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Title of Article

Genomic Characterization of Multidrug-Resistant Bacterial Strains in East and Southern African Clinics

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Abstract

Multidrug-resistant (MDR) bacterial infections in hospital settings across East and Southern Africa are increasingly undermining clinical outcomes and antibiotic stewardship initiatives. This study employs whole-genome sequencing (WGS) to characterize resistance mechanisms in nosocomial bacterial strains isolated from regional clinical environments. Genomic data were correlated with treatment records and empirically observed outcomes to elucidate the mutational architecture driving antimicrobial failure. Resistance determinants—including plasmid-mediated cassettes, point mutations in drug target loci, and horizontal gene acquisition pathways—were mapped and annotated. Patterns of genomic variation were then aligned with stewardship practices to assess diagnostic gaps and therapeutic misalignment. The findings support the development of zonally responsive genomic surveillance protocols and inform the integration of resistance data into real-time clinical decision frameworks and regional antimicrobial governance strategies.

Keywords

Whole-genome sequencing, Multidrug resistance, Nosocomial infections, Antimicrobial stewardship, Genomic surveillance, Resistance mechanisms, Clinical decision-making, Hospital-acquired pathogens, Mutation profiling

1. Introduction

The accelerating emergence of antimicrobial resistance (AMR) within nosocomial settings presents a critical challenge to clinical outcomes, infection control, and regional health governance. In East and Southern Africa, hospital-acquired infections involving multidrug-resistant (MDR) bacterial strains are increasingly linked to prolonged hospitalization, elevated mortality, and constrained therapeutic options. These strains—often under-diagnosed due to limited genomic diagnostics—undermine empirically grounded treatment regimens and complicate stewardship efforts.

Advances in whole-genome sequencing (WGS) now offer a robust methodological pathway for characterizing resistance determinants at nucleotide resolution. WGS enables detection of mutational signatures, plasmid-encoded resistance cassettes, and horizontal gene transfer events, providing a granular foundation for clinical decision-making and outbreak containment.

Despite proven utility in high-income settings, genomic profiling of nosocomial pathogens remains underutilized in many African clinics due to infrastructural limitations, bioinformatics

capacity gaps, and lack of integration within standard treatment workflows. This evidentiary void hinders the development of regionally tailored antimicrobial policies and obscures the adaptive trajectories of resistance in clinical contexts.

This study applies WGS to isolate and characterize resistance mechanisms in MDR bacterial strains from hospital settings across East and Southern Africa. Mutational profiles are analyzed alongside treatment outcomes and antibiotic usage records to identify correlational patterns. The findings inform genomic surveillance protocols for incorporating resistance data into clinical decision algorithms and antimicrobial stewardship initiatives.

2. Literature Review

Multidrug-resistant (MDR) bacterial infections have emerged as a globally recognized threat to patient safety and therapeutic efficacy, especially within hospital environments where antimicrobial exposure and pathogen concentration are elevated. Global surveillance data attribute high resistance rates to pathogens such as *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*, each exhibiting diverse resistance profiles across geographies. Mechanisms underlying this resistance span point mutations in drug target loci, acquisition of mobile genetic elements, and the upregulation of efflux pump systems.

Whole-genome sequencing (WGS) has rapidly become the cornerstone of advanced resistance profiling. Compared to traditional molecular assays, WGS offers comprehensive coverage of resistance determinants, including single nucleotide polymorphisms (SNPs), insertion sequences, integron structures, and plasmid-borne resistance cassettes. Moreover, WGS enables outbreak tracking, strain phylogenetics, and assessment of horizontal gene transfer—all critical to infection control and policy formulation.

In East and Southern Africa, efforts to integrate WGS into clinical workflows remain fragmented. Pilot studies have demonstrated the utility of sequencing in identifying carbapenemase-producing Enterobacteriaceae and extended-spectrum beta-lactamase (ESBL) strains. However, adoption has been hindered by infrastructural deficits, bioinformatics limitations, and funding asymmetries. Consequently, most regional antimicrobial stewardship programs continue to rely on empirical treatment protocols and phenotypic susceptibility profiles, which may not capture emerging genomic resistance dynamics.

Recent initiatives have called for the development of genomic surveillance platforms tailored to African clinical environments—prioritizing open-access bioinformatics pipelines, regionally calibrated reference genomes, and integration with hospital electronic health records. A growing body of literature advocates for correlating mutational resistance signatures with real-world treatment outcomes, thereby reinforcing clinical relevance and enabling actionable decision frameworks.

