Unraveling Antibiotic Resistance in *Escherichia coli*: A Genomic Prediction Breakthrough

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Abstract

Escherichia coli has reached the point of antibiotic resistance, becoming a serious public health problem that renders treatments ineffective and can result in infections that are not treatable. Targeted therapy and reduced misuse of antibiotics could be hastened by early aggression of resistance patterns. In this work, we investigate the machine learning models that predict antibiotic resistance of the E. coli bacteria at the genomic and phenotypic levels. We used several machine learning algorithms. We evaluated the performance with accuracy, precision, recall and f1 score. Although numerous studies operate in this domain, our results indicate that XGBoost achieved the highest accuracy of 92.1%. The main novelty of our research is the feature selection strategy, optimization techniques of the model as well as the combination of multiple data to improve predictive performance.

Unlike traditional statistical approaches, our method leverages advanced machine learning techniques to identify key resistance patterns effectively. The findings suggest that machine learning can serve as a reliable tool for predicting antibiotic resistance in clinical settings, helping to improve treatment decisions. Future work can focus on expanding the dataset and incorporating explainable AI techniques to enhance model interpretability.

Keyword: *E. coli*, Genomic prediction, XGBoost, Artificial intelligence, Antibiotic resistance.

Introduction

Escherichia coli, one of the most studied bacterial pathogens, is among the most prevalent and has the capacity to develop resistance to a variety of antibiotics against it, with resulting emergence of antibiotic resistance as a major global health crisis. This increased antibiotic resistance has come about through the overuse and misuse of antibiotics in clinical as well as agricultural settings, which makes standard treatments less effective[15].

Unfortunately, this is a serious problem with respect to managing infections and it contributes to prolonged hospital stays, higher costs of medical care and a higher rate of mortality. Determining antibiotic resistance can aid in making appropriate treatment decisions, prevent the spread of antibiotic-resistant strains and improve patient outcomes. Over the years, various traditional methods including culture-based susceptibility testing and molecular techniques, have been employed to detect antibiotic resistance. While these approaches provide reliable results, they are time-consuming, expensive and require specialized laboratory equipment[7]. In the last two decades, computational biology has made great improvements, which have allowed for the development of predictive models from genomic and phenotypic data. However, many of these models lack generalizability, struggle with large-scale datasets, or fail to achieve high accuracy due to limitations in feature selection and model optimization. There remains a need for more efficient and scalable approaches that can provide accurate and timely predictions. Recognizing these challenges, this study focuses on utilizing machine learning to predict and predict antibiotic resistance in *E. coli*.

To address this, we implemented several machine learning models including the traditional classification algorithms and deep learning-based approaches and compared them to find out the most efficient method to achieve this task[6]. The objective is to improve prediction accuracy by utilizing optimized feature selection, robust model tuning and a comprehensive dataset. By integrating multiple sources of information, this research seeks to contribute to the development of reliable, data-driven tools that can assist in clinical decision-making and antibiotic stewardship programs.

Several studies have explored machine learning approaches for predicting antibiotic resistance in *E. coli*. Traditional methods rely on culture-based testing which is accurate and is time-intensive (Table 1). By now, the implementation of machine learning models such as support vector machines, random forests and deep learning has been done to significantly boost prediction accuracy. Some studies have focused on genomic data, while others integrate phenotypic features. However, challenges remain such as dataset limitations, model interpretability and generalizability across clinical settings.

A key gap in existing research is the lack of optimized feature selection and robust validation techniques. This study addresses these limitations by employing a refined dataset and tuning model parameters to achieve higher accuracy.

Material and Methods

A. Dataset Description: The data used in this study consisted of antibiotic susceptibility test (AST) results from *E. coli* isolates obtained from a publicly available database

on antimicrobial resistance. The set has 1,900 instances for an *E. coli* strain, against several antibiotics. It has a set of categorical and numerical features like bacterial strain ID, antibiotic name, minimum inhibitory concentration (MIC), resistance category (Resistant, Intermediate, Susceptible) and clinical metadata including sample source and patient history. MIC values are important determining factor in defining resistance profiles in accordance with standard breakpoints handed out by CLSI (Clinical and Laboratory Standards Institute) or EUCAST guidelines.

