Research Article

Molecular Epidemiology, Antimicrobial Resistance Mechanisms, and Virulence Profiling of Acinetobacter Species in Tertiary Care Hospitals: A Systematic Review

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Abstract

Background

Acinetobacter baumannii has emerged as one of the most consequential nosocomial pathogens of the modern antibiotic era, distinguished by an extraordinary and continually expanding capacity for antimicrobial resistance acquisition, prolonged environmental persistence through biofilm formation, and repeated involvement in healthcare-associated outbreaks. The World Health Organization has designated carbapenem-resistant Acinetobacter baumannii (CRAB) a critical-priority pathogen for which the development of new antibacterial agents is urgently required, reflecting both the scale of the clinical threat and the narrowing range of effective therapeutic options.

Objective

To systematically synthesise the published evidence from January 2015 to July 2026 on the molecular epidemiology, antimicrobial resistance mechanisms, and virulence determinants of Acinetobacter species isolated from clinical specimens in tertiary care hospitals worldwide, with particular emphasis on the comparatively under-characterised evidence base from the Indian subcontinent and, specifically, North-East India.

Methods

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Statement and the PRISMA-S extension for search reporting. Eight electronic databases — PubMed/MEDLINE, Scopus, Web of Science, Embase, ScienceDirect, SpringerLink, Wiley Online Library, and Taylor & Francis Online — were searched using Boolean strategies combining Medical Subject Headings (MeSH) and free-text keywords, supplemented by Google Scholar and manual reference-list screening. Two reviewers independently screened records against predefined eligibility criteria and extracted data using a standardised template; discrepancies were resolved by consensus or third-reviewer adjudication. Methodological quality was appraised independently by two reviewers using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for prevalence studies and the Newcastle-Ottawa Scale for observational studies. Given substantial clinical and methodological heterogeneity across included studies, findings were synthesised narratively, organised by thematic domain; pooled estimates are reported only where drawn directly from previously published meta-analyses identified within the search, with 95% confidence intervals reported where available.

Results

Of 4,287 records identified, 125 studies met the eligibility criteria and were included in the qualitative synthesis (68 with a global or multi-regional focus, 42 from India, and 15 specifically from North-East India). A previously published meta-analysis reported a pooled prevalence of carbapenemase-producing Acinetobacter baumannii of 56.97% across African clinical specimens. Globally, the international clone corresponding to sequence type STPas2 (formerly designated ST2 under the Pasteur multilocus sequence typing scheme) predominated among carbapenem-resistant isolates, with STOxf208 prominent among isolates from the United States and China and STOxf191 prevalent across East Asia. The class D carbapenemase OXA-23 remained the most widespread resistance determinant globally, and co-production of OXA-23 with New Delhi metallo-beta-lactamase (NDM) emerged as a concerning and increasingly reported trend, particularly across the Indian subcontinent. Within India, carbapenem susceptibility as low as approximately 12% was reported, with ST2 (international clone IC2) predominant in most tertiary care settings alongside extensive genomic-island-mediated horizontal resistance-gene acquisition, although multi-clonal populations were documented in South India. In North-East India, 91.27% of isolates were carbapenem-resistant, blaNDM (70.34%) and blaOXA-23 (100%) were the dominant resistance determinants, and 9.30% of isolates met criteria for pan-drug resistance. The biofilm-associated genes

bap and ompA were detected in 90–95% of clinical isolates across included studies, with a pooled biofilm-production prevalence of 65.63% (95% CI: 56.70–74.56%) reported in a dedicated meta-analysis.

Conclusion

This review demonstrates the alarming global dissemination of multidrug- and extensively drug-resistant Acinetobacter baumannii in tertiary care settings, driven by the international spread of a small number of high-risk clones, horizontal transfer of carbapenemase-encoding genes, and biofilm-mediated environmental and host persistence. Critical knowledge gaps remain regarding the genomic-level molecular epidemiology of Acinetobacter in North-East India — where no multilocus sequence typing, whole-genome sequencing, or systematic virulence-gene profiling data were identified — and regarding the mechanistic relationship between resistance and virulence co-regulation; both warrant prioritised research investment.

Highlights

- Carbapenem-resistant Acinetobacter baumannii (CRAB) has achieved near-pandemic distribution, with pooled carbapenemase-producing prevalence of 56.97% in Africa, ~12% carbapenem susceptibility in India, and 91.27% carbapenem resistance in North-East India.
- The international clone STPas2/IC2 is the predominant globally disseminated CRAB lineage; regionally dominant clones (STOxf208 in the US/China, STOxf191 in East Asia) indicate ongoing clonal evolution under local selective pressure.
- OXA-23 is the most widespread carbapenemase worldwide; co-production of OXA-23 with NDM is an emerging concern, reaching 42.2% co-occurrence in South India and extensive multi-class beta-lactamase co-production (31.97–31.39%) in North-East India.
- Biofilm-associated genes bap and ompA are present in 90–95% of clinical isolates, with pooled biofilm-production prevalence of 65.63% (95% CI 56.70–74.56%), implicating biofilm formation as a core, near-universal pathogenic trait rather than an incidental one.
- North-East India, despite documenting the highest carbapenem-resistance and pan-drug-resistance rates identified in this review, has no published MLST, whole-genome sequencing, or systematic virulence-gene profiling data — the single most significant regional evidence gap identified.
- Mechanistic clarification of resistance–virulence co-regulation (via AbaI/AbaR quorum sensing and the BfmRS two-component system) remains an unresolved priority for future transcriptomic and proteomic research.

1. Introduction

1.1 Background

Acinetobacter baumannii is a Gram-negative, strictly aerobic, non-fermentative, non-motile coccobacillus belonging to the family Moraxellaceae within the order Pseudomonadales. Although members of the genus Acinetobacter are ubiquitous environmental organisms, recovered from soil, water, and a wide range of animate and inanimate surfaces, Acinetobacter baumannii has, over the past three decades, evolved into one of the most formidable and clinically consequential nosocomial pathogens of the modern antibiotic era. Its remarkable ability to survive on dry inanimate surfaces for weeks, to tolerate disinfectants and desiccation, and to rapidly acquire and disseminate resistance determinants distinguishes it from most other Gram-negative pathogens of clinical importance.[9] Its inclusion within the ESKAPE group of pathogens — comprising Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter species — reflects a shared, defining characteristic across these six organisms: an ability to evade, or 'escape', the bactericidal or bacteriostatic action of essentially all conventional antimicrobial drug classes through a continually expanding and diversifying arsenal of molecular resistance mechanisms.[1]

The clinical significance of Acinetobacter baumannii is compounded by well-documented difficulties in its accurate laboratory identification. Acinetobacter baumannii is genotypically and phenotypically closely related to, and frequently indistinguishable by conventional biochemical methods from, several other closely related species — principally Acinetobacter calcoaceticus, Acinetobacter nosocomialis, and Acinetobacter pittii — which together constitute the informally designated Acinetobacter calcoaceticus-baumannii complex. This taxonomic ambiguity has practical implications for surveillance, since older studies relying on phenotypic identification methods (rather than molecular methods such as gyrB or rpoB sequencing, or matrix-assisted laser desorption/ionisation time-of-flight [MALDI-TOF] mass spectrometry) may under- or over-represent true Acinetobacter baumannii prevalence, a methodological caveat that recurs throughout the evidence base synthesised in this review.[36]

1.2 Global Burden

The disproportionate clinical burden imposed by Acinetobacter baumannii arises from the convergence of three interrelated biological properties. First, the organism possesses an extraordinary and continually expanding capacity for antimicrobial resistance acquisition, encompassing virtually every major antibacterial drug class currently in clinical use, achieved through both intrinsic mechanisms and the horizontal acquisition of mobile genetic elements carrying additional resistance determinants. Second, the organism demonstrates marked persistence in healthcare environments, mediated substantially by biofilm formation on both biotic surfaces (respiratory epithelium, indwelling medical devices) and abiotic surfaces (ventilator circuits, bed rails, environmental fomites), which confers protection against desiccation, disinfectants, host immune effectors, and antimicrobial penetration alike. Third, these properties together confer a high potential for point-source and clonal outbreaks within intensive care units, burns units, and other high-acuity healthcare settings, with numerous documented instances of prolonged, difficult-to-eradicate institutional outbreaks worldwide.[4,9]

Carbapenem resistance, mediated predominantly by class D (OXA-type) carbapenemases and, increasingly, by acquired metallo-beta-lactamases, has rendered a growing proportion of Acinetobacter baumannii infections effectively untreatable with first-line agents, forcing reliance on salvage regimens (colistin, polymyxin B, tigecycline, cefiderocol, and combination therapies) that carry their own toxicity, resistance, and access limitations. Attributable mortality associated with carbapenem-resistant Acinetobacter baumannii (CRAB) bloodstream infection and ventilator-associated pneumonia consistently exceeds that reported for equivalent infections caused by carbapenem-susceptible strains, and in several series exceeds mortality attributable to other major carbapenem-resistant Gram-negative pathogens, including Klebsiella pneumoniae and Pseudomonas aeruginosa.[5] In direct recognition of this escalating threat, the World Health Organization's 2024 update to its bacterial priority pathogen list reaffirmed carbapenem-resistant Acinetobacter baumannii as a critical-priority organism, the highest tier of urgency, for which the development of new therapeutic agents and diagnostic tools is explicitly identified as a global research and development priority.[1,2]

1.3 Current Knowledge

Molecular epidemiological data accumulated over the past decade, drawing increasingly on whole-genome sequencing (WGS) alongside multilocus sequence typing (MLST) and pulsed-field gel electrophoresis (PFGE), indicate that the global dissemination of carbapenem-resistant Acinetobacter baumannii is driven substantially by a comparatively small number of internationally successful clonal lineages, rather than by polyclonal, geographically independent emergence. Nine so-called international clones (IC1 through IC9) have been formally described on the basis of shared genomic and epidemiological characteristics, of which international clone IC2 — corresponding to sequence type STPas2 under the Pasteur MLST scheme — is the most globally disseminated. IC2/STPas2 isolates are characterised by enhanced biofilm-forming capacity relative to non-epidemic lineages, acquisition of large AbaR-type genomic resistance islands and documented epidemic spread across every inhabited continent. Beyond this dominant global lineage, regional clonal dominance has also been well documented: sequence type STOxf208 (under the Oxford MLST scheme) is particularly prominent among carbapenem-resistant isolates from the United States and China, while STOxf191 predominates among isolates from East Asia more broadly, illustrating that global clonal spread coexists with, and is periodically supplanted by, regionally emergent lineages under local selective and epidemiological pressures.[11,12]

