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AI FOR PREDICTING ANTIBIOTIC RESISTANCE IN CLINICAL PATHOGENS

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ABSTRACT

Antibiotic resistance (AR) has emerged as one of the most critical threats to global public health, undermining the effectiveness of existing therapies and complicating the management of infectious diseases. Conventional diagnostic and susceptibility testing methods, while reliable, are often time-consuming and insufficient for addressing the rapid emergence of multidrug-resistant pathogens. In recent years, artificial intelligence (AI) has gained prominence as a powerful tool for predicting antibiotic resistance by leveraging large-scale genomic, phenotypic, and clinical datasets. Machine learning and deep learning models have been employed to identify resistance genes, forecast antimicrobial susceptibility patterns, and support clinical decision-making. Applications range from predicting resistance in *Staphylococcus aureus*, *Escherichia coli*, and *Klebsiella pneumoniae* to guiding personalized treatment strategies for tuberculosis and other high-burden infections. Despite promising advances, challenges such as data heterogeneity, model interpretability, and ethical concerns remain significant barriers to clinical translation. This review summarizes recent progress in AI-based approaches for antibiotic resistance prediction, highlights notable case studies, and

discusses limitations and future directions. The integration of AI into diagnostic workflows holds potential for real-time surveillance, personalized medicine, and global antibiotic stewardship.

KEYWORDS: Antibiotic resistance, Artificial intelligence, Machine learning, Deep learning, Clinical pathogens, Predictive models, Antimicrobial stewardship.

1. INTRODUCTION-

Antibiotic resistance (AR) is recognized as one of the most pressing global health challenges of the 21st century. The World Health Organization has declared antimicrobial resistance a major threat to human health, food security, and development, predicting that drug-resistant infections could cause up to 10 million deaths annually by 2050 if left unaddressed (Dhingra et al., 2020). Resistance mechanisms including enzymatic drug inactivation, efflux pump activity, and target site modification have been documented in a wide range of pathogens, such as *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Mycobacterium tuberculosis* (Salam et al., 2023). The primary problem with current antibiotic treatments is that antimicrobial resistance is rapidly spreading in hospitals and communities (Kushwaha et al., 2025). These organisms are frequently associated with hospital-acquired and community-acquired infections, increasing morbidity, mortality, and healthcare costs (Tobin & Zahra, 2025). Traditional antimicrobial susceptibility testing (AST), such as disk diffusion and broth dilution, provides reliable information on drug resistance but is often time-consuming, requiring 24–72 hours to yield results (Alekshun & Levy, 2007). Molecular techniques, including PCR-based detection of resistance genes, offer faster results but are limited to known genetic markers and may fail to detect novel or rare resistance mechanisms (van Belkum & Dunne, 2013). With the rapid emergence of multidrug-resistant and extensively drug-resistant pathogens, there is a growing need for predictive approaches capable of anticipating resistance patterns before clinical treatment failure occurs (Arango-Argoty et al., 2018). Predictive models can enable clinicians to make evidence-based decisions, optimize antibiotic prescriptions, and reduce the misuse of broad-spectrum antimicrobials, which further drive resistance (Pesesky et al., 2016). Artificial intelligence (AI) offers a transformative solution for tackling the antibiotic resistance crisis. By integrating machine learning (ML) and deep learning (DL) algorithms with large-scale genomic, phenotypic, and clinical data, AI systems can identify subtle patterns and predict antimicrobial resistance with high accuracy (Nguyen et al., 2019). The choice for

antimicrobial therapy is usually straight forward when the etiologic agents and their susceptibility patterns are known (Singh & Kumar, 2025). AI-based tools have been successfully applied to whole-genome sequencing data for predicting resistance genes, analyzing electronic health records to anticipate resistance trends, and developing clinical decision-support systems that guide personalized therapy (Rabaan et al., 2022). Moreover, AI facilitates real-time surveillance, enabling healthcare systems to monitor resistance evolution at local and global scales (Rawson et al., 2019). These advances highlight the potential of AI to revolutionize diagnostic microbiology, improve patient outcomes, and strengthen antibiotic stewardship programs in shown figure 1.

