Review Article

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The integration of machine learning (ML) models with genomic data to predict future trends in *Klebsiella* antimicrobial resistance

Abstract

The rising antimicrobial resistance (AMR) among *Klebsiella* species presents the need for a transformative approach to understanding and combating the public health crisis crises with by integrating cutting-edge artificial intelligence (AI) in microbiological insights by employing machine learning techniques like deep learning, support vector machines and ensemble methods. Researchers can analyse and analyse vast datasets out discover intricate relationships between specific genomic features and resistance profiles. This synergy of microbiology also enhances it and informs targeted public health strategies and personalized treatment modalities. Various enigmas can like the challenges of data quality, interpretation and the need for robust validation frameworks to ensure the findings across diverse scientific contexts. Recent advancements have illuminated the genetic underpinnings of resistance to critical antibiotic classes, including carbapenems, cephalosporins, aminoglycosides, fluoroquinolones and tetracyclines. Ultimately, this review underscores the recent innovations in genomic data utilization utilisation, the potential of AI-driven approaches, and types of machine learning frameworks for the understanding *Klebsiella* AMR, fostering a proactive stance in antibiotic stewardship and improving human health where resistance is increasing humdrum.

Keywords: antibiotics, *Klebsiella*, AMR, machine learning, artificial intelligence

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Abbreviations: AMR, Antimicrobial resistance; ML, Machine learning; SVM, Support vector machine; WHO, World health organization; MDR, Multidrug resistance; WGS, Whole genome sequencing; ESBL, Extended spectrum beta-lactamase

Introduction

Antimicrobial resistance (AMR) has emerged as a significant threat to global health. The bacterial strains of *Klebsiella* are the cause of prominent pathogens responsible for a wide range of human infections of the bloodstream, pneumonia and urinary tract. The World Health Organization has classified *Klebsiella pneumoniae* as a critical priority pathogen due to its increasing resistance to commonly used antibiotics, particularly carbapenems and cephalosporins.[1] This resistance is exacerbated by the overuse and misuse of antibiotics, leading to treatment failures and increased morbidity and mortality rates in infected patients.[2] Generally microbial secretions are hazardous to human health and the environment.[3] Recent advances in genomic sequencing technologies have provided invaluable insights into the genetic mechanisms underlying AMR in *Klebsiella*. However, the sheer volume of generated genomic data necessitates applying machine learning (ML) models to analyze and interpret this information efficiently. Whole-genome sequencing (WGS) enables the identification of specific resistance genes and mutations associated with antimicrobial resistance.[4] WGS facilitates a better understanding of the epidemiology of resistance patterns.[5] Machine learning is a subset of artificial intelligence (AI) offering promising approaches to predict AMR patterns based on genomic data.[6] By leveraging diverse datasets, ML algorithms can identify complex relationships and patterns that may not be apparent through traditional statistical methods.[7]

Adaptive evolution of Klebsiella with different class antibiotics

a) Carbapenems

Carbapenems are a class of broad-spectrum beta-lactam antibiotics characterized by their broad-spectrum efficacy against Gram-positive and Gram-negative bacteria. They are considered last-resort drugs for treating severe infections, mainly caused by multi-drug-resistant bacteria like *Klebsiella pneumoniae*. The mechanism of action involves bacterial cell death due to inhibition of cell wall synthesis. Generally, such as peptidoglycan-inhibiting cross-linking antibiotics, including imipenem and meropenem, are used in treating meningitis and sepsis. However, the emergence of carbapenem-resistant bacterial strains highlights the urgent need for novel therapies and prudent antibiotic stewardship to mitigate resistance.[8]

b) Cephalosporins

Cephalosporins are a group of beta-lactam antibiotics divided into generations based on their antimicrobial spectrum and pharmacological properties. There are five generations of cephalosporin meningitis that treat pneumonia, skin infections, meningitis, and other associated infections. The first generation primarily targets Gram-positive bacteria, while subsequent generations have enhanced activity against Gram-negative pathogens. Cephalosporins like ceftriaxone and ceftazidime are commonly employed in treating respiratory, urinary and skin infections. Their ability to penetrate the blood-brain barrier makes certain cephalosporins effective against central nervous system infection the past, resistance rates in constant surveillance and sensitivity testing have been seen to increase. It needs to conduct a precise study to ensure the effectiveness of cephalosporins in clinical practice with concerning appropriate therapeutic decisions.[9]