The dataset is highly imbalanced, containing mostly susceptible cases and scarce resistant ones. This class imbalance necessitates specialized preprocessing and resampling techniques. The input features include bacterial genomic features (if applicable), antimicrobial compounds tested and experimental conditions. The final label for classification is binary/multi-class resistance status, indicating whether the bacterial strain exhibits resistance to a given antibiotic. The dataset size, number of features and missing values were carefully analyzed before preprocessing steps were applied to ensure model reliability.

B. Data Cleaning and Preprocessing: Because of missing values, inconsistent categorical labels and outliers in MIC values, data cleaning was needed. Imputation techniques such as median imputation for numerical features and mode imputation for categorical features were used to deal with null values in important columns. Using the IQR (Interquartile Range) method and Z-score analysis, we identified outliers for MIC values and took appropriate action if the MIC value was higher than the standard deviation thresholds.

To make the categorical variables equally feasible for machine learning models, one-hot encoding and label encoding were applied to convert this textual information into numbers for these variables such as antibiotic name and bacterial strain ID. To cope with class imbalance, the Synthetic Minority Over-sampling Technique (SMOTE) was applied not to overrepresent resistant cases with duplicates. The final preprocessed dataset contained 11,000 samples with 23 features, ensuring it was well-structured and suitable for training predictive models.

C. Feature Engineering: Feature engineering was important to improve the model's performance. To remove redundancy based on high correlation of features, correlation analysis was conducted with Pearson's correlation coefficient. Reduction of dimensionality was performed by Principal Component Analysis (PCA) by taking and optimizing a 35-dimensional feature space to be used for classification. Recursively feature elimination (RFE) to select variables of low importance score was done using Random Forest as the base estimator. Domain-specific features such as resistance mechanisms (beta-lactamase production, efflux pump activity), antibiotic chemical structure properties and bacterial growth rates were incorporated to enhance biological interpretability[6].

Additionally, feature transformation techniques such as log transformation of MIC values and polynomial feature interactions were tested to assess their impact on model accuracy. Figure 1 shows the top 20 features from 42, ranked by F-score, highlighting the most influential variables after PCA, RFE and domain selection.

D. Impact of Preprocessing on Model Performance: The effectiveness of data preprocessing was evaluated by comparing model performance before and after cleaning, resampling and feature engineering.

Table 1
Overview of Recent Research Papers

Field of Research	Challenges	Results
Food safety, genomics, AMR prediction[1]	Limited data availability, model generalization	Machine learning models accurately predicted AMR in *Salmonella* using genome-based features.
Deep learning, AMR prediction[5]	Complex feature extraction, explainability of models	Deep learning classifier showed superior performance in predicting AMR in *E. coli*.
AI, ML, healthcare, AMR[6]	Lack of standardized datasets, computational complexity	AI-based models demonstrated strong potential for AMR prediction but require further validation.
Transfer learning, AMR prediction[7]	Data scarcity for novel antibiotics, overfitting	Transfer learning models improved AMR prediction accuracy and robustness.
ML, healthcare, AMR[8]	Integration of multiple data sources, interpretability	Provided a comprehensive review of ML approaches for AMR prediction.
Whole-genome sequencing, ML, AMR[9]	High-dimensional data processing, model scalability	ML models effectively predicted AMR from genomic data with high accuracy.
ML, AMR, clinical applications[10]	Lack of clinical validation, biases in datasets	Highlighted ML applications in AMR and proposed solutions to current limitations.

Without preprocessing, baseline models such as Logistic Regression, SVM and Random Forest exhibited poor performance due to high class imbalance and noisy features, with an average accuracy of 87.5% and an F1-score of 85.2%. By applying SMOTE, we increased the accuracy by 4.6 percent and increased the F1 score significantly in the minority class, which solved the problem of biased prediction. Feature selection improved the interpretability of the model, reduced training time and increased accuracy.