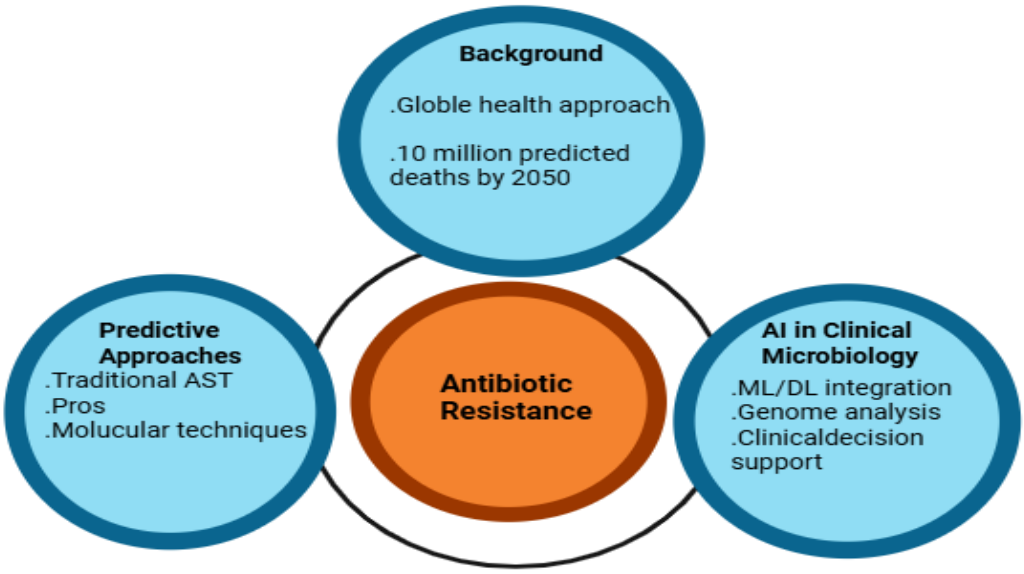

Figure 1: Antibiotic Resistance.

2. Antibiotic Resistance in Clinical Pathogens-

2.1 Mechanisms of Resistance- Numerous strategies, many of which have been thoroughly studied at the molecular level, are used by bacteria to avoid the effects of antibiotics. The most prevalent ones include reduced permeability from porin loss or modification, active efflux pumps that extrude antibiotics from the cell, enzymatic inactivation (e.g., β-lactamases hydrolyzing β-lactam antibiotics), and target modification (e.g., ribosomal RNA or DNA gyrase mutations that prevent drug binding) (Blair et al., 2015; Munita & Arias, 2016). The global development of multidrug resistance is accelerated by mobile genetic elements such as

transposons, integrons, and plasmids, which enable the horizontal transmission of resistance determinants between bacterial species (Partridge et al., 2018).

2.2 Key Multidrug-Resistant Pathogens- A number of bacterial species are regarded as high-priority concerns because of their clinical significance and wide range of resistance profiles. Enterococcus fecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter spp. are among the ESKAPE bacteria that are especially dangerous since they "escape" the effects of the majority of modern antibiotics (Mancuso et al., 2021). Methicillin-intolerant in certain areas, Staphylococcus aureus (MRSA) has fatality rates higher than HIV/AIDS and is a leading cause of pneumonia and bloodstream infections (Hidron et al., 2010). Resistant to carbapenem Colistin is frequently used as a last resort in hospitals with intensive care because to the serious problems posed by K. pneumoniae along with A. baumannii able to withstand multiple drugs another global burden is Mycobacterium tuberculosis (MDR-TB), which necessitates lengthy treatment regimens of costly and hazardous second-line medications (Rojas et al., 2017).

