



Utilising clinical covariates to predict multi-drug resistance genotypes in WHO priority pathogens: a genomic study of eight African countries

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The escalating threat of antimicrobial resistance (AMR) poses a significant challenge to global health, particularly in resource-limited settings where genomic surveillance remains sparse. We performed a genomic analysis to characterise AMR gene distributions and evaluate the predictive value of clinical metadata for multidrug-resistant (MDR) phenotypes across Africa. In this study, a total of 1,239 whole genome sequences from four WHO priority pathogens (*Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, and *Pseudomonas aeruginosa*) from 8 African countries: Nigeria, Ghana, Senegal, Tunisia, Gabon, South Africa, Algeria, and Egypt were analysed. Genetic determinants of AMR across 11 antibiotic classes were identified using established WGS-based pipelines. Co-resistance patterns were assessed by correlation analyses, and classifier models with cross-validation were employed to model associations between clinical covariates and MDR genotypes. Over 90% of the sequenced genomes were MDR, exhibiting high frequencies of resistance genes against beta-lactams, tetracyclines, and aminoglycosides. Co-resistance profiling demonstrated that tetracycline resistance rarely co-occurred with resistance to most other drug classes. Furthermore, we demonstrated that clinical covariates, such as infection sites and clinical indication, can accurately predict MDR genotypes with >80% accuracy. These findings highlight the widespread burden of MDR among priority pathogens in Africa, and the high predictive accuracy of clinical indicators suggests that clinical metadata can serve as a reliable proxy for genomic resistance profiling in low resource settings. The identification of distinct co-resistance patterns, alongside the predictive utility of clinical covariates, provides a foundation for developing cost-effective, metadata-driven decision support tools to guide empirical treatment strategies in low resource healthcare environments.