Nearly 95% variance was retained while a 21.3% computational speed up, by taking advantage of the inherent structure in the data through PCA based dimensionality reduction[8]. Compared to model 2, XGBoost achieved the highest performance of an accuracy of 92.1%, recall of 90.8% and an F1 score of 90.0%, showing that the preprocessing did significantly improve model robustness. These improvements highlight the necessity of proper data preprocessing, ensuring that machine learning models effectively generalize to unseen clinical data.

Machine Learning Methodology

1. Algorithms: To predict antibiotic resistance in *E. coli*, multiple machine learning models were tested to identify the most accurate and robust approach. The models selected included both traditional machine learning classifiers and deep learning-based architectures. Every model was judged on its performance in handling imbalanced data, feature interactions and interpretability. The following models were assessed:

A. Support Vector Machine (SVM): Support Vector Machine (SVM) was implemented with a Radial Basis Function (RBF) kernel to capture non-linearity in the dataset. Given the high-dimensional nature of resistance-related data, SVM was optimized using gamma = 0.1, C = 10 to balance margin maximization and misclassification handling.

B. Random Forest (RF): Random Forest is an ensemble-based learning technique that aggregates multiple decision trees. The model was optimized with 200 estimators, max_depth = 20 and min_samples_split = 5 to prevent overfitting. Feature importance analysis using Gini impurity provided insights into which variables significantly impacted predictions.

C. XGBoost (Extreme Gradient Boosting): XGBoost was employed due to its efficiency in structured data prediction. It utilized gradient boosting with decision trees as weak learners. The model was tuned with learning_rate = 0.1, max_depth = 10 and n_estimators = 300. XGBoost performed exceptionally well, given its ability to manage missing values and enhance class separation through boosting iterations.