2.3 Clinical and Economic Impact- There are significant economic and health consequences associated with antibiotic resistance. Resistant infections are associated with increased mortality, morbidity, as well as duration of hospital stay (National Academies of Sciences et al., 2021). For example, multiple studies have shown that over 40% of patients with carbapenem K. pneumoniae resistance pass away (Xu et al., 2017). Immunosuppression, diabetes, indwelling catheters and long-term antibiotic use are risk factors. Due to the potential for increased morbidity and mortality from insufficient or delayed therapy the advent of drug-resistant NAC species has complicated patient management. Antimicrobial resistance, or AMR, expenses hospitals and medical centers billions of dollars annually due to infection control measures, expensive alternative medications, and prolonged hospital stays. AMR could kill 10 million people a year by 2050 and cost the global economy up to $1 trillion, according to a landmark O'Neill Commission report (Dadgostar, 2019). These results emphasize how crucial it is to develop prediction tools, like AI-driven models, in order to reduce the likelihood of resistant bacteria in clinical illnesses in shown table 1.

Table 1: Key Multidrug-Resistant Pathogens and Resistance Mechanisms.

Pathogen	Common Resistance Mechanisms	Antibiotics Affected	Clinical Relevance
Staphylococcus aureus (MRSA)	mecA gene (PBP2a), efflux pumps	β-lactams, macrolides	Skin infections, bacteremia, pneumonia (Lade &

			Kim, 2021).
Escherichia coli	ESBLs, plasmid-mediated quinolone resistance, efflux	β-lactams, fluoroquinolones	UTI, bloodstream infections (Afsharikhah et al., 2023).
Klebsiella pneumoniae	Carbapenemases (KPC, NDM), efflux, porin loss	Carbapenems, cephalosporin	Nosocomial infections, sepsis (J. Li et al., 2025).
Pseudomonas aeruginosa	Efflux pumps, β-lactamases, biofilm formation	Carbapenems, aminoglycosides	Hospital-acquired infections (Elfadadny et al., 2024).
Mycobacterium tuberculosis	rpoB, katG, inhA mutations	Rifampicin, Isoniazid	MDR-TB, XDR-TB (Click et al., 2020).

3. Artificial Intelligence in Antibiotic Resistance Prediction-

3.1 Overview of AI, ML, and DL Approaches: Because of its ability to analyze large, complicated data sets that are beyond the scope of traditional statistical methods, artificial intelligence, or AI, has quickly become an essential instrument in the investigation of infectious illnesses. In order to predict antibiotic resistance, or simply AMR, using genetic and clinical data, the artificial intelligence concept has been heavily utilizing machine learning (ML) methods, such as supporting vector machines (SVM), randomized forest structures and decision trees (Sakagianni et al., 2023). Convolutional neural networks are algorithms that (also called CNNs) and RNNs (recurrent neural networks) are two examples of deep learning (DL) techniques that have been developed in recent years to handle extremely dense inputs like microbiome profiles and WGS (whole-genome sequencing) data, respectively (Vakalopoulou et al., 2023). These models excel at automatically identifying hidden patterns and nonlinear relationships, which are often missed by rule-based diagnostics (Pettit et al., 2021). Ensemble learning methods that integrate multiple algorithms enhance prediction accuracy and dependability in clinical settings (Naderalvojoud & Hernandez-Boussard, 2024).

3.2 Data Sources (Genomic, Phenotypic, Clinical, EHRs): The predictive performance of AI models depends heavily on the quality and diversity of data sources. Genomic data**,** particularly WGS, provide comprehensive insights into resistance-associated genes and mutations, enabling prediction of minimum inhibitory concentrations (MICs) without the need for lengthy culture-based assays (Ardila et al., 2024). Phenotypic data**,** such as traditional antimicrobial susceptibility testing (AST) results, serve as essential training and validation benchmarks for AI models (Liao et al., 2025). Integrating electronic health records, or EHRs, which include data on the patient's background, comorbidities, prior antibiotic

exposures, and hospital environment, can further enhance predictions and enable personalized risk assessment (Rezel-Potts & Gulliford, 2022). Moreover, multi-omics data, including transcriptomic, proteomics, and metabolomics, are being integrated to improve prediction resolution and more accurately represent the complexity of host-pathogen interactions (Chen et al., 2023).