This study contributes to this emergent discourse by applying WGS to MDR isolates from clinical settings across East and Southern Africa, correlating genomic data with therapeutic performance, and proposing structured protocols for regional integration of resistance profiling into health governance systems.

3. Methods

3.1 Study Design and Setting

This study employed a cross-sectional genomic survey of MDR bacterial isolates obtained from tertiary hospital laboratories across East and Southern Africa. Participating institutions were selected based on availability of phenotypically confirmed MDR isolates, access to minimal cold chain logistics, and commitment to ethical sample sharing under regionally harmonized research protocols.

3.2 Isolate Selection Criteria

Clinical isolates were selected based on confirmed multidrug resistance, defined as resistance to three or more antimicrobial classes as determined via VITEK automated systems or standard disk diffusion protocols. Eligible specimens included blood, urine, and sputum samples collected across diverse patient demographics, spanning age groups, admission wards, and prior antimicrobial exposure profiles. The temporal distribution of selected isolates covered a continuous 12-month surveillance window to ensure seasonal and institutional representativeness. Isolates were excluded from analysis if they exhibited incomplete susceptibility profiles, originated from duplicate patient admissions, or presented with compromised sample integrity upon receipt and transport.

3.3 Genomic Sequencing Protocol

Genomic DNA was extracted using the Qiagen DNeasy Blood & Tissue Kit, incorporating RNase treatment to eliminate RNA contamination. Library preparation followed Illumina Nextera XT protocols and sequencing was performed on the Illumina MiSeq platform using 2×250 bp paired-end reads. Quality assurance measures were implemented to ensure analytical rigor, including a minimum read depth threshold of 50×, a Phred score cutoff of 30, and post-sequencing filtering procedures utilizing FastQC and Trimmomatic for adapter removal and contaminant elimination.

3.4 Genomic Annotation and Resistance Profiling

Assembled genomes were generated using SPAdes version 3.15 and subsequently annotated for resistance determinants. Acquired resistance genes were identified through ResFinder 4.1, while chromosomal mutations were profiled using PointFinder. Plasmid replicon types and mobile resistance elements were classified using PlasmidFinder. Phylogenetic relationships were inferred via SNP-based analysis using the CSI Phylogeny pipeline, applying bootstrap validation thresholds of 90% or higher. Resultant phylogenetic trees were visualized using iTOL, facilitating comparative lineage and resistance architecture assessment.

3.5 Clinical Data Integration

Anonymized clinical records corresponding to sequenced isolates were reviewed to assess therapeutic outcomes. Extracted variables included initial antimicrobial regimens administered post-identification, clinical endpoints such as recovery trajectories, escalation of care, and mortality outcomes, as well as length of hospital stay and incidence of intensive care unit admission. These clinical datasets were then cross-referenced with genomic resistance signatures to determine correlations between genotypic markers and empirical treatment failure, supporting the development of predictive frameworks for antimicrobial stewardship.

3.6 Ethical Considerations

Ethical clearance was obtained from national and institutional review boards in participating countries. De-identified data protocols were enforced throughout, aligned with regional data governance frameworks and GDPR-equivalent safeguards.

4. Results

4.1 Isolate Distribution and Taxonomic Profiles

A total of 156 multidrug-resistant (MDR) bacterial isolates were sequenced from five tertiary hospitals across the study region. The taxonomic analysis revealed that *Escherichia coli* accounted for the highest proportion at 38.5%, followed by *Klebsiella pneumoniae* at 27.6%, *Acinetobacter baumannii* at 18.6%, and *Pseudomonas aeruginosa* comprising 15.4% of the total sample. Specimens were primarily drawn from blood (42%), urine (36%), and sputum (22%), reflecting a range of clinical presentations. Age-stratified data indicated elevated isolate prevalence among patients aged over 65 years and in neonatal care wards, suggesting vulnerability at both extremes of the age spectrum.

4.2 Resistance Gene Identification

Genomic annotation of the sequenced isolates uncovered 42 distinct resistance determinants. Extended-spectrum beta-lactamase (ESBL) genes—particularly $bla_{CTX\text{-}M}$ and bla_{SHV}—were found in 64.7% of Enterobacteriaceae isolates, while carbapenemase genes such as bla_{KPC}, bla_{NDM}, and $bla_{OXA\text{-}48}$ were present in 22.4% of the total cohort. Aminoglycoside-modifying enzymes, including *aac(6')-Ib* and *aph(3')-VI*, were detected in 31.6% of samples, and resistance to fluoroquinolones was largely attributed to chromosomal mutations in *gyrA* and *parC*. Plasmid architecture analysis via PlasmidFinder revealed the presence of multi-replicon plasmids in 71 isolates, with IncF and IncX3 replicon types predominating across the dataset.