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c) Aminoglycosides

Aminoglycosides are antibacterial antibiotics that inhibit protein synthesis in aerobic bacteria. These antibiotics contain an amino-modified glycoside. They function by irreversibly binding to the 30S ribosomal subunit, disrupting protein synthesis and finally causing bacterial cell death. Commonly used aminoglycosides include gentamicin, amikacin and tobramycin. Aminoglycosides are often used in combination therapies to enhance efficacy against resistant infections like sepsis and pneumonia. Frequent resistance mechanisms of enzymatic modification are emerging concerns related to aminoglycosides in clinical settings.[10]

d) Fluoroquinolones

Fluoroquinolones are a class of broad-spectrum synthetic antibiotics that inhibit bacterial DNA synthesis by targeting topoisomerases like DNA gyrase and topoisomerases IV. Their broad-spectrum activity makes them effective against various pathogens, including *Klebsiella pneumoniae* and other Gram-negative and Gram-positive bacteria. Some fluoroquinolones used in wide arena are ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin. These are frequently prescribed for urinary tract infections, respiratory infections and gastroenteritis. These antibiotics can be taken orally, intravenous the and as drops related to ear and eye enigmas. However, increasing resistance among bacterial strains raises concerns regarding their long-term efficacy. A careful risk assessment consideration is required for reasonable use to mitigate the risk of further resistance development in maintaining better health and life should be of prime importance.[11]

e) Tetracyclines

Tetracycline is a broad-spectrum polyketide secondary metabolite produced by the *Actinobacteria Streptomyces*. It exerts a bacteriostatic effect on bacteria by reversibly binding to the bacterial 30S ribosomal subunit and blocking incoming aminoacyl tRNA from binding to the ribosome acceptor site.

It is used to treat various bacterial infections of the skin, intestines, respiratory tract, urinary tract, genitals, lymph nodes and other body systems. Commonly used tetracyclines include doxycycline and minocycline, which also have anti-inflammatory properties. Tetracyclines have a unique mechanism of action and are employed in combination therapies to combat resistant infection. Apart from their effectiveness, the rising rates of tetracycline resistance through efflux pumps and ribosomal protection ways are subject to exhaustive research. Resistance in bacterial strains is becoming a significant challenges to address these resistance issues.[12,13]

Current trends of antimicrobial resistance Klebsiella spp.

The hasty surfacing of multidrug resistance of *Klebsiella pneumonia* poses a critical menace to global health. These nosocomial pathogens have acquired resistance genes and give rise to severe enigmas for the treatment of severe infections. The prevalence of multidrug-resistant strains has surged produce spectrum extended-spectrum carbapenemases lactamase beta-lactamases like *Klebsiella pneumoniae* carbapenemases (KPC) has rendered standard treatments ineffective of rapidly disseminating resistance genes through mobile genetic elements further complicates infection control efforts. Geographic variations in resistance rates are evident, with higher prevalence in areas lacking robust antibiotic stewardship. These trends emphasise the urgent need for enhanced surveillance and targeted strategies to combat *Klebsiella*-associated infections effectively.[3,14] Using genomic data, the machine learning framework for predicting AMR in *Klebsiella* represents a transformative approach to tackling resistance challenges. This framework incorporates genomic sequences, single nucleotide polymorphisms and gene expression profiles to develop predictive models. Key stages, mainly data pre-processing, feature selection and model training with machine learning algorithms such as support vector machines and neural networks, are important. Analysis by annotated datasets to link genetic information with resistance patterns such models can effectively predict resistance trends and emerging mechanisms. Ultimately, Table 1 reveals the framework that enhances our understanding of *Klebsiella* AMR, guiding public health interventions and improving treatment strategies.[15,16]

Table 1 Machine learning framework for predicting antimicrobial resistance in *Klebsiella* using genomic data

Feature	Description	Machine learning (ML) models	Application in *Klebsiella* research
Source of genomic data	Genomic sequences of *Klebsiella* sps. as WGS, SNPs and gene expression	NCBI Gen Bank and European Sequence Database	Basic information that serves as the input for ML models
Pre-processing	Data extraction for gene presence, mutation & resistance	Bioinformatics GATK	Precisely preparation of model input
Machine learning models	Based on genomic features predict antimicrobial resistance (AMR)	Neural Networks (NN) and Gradient Boosting Machines (GBM).	Based on historical data predicts resistance and trends in *Klebsiella*.
Feature Selection	Key genetic markers identification associated with resistance	Recursive Feature Elimination RFE and Principal Component Analysis PCA	Genes and mutations are highlighted responsible for AMR in *Klebsiella*
Model evaluation	Accuracy and precision to assess model performance.	ROC curves Cross validation	Ensures the model reliably predicts AMR trends
precise prediction	Future trends in resistance to specific antibiotics	Resistance probabilities for diverse antibiotics	Guides public health interventions for *Klebsiella*
Challenges	Integrating ML with genomic data, Data quality	Large datasets, interpretability of ML models	Rigorous data updates and validation in clinical tests
Future prospects	Innovations to predict narrative resistance mechanisms	Techniques like deep learning as clustering to improve prediction accuracy	Helpful in outbreaks prediction and optimize antibiotic stewardship