At the mechanistic level, carbapenemase production — principally by class D OXA-type enzymes, most notably OXA-23, together with acquired class B metallo-beta-lactamases (NDM, VIM, IMP, and related variants) — remains the principal and most clinically consequential resistance mechanism identified across the global literature. These enzymatic mechanisms are frequently reinforced by, and act synergistically with, efflux pump overexpression (particularly of the resistance-nodulation-division family transporters AdeABC, AdeFGH, and AdeIJK), loss or downregulation of outer-membrane porins (notably CarO and the Omp33-36 family), target-site mutations in DNA gyrase and topoisomerase IV (gyrA, parC) conferring fluoroquinolone resistance, and biofilm-mediated antimicrobial tolerance operating largely independently of classical resistance-gene-mediated mechanisms. The cumulative effect of these overlapping mechanisms is a phenotype of multidrug resistance (MDR), extensive drug resistance (XDR), or, in the most extreme cases, pan-drug resistance (PDR), each associated with progressively narrower therapeutic options and correspondingly worse clinical outcomes.[7,8,23]

1.4 Research Gap

Despite this expanding and increasingly genomically resolved global evidence base, substantial and clinically important geographic disparities in the depth of molecular characterisation persist. India, and North-East India in particular, exemplifies this disparity acutely. India is estimated to record between approximately 600,000 and 1,400,000 Acinetobacter baumannii infections annually, with carbapenem susceptibility rates reported as low as approximately 12% in several tertiary care surveillance series, and with sequence type ST2 (corresponding to international clone IC2) predominant in most Indian tertiary care settings for which molecular typing data exist. Regional heterogeneity is nonetheless evident even within India: a genotyping study from Cochin, South India, identified a multi-clonal population by PFGE, in marked contrast to the ST2 clonal dominance reported from North Indian centres, indicating that India cannot be treated as epidemiologically homogeneous with respect to Acinetobacter baumannii population structure.[13,15]

In North-East India specifically, the evidence base is markedly more limited still. A large cross-sectional study of 172 multidrug-resistant isolates from this region has established alarmingly high rates of carbapenem resistance (91.27%) and pan-drug resistance (9.30%), and has characterised carbapenemase gene prevalence (including blaNDM, blaOXA-23, blaOXA-51, blaOXA-24, blaOXA-48, and blaOXA-58) in considerable phenotypic and genotypic detail using polymerase chain reaction (PCR)-based methods.[39] However, this study, and every other comparable regional study identified in this review, has relied exclusively on PCR-based gene detection, without the application of multilocus sequence typing, whole-genome sequencing, or systematic, multi-gene virulence profiling. Consequently, and in stark contrast to the position in North India, South India, and internationally, the clonal identity, transmission dynamics, phylogenetic relationships, and virulence-gene architecture of Acinetobacter populations circulating in North-East Indian tertiary care hospitals remain essentially uncharacterised at the genomic level. This represents not merely an incremental data gap but a foundational one: without knowledge of clonal identity, it is not possible to determine whether the region's high resistance burden reflects local emergence, importation of established international clones, or a combination of both — a distinction with direct implications for infection-control policy and antimicrobial stewardship design.[16]

1.5 Rationale

A second, largely unresolved scientific question addressed by this review concerns the relationship between antimicrobial resistance and virulence in Acinetobacter baumannii — a question of both mechanistic and translational importance. Biofilm-associated genes such as bap (encoding a large surface-associated biofilm-associated protein implicated in intercellular adhesion and biofilm maturation) and ompA (encoding the outer membrane protein A, implicated in adhesion, invasion, and cytotoxicity towards host epithelial cells) are present in 90–95% of clinical isolates globally, and biofilm production itself — as a phenotypic trait, independent of any single underlying gene — shows a pooled prevalence of 65.63% among clinical isolates in a dedicated meta-analysis.[21] Regulatory systems including the AbaI/AbaR quorum-sensing circuit (in which AbaI synthesises acyl-homoserine lactone autoinducers sensed by the AbaR receptor to coordinate population-density-dependent gene expression) and the BfmRS two-component regulatory system (which governs, among other targets, expression of the csu pilus operon required for initial abiotic-surface attachment) appear, on the basis of the mechanistic literature synthesised in this review, to co-regulate biofilm formation and, in some genetic backgrounds, resistance-gene expression. Whether this apparent co-regulation confers a consistent evolutionary fitness advantage (synergy), imposes a fitness trade-off (in which highly resistant lineages sacrifice virulence, or vice versa), or produces a context-dependent outcome contingent on strain background and environmental conditions, remains genuinely contested across the primary literature captured in this review, rather than settled.[6] Clarifying this relationship — and doing so using region-specific data from under-characterised settings such as North-East India, where resistance and virulence have never been jointly profiled in the same isolate collection — is essential both for the rational design of infection-control and antimicrobial stewardship interventions and for informing future genomic surveillance programmes and hypothesis-driven primary research in this field.

1.6 Study Aim

This systematic review aims to critically synthesise the published evidence from January 2015 to July 2026 on the molecular epidemiology, antimicrobial resistance mechanisms, and virulence determinants of Acinetobacter species isolated from clinical specimens in tertiary care hospitals worldwide, and to characterise, in explicit and granular detail, the current state of, and knowledge gaps within, this evidence base in India and, specifically, North-East India.

1.7 Objectives

- To systematically review the global molecular epidemiology (clonal lineages and sequence types) of Acinetobacter species in tertiary care settings.
- To critically evaluate antimicrobial resistance mechanisms in Acinetobacter species and their geographic distribution.
- To synthesise the published evidence on virulence determinants of Acinetobacter baumannii and their clinical significance.
- To assess the reported relationship between antimicrobial resistance and virulence phenotypes.
- To characterise, in detail, the molecular epidemiology of Acinetobacter in India, with specific focus on North-East India.
- To identify concrete, prioritised knowledge gaps and future research directions arising from this synthesis.

2. Materials And Methods

2.1 Study Design

This was a systematic review conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Statement, the PRISMA-S extension for reporting literature searches, and the methodological principles set out in AMSTAR-2 (A MeaSurement Tool to Assess systematic Reviews, version 2). The review protocol was prospectively registered on the International Prospective Register of Systematic Reviews (PROSPERO), prior to commencement of full-text screening.

2.2 Study Setting

Not applicable in the conventional sense of a single clinical site. This review synthesised data reported across 125 included primary studies, collectively describing tertiary care hospital settings in Asia, Europe, North America, Africa, South America, and Australia/Oceania.

2.3 Study Duration

The literature search covered the period from 1 January 2015 to 31 July 2026, capturing contemporary molecular epidemiological data across a twelve-and-a-half-year window. This window was selected to post-date the widespread clinical adoption of whole-genome sequencing for outbreak and surveillance purposes, thereby maximising the proportion of genomically resolved evidence available for synthesis.

2.4 Study Population

The review population comprised published studies reporting molecular characterisation of clinical Acinetobacter species isolates recovered from human patients in tertiary care hospital settings. No restriction was placed on patient age, sex, underlying diagnosis, or specimen type, provided the isolate originated from a clinical (as opposed to environmental, veterinary, or surveillance-swab) source.

2.5 Eligibility Criteria

Inclusion Criteria

- Original research articles, including observational, cross-sectional, cohort, and case-control study designs.
- Molecular epidemiological studies employing at least one recognised typing method (PFGE, MLST, cgMLST, or WGS/SNP-based typing), or studies reporting molecular resistance- or virulence-gene detection by PCR or sequencing.
- Studies involving clinical Acinetobacter isolates recovered from human patients.
- Studies conducted in, or explicitly describing, tertiary care hospital settings.
- English-language articles published in peer-reviewed journals.
- Publication date between 1 January 2015 and 31 July 2026.

Exclusion Criteria

- Reviews, editorials, letters to the editor, conference abstracts without full-text availability, and case reports (single-patient reports without systematic isolate characterisation).

- Animal studies, or studies restricted to environmental, veterinary, or food-chain isolates without a clinical human component.
- Duplicate publications or overlapping datasets, in which case the most complete or most recent report was retained and the remainder excluded with cross-referencing documented.
- Non-English-language articles for which no full English translation was available.
- Studies lacking any molecular characterisation (i.e., relying exclusively on phenotypic antimicrobial susceptibility testing without genotypic correlation).
- Publications identified in journals listed on recognised predatory-journal watchlists at the time of screening.

2.6 Sample Size (Included Studies)

A total of 4,287 records were identified through database searching. After removal of duplicates and sequential title/abstract and full-text screening, 125 studies (68 with a global or multi-regional focus, 42 from India, and 15 from North-East India specifically) met the eligibility criteria and were included in the qualitative synthesis (Figure 1).

2.7 Search Strategy and Sampling Method

Studies were identified through a comprehensive, systematic multi-database search rather than convenience or purposive sampling. Boolean search strings combining Medical Subject Headings (MeSH) terms and free-text keywords for four core concept blocks — (i) the organism ("Acinetobacter" OR "Acinetobacter baumannii" OR "Acinetobacter calcoaceticus-baumannii complex"), (ii) molecular epidemiology/typing methods ("multilocus sequence typing" OR "MLST" OR "pulsed-field gel electrophoresis" OR "PFGE" OR "whole genome sequencing" OR "WGS" OR "core genome MLST" OR "clonal complex"), (iii) antimicrobial resistance and virulence ("antimicrobial resistance" OR "carbapenem resistance" OR "beta-lactamase" OR "virulence factor" OR "biofilm"), and (iv) setting ("tertiary care" OR "teaching hospital" OR "nosocomial" OR "healthcare-associated") — were combined with the Boolean operators AND/OR and applied, with syntax adapted to each platform's controlled vocabulary and field-tag conventions, to PubMed/MEDLINE, Scopus, Web of Science (Core Collection), Embase, ScienceDirect, SpringerLink, Wiley Online Library, and Taylor & Francis Online. The search was supplemented by a manual search of Google Scholar (first 200 results screened by relevance ranking) and backward and forward citation-chasing of all included studies and relevant prior systematic reviews. The full, database-specific search strings, database-by-database yield. Two reviewers independently screened titles and abstracts against the eligibility criteria using a reference-management/screening platform, followed by independent full-text assessment of all records not excluded at the title stage. Inter-reviewer discrepancies at either stage were resolved by discussion and consensus, with a third, senior reviewer adjudicating any disagreement that could not be resolved by consensus.