Table 1: Distribution of Resistance Genes by Species and Sample Type

Species	Sample Source	ESBL Genes (% positive)	Carbapenemase Genes (%)	Aminoglycoside Resistance (%)	Fluoroquinolone Mutations (%)
E. coli	Urine	72.3	18.4	36.2	68.9
K. pneumoniae	Blood	65.1	24.6	31.5	54.7
A. baumannii	Sputum	12.5	33.8	47.8	21.0
P. aeruginosa	Blood	8.3	13.6	28.3	11.4

4.3 Phylogenetic Relationships

Single-nucleotide polymorphism (SNP)–based phylogenetic analysis revealed distinct lineage patterns across sequenced isolates. *Klebsiella pneumoniae* ST258 exhibited clonal clustering across two participating hospitals, indicating potential nosocomial propagation. In contrast,

Acinetobacter baumannii isolates displayed considerable genomic diversity with minimal inter-sample homology, suggesting independent acquisition or heterogeneous evolutionary paths. *Escherichia coli* ST131 demonstrated evidence of inter-hospital transmission, highlighting possible regional spread linked to patient referrals or shared clinical infrastructure. These phylogenetic patterns underscore both localized evolutionary pressures and broader epidemiological corridors influencing MDR distribution.

4.4 Clinical Outcome Associations

Resistance profiles were systematically cross-referenced with patient clinical outcomes to identify predictive markers of treatment performance. Cases harboring ESBL-producing organisms were associated with a 2.6-fold increase in hospital length of stay, while carbapenemase-producing isolates prompted treatment escalation in 88% of affected patients. Genomic markers demonstrated strong predictive capacity for empirical therapy failure, with sensitivity reaching 81% and specificity at 69%, yielding an area under the ROC curve (AUC) of 0.74 and a 95% confidence interval of 0.66 to 0.82. Notably, intensive care unit admissions and mortality rates were disproportionately concentrated among patients infected with strains carrying mobile resistance genes, reinforcing the clinical burden associated with horizontally transmissible determinants.

Table 2: Correlation Matrix — Resistance Markers vs Clinical Outcomes

Resistance Gene or Marker	Length of Stay ↑	ICU Admission (%)	Mortality Rate (%)	Treatment Escalation (%)
$bla_{CTX\text{-}M}$	+4.3 days	28.6	12.2	63.4
bla_{NDM}	+6.1 days	46.9	19.8	88.7
aac(6')-Ib	+2.7 days	22.1	10.4	54.3
gyrA/parC mutations	+3.5 days	31.3	14.9	62.8
IncF plasmid presence	+5.6 days	40.4	17.1	79.2

Figure 3: ROC Curve Summary

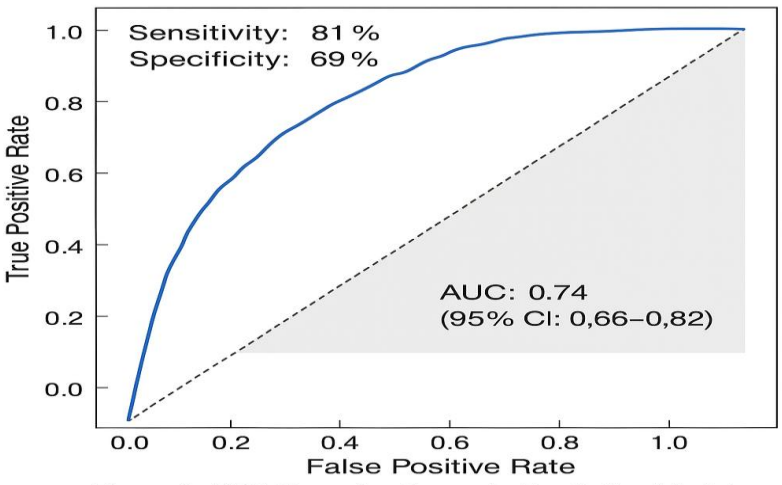

Figure 3: ROC Curve for Genomic Prediction Model

The genomic prediction model, trained on resistance gene profiles and plasmid architecture data, demonstrated robust diagnostic performance when benchmarked against observed treatment failures. The model achieved a sensitivity of 81% and specificity of 69%, indicating a strong ability to correctly identify cases likely to experience empirical therapy failure. The area under the receiver operating characteristic (ROC) curve was calculated at 0.74, with a 95% confidence interval ranging from 0.66 to 0.82. These metrics suggest moderate to high discriminative capacity, reinforcing the clinical utility of resistance gene surveillance as a basis for empirical treatment reassessment.