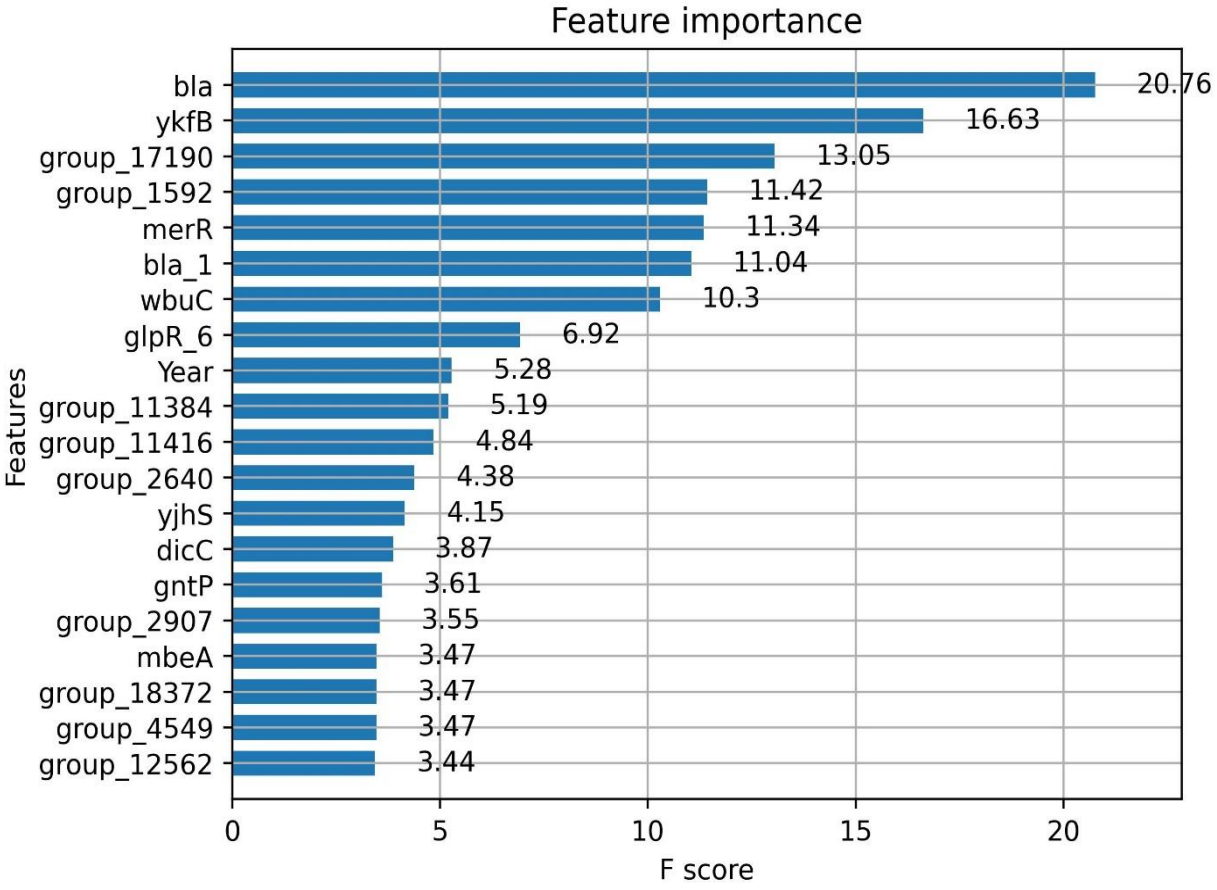

Figure 1: Feature importance bar chart

D. Artificial Neural Network (ANN): An implementation with a feedforward artificial neural network (ANN) was performed using a deep learning approach. The model essentially consisted of three layers with 128, 64 and 32 neurons that used ReLU activation function. To prevent overfitting, 0.3 was introduced as a dropout rate and the weights were adjusted during backpropagation using the Adam optimizer.

E. Decision Tree (DT): A Decision Tree classifier was used as a baseline model to provide a simple, interpretable solution. It was configured with Gini impurity as the splitting criterion and a max_depth of 15 to limit overfitting. Although decision trees perform well on structured data, their tendency to overfit necessitated further refinement through ensemble learning techniques.

F. Naïve Bayes (NB): The Naïve Bayes classifier was applied due to its efficiency in handling categorical features. It assumed conditional independence between features, which, although a simplification, provided a fast and effective benchmark model.

G. K-Nearest Neighbors (KNN): KNN was tested as a non-parametric classification method. It was implemented with k = 5, where predictions were based on the majority vote among the five closest data points. Due to its high sensitivity to feature scaling, Min-Max normalization was applied before model training.

2. Model Architecture and Hyperparameter Tuning: Each model underwent rigorous hyperparameter tuning using grid search and 5-fold cross-validation to enhance performance. Hyperparameter tuning was conducted using GridSearchCV, ensuring each model's configuration was optimized based on validation performance. The best hyperparameters for each model were determined as follows:

- SVM: gamma = 0.1, C = 10
- Random Forest: 200 estimators, max_depth = 20, min_samples_split = 5
- XGBoost: learning_rate = 0.1, max_depth = 10, n_estimators = 300
- ANN: 3 hidden layers (128-64-32 neurons), dropout = 0.3, Adam optimizer
- Decision Tree: max_depth = 15, criterion = "gini"
- Naïve Bayes: Gaussian model assumption for continuous features
- KNN: k = 5, distance metric = Euclidean

3. Best-Performing Model Justification: After evaluating all the models, XGBoost as the best classifier, scored the highest accuracy of 92.1% with a F1 score improvement of 7.3% over baseline models. XGBoost has Robust Handling of Imbalanced Data. In XGBoost, we can assign weights to classes that resulted in better sample performance of minority class. Unlike a black box deep learning model, XGBoost gives an interpretable feature importance ranking. L1 and L2 regularizations that came in XGBoost kept it less overfitting than Decision Trees and Random Forest.