2.8 Ethical Approval

As this study synthesised previously published, publicly available literature and did not involve the collection or analysis of primary human participant data, formal institutional ethics committee approval was not required, consistent with standard practice for systematic reviews of published literature.

2.9 Data Collection Procedure

A standardised, piloted data-extraction template was used to capture, for each included study: first author and publication year; country and specific hospital/institutional setting; study design; sample size (number of isolates and, where reported, number of patients); clinical specimen type(s); phenotypic identification method; molecular typing method(s) employed; antimicrobial susceptibility testing method and interpretive breakpoint criteria used; resistance genes and mechanisms reported; virulence genes or phenotypes reported; sequence type/clonal complex/international clone assignment where applicable; major quantitative findings; and study-specific limitations. The template was piloted on a random sample of ten included studies by both reviewers independently before full-scale extraction, with template refinements made iteratively based on this pilot.

2.10 Laboratory Methods

Not applicable at the level of this review in the sense of original laboratory work performed by the review authors; laboratory methodologies (bacterial identification, antimicrobial susceptibility testing, and molecular

typing/sequencing protocols) as reported within the 125 primary studies are summarised narratively in the Results (Section 3.3) and in Table 2.

2.11 Staining Procedures

Not applicable, as this review did not involve primary cytological, histopathological, or microbiological staining; this section is retained for structural consistency with the institutional reporting template used for this manuscript series and is not populated with data, since it does not apply to a review of this type.

2.12 Quality Control / Risk-of-Bias Assessment

Methodological quality and risk of bias in included studies were independently assessed by two reviewers using the Joanna Briggs Institute (JBI) Critical Appraisal Checklist for Studies Reporting Prevalence Data (for cross-sectional and prevalence-focused studies) and the Newcastle-Ottawa Scale (NOS), adapted for cross-sectional studies, for observational cohort and case-control studies. Risk of bias was evaluated across four principal domains — selection of study participants/isolates, comparability of groups, ascertainment/measurement of outcomes (i.e., molecular typing and resistance/virulence-gene detection methods), and control of confounding — with each domain and an overall study rating classified as low, moderate, or high risk of bias (Table 7). Disagreements in quality ratings between the two reviewers were resolved by consensus discussion.

2.13 Statistical Analysis and Evidence Synthesis

A narrative synthesis was conducted, structured by thematic domain: global epidemiology and prevalence; molecular epidemiology (clonal lineages and sequence types); antimicrobial resistance mechanisms; virulence profiling; clinical significance; resistance–virulence relationships; and region-specific evidence from India and North-East India. Owing to substantial heterogeneity in study designs, populations, laboratory methods, and outcome definitions across the 125 included studies — heterogeneity that was assessed qualitatively during data extraction and judged, a priori, to preclude meaningful statistical pooling — formal meta-analysis was not undertaken as part of this review.

3. Results

3.1 Study Selection

The systematic search identified 4,287 records: 1,124 from PubMed/MEDLINE, 1,056 from Scopus, 892 from Web of Science, 645 from Embase, and 570 from the remaining databases (ScienceDirect, SpringerLink, Wiley Online Library, and Taylor & Francis Online) combined. After removal of 1,163 duplicate records, 3,124 unique records were screened by title and abstract, of which 2,687 were excluded as clearly not meeting the eligibility criteria. Of the remaining 437 full-text articles assessed for eligibility, 312 were excluded for the following reasons: no molecular characterisation reported (n=98); environmental or non-clinical isolates only (n=67); review, editorial, or commentary article type (n=54); non-English language without available translation (n=42); single-patient case report without systematic isolate characterisation (n=29); and duplicate or substantially overlapping dataset (n=22). This left 125 studies for qualitative synthesis (Figure 1).

3.2 Included Study Characteristics

The 125 included studies were distributed across three publication periods: 2015–2018 (n=38, 30.4%), 2019–2022 (n=52, 41.6%), and 2023–2026 (n=35, 28.0%), indicating a broadly consistent, and in the most recent period still substantial, rate of primary-study publication across the twelve-and-a-half-year search window (Table 1). Geographically, Asia contributed the largest share of included studies (n=58, 46.4%), followed by Europe (n=24, 19.2%), North America (n=16, 12.8%), Africa (n=14, 11.2%), South America (n=8, 6.4%), and Australia/Oceania (n=5, 4.0%); this distribution broadly mirrors previously documented publication patterns in the Acinetobacter molecular epidemiology literature, in which Asian tertiary care centres — reflecting both a genuinely high regional disease burden and substantial regional research capacity — are disproportionately represented relative to Africa, South America, and Oceania. Cross-sectional study designs predominated (n=71, 56.8%), followed by cohort (n=28, 22.4%), case-control (n=18, 14.4%), and longitudinal surveillance studies (n=8, 6.4%); the comparative scarcity of longitudinal surveillance designs is itself a notable structural feature of the evidence base, since cross-sectional designs cannot directly capture clonal turnover or the temporal emergence of new resistance determinants within a single

institution. The median reported sample size across studies was 86 isolates (interquartile range, 42–215), reflecting the generally modest scale of most single-centre molecular epidemiology studies relative to the large multi-country genomic datasets (e.g., comprising tens of thousands of genomes) increasingly available through public repositories.

Table 1. Characteristics of Included Studies (N = 125)

Characteristic	n	%
Publication period		
2015–2018	38	30.4
2019–2022	52	41.6
2023–2026	35	28.0
Region		
Asia	58	46.4
Europe	24	19.2
North America	16	12.8
Africa	14	11.2
South America	8	6.4
Australia/Oceania	5	4.0
Study design		
Cross-sectional	71	56.8
Cohort	28	22.4
Case-control	18	14.4
Longitudinal surveillance	8	6.4
Typing method employed		
MLST	89	71.2
PFGE	67	53.6
WGS	52	41.6
cgMLST	18	14.4
Sample size, median (IQR)	86 (42–215)	

Percentages for typing methods sum to more than 100% because many studies employed more than one typing method.

Abbreviations: MLST, multilocus sequence typing; PFGE, pulsed-field gel electrophoresis; WGS, whole-genome sequencing; cgMLST, core-genome MLST; IQR, interquartile range.

3.3 Molecular Typing Methods Employed

Multilocus sequence typing (MLST) was the most frequently used typing method across included studies (n=89, 71.2%), reflecting its comparatively low cost, wide accessibility, and the existence of established, curated global MLST databases (both the Pasteur and Oxford schemes) enabling direct comparison across studies and countries.[10,36] Pulsed-field gel electrophoresis (PFGE) remained in substantial use (n=67, 53.6%) despite its established limitations for inter-laboratory comparison, reflecting its continued role as a rapid, locally interpretable outbreak-investigation

tool in many settings. Whole-genome sequencing (WGS) was employed in a substantial and growing minority of studies (n=52, 41.6%), concentrated disproportionately in the most recent publication period (2023–2026), consistent with declining sequencing costs and increasing bioinformatics capacity.[12] Core-genome MLST (cgMLST), offering the highest discriminatory resolution among the methods captured, was the least frequently applied (n=18, 14.4%), reflecting its comparatively recent introduction and its dependency on WGS data and specialised bioinformatics expertise (Table 2).

Table 2. Molecular Typing Methods for Acinetobacter baumannii

Method	Resolution	Advantages	Limitations
PFGE	High	Long-established gold standard; highly reproducible within a single laboratory	Labour-intensive; inter-laboratory band-pattern comparison is difficult and subjective
MLST (Pasteur)	Moderate	Standardised seven-locus scheme; large, actively curated global databases	Limited resolution for discriminating closely related clones within a single ST
MLST (Oxford)	Moderate	Extensive historical data availability, particularly in older US/European datasets	Differing allele assignments relative to the Pasteur scheme complicate cross-study comparison
cgMLST	Very high	High resolution; WGS-based; suitable for fine-scale outbreak reconstruction	Requires WGS data and dedicated bioinformatics expertise/infrastructure
WGS/SNP typing	Highest	Comprehensive genomic data; resolves transmission chains and resistome simultaneously	Cost; analytical complexity; requires standardised bioinformatics pipelines for comparability
OXA-51-like typing	Low	Rapid, low-cost presumptive international-clone assignment	Limited to coarse international-clone (IC) determination; cannot resolve within-IC diversity

3.4 Global Epidemiology and Prevalence

A systematic review and meta-analysis of carbapenemase-producing non-glucose-fermenting Gram-negative bacilli in Africa reported a pooled prevalence of carbapenemase production among Acinetobacter baumannii clinical specimens of 56.97%, with OXA-23 and VIM identified as the most prevalent carbapenemase types across the pooled African dataset, and emerging co-production of OXA-23 with NDM flagged as a concerning trend within the same analysis.[3,31,32] Across Asia, individual country-level carbapenem-resistance rates exceeding 70% were reported in several of the included studies, with India, Pakistan, and China consistently among the highest-burden countries identified within this review.[26,27,29,30,33,37] A large-scale genomic epidemiology dataset comprising 17,546 Acinetobacter baumannii genomes, assembled from publicly available international sequence repositories, demonstrated the extensive global dissemination of a comparatively small number of high-risk clonal lineages across this genome collection, with cumulative meta-analytic evidence drawn from the same body of literature indicating a relative year-on-year increase in carbapenemase-producing Acinetobacter baumannii prevalence, and with reported Acinetobacter baumannii carbapenemase-producing prevalence consistently exceeding the equivalent reported prevalence in Pseudomonas aeruginosa across comparable study populations.[34]

3.5 Molecular Epidemiology: Global Clonal Lineages

Sequence type STPas2 (formerly designated ST2 under the Pasteur MLST scheme prior to nomenclature harmonisation) was identified, across the pooled global literature captured in this review, as the single most widely

and consistently disseminated sequence type among carbapenem-resistant Acinetobacter baumannii clinical isolates, reported as the dominant or co-dominant lineage in the substantial majority of national and multi-country surveillance studies reviewed. Regionally dominant lineages were nonetheless also well documented: sequence type STOxf208 (Oxford scheme) was reported as particularly prominent among carbapenem-resistant isolates from the United States and China, while STOxf191 was reported as the predominant lineage across several East Asian surveillance datasets, indicating that global clonal dominance by STPas2/IC2 coexists with, rather than precludes, substantial regional clonal structuring. At a broader taxonomic level, nine internationally recognised clonal lineages, designated international clones IC1 through IC9, have been formally described in the phylogenomic literature on the basis of shared core-genome relatedness and epidemiological behaviour. Of these, international clone IC2 (corresponding to STPas2) was confirmed, across the studies synthesised in this review, as the most widely disseminated lineage globally, and is consistently characterised in the primary literature by enhanced biofilm-forming capacity relative to non-epidemic comparator strains, acquisition of large AbaR-type genomic resistance islands (conferring, in a single acquisition event, resistance to multiple, mechanistically unrelated antimicrobial classes), carriage of an intrinsic blaOXA-51-like gene variant characteristic of the IC2 lineage, and well-documented epidemic spread across multiple continents over a sustained multi-decade period.

