Experimental and Applied Medical Science, 5, 2:95-106, 2024. DOI: 10.46871/eams.1497329

Artificial Intelligence in Clinical Applications for Infectious Diseases: Diagnosis, Treatment and Immunization

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Abstract

Despite scientific and technological advances in recent years, infectious diseases continue to pose a significant threat to public health. These diseases can cause serious health problems as they have the potential to spread rapidly. In addition, they occur in the form of epidemics and affect populations. The difficulty of rapid and accurate diagnosis and increasing antimicrobial resistance create difficulties in the treatment of infectious diseases. Artificial intelligence technology has developed useful applications in many areas such as the development of diagnosis and treatment methods, anti-infective drug and vaccine discovery, and prevention of increasing anti-infective drug resistance. In particular, AI-assisted clinical decision support systems can help predict disease outbreaks, support diagnosis of diseases, optimise treatment options and monitor epidemiological trends by analysing large datasets. It can also provide more accurate and faster results in analysing diagnostic images and identifying diseases. Advances in this field need to be supported by multidisciplinary studies and a strong ethical framework. In this review, we outline approaches to the application and use of artificial intelligence in infectious diseases, highlight the progress supported by artificial intelligence, and discuss how it can be used. We outline the applications and benefits of AI in infectious diseases. In this way, more effective intervention strategies can be developed to control infectious diseases and protect public health.

Key words: *Artificial intelligence, Machine learning, Infectious diseases*

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Artificial intelligence is not a threat; it is about how we choose to use it
(Moedas, 2017)

Introduction

In recent years, developments in the field of technology have been rapidly progressing, profoundly influencing and shaping societal life. Artificial intelligence (AI) studies have created a revolution by leading to radical changes in human life. In this context, just as in all other fields, efforts are being made to develop future-oriented designs in the field of medicine through AI applications. AI is a comprehensive branch of computer science that aims to create intelligent machines that can mimic human intelligence. At the same time, it is the general name of technologies that can fulfil the tasks of prediction and decision-making; whether it uses machine learning or not is a factor affecting this process. The process of acquiring rules includes the processes of making logical inferences and self-correction using these rules and produces output as a result.

This learning method is capable of making inferences and decisions similar to or even better than humans. AI includes many disciplines such as machine learning, deep learning, neural networks (Figure 1).

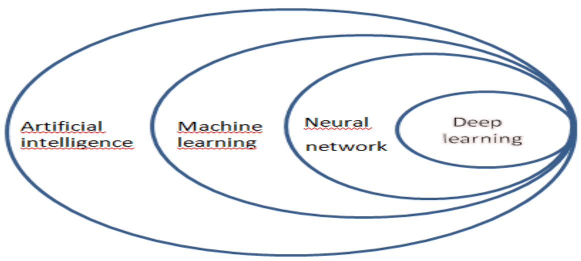

Figure 1: Learning relationship.

The origins of the concept of AI started with Alan Turing's question "Can machines think?" (1). The first examples of AI applications in the field of medicine are a mechanical machine developed in 1954 to assist clinicians in symptom-based diagnosis and a Naïve Bayes-based digital system developed in 1972 for the diagnosis of acute abdominal pain (2).

The first system used in health services was the MYCIN system developed in 1976. It is also one of the first attempts towards a computer-based clinical decision support system for infectious diseases.

This system utilised more than 500 rules to identify the bacterial species responsible for infection, make a diagnosis and recommend an antibiotic regime. The aim of the system was to recommend antibiotic treatment regimens for serious bacterial infections. However, the use of the system was limited due to the inability to integrate the system with clinical studies and the size of the data (3).

With the developed AI applications, more specialised programmes have started to be developed in health services as a result of interviews with medical specialists (4).

In the following years, especially after the 2000s, developments in the field of technology have revolutionised medical sciences in the field of artificial intelligence. The systematic recording of electronic health records and other medical data has provided a rich resource for the development of AI technologies. Different AI applications have been developed using medical data in many areas such as diagnosis and imaging, treatment planning and personalised medicine, drug discovery and development, patient monitoring and prediction, medical tissue and cell analysis, health systems and data management. Developments in the field of medicine aim to provide more accurate diagnoses, more effective treatments, better patient care and improve the overall quality of healthcare services. At the same time, it finds an intensive use in the field of medicine due to its potential expectations and promising prospects (5). It is expected that the expenditures on this new developing technology in healthcare services will reach 45 billion US dollars by 2026 worldwide (6).

Despite advances in medical sciences in recent years, infectious diseases caused by pathogens such as bacteria, fungi and viruses still challenge scientists and clinicians. The difficulty of rapid and accurate diagnosis and increasing antimicrobial resistance create challenges in the treatment of infectious diseases. Joint interdisciplinary efforts are required to overcome these challenges. Interdisciplinary collaborative efforts are required to address these challenges.