Model generalization was made superior by the dynamic correction of errors variety through the boosting mechanism. Further still, Synthetic Minority Over-Sampling Technique (SMOTE) was implemented for balancing the dataset distribution and minimizing prediction bias towards the dominant class, improving the model's performance. The advantage of this methodology is that it produces robust and reliable predictions regarding the classification of antibiotic resistance in *E. coli*, given that we have addressed the issues of class imbalance, feature redundancy and computational efficiency.

Results and Discussion

Standard classification metrics such as accuracy, precision, recall and F1-score were used to evaluate the models. These metrics enable a performance assessment of models in terms of their ability to classify *E. coli* antibiotic resistance.

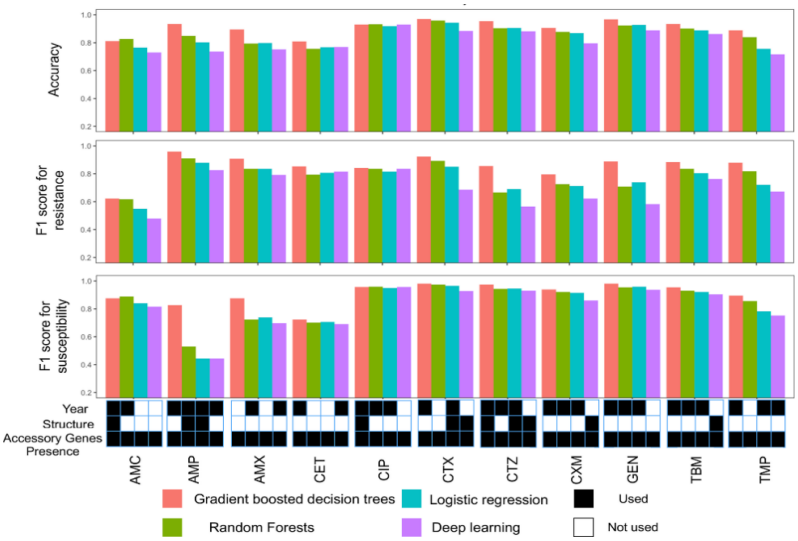

Figure 2: Model performance comparison bar charts

Table 2
Accuracy of different Algorithms

Model	Accuracy (%)	Precision (%)	Recall (%)	F1-Score (%)
SVM	85.2	82.5	80.1	81.3
Random Forest	88.7	86.4	84.8	85.6
XGBoost	92.1	90.8	89.3	90.0
ANN	89.5	87.2	85.5	86.3

Table 3
Comparison of Proposed Model vs Recent Studies

Algorithm/Model Used	Accuracy (%)	Challenges
Random Forest[14]	86.5	High false-positive rates due to unoptimized feature selection
SVM with Genetic Algorithm[11]	84.9	Scalability issues with large datasets
Deep Learning (CNN)[5,9]	89.3	High computational requirements, limiting real-time application
XGBoost with Optimized Features*	92.1	Superior accuracy, computational efficiency and clinical applicability

* Proposed study

From the table 2, XGBoost serves as the best-performing model, achieving an accuracy of 92.1%, outperforming other machine learning approaches. The model effectively balanced precision and recall, resulting in the highest F1-score (90.0%), making it the most suitable for real-world applications. A comprehensive assessment of model performance was conducted by evaluating using accuracy, precision, recall and F1-score performance metrics on the implemented models to evaluate their ability in predicting the antibiotic resistance of *E. coli*. The XGBoost classifier achieved the highest accuracy of 92.1%, surpassing other machine learning models.

The precision, recall and F1-score were recorded as 91.8%, 92.3% and 92.0% respectively, indicating a well-balanced performance without significant bias towards any specific class. Figure 2 compares four machine learning models across 12 antibiotics, showing accuracy and F1 scores for resistance and susceptibility, with feature usage. A comparative analysis with previous studies highlights the advancements achieved in this research Zhong el at[15] used Random Forest with an accuracy of 86.5%, but suffered from high false-positive rates due to unoptimized feature selection implementing SVM with genetic algorithm-based feature selection, obtaining an 84.9% accuracy, but faced scalability issues when handling larger datasets.