Recent innovations in utilising genomic data for predicting AMR have significantly enhanced our understanding of resistant pathogens. Table 2 reveals that advances in whole-genome sequencing (WGS) allow researchers to identify specific genetic mutations associated with resistance in bacteria like *Klebsiella*. Additionally, machine learning algorithms analyse vast genomic effectively uncover patterns and predict resistance trends. Techniques such as single nucleotide polymorphism (SNP) analysis and gene expression profiling further

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refine these predictions. By integrating genomic data with clinical information, these innovations enable the development of tailored treatment strategies, facilitating early detection of resistance and informing public health initiatives to combat AMR effectively.[15,17,18]

Table 2 Innovations in genomic data utilization for AMR prediction

Element	Genomic feature	Associated resistance	ML model
Resistance gene	blaKPC Gene	Carbapenem	Random Forest SVM
Mutation	oqxAB Efflux Pump	Fluoroquinolone	Gradient Boosting
Mutation)	porin loss mutation (OmpK	Cephalosporin	Neural Networks

Integrating artificial intelligence (AI) in predicting AMR in *Klebsiella* represents a ground-breaking advancement in microbiological research. Recent innovations include machine learning algorithms that analyse genomic data, identify resistance patterns and predict future trends. These AI models utilise various data sources, such as genomic sequences and clinical records, to enhance accuracy in resistance prediction. Table 3 depicts advancements in deep learning techniques to improve the ability to detect novel resistance mechanisms. Implementing these AI-driven approaches not only aids in understanding *Klebsiella* resistance dynamics but also supports personalised treatment strategies, ultimately contributing to better patient outcomes and public health management.[17,19–21]

Table 3 AI innovations for AMR prediction in *Klebsiella*

AI Innovation	Key features	Purpose
Deep AMR	Uses deep learning for AMR classification	Predict AMR genes from sequencing
Res Finder 4.0	Focuses on gene-based AMR prediction in Gram-negative bacteria	AMR gene detection
Pathogen Watch	Monitors AMR trends using genomic data	Genomic surveillance
K-mer Resistance Classifier	High accuracy in resistance prediction	Identifies AMR profiles from k-mers

Antibiotic resistance trend in Klebsiella

Over the past few years, antibiotic resistance in *Klebsiella* species has escalated significantly. *Klebsiella* has cause serious threat to public health in South East Asian countries including India. Figure 1 enshrines the epidemic pattern and percentage of resistance occurrence in *Klebsiella* to the mentioned antibiotics, which have become infections harder to treat like carbapenems, cephalosporins, aminoglycosides, fluoroquinolones and tetracyclines.[1,12,15–18] Resistance among the bacterial strains against these antibiotics has risen due to the organism's ability to adapt and survive despite therapeutic interventions. These rising trends emphasize the urgent need for improved surveillance, new therapeutic strategies and public health measures to combat *Klebsiella* associated infections and preserve the effectiveness of existing antibiotics in clinical practice.
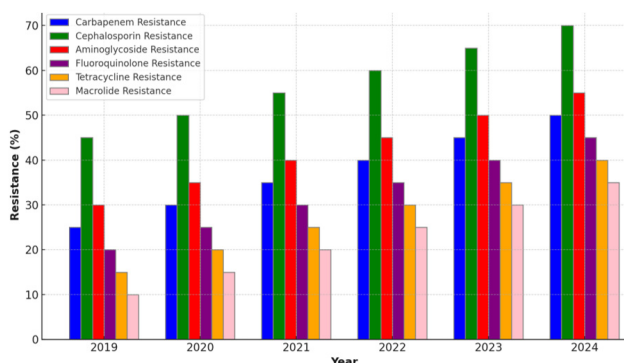

Figure 1 Selected antibiotic resistance trends in *Klebsiella* since 2019-2024.

Conclusion

Integrating machine learning models with genomic data offers a transformative approach to predicting antimicrobial resistance in *Klebsiella pneumoniae*. By identifying resistance patterns and genetic markers, ML models can provide critical insights into the evolution and spread of AMR, aiding in more effective treatment strategies and infection control measures. As the threat of AMR continues to grow, machine learning in microbiology will become increasingly important in addressing one of the most pressing challenges in modern healthcare. Incorporating ML into microbiological research and clinical practice will enable a more proactive approach to combating *Klebsiella* resistance, helping to reduce the impact of multidrug-resistant infections and improve patient outcomes.

Acknowledgments

None

Conflicts of interest

The authors declare that there are no conflicts of interest.

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