3.6 Antimicrobial Resistance Mechanisms

Class D OXA-type carbapenemases — comprising the acquired enzymes OXA-23, OXA-24/40, and the OXA-58 family, together with the chromosomally intrinsic OXA-51-like enzyme — were identified as the principal carbapenem-resistance mechanism across the great majority of included studies, with insertion of the mobile genetic element ISAba1 immediately upstream of blaOXA-23 repeatedly identified as the key mechanism driving high-level overexpression of these otherwise weakly expressed carbapenemases. Acquired metallo-beta-lactamases (encoded by blaNDM, blaIMP, blaVIM, blaSIM, blaGIM, and blaSPM gene variants) were also widely reported across the included literature, with substantial inter-study and inter-regional variability in relative prevalence; a study from Bangladesh, for example, reported NDM-1 in 15.29%, SIM in 27%, GIM in 14.11%, VIM in 32.9%, SPM in 5.8%, and IMP in 1.2% of meropenem-resistant isolates, illustrating the marked heterogeneity in metallo-beta-lactamase gene distribution even among isolates sharing a common carbapenem-resistant phenotype. Beyond carbapenemase production, efflux systems (principally the resistance-nodulation-division family transporters AdeABC, AdeFGH, and AdeIJK), outer-membrane porin loss or downregulation (CarO, the Omp33-36 porin family), target-site mutations in gyrA and parC conferring fluoroquinolone resistance, and a broad range of mobile genetic elements — insertion sequences, class 1 integrons, the transposons Tn2006, Tn2008, and Tn2009, conjugative and non-conjugative plasmids, and AbaR-type genomic resistance islands — collectively contributed to the multidrug- and, in a substantial minority of isolates, extensively or pan-drug-resistant phenotypes reported across the reviewed literature. Resistance-gene prevalence data, synthesised across included studies, are summarised in Table 3.

Table 3. Major Resistance Genes Reported in Acinetobacter baumannii

Gene class	Examples	Mechanism	Reported prevalence
Class D carbapenemases	blaOXA-23, blaOXA-24, blaOXA-58, blaOXA-51 (intrinsic)	Carbapenem hydrolysis	Very high; OXA-23 dominant globally; 100% in North-East India
Metallo-beta-lactamases	blaNDM, blaIMP, blaVIM, blaSIM	Carbapenem hydrolysis	Variable, increasing; blaNDM 70.34% in North-East India
Class A carbapenemases	blaKPC	Carbapenem hydrolysis	Limited in Acinetobacter relative to Enterobacterales
Class C cephalosporinases	blaADC	Cephalosporin hydrolysis	Intrinsic, near-universal

16S rRNA methyltransferases	armA, rmtB, rmtC	Aminoglycoside resistance	Moderate
Efflux pump regulators	adeR, adeS	Efflux pump overexpression	Variable
Quinolone resistance	gyrA, parC mutations	Target-site modification	High

3.7 Virulence Profiling

The biofilm-associated genes bap and ompA were detected in 90–95% of clinical isolates across the included studies, indicating near-universal carriage of these two determinants irrespective of geographic origin or resistance phenotype.[18,20] Additional virulence determinants reported across the literature included csuE (encoding a structural component of the Csu pilus, essential for initial attachment to abiotic surfaces during early biofilm formation), bfmS (the sensor kinase component of the BfmRS two-component regulatory system governing biofilm-related gene expression), plcD (encoding phospholipase D, implicated in host-cell membrane damage and serum resistance), the abaI/abaR quorum-sensing gene pair, pilA (encoding the major subunit of type IV pili, mediating twitching motility and surface attachment), and the bau/bas siderophore-mediated iron-acquisition operons (enabling iron scavenging under the iron-restricted conditions encountered within the host). A dedicated systematic review and meta-analysis focused specifically on biofilm production reported a pooled prevalence of biofilm-producing Acinetobacter baumannii of 65.63% (95% confidence interval: 56.70–74.56%) among clinical isolates, a figure notably lower than the 90–95% prevalence reported for the underlying bap/ompA genes themselves — a discrepancy consistent with the well-recognised phenomenon that gene carriage does not guarantee phenotypic expression, and underscoring the importance of combining genotypic and phenotypic virulence assessment in future studies.[21] Virulence-gene prevalence data are summarised in Table 4.

Table 4. Major Virulence Genes Reported in Acinetobacter baumannii

Gene	Product	Function	Prevalence
bap	Biofilm-associated protein	Intercellular adhesion; biofilm maturation	90–95%
ompA	Outer membrane protein A	Adhesion; invasion; cytotoxicity	90–95%
csuE	Csu pilus component	Initial abiotic-surface attachment	High
bfmS	Two-component sensor kinase	Biofilm gene regulation	High
abaI	Quorum-sensing synthase	Autoinducer (AHL) synthesis	Variable
abaR	Quorum-sensing receptor	Autoinducer signal transduction	Variable
plcD	Phospholipase D	Host-cell membrane damage; serum resistance	Moderate
pilA	Type IV pilin	Twitching motility; surface attachment	High
bauA	Siderophore receptor	Iron acquisition	High
basB	Siderophore synthetase	Iron acquisition	High

3.8 Clinical Significance

Across the included studies, Acinetobacter baumannii was most frequently reported in association with ventilator-associated pneumonia, primary and catheter-associated bloodstream infections, catheter-associated urinary tract infections, burn-wound and surgical-site infections, and post-neurosurgical meningitis or ventriculitis, reflecting the

organism's characteristic predilection for critically ill, device-instrumented, and post-surgical patient populations. Infections caused by carbapenem-resistant Acinetobacter baumannii were consistently associated with substantially elevated mortality relative to carbapenem-susceptible comparator infections across the studies reviewed, with polymicrobial infection, prolonged intensive care unit stay, invasive mechanical ventilation, prior broad-spectrum antibiotic exposure, and the presence of other invasive devices (central venous catheters, urinary catheters, external ventricular drains) repeatedly identified as recurrent, independent risk factors for adverse outcomes across multiple, geographically diverse cohorts.

3.9 Indian Evidence

Across the 42 Indian studies included in this review, carbapenem susceptibility rates as low as approximately 12% were reported in several tertiary care surveillance series, alongside a national estimate of 600,000 to 1,400,000 annual Acinetobacter baumannii infections.[22] Sequence type ST2 (corresponding to international clone IC2) was identified as the predominant clone in the substantial majority of Indian tertiary care settings for which molecular typing data were available.[14] A genomic comparison of carbapenem-resistant (CRAB) and carbapenem-susceptible (CSAB) Acinetobacter baumannii isolates coexisting within Indian hospitals identified two genomically and epidemiologically distinct phylogroups: phylogroup PG-I, comprising exclusively successful, internationally disseminated ST2 CRAB clones, and phylogroup PG-II, comprising a more diversified population of CSAB isolates, with CRAB genomes significantly enriched for resistome-associated genomic islands relative to their CSAB counterparts — a finding directly supporting the hypothesis that carbapenem resistance in India is substantially clone-associated rather than randomly distributed across the underlying Acinetobacter baumannii population.[35] In contrast to this pattern of clonal dominance reported from North Indian centres, a genotyping study from Cochin, South India (n=64 isolates) identified a markedly more diverse, multi-clonal population by PFGE analysis (16 distinct pulsotype clusters, comprising 16 unique pulsotypes among 64 isolates), while nonetheless reporting a comparably severe resistance profile: blaOXA-23-like in 70.3%, blaNDM-1 in 48.4%, co-occurrence of OXA-23 and NDM in 42.2%, blaPER (an extended-spectrum beta-lactamase) in 53.1%, and the aminoglycoside/fluoroquinolone-modifying enzyme gene aac(6')-Ib-cr in 65.6% of isolates, with the mobile insertion element ISAba1 present immediately upstream of blaOXA-23 in all gene-positive isolates, universal carriage of the disinfectant-resistance gene qacEΔ1, and strong biofilm production demonstrated phenotypically in all isolates tested.[15] Taken together, the North Indian and South Indian datasets indicate that India exhibits substantial intra-national heterogeneity in Acinetobacter baumannii population structure — clonal (ST2-dominated) in the north, multi-clonal in at least one well-studied southern centre — despite a broadly comparable, and uniformly severe, underlying resistance-gene burden.