3.3 Advantages over Conventional Methods: The advantages of AI-based prediction systems over conventional diagnostic methods are numerous. They first make it possible to forecast resistant patterns quickly, often within hours after decoding, as opposed to days as culture-based AST may Second, AI models can detect novel resistance processes even in the absence of known resistance genes by identifying indirect genetic or phenotypic cues (Bilal et al., 2025a). Thirdly, they are scalable, making them suitable for vast hospital and even global health network monitoring. Furthermore, unlike static molecular assays, AI-driven models can learn continuously, adjusting to new data and changing pattern of resistance over time (Ruyobeza et al., 2022).Collectively, these advantages highlight AI as a promising solution for advancing antimicrobial stewardship and improving patient outcomes in the face of growing resistance.

4. AI Models and Approaches-

4.1 Machine Learning Models (SVM, Random Forest, etc.): Techniques based on machine learning (ML) have been used to predict antimicrobial resistance (AMR) due to their ability to detect unpredictable connections between genetic markers as well as phenotypic resistance results. One of the earliest machine learning methods for AMR prediction was to use support vector machines (SVMs), which perform well on dimensional genomics datasets (Kim et al., n.d.-a). Random forests (RF); these classifiers, which reduce overfitting by building many trees of decisions and aggregating their outputs, are specifically known to exhibit resistance-associated features (Khan et al., 2024a). Additionally, young Bayes as well logistic regression models have been used to predict resistance, often as benchmarks for more intricate algorithms (Bilal et al., 2025b). These classic machine learning methods still provide interpretable decision bounds and can be used in clinical settings on moderately sized datasets.

4.2 Deep Learning Architectures (CNN, RNN, Transformers): Deep learning (DL) techniques have improved the predictive ability of AI in AMR research by automatically extracting hierarchical features from raw genomic or phenotypic data. Convolutional neural networks, or CNNs, have been successfully used to classify genes that are resistant from

sequencing data by detecting local sequence motifs (Y. Li et al., 2024a). The unique suitability of recurrent neural networks (RNNs) and their variants, such as LSTM (long-term and short-term memories) networks, for sequential data allows for accurate forecasting of mutations which raise resistance across bacterial genomes (Waqas & Humphries, 2024). In recent years, transformer-based architectures, based on self-attention mechanisms, have been introduced to AMR prediction due to their improved scalability and ability to capture long-term usage in biological information (Choi & Lee, 2023). These models hold promise for integrating diverse data types, including genome sequences, clinical metadata, and drug exposure histories.

4.3 Hybrid and Ensemble Models: Hybrid models that combine methods such as ML and DL have emerged in an effort to leverage the benefits of both paradigms. For instance, CNN-based feature extraction combined with RF classifiers has been used to improve both interpretability and accuracy in the resistance prediction (Almulihi et al., 2022). Ensemble models, which incorporate many classifiers, often outperform individual algorithms by reducing bias and variance (Khan et al., 2024b). Stacking approaches, in which a meta-classifier adds predictions to base learners, have shown promise in predicting patterns of resistance across a range of bacterial species (T. Zhang et al., 2025). These hybrid or ensemble techniques are becoming increasingly important in clinical microbiological research, where optimizing prediction accuracy is essential.

