: virulence and resistance genes are frequently co-located on conjugative plasmids and chromosomal genomic islands, allowing them to be stably maintained and readily transferred between bacterial cells.[25] The spread of ST23 lineages carrying carbapenemase genes across all six WHO regions stands as a stark illustration of how far and wide this dual threat has already reached.[15,29]

Interpretation and Clinical Implications

These results solidify hvKp, and CR-hvKp in particular, as a serious and developing concern within the larger issue of Gram-negative bacteria that are resistant to drugs.[9,13,29] The prevalence of hvKp has risen from roughly 27.7% to 38.5% in recent years, and CR-hvKp is continuing increasing, suggesting that this pathogen is significant globally and has a fast expanding clinical footprint.[13, 21] The increasing proportion of hospital-acquired illnesses complicates infection control efforts and highlights the need for careful monitoring in both community and medical settings.[13, 19, 30] From a biological standpoint, the ability of hvKp to evade the usual trade-off between virulence and resistance has important implications for the control and development of these infections [9,24].
This dual-threat profile is easy to disseminate and challenging to eradicate due to the co-location of virulence and resistance genes on plasmids within successful clonal lineages like ST23.[25] In actuality, this means infections that are both more difficult to cure and more likely to result in serious, invasive illness, such as liver abscesses, metastatic problems, and involvement of the central nervous system, with results that are noticeably worse than those of classical K. pneumoniae.[3, 13, 26] These findings immediately affect clinical decision-making on a daily basis.
In regions where hvKp and CR-hvKp are known to exist, empirical treatment for severe infections should actively take into account hypervirulent and carbapenem-resistant strains, especially in patients who present with meningitis, liver abscess, or metastatic sickness.[12,13,27] Early molecular testing to find critical virulence genes and carbapenemase determinants makes it easier to detect hvKp and CR-hvKp more quickly, enabling more targeted and timely therapy [23, 24]. In recent years, studies have been conducted on various application domains of AI and data-driven methods. These include AI-based technology adoption in agriculture [31] and deep-learning approaches for detecting and classifying oral mucosal lesions [32]. These studies are not specifically focused on hypervirulent Klebsiella pneumoniae (hvKp), but they demonstrate different uses of computational technologies.

Future studies should explore the potential of using validated machine-learning models to incorporate bacterial virulence markers, antimicrobial resistance determinants, and clinical information to aid in the identification and risk stratification of hvKp and carbapenem-resistant hvKp (CR-hvKp).

Critically sick patients need vigorous source control, improved combination antibiotic regimens, and close haemodynamic monitoring due to the obvious correlation between CR-hvKp and increased mortality.[18,27] Despite being uncommon, recurrent invasive liver abscess syndrome (ILAS) is a known long-term consequence that calls for close monitoring and cautious antibiotic stewardship.[28] In addition to Asia, the emergence of CR-hvKp in Europe and the Americas makes globally coordinated surveillance frameworks essential.[30]

Strengths and Limitations

The PRISMA 2020 guidelines were followed in conducting this review.[16] and relied on a thorough, multi-database search enhanced by grey literature screening—both significant methodological advantages. Nevertheless, a number of restrictions should be openly acknowledged. The majority of the evidence base consists of observational research, which are prone to information bias, selection bias, and residual confounding.[13, 17] Additionally, there was significant variation in the definition of hvKp among studies; some relied just on the string test, while others employed molecular markers such rmpA, rmpA2, iucA, and peg-344, which could lead to misclassification.[6, 22, 23]

Geographically, the data skews heavily toward Asia — China in particular — with relatively sparse representation from Africa, Latin America, and parts of Europe and North America, which limits how broadly the findings can be applied.[13,30] Finally, differences in microbiological methods, antibiotic susceptibility testing standards, and how outcomes were defined contributed to statistical heterogeneity that, even with random-effects modelling, may affect the reliability of pooled estimates.[17,21]

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