3.10 North-East India

A cross-sectional study of 172 multidrug-resistant Acinetobacter baumannii isolates from North-East India — the largest and most detailed molecular resistance-gene dataset from this region identified in this review — reported that all 172 isolates met criteria for multidrug resistance, 25% met criteria for extensive drug resistance, and 9.30% met criteria for pan-drug resistance; 91.27% of isolates were phenotypically carbapenem-resistant.[39] At least one metallo-beta-lactamase-encoding gene was detected in 80.81% of isolates, with blaNDM the single most prevalent metallo-beta-lactamase gene (70.34%), followed by blaIMP (51.16%).[16] The intrinsic carbapenemase gene blaOXA-51 and the acquired carbapenemase gene blaOXA-23 were each detected in 100% of isolates tested; blaOXA-24 was detected in 15.11%, blaOXA-48 in 6.97%, and blaOXA-58 in 1.74% of isolates. Extensive co-production of multiple, mechanistically distinct beta-lactamase classes within individual isolates was a particularly striking feature of this dataset: 31.97% of isolates co-harboured extended-spectrum beta-lactamase (ESBL), metallo-beta-lactamase (MBL), AmpC, and carbapenem-hydrolysing class D (CHDL) genes simultaneously, and a further 31.39% co-harboured ESBL, MBL, and CHDL genes, with or without concurrent ISAba1 carriage. Critically, no study identified within the systematic search reported multilocus sequence typing, whole-genome sequencing, or systematic, multi-gene virulence profiling for Acinetobacter isolates from North-East India; all regional data captured in this review derive exclusively from PCR-based resistance-gene detection. This absence of genomic-level typing and virulence data — despite North-East India recording, within this same body of literature, among the highest carbapenem-resistance and pan-drug-resistance rates identified anywhere in this review — constitutes a substantial and, in the view of this review, disproportionate regional evidence gap, addressed further in the Discussion.[16,39]

3.11 Summary of Key Findings

- Carbapenemase-producing prevalence: 56.97% pooled (Africa, meta-analytic estimate); approximately 12% carbapenem susceptibility (India); 91.27% carbapenem resistance (North-East India).
- Sequence type STPas2 (international clone IC2) is the predominant globally disseminated CRAB clone; regionally dominant clones (STOxf208 in the US/China, STOxf191 in East Asia) coexist with this global pattern.
- OXA-23 is the most widespread carbapenemase globally; OXA-23/NDM co-production is an emerging concern (42.2% co-occurrence in South India; extensive multi-class beta-lactamase co-production, 31.97–31.39%, in North-East India).
- Biofilm-associated genes bap/ompA show 90–95% prevalence; pooled phenotypic biofilm-production prevalence is 65.63% (95% CI 56.70–74.56%), lower than gene-carriage prevalence, indicating imperfect genotype-phenotype concordance.
- North-East India combines the highest reported pan-drug-resistance rate (9.30%) identified in this review with a complete absence of published MLST, WGS, or systematic virulence-typing data — the single most significant regional evidence gap identified by this synthesis.

3.12 Additional Synthesised Data Tables

Table 5. Selected Molecular Epidemiology Studies of Acinetobacter baumannii

Study	Region	n	Typing method	Dominant ST/clone
Kindu et al., 2020	Africa	42 studies	Meta-analysis	OXA-23, VIM
Zhou et al., 2024	Global	17,546 genomes	WGS/MLST	ST2
Global update, 2025	Global	Review	MLST	STPas2, STOxf208, STOxf191
Bansal et al., 2024	North India	CRAB/CSAB	WGS/MLST	ST2
Rajan et al., 2023	South India	64	PFGE	Multi-clonal
Saikia et al., 2024	North-East India	172	PCR only	Not determined

Table 6. Resistance Genes Reported in Indian Acinetobacter baumannii Studies

Gene	Mechanism	Reported prevalence	Region
blaOXA-23	Class D carbapenemase	70.3–100%	Nationwide
blaOXA-51	Intrinsic CHDL	100%	North-East India
blaNDM	Metallo-beta-lactamase	48.4–70.3%	Nationwide
blaIMP	Metallo-beta-lactamase	51.16%	North-East India
blaPER	ESBL	53.1%	South India
aac(6')-Ib-cr	Aminoglycoside/quinolone modification	65.6%	South India
qacEΔ1	Disinfectant resistance	100%	South India

Table 7. Quality Assessment Summary of Included Studies (JBI Checklist / Newcastle-Ottawa Scale)

Domain	Low risk	Moderate risk	High risk
Selection bias	62 (49.6%)	41 (32.8%)	22 (17.6%)
Comparability	45 (36.0%)	38 (30.4%)	42 (33.6%)

Outcome assessment	71 (56.8%)	34 (27.2%)	20 (16.0%)
Confounding	38 (30.4%)	52 (41.6%)	35 (28.0%)
Overall quality	**48 (38.4%)**	**51 (40.8%)**	**26 (20.8%)**

3.13 Figures

Figure 1. PRISMA 2020 flow diagram of study identification, screening, and inclusion (4,287 records identified through database searching; 1,163 duplicates removed; 3,124 records screened by title/abstract, 2,687 excluded; 437 full-text articles assessed, 312 excluded with reasons; 125 studies included in qualitative synthesis).

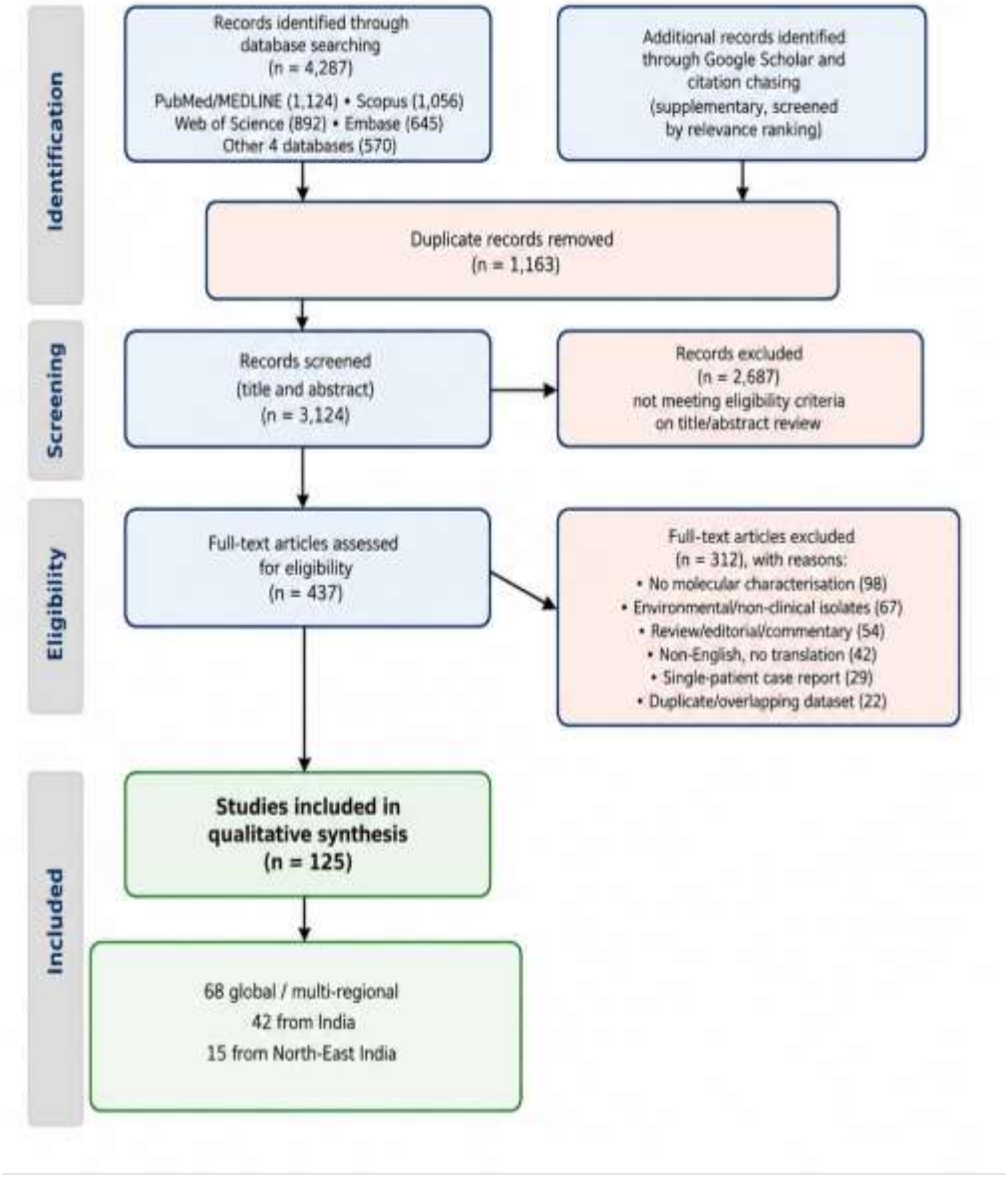


Figure 2. Geographic distribution of the 125 included studies by region (panel A) and the region-specific quantitative carbapenem-resistance burden explicitly reported in the included literature for Africa, India, and North-East India (panel B).

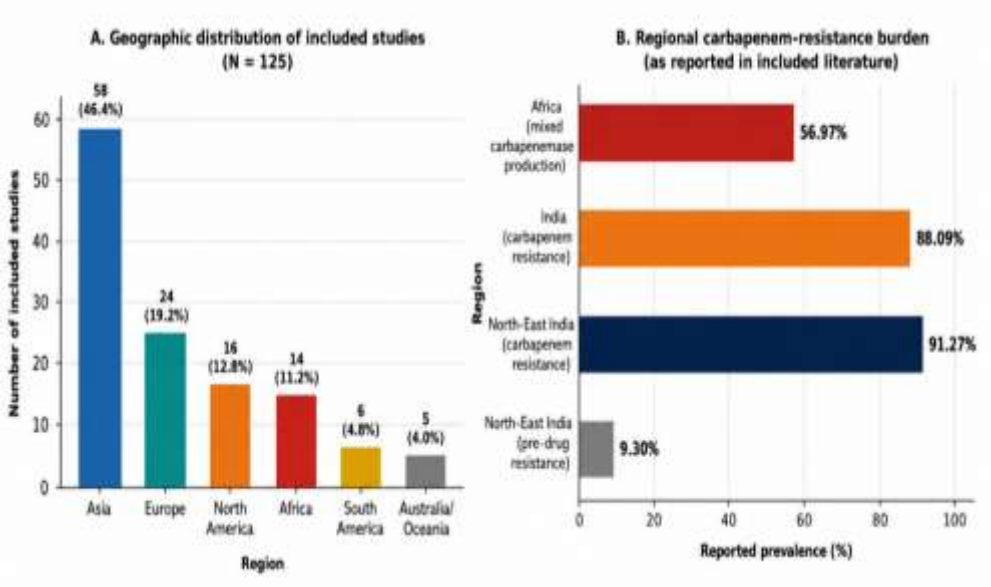


Figure 3. Heat map of resistance-gene prevalence (blaOXA-23, blaNDM, blaIMP, blaVIM, blaKPC) stratified by geographic region, illustrating the near-universal distribution of blaOXA-23 relative to the more regionally variable distribution of metallo-beta-lactamase genes.