4.4 Integration of Multi-Omics and Big Data: With the integration of several omics datasets, including transcriptomic, proteomics, metabolomics and genomes, AI-driven AMR prediction is at the forefront. Multi-omics integration enables systems-level understanding of bacterial resistance mechanisms and host-pathogen interactions (Eicher et al., 2020). By combining whole-genome sequencing (WGS), electronic medical records, and real-time surveillance data, big data platforms are being developed to enhance clinical interpretation and prediction capabilities (Kulynych & Greely, 2017). For example, AI models trained regarding transcriptomic as well genomic data have demonstrated higher accuracy than only one source models in predicting MICs (minimal inhibitory concentrations) (Chung et al., 2024). In addition to enhancing clinical decision-making, these integrative approaches support global AMR surveillance programs.

5. Applications and Case Studies-

5.1 AI in Predicting Resistance in *Staphylococcus aureus*, *E. coli*, *Klebsiella,etc*: Many artificial intelligence applications have been developed to predict resistance trends in highly

significant clinical pathogens. When combined with machine learning classifiers, whole-genome sequencing (WGS) has enabled the rapid detection of mecA-mediated resistance in methicillin-resistant Staphylococcus (MRSA) and the prediction of minimal inhibitory concentrations (MICs) for β-lactam antibiotics (Y. Li et al., 2024b). Similarly, fluoroquinolone as well amoxicillin resistance in a strain of Escherichia coli has been predicted using random forest and deep learning techniques; training on large genetic databases has produced accuracies of over 90% (Moradigaravand et al., 2018). Artificial intelligence (AI) predictive models have proven effective in predicting carbapenem resistance, even in Klebsiella pneumoniae isolates with distinct resistance mechanisms the fact that are not identified by traditional gene panels (Alparslan et al., 2025). These uses demonstrate how AI can detect hidden genetic markers and outperform traditional molecular diagnostics.

5.2 AI in Tuberculosis Drug Resistance Prediction: Tuberculosis (TB) remains a major global health burden, particularly due to multidrug-resistant (MDR-TB) and extensively drug-resistant (XDR-TB) strains. AI models trained on large WGS datasets have demonstrated high accuracy in predicting resistance to first-line drugs such as isoniazid and rifampicin, as well as second-line agents (Tan et al., 2025). Deep learning architectures have further improved predictive capacity by capturing complex interactions between resistance-conferring mutations (Green et al., 2022). In addition, large-scale projects such as the CRyPTIC consortium have applied machine learning to thousands of *Mycobacterium tuberculosis* genomes, generating comprehensive resistance prediction tools that can inform personalized treatment regimens (Bustad et al., 2025). These developments position AI as a critical enabler in the global fight against TB, particularly in resource-limited settings where rapid diagnostics are urgently needed.

5.3 Clinical Decision-Support Systems and Diagnostic Tools: Artificial intelligence, or AI, has been incorporated into the CDSS in order to assist physicians in choosing the most effective antimicrobial treatments, regardless of the specific infection. These systems combine patient-specific information, regional resistance patterns, or electronic medical records (EHRs) to recommend personalized treatment options (Gomez-Cabello et al., 2024). For example, hospital antimicrobial stewardship programs have incorporated predictive models to reduce unnecessary prescriptions and improve patient outcomes (MacDougall & Polk, 2005). AI-enhanced diagnostic tools, like those that integrate real-time micro pore sequencing data with ML classifiers, are being developed to generate same-day resistance predictions (Suster et al., 2024). Importantly, these methods expedite clinical decision-

making and offer comprehensive surveillance of antibiotic resistance, providing valuable data for public health campaigns in shown table 2 (Infections et al., 2003).

Table 2: AI Models for Predicting Antibiotic Resistance.

AI Approach	Examples	Input Data	Key Applications	Accuracy / Performance
Machine Learning (ML)	Random Forest, SVM, Logistic Regression	Genomic sequences, AST results	Predict MICs, resistance phenotype	85–95% (Kim et al., n.d.-b).
Deep Learning (DL)	CNN, RNN, Transformers	WGS, transcriptomics	Resistance gene detection, mutation analysis	90–98% (J. Zhang et al., 2025).
Hybrid / Ensemble	CNN + Random Forest, Stacking models	Multi-omics + EHR	Improved prediction, interpretability	92–99% (van Hilten et al., 2024).
Multi-Omics Integration	AI pipelines combining genomics, proteomics, metabolomics	Genomic + transcriptomic + proteomic	Personalized therapy, global surveillance	93–97% (Lin et al., 2025).