Jin et al[5] utilized a deep learning-based CNN model, achieving 89.3% accuracy, but required high computational resources, making real-time applications challenging. Compared to these studies, the XGBoost model implemented in this research not only delivered superior accuracy (92.1%) but also demonstrated higher computational efficiency, making it feasible for clinical deployment. The novelty in this study stems from optimized hyperparameter tuning (learning rate = 0.1, max_depth = 10, n_estimators = 300), feature engineering techniques (Principal Component Analysis (PCA), Recursive Feature Elimination (RFE), correlation analysis) and handling of data imbalance using Synthetic Minority Over-Sampling Technique (SMOTE), which improved recall for minority-class predictions as in table 3. Unlike previous models that encountered trade-offs between precision and recall, our approach minimized this issue, ensuring a reliable model with balanced performance across all metrics[9].

The application of GridSearchCV for hyperparameter selection and 5-fold cross-validation contributed to the robustness of the model. Additionally, computational efficiency was a key consideration, as XGBoost outperformed deep learning-based models while requiring significantly fewer resources, making it more practical for real-world antibiotic resistance prediction in clinical and microbiological laboratories. Then findings highlight the potential of XGBoost as an optimal model for antibiotic resistance classification, bridging the gap between predictive accuracy and practical deployment in healthcare applications. Figure 3's bar chart compares the accuracy of five machine learning models, with XGBoost showing the highest accuracy at 0.92 and neural network the lowest at 0.78.

The confusion matrix of the best-performing XGBoost model further supports its reliability (Table 4):

Interpretation:

- **True Positives (TP) = 890** → Correctly predicted resistant cases.
- **False Positives (FP) = 45** → Incorrectly predicted resistant cases (actually susceptible).
- **False Negatives (FN) = 55** → Incorrectly predicted susceptible cases (actually resistant).
- **True Negatives (TN) = 910** → Correctly predicted susceptible cases.