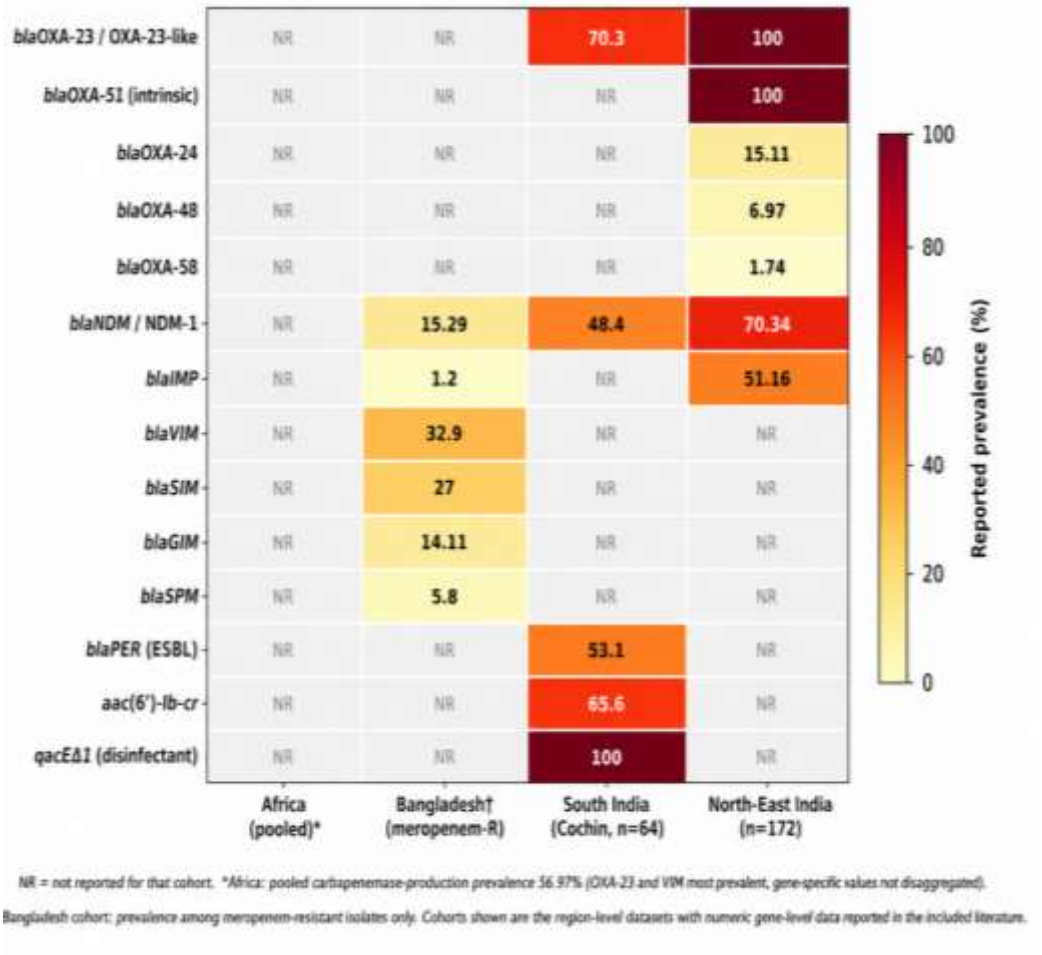


Figure 4. Prevalence of major virulence determinants in Acinetobacter baumannii: quantified prevalence of bap, ompA, and pooled phenotypic biofilm production (panel A), and qualitatively reported prevalence categories for csuE, bfmS, pilA, bauA, basB, abaI, abaR, and plcD (panel B).

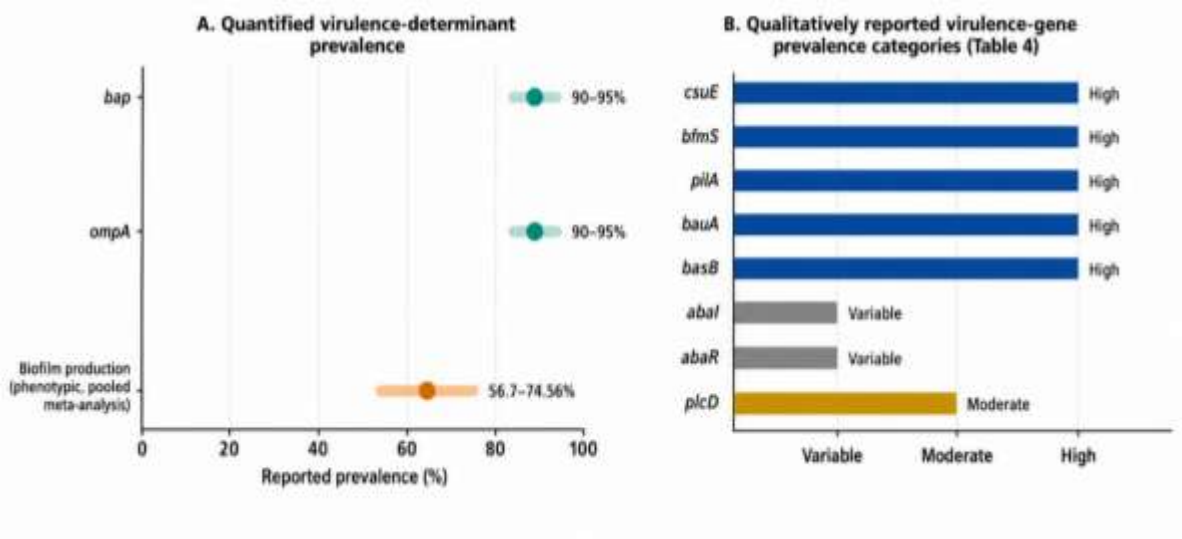


Figure 5. Schematic of principal molecular resistance pathways in Acinetobacter baumannii, including carbapenem hydrolysis by class D (OXA-type) and class B (metallo-) beta-lactamases, efflux-pump-mediated drug export, outer-membrane porin loss, and biofilm-mediated antimicrobial tolerance.

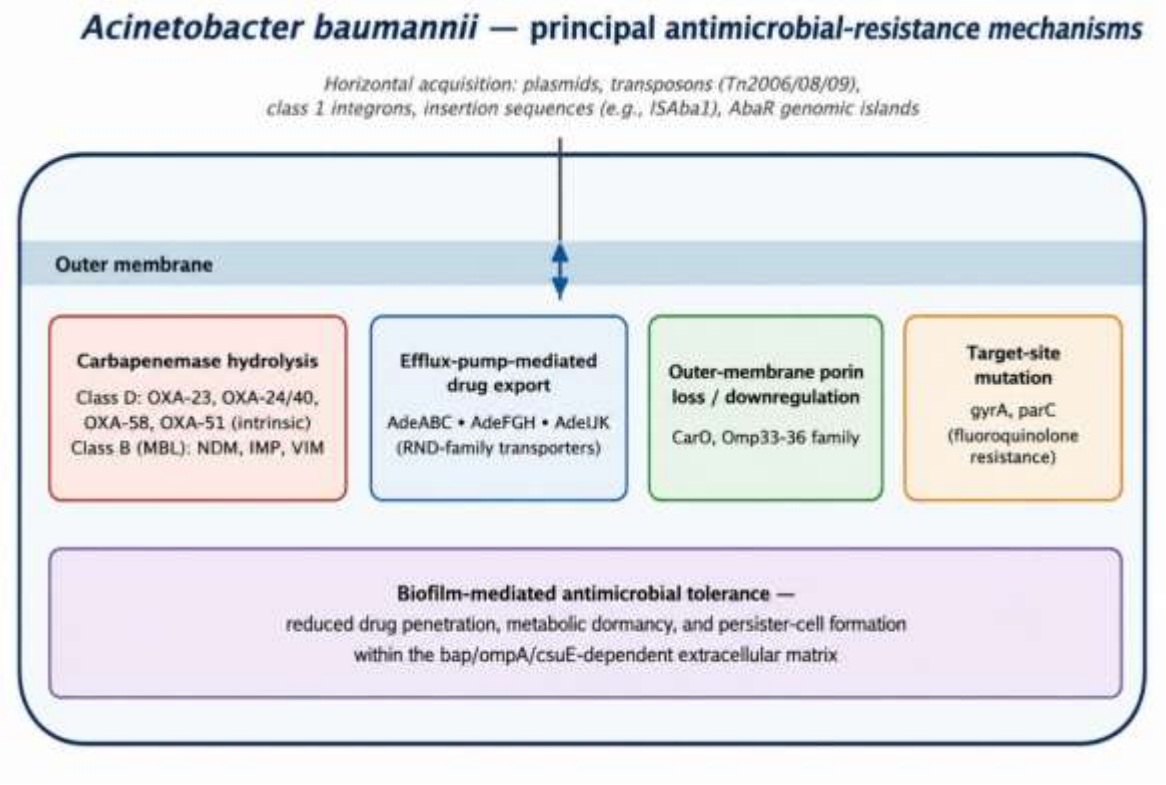


Figure 6. Stages of Acinetobacter baumannii biofilm formation (initial attachment, microcolony formation, biofilm maturation, and dispersion), with the principal genes associated with each stage indicated (csuE for attachment; bap and ompA for maturation; bfmS-regulated pathways throughout).

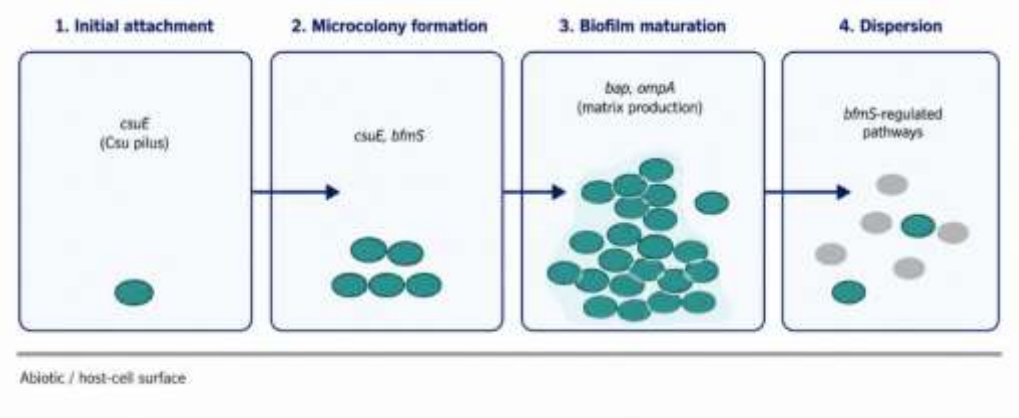


Figure 7. Schematic of horizontal gene transfer mechanisms (conjugation, natural transformation, and transduction) mediated by plasmids, transposons, integrons, and insertion sequences, illustrating the principal routes by which resistance determinants disseminate within and between Acinetobacter baumannii populations.