6. CHALLENGES AND LIMITATIONS

6.1 Data Quality and Availability: How well AI models predict antimicrobial resistance (AMR) depends largely on the volume, diversity, and quality of the input data. Biased or incomplete datasets may result in poor generalization, overfitting and erroneous predictions (Kim et al., n.d.-c). Reduced representation of regions with middle or low incomes is a result of many genome databases being biased toward isolates form high-income nations (Ruderman, 2023). Additionally, due to methodological variations, phenotypic resistance data, including minimal inhibitory concentrations (MICs). These values may fluctuate between laboratories, leading to noise in training datasets (Kowalska-Krochmal & Dudek-Wicher, 2021). Significant obstacles to creating AI models that are applicable worldwide are presented by these data restrictions.

6.2 Model Interpretability and Transparency: Deep learning and ensemble models often function as "black boxes," providing high predictive accuracy but limited interpretability (Hassija et al., 2024). Lack of transparency can hinder clinical adoption, as healthcare providers require clear rationales for AI-generated recommendations. Efforts to enhance interpretability, such as feature importance analysis and attention mechanisms, are ongoing but not yet standardized (Kiseleva et al., 2022). Without interpretable outputs, AI models risk

being viewed as untrustworthy, particularly in critical settings like antimicrobial stewardship and infection management.

6.3 Generalizability across Populations: AI models trained on data from specific hospitals, regions, or patient populations may not generalize effectively to other settings due to variations in local resistance patterns, pathogen diversity, and clinical practices (Muteeb et al., 2023). For example, a model developed for predicting MRSA resistance in European hospitals may perform poorly in Asian or African healthcare settings (Nandhini et al., 2022). Continuous retraining with new and diverse datasets is required to maintain performance, but this presents logistical and computational challenges.

6.4 Ethical, Regulatory, and Privacy Concerns: The deployment of AI in clinical microbiology raises ethical and regulatory questions. Patient-level data used for training AI models often include sensitive health information, raising concerns about privacy and data security (Mennella et al., 2024). Additionally, accountability for AI-driven decisions remains unclear; incorrect predictions could have serious consequences for patient outcomes (Cross et al., 2024). Regulatory frameworks for AI in healthcare are evolving, but harmonized global standards are lacking (Palaniappan et al., 2024). Ensuring equitable access and preventing algorithmic bias where models inadvertently reinforce existing healthcare disparities are critical considerations for ethical deployment.

7. FUTURE DIRECTIONS

7.1 AI Integration with Point-of-Care Diagnostics: Combining artificial intelligence with point-of-care (POC) diagnostic technologies is a promising method for the rapid and autonomous identification of antimicrobial resistance, or AMR.By evaluating data from portable devices such as nanopore sequencers or microfluidic platforms, systems utilizing AI can produce nearly instantaneous resistance predictions (Lawal et al., 2025). This integration reduces reliance on one centralized laboratory and shortens turnaround time from days to hours, allowing targeted therapy to be initiated on time in clinical settings (Cherie et al., 2024). Furthermore, by facilitating remote monitoring in areas with limited resources, POC-AI systems can improve patient outcomes and help close healthcare distances globally (Maleki Varnosfaderani & Forouzanfar, 2024a).

7.2 Precision Medicine and Personalized Therapy: Predictive models powered by AI could improve infectious illness precision medicine. AI can detect patient-specific risk factors and pathogen-specific resistance mechanisms by integrating genetic, transcriptomic, and proteomic as well as clinical data, allowing for customized antimicrobial regimens (Alsaedi

et al., 2025). This method increases treatment efficacy, decreases the development of resistance and minimizes the needless use of broad-spectrum antibiotics (Muteeb et al., 2023). For instance, it has been demonstrated that AI models that combine patient comorbidities and WGS data can direct tailored treatment in cases of multidrug-resistant tuberculosis (MDR-TB) (K et al., n.d.).