The first applications of artificial intelligence in the field of infectious diseases were carried out with easily accessible medical data (demographic information, laboratory measurements, medical history and physical examination data) (7). In the following process, AI applications together with systems and synthetic biology aimed to reveal new approaches in diagnosis and treatment methods in the field of infectious diseases. In particular, biotechnological and medical innovations (including drug therapies and modalities, vaccines and diagnostics) are aimed to overcome the challenges. In this review, we aim to understand the relationship between artificial intelligence applications and infectious diseases and to understand how artificial intelligence can be utilised.

The systematic recording of electronic health records and other medical data has significantly increased the availability of healthcare data (8). Clinical decision support systems (CDSS) software has started to be used to integrate and make sense of this large amount of data (9). These systems have the ability to provide patient-specific assessments and suggestions and solutions for the clinician (10). In the following process, interest in this system has increased since data can be analysed more effectively with Machine Learning-Clinical Decision Support Systems (ML-CDSS). With these systems, large amounts of data can be used, the logic system is automatically derived and most of the problems can be solved (11).

In a review by Peiffer-Smadja et al. in 2020, 60 different ML-CDSS applications were analysed (7). It was determined that structured and easily accessible medical data types, including vital signs, laboratory measurements, demographic information, medical history and physical examination data, were used in the first AI applications related to infectious diseases. In the review, ML-CDSS applications were analyzed, revealing that 62% (37 applications) included bacterial infections, 17% (10 applications) included viral infections, 15% (nine applications) included tuberculosis, and 7% (four applications) included any type of infection. Among these applications, it was noted that 33% (20 applications) focused on diagnosing infections, 30% (18 applications) on predicting, early detecting, or classifying sepsis, 22% (13 applications) on predicting treatment response, 7% (four applications) on predicting antibiotic resistance, 5% (three applications) on selecting antibiotic regimens, and 3% (two applications) on selecting antiretroviral treatment combination.

1. AI Applications in Medical Diagnosis of Infectious Diseases

It is important to take infectious diseases under control with early diagnosis and to prevent them from turning into epidemics or pandemics. Early diagnosis of infectious diseases is of vital importance (12). For this reason, studies are carried out in order to develop models for the diagnosis of diseases in the early stages.

Humans can usually easily interpret and integrate up to 4 variables at the same time (13). Computers, on the other hand, can process a wider range of variables simultaneously due to their ability to recognize and process complex patterns invisible to the human eye.

Therefore, they do not share the limitations of variable interpretation and integration that humans have. Consequently, the development of predictive analytics through AI/ML will continue. With the developed AI, the spread of infectious diseases is classified and predictions are tried to be made (14).

When literature was reviewed, it was observed that different machine learning methods were used for modeling in various infectious diseases. In one study, clinical and laboratory data were used for early diagnosis and prediction of mortality rates of COVID-19, which created a global pandemic at the end of 2019. In another study, diagnosis and prognosis were predicted with different modelling types using many data, including images (15,16). Additionally, various applications have been used in areas such as drug and vaccine development (17). During the COVID-19 pandemic, contact tracing was performed using an AI application called FITAS (Filiation and isolation tracking system). The rate of case increase was reduced with the measures taken in line with the analysis of the filiation data (18).

In a study by Kar et al. it was stated that only clinical tests could be used for hepatitis (19). In another study, ML models were established using laboratory and pathology scoring system data to predict the progression of chronic hepatitis C infection (20). The use of ML approaches to predict early virological relapse following cessation of treatment in chronic hepatitis B infection is promising. ML models have been established with the combination of interleukin-2, interferon gamma, T cell activation, stem cell factor and tumour necrosis factor-associated apoptosis-inducing ligand to determine the highest predictive values for early virological relapse (21). It was predicted that only signs and symptoms may be insufficient in the modelling to be performed in the detection of pneumonia, and the combination with imaging may detect more infections (22). For the diagnosis of tuberculosis, which is widespread globally, the combination of clinical signs, symptoms, and radiological images, or the use of only chest X-ray images, or the use of only clinical and laboratory data as inputs have been examined, and modeling has been performed using AI approaches (23,24).

For influenza A virus, which causes epidemics, genomic or proteomic inputs have been used for AI applications to predict the phenotypic characteristics of influenza virus in surveillance laboratories (25).

Using AI applications in the diagnosis of infectious diseases can help shorten the time required for medical diagnosis. Various medical diagnostic tools such as clinical examination findings, biochemical data, and radiological images can be analyzed with the assistance of AI to predict rapid and accurate results and provide effective treatment planning.

2. AI Applications in Imaging Methods in Infectious Diseases

One of the auxiliary methods used in the diagnosis of infectious diseases is imaging systems. ML models are also used in the field of imaging methods. The first FDA approval for AI applications in this field was granted in 2018 for the detection of diabetic retinopathy in retinal fundus photographs (26). In the following period, the use of AI applications for the analysis of medical imaging techniques increased rapidly with the COVID-19 pandemic. However, it was realized that measuring more complex (unstructured) data types, especially three-dimensional (3D) and time-series images, would be difficult. Therefore, it was realised that further studies are needed to develop specialised AI applications for imaging systems.