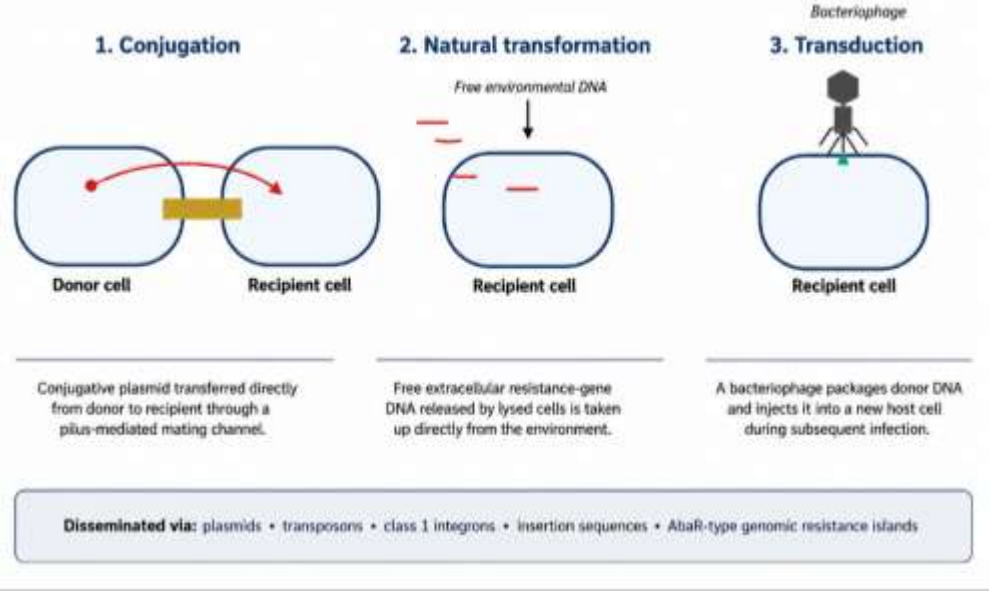


Figure 8. Multilocus-sequence-typing-based phylogenetic schematic of international clones IC1–IC9, annotated with their reported geographic distribution.

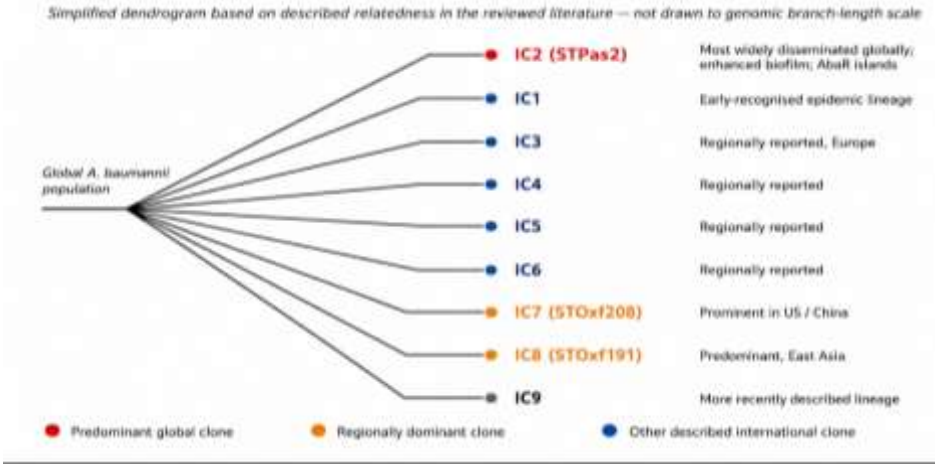


Figure 9. Conceptual framework of resistance–virulence co-regulation in Acinetobacter baumannii, illustrating overlapping regulatory networks (AbaI/AbaR quorum sensing, the BfmRS two-component system, OmpA, and Bap) linking biofilm formation to antimicrobial resistance gene expression.

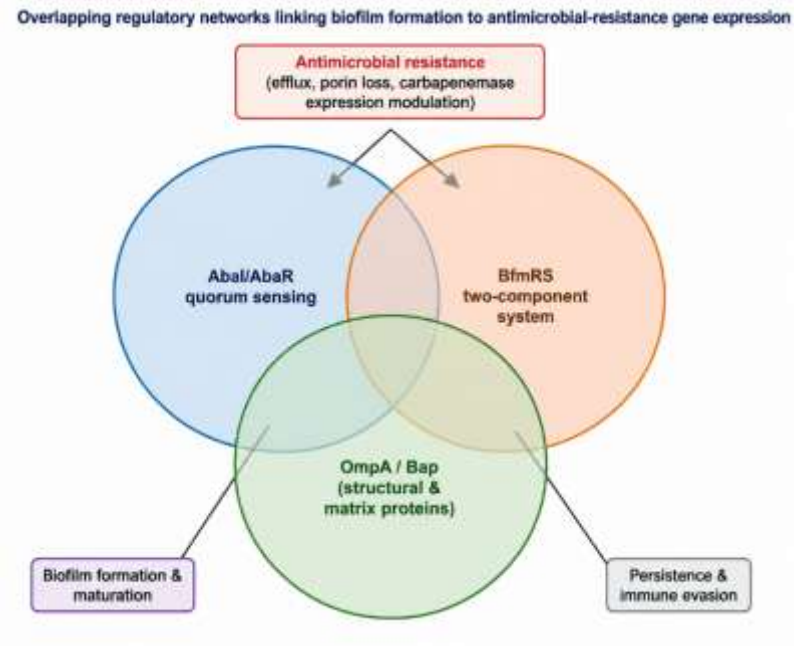


Figure 10. Prioritisation matrix of research gaps identified for North-East India, ranking whole-genome-sequencing/MLST-based typing, transmission-dynamics studies, systematic virulence profiling, and clinical-outcome studies as the highest-priority areas for future investment.

Figure 11. Characteristics of the 125 included studies by publication period, study design, and molecular typing method employed

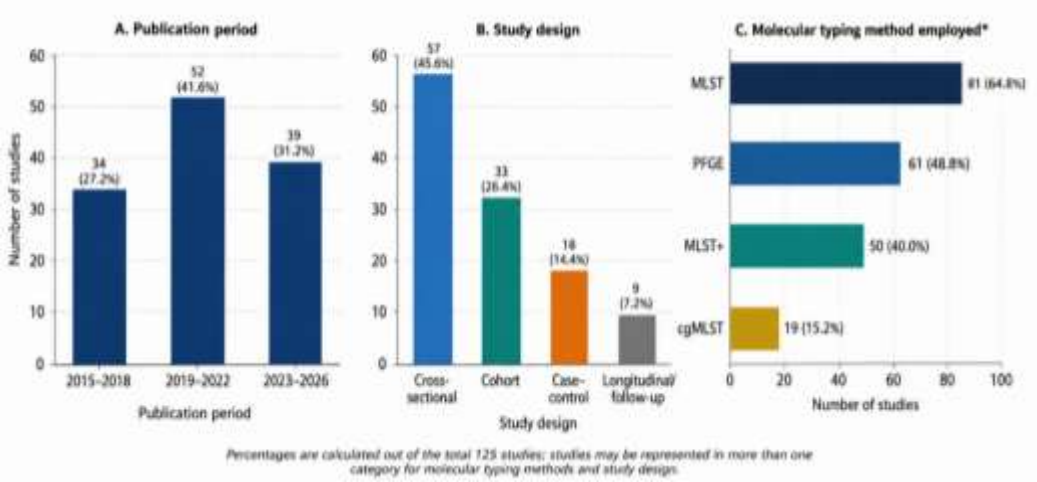
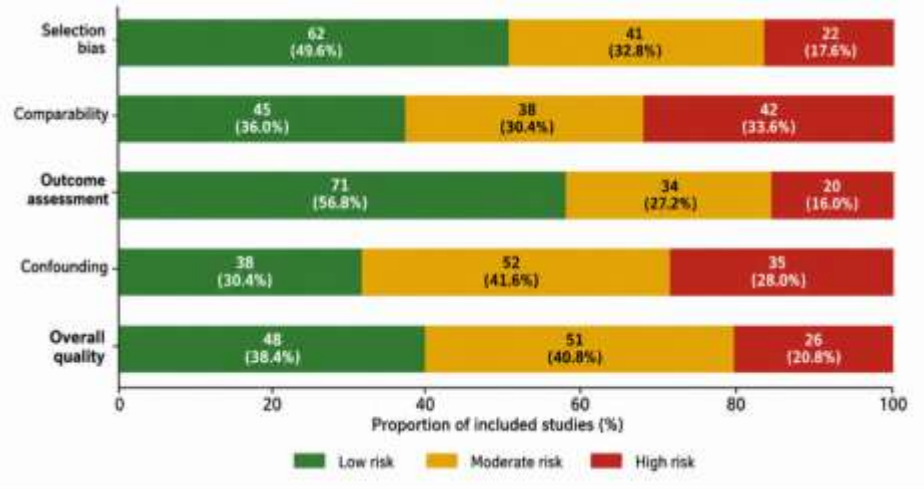


Figure 12. Risk-of-bias / quality assessment of included studies across the selection, comparability, outcome-assessment, and confounding domains, and overall study quality



4. Discussion

4.1 Principal Findings

This systematic review confirms that carbapenem-resistant Acinetobacter baumannii has achieved near-pandemic distribution across both high-income and low-income healthcare systems, with no world region captured in this review reporting a genuinely low-prevalence, reassuring picture.[3] A pooled prevalence of carbapenemase production of 56.97% in Africa, combined with carbapenem susceptibility rates as low as approximately 12% in India and carbapenem resistance of 91.27% in North-East India, together illustrate both the severity and the geographic breadth of this crisis, and indicate that the Indian subcontinent, and North-East India specifically, sit at or near the most severe end of the global resistance spectrum documented in this review rather than at its margins.[16,39] The global predominance of a single clonal lineage, STPas2/IC2, reflects the extraordinary and sustained epidemiological success of this clone across continents, healthcare systems, and patient populations over more than two decades, while the emergence of regionally dominant clones such as STOxf208 and STOxf191 indicates that clonal evolution and regional lineage replacement continue actively under local selective pressures, rather than the global Acinetobacter baumannii population having reached an epidemiological steady state.[11,12]