7.3 Global Surveillance and Resistance Monitoring: AI can enhance global AMR surveillance by analyzing large datasets from hospitals, environmental monitoring networks and public health databases (Ayesiga et al., 2024). Machine learning algorithms have the potential to forecast outbreak areas, detect emerging resistance trends and produce early warning alerts for high risk infections (Villanueva-Miranda et al., 2025). Geographic information systems (GIS) and artificial intelligence (AI) can be combined to map resistance patterns in real time, which helps with resource allocation and infection control policymaking (Prakash Nayak et al., 2025). Such surveillance programs are crucial for directing public health efforts and halting the spread of treatment resistant infections.

7.4 AI-Driven Antibiotic Stewardship: There are several chances to enhance antimicrobial stewardship programs with artificial intelligence. Based on individual traits, geographic resistance patterns and pathogen genetic information, predictive AI models can suggest the best treatment options, dosages and durations (de la Lastra et al., 2024). AI lowers selection pressure, decreases the overuse of antibiotics, and helps maintain the effectiveness of currently available antimicrobial drugs through evidence-based prescribing (Branda & Scarpa, 2024). Additionally, AI-based monitoring systems can provide clinicians and hospital managers with ongoing feedback, allowing them to bring about dynamic stewardship adjustments to their approach in shown figure 2 (Maleki Varnosfaderani & Forouzanfar, 2024b).

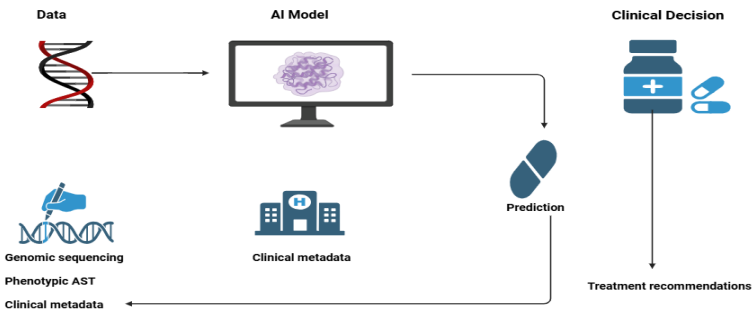

Figure 2: Future Directions.

8. CONCLUSION

Due to the rise of multidrug-resistant organisms such as Escherichia coli, Staphylococcus the bacteria Klebsiella pneumoniae, as well as Mycobacterium TB, antimicrobial resistance (AMR) remains a serious danger to world health. Even though they are necessary, traditional diagnostic and sensitivity testing techniques are frequently laborious and unable to keep up with the quickly changing patterns of resistance. Antibiotic resistance can now be predicted from genomic, phenotypic, or clinical data using artificial intelligence (AI), which includes the use of machine learning (ML) along with deep machine learning (DL), and hybrid techniques. Personalized therapy for tuberculosis, excellent prediction for a variety of diseases, and the creation of clinical decision-support programs to direct the best use of antibiotics have all been made possible by AI-based models. Despite these developments, there are still issues, such as restrictions on the availability and quality of data, interpretability issues with models, issues with population generalizability, or legal and ethical problems. If research-based AI models are to be used in healthcare settings, these problems need to be fixed. Future paths will focus on integrating AI with multi-omics data, point-of-care exams, and global monitoring platforms to enhance clinical accuracy along with antimicrobial stewardship initiatives. Ultimately, artificial intelligence (AI) has the potential to transform antibiotic resistance treatment by providing more precise, quick, and patient-specific interventions that can lessen the impact of resistant diseases everywhere.

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