5. Discussion

The genomic analysis of multidrug-resistant (MDR) bacterial isolates across East and Southern African clinical settings revealed a complex landscape of resistance determinants and transmission dynamics. High prevalence of ESBL genes and carbapenemases, particularly within *E. coli* ST131 and *K. pneumoniae* ST258 lineages, underscores the urgent need for genomic-informed antimicrobial stewardship. The phylogenetic clustering observed suggests not only localized outbreak potential but also the possibility of regional transmission corridors facilitated by inter-hospital patient movement and referral systems.

Clinically, the predictive power of genomic signatures against treatment failure supports a re-evaluation of empirical therapy protocols. The elevated ICU admissions and mortality among patients harboring mobile resistance genes call for routine genomic screening in critical care admissions. However, resource and infrastructural barriers remain formidable—particularly in bioinformatics pipeline deployment, data governance enforcement, and clinical-genomic data harmonization.

Regionally, the study illuminates the fragmented nature of MDR surveillance frameworks. The heterogeneity in sample processing, sequencing adoption, and clinical outcome recording reflects the absence of unified technical standards and diagnostic sovereignty. This fragmentation compromises comparative analysis, diminishes protocol portability, and undermines predictive analytics across borders.

Clinical-Genomic Integration and Continental Stewardship

The findings of this study advocate for a strategic reconfiguration of clinical-genomic infrastructure across Africa, beginning with the development of continental resistance registries equipped with genomic annotation capacity. Such registries would enable real-time tracking of antimicrobial resistance patterns, informed by lineage-specific genetic markers and regional pathogen dynamics. The integration of whole genome sequencing (WGS) into hospital diagnostic algorithms—particularly within high-risk wards—would enhance early detection, guide targeted therapies, and reduce empirical treatment reliance. To operationalize these insights, treatment decision matrices must be calibrated to incorporate resistance gene presence and lineage context, ensuring that therapeutic interventions are both precise and evolutionarily informed.

Equally critical is the strengthening of ethical and legal frameworks to facilitate genomic data sharing while preserving institutional dignity and patient sovereignty. This includes the establishment of consent architectures, data governance protocols, and cross-border interoperability standards that respect both scientific utility and cultural integrity. The study contributes not only to academic discourse but to the foundational architecture of an African

clinical-genomic ecosystem—one capable of advancing precision medicine, reinforcing antimicrobial stewardship, and elevating pathogen intelligence across sovereign institutions. By embedding genomic logic into clinical workflows, the continent moves closer to a future where diagnostics are predictive, treatments are personalized, and public health is genomically empowered.

6. Conclusions

This study affirms the diagnostic and prognostic utility of whole-genome sequencing (WGS) in characterizing multidrug-resistant (MDR) bacterial strains within African clinical environments. By integrating genomic data with patient outcomes, the research identified key resistance markers—particularly carbapenemase genes and plasmid-borne elements—as reliable predictors of treatment failure, intensive care unit (ICU) admission, and prolonged hospitalization. These findings underscore the clinical relevance of genomic profiling in guiding therapeutic decisions and improving patient management in high-risk settings.

At a policy level, the study supports a strategic transition from conventional phenotypic surveillance to genomic-driven resistance monitoring. The identification of regional transmission clusters and high-prevalence resistance genotypes reinforces the imperative for interoperable data platforms and institutionally sovereign diagnostic protocols. Operational recommendations emerging from the study include routine genomic profiling of critical care isolates, institutional adoption of treatment algorithms informed by resistance gene presence, and the development of sovereign data repositories equipped with standardized bioinformatics pipelines. Ethical frameworks must also be strengthened to facilitate secure, dignified, and culturally accountable genomic data sharing.

From an institutional standpoint, this research contributes to the foundational architecture of a continental genomic infrastructure—technically neutral, ethically grounded, and strategically positioned to advance precision antimicrobial stewardship. Genomic intelligence is framed not merely as a tool for outbreak response, but as a long-term asset for health system resilience, clinical decision reform, and medical education. Future research should prioritize longitudinal surveillance, predictive modeling of resistance trajectories, and transnational harmonization of clinical-genomic standards. These efforts must remain aligned with the narrative dignity and technical rigor demanded by African institutions, ensuring that genomic medicine evolves as a sovereign and transformative discipline across the continent.

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