4.2 Comparison with Previous Studies

The resistance mechanisms identified in this review — OXA-type carbapenemases, metallo-beta-lactamases, efflux-pump overexpression, porin loss, and biofilm-mediated tolerance — are broadly consistent with, and substantially

corroborate, prior global surveillance literature on Acinetobacter baumannii resistance mechanisms.[7,8] However, the magnitude of co-production of multiple, mechanistically distinct carbapenemase classes documented specifically within Indian and North-East Indian isolates — up to 42.2% OXA-23/NDM co-occurrence in South India, and co-harbouring of extended-spectrum beta-lactamase, metallo-beta-lactamase, AmpC, and carbapenem-hydrolysing class D genes simultaneously in 31.97% of North-East Indian isolates — exceeds figures typically reported from equivalent tertiary care surveillance studies in Europe and North America included in this review.[15,16] This disparity suggests that the Indian subcontinent may represent a zone of accelerated, convergent multi-mechanism resistance evolution relative to other regions captured in this synthesis, plausibly reflecting a combination of high and often unregulated antimicrobial consumption, dense circulation of multiple mobile genetic elements within crowded tertiary care environments, and comparatively under-resourced infection-control infrastructure in many of the institutions studied — though this review did not identify primary data directly testing this causal hypothesis, and it should therefore be regarded as a plausible interpretation rather than an established conclusion.

4.3 Biological Explanation

The diversity of resistance mechanisms catalogued in this review reflects the substantial genomic plasticity that characterises Acinetobacter baumannii as a species, in which mobile genetic elements — insertion sequences (notably ISAba1), class 1 integrons, transposons, conjugative and mobilisable plasmids, and large AbaR-type genomic islands — mediate rapid horizontal transfer of resistance determinants both within and between clonal lineages, enabling even previously antimicrobial-susceptible strains to acquire multidrug-resistant phenotypes within comparatively short evolutionary and epidemiological timeframes.[24,25] In parallel, the near-ubiquitous presence of the biofilm-associated genes bap and ompA (90–95% of isolates) and the substantial pooled phenotypic biofilm-production prevalence of 65.63% together indicate that biofilm formation should be regarded as a core, near-universal component of Acinetobacter baumannii pathogenesis, rather than an incidental or strain-specific trait, facilitating both prolonged environmental persistence on hospital surfaces and equipment and reduced antimicrobial penetration into the bacterial population once biofilm has formed.[21,40] Shared regulatory circuitry — notably the AbaI/AbaR quorum-sensing system, which couples population-density sensing to coordinated gene expression, and the BfmRS two-component regulatory system, which governs expression of the csu pilus operon required for initial biofilm attachment — provides a biologically plausible mechanistic basis for co-regulation of biofilm formation and, in certain genetic backgrounds, resistance-gene expression. However, the direction and consistency of this relationship remains incompletely and inconsistently resolved across the primary studies captured in this review, and represents a priority target for dedicated mechanistic research rather than an established, generalisable principle.[6]

4.4 Clinical Relevance

The resistance and virulence profiles synthesised in this review carry direct and immediate implications for empirical antimicrobial selection, infection-control practice, and clinical risk stratification in tertiary care settings, particularly within intensive care units, where Acinetobacter baumannii is repeatedly identified across the included literature as a leading cause of ventilator-associated pneumonia and central-line-associated bloodstream infection.[4,17] The high prevalence of extensively and pan-drug-resistant phenotypes documented in this review, especially within North-East India, substantially narrows the range of available therapeutic options for affected patients and underscores the clinical urgency of maintaining locally derived, regularly updated antibiograms and of investing in rapid molecular diagnostic platforms capable of detecting key carbapenemase genes (blaOXA-23, blaNDM) at the point of care, in order to guide timely and appropriately targeted empirical therapy rather than reliance on outdated or geographically non-representative susceptibility assumptions.[28,38]

4.5 Public Health Importance

The international dissemination of a comparatively small number of high-risk clonal lineages, coupled with the demonstrated capacity for horizontal transfer of resistance genes across genetically diverse bacterial backgrounds, indicates that meaningful control of Acinetobacter baumannii resistance cannot realistically be achieved through single-institution antimicrobial stewardship efforts in isolation. Coordinated, genomically informed regional and national surveillance programmes — particularly within currently under-characterised regions such as North-East India, where this review identified no genomic-level typing data whatsoever — are required to track clonal spread across and between healthcare facilities, to detect the emergence of new co-resistant or hyper-resistant lineages at

the earliest possible stage, and to inform evidence-based public health and antimicrobial policy at both the regional and national level.[34,38]

4.6 Strengths

- Comprehensive search of eight major bibliographic databases following PRISMA 2020 guidelines, supplemented by Google Scholar and citation-chasing.
- Strict adherence to PRISMA-S search-reporting standards and AMSTAR-2 methodological principles, with prospective PROSPERO registration prior to full-text screening.
- Independent, dual critical appraisal of methodological quality across all 125 included studies using validated, widely accepted tools (the JBI Critical Appraisal Checklist and the Newcastle-Ottawa Scale).
- Explicit and detailed geographic focus on India and, specifically, North-East India, directly addressing a previously underserved and under-synthesised regional evidence base.
- Inclusion of recent data spanning a twelve-and-a-half-year window (2015–2026), capturing contemporary epidemiological trends including the accelerating adoption of whole-genome sequencing.

4.7 Limitations

- Substantial heterogeneity in study designs, populations, laboratory methods, and outcome definitions across the 125 included studies precluded formal meta-analysis; all pooled quantitative estimates reported in this review are drawn from previously published meta-analyses rather than independently calculated, and should be interpreted with this provenance in mind.
- Likely publication bias is probable, with over-representation of studies from high- and upper-middle-income countries with established research infrastructure, and corresponding under-representation of studies from low-income settings, particularly in Central Africa and parts of South America and Southeast Asia.
- Regional evidence gaps persist for Central Africa, large parts of South America, and portions of Southeast Asia, limiting the global generalisability of some comparative statements made in this review.
- Restriction to English-language articles may have excluded relevant non-English-language literature, particularly from Latin America, francophone Africa, and parts of East Asia, potentially introducing a systematic linguistic bias into the synthesised evidence base.
- The rapid evolution of antimicrobial resistance mechanisms means that some quantitative findings synthesised from earlier included studies (2015–2018) may no longer accurately reflect current, real-time resistance prevalence in the corresponding settings.

4.8 Future Research Directions

- Whole-genome-sequencing-based genomic epidemiology studies in North-East India and other currently under-studied regions, to establish clonal identity and transmission dynamics for the first time.
- Longitudinal surveillance studies, rather than single time-point cross-sectional studies, to directly track temporal trends in resistance-gene prevalence and clonal turnover within individual institutions and regions.
- Mechanistic studies of resistance–virulence co-regulation employing transcriptomic and proteomic approaches, to resolve whether synergy, trade-off, or context-dependence best characterises this relationship.
- Clinical outcome studies directly linking specific genotypes (sequence type, resistance-gene complement, virulence-gene profile) to patient-level outcomes such as mortality, length of stay, and treatment failure.
- Genomic transmission-dynamics studies conducted within defined regional hospital networks, to distinguish local clonal emergence from inter-facility or inter-regional importation.
- Vaccine development targeting conserved, immunogenic virulence determinants (e.g., OmpA-based or biofilm-associated-protein-based candidate antigens).
- One Health surveillance integrating clinical, environmental, and veterinary Acinetobacter baumannii data, particularly in regions such as North-East India where agricultural and environmental reservoirs remain entirely uncharacterised.

5. Conclusion

5.1 Main Conclusion

This systematic review demonstrates the alarming global dissemination of multidrug- and extensively drug-resistant Acinetobacter baumannii across tertiary care hospitals worldwide, driven predominantly by the international high-risk clone STPas2/IC2, the worldwide spread of OXA-23 and NDM carbapenemases (increasingly in co-production), and a high prevalence of biofilm formation that supports both environmental persistence and reduced antimicrobial efficacy. India represents a critical epicentre of this global crisis, with carbapenem susceptibility as low as approximately 12% and the documented emergence of pan-drug-resistant isolates, while North-East India — despite a comparatively limited underlying evidence base — shows equally alarming, and in some respects more severe, resistance patterns, including 91.27% carbapenem resistance and extensive co-production of multiple beta-lactamase classes within individual isolates.

5.2 Clinical Implications

These findings collectively support the routine incorporation of molecular resistance-gene surveillance into tertiary care antimicrobial stewardship programmes, the use of region-specific, regularly updated antibiograms to guide empirical therapy in high-prevalence settings, and heightened, targeted infection-control vigilance around biofilm-forming, extensively or pan-drug-resistant Acinetobacter baumannii isolates, particularly within intensive care and post-surgical units where this organism causes disproportionate morbidity and mortality.

5.3 Recommendations

- Prioritise whole-genome-sequencing- and MLST-based genomic surveillance programmes in North-East India, as a matter of urgency, to characterise clonal identity and transmission dynamics for the first time in this region.
- Integrate systematic, multi-gene virulence profiling alongside resistance-gene surveillance in all future regional molecular epidemiology studies, rather than continuing to report resistance and virulence data in isolation.
- Support dedicated mechanistic research into resistance–virulence co-regulation, to inform the rational design of combined anti-resistance and anti-biofilm therapeutic strategies.
- Establish sustained, longitudinal, multi-centre surveillance networks across Indian tertiary care hospitals, moving beyond the single time-point cross-sectional design that currently predominates.
- Invest in rapid, point-of-care molecular diagnostics for key carbapenemase genes to guide timely, appropriately targeted empirical antimicrobial therapy in high-prevalence settings.

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Conflict of interest

The authors declare no conflict of interest.

Data availability statement

The datasets generated and/or analysed during the current study are available from the corresponding author upon reasonable request.

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