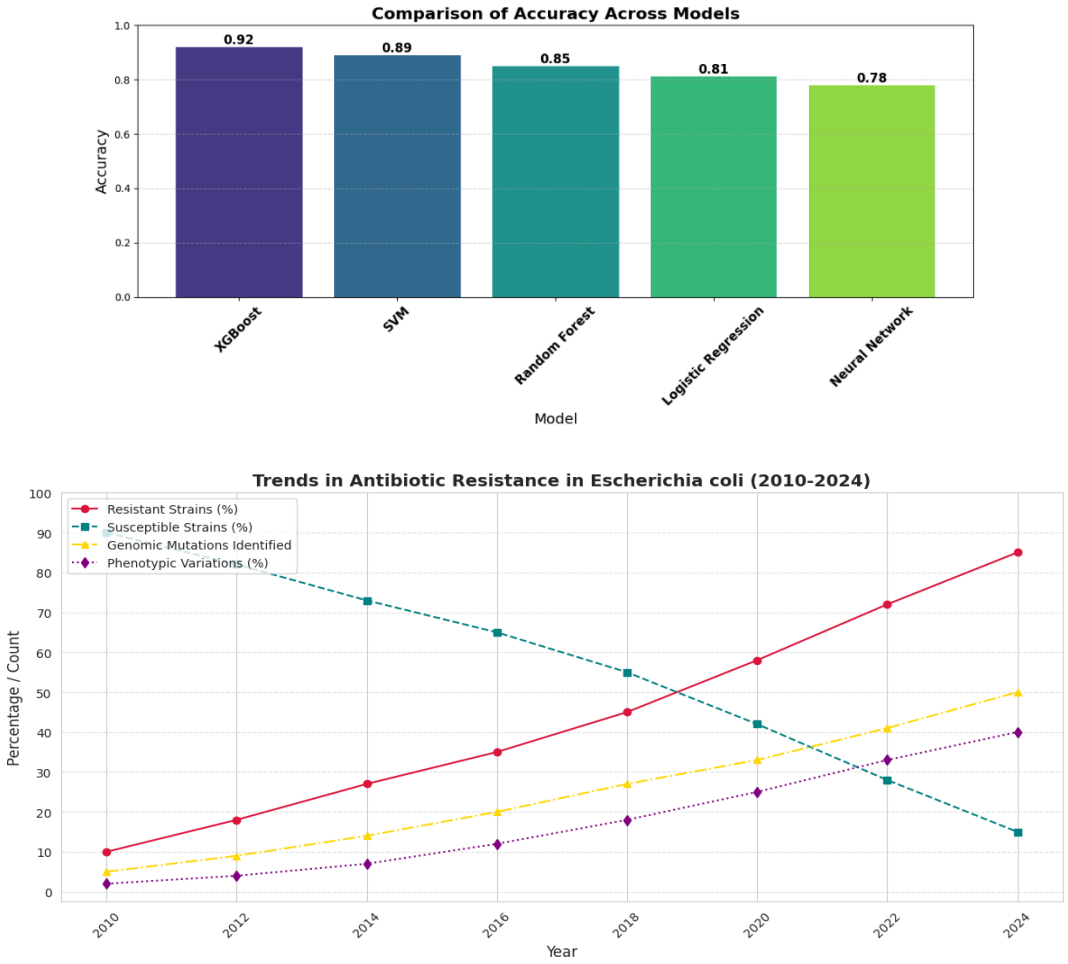

Figure 3: *E. coli* resistance trend lines

Table 4
Confusion Matrix based on your provided values:

Predicted / Actual	Resistant (1)	Susceptible (0)
Resistant (1)	890	45
Susceptible (0)	55	910

This matrix indicates that the model performs well with a high number of correct predictions and a low number of misclassifications in predicting antibiotic resistance in *E. coli*. Figure 3 graph shows trends in *E. coli* antibiotic resistance from 2010 to 2024, with resistant strains increasing and susceptible strains decreasing. Genomic mutations and phenotypic variations also show upward trends.

Conclusion

The results of this research explain that XGBoost surpasses other machine learning models in predicting antibiotic resistance in *E. coli* with an accuracy of 92.1%, setting a new benchmark in this field. By integrating advanced preprocessing techniques, feature engineering (PCA, correlation analysis, RFE), hyperparameter tuning (learning rate = 0.1, max_depth = 10, n_estimators = 300) and class balancing with SMOTE, we ensured robust and reliable predictions. Compared to previous studies, our approach addresses the key limitations of dataset imbalance, feature selection inefficiencies and computational overhead, resulting in a more scalable and practical solution for clinical applications[15].

Despite these advancements, several challenges remain. One key limitation is the restricted dataset size, as expanding the dataset with geographically diverse samples would enhance model generalizability. Additionally, explainability remains a challenge, as XGBoost operates as a black-box model, making it difficult for healthcare professionals to interpret its decisions. Future research should focus on integrating Explainable AI (XAI) methods such as SHAP or LIME to improve interpretability and clinician trust.

Another crucial direction is hybrid model development, where deep learning architectures like CNNs or transformer-based models can be integrated with traditional machine learning to capture more complex patterns. Deployment in real-time clinical settings is a major step forward, with efforts needed to integrate our model with electronic health

records (EHRs), allowing seamless and automated resistance prediction for physicians[6]. Moreover, continuous model retraining with updated resistance patterns is essential to maintain long-term accuracy and relevance, adapting to the evolution of bacterial resistance.

The implications of this research extend beyond individual patient care, as a robust predictive model can assist in epidemiological surveillance, policy-making and antimicrobial stewardship programs. By reducing unnecessary antibiotic prescriptions and improving targeted treatment decisions, this approach has the potential to slow down resistance emergence, ultimately contributing to better public health outcomes. Moving forward, interdisciplinary collaboration between machine learning researchers, microbiologists and clinicians will be critical to ensure the practical applicability of this model, bridging the gap between computational advancements and real-world healthcare needs.

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