Segmentation and classification of images are two main challenges in imaging applications for infectious diseases. Images have to be segmented manually and this process is time-consuming, especially for high field of view and high-resolution 3D images such as CT, MR and PET. Therefore, the development of reliable automated segmentation methods was crucial for advancing infectious disease imaging research and improving clinical applications. In the following period, with the use of artificial intelligence techniques, images could be automatically segmented and utilized in the diagnosis of various infectious diseases.

In infectious diseases, it is crucial to address questions regarding the infection status, severity or stage of the disease, and predicting the response to therapeutic interventions.

AI approaches are employed across a broad spectrum of applications, ranging from simple algorithms to more complex deep learning algorithms. Convolutional neural networks (27) and image transducers (28), a special type of deep learning, have led to significant advances in this field. AI imaging methods have been extensively utilized in various contexts, including human immunodeficiency virus (HIV), tuberculosis, Ebola and Marburg virus infections, Lassa virus and Nipah virus infections, liver CT scanning, influenza, and throughout the COVID-19 pandemic (29).

Imaging data in infectious diseases are more complex due to uncontrolled and confounding factors. This complexity can adversely affect model performance because there can be spurious correlations between data. With the widespread use of

AI techniques, predictions based on imaging data can become more accurate.

3. AI Applications in Antibiotic Resistance and Treatment Methods

Antimicrobial resistance is one of the greatest threats to global public health and development. In 2019, it is estimated that bacterial resistance directly caused 1.27 million deaths and contributed to 4.95 million deaths (30). The acquisition of resistance with the increasing use of anti-infective drugs leads to a decrease in treatment options. Therefore, the detection of resistant organisms is crucial. In vitro antimicrobial susceptibility testing (AST) can be determined by microdilution or molecular approaches. While the microdilution method determines the minimum inhibitory concentration, molecular approaches target specific genes to rapidly identify genotypic resistance.

In this field, AI applications are also utilized. ML models are used to make predictions with techniques such as gene expression and mass spectrometry. When performing AST, methods such as gene expression and mass spectrometry are also used. Typical culture-based AST can take at least a few days to complete. However, in acute systemic infections such as sepsis, accurate and early initiation of antimicrobial therapy is vital. AI technology has combined gene expression and structural mutation mapping with ML (31,32). Bacterial proteins were used to predict MALDI-TOF mass spectra and antibiotic resistance profiles. Results can be finalised within 24 hours after sample collection (33). The creation of multidimensional data resistance profile clusters will enable ML to produce accurate predictions. Despite high-quality data sources like the PATRIC database (34), it remains unclear whether the antimicrobial resistance predictions generated from these data can be generalized to infections worldwide. With the advances in the field of ML, antibiotic resistance can be predicted accurately and rapidly using proteins, peptides and nucleic acids.

Antibiotic resistance is a global threat. Inappropriate use can be prevented with rational antibiotic use in our country as in the world. Drugs should be used in appropriate duration and dose by evaluating clinical findings and individual characteristics. Determining prescribing rules with AI applications requires the integration of broad and complex information. In a study conducted by Rawson et al., fifty-eight articles were reviewed and 38 CDSS applications were analysed. It was observed that the majority of systems aimed at prescribing antimicrobial drugs (76%), integrating with electronic medical records (74%), and having a rule-based infrastructure (76%). However, it was observed that CDSS studies were unsuccessful when considering workflow. Additionally, clinicians were reluctant to use CDSS (10).

In the field of infectious diseases, the most significant challenge in antimicrobial prescription CDSS applications is that decision support is influenced not only by human factors but also by pathogen factors, the antibiotic prescribed in the context of individual polypharmacy, the evolution of resistance, symbiotic microbiome, and environmental factors. In the field of infectious diseases, AI applications are still in their early stages, and personalized treatment decision-making systems need to be developed to avoid undesired outcomes.

4. AI Applications in Pharmaceutical and Vaccine Production

Anti-infective drugs, including antibacterials, antivirals, antifungals and antiparasitics, have become less effective treatments as a result of the spread of drug resistance. The use of anti-infective drugs is increasing worldwide, leading to the development of resistance as a consequence. Every year, the diminishing number of effective anti-infective drugs presents a serious public health concern. In addition, some pathogenic microorganisms have developed resistance to all existing antibiotics and this situation causes difficulties in treatment processes (35).

Traditional drug production includes many stages such as drug ingredient design, drug performance tests, clinical trials. Phase 0,1,2,3 and phase 4 studies are carried out for each drug and production is realised at the end of a long process. However, this process involves expensive, time-consuming, and labor-intensive stages that can decrease production performance. Moreover, due to the decrease in the share of research and development (R&D) expenditures, research for the development of new drug molecules cannot be supported adequately.

Artificial intelligence technologies contribute to drug development studies at molecular level by shortening the processes. Due to the extensive time and effort required for drug discovery, AI technologies have also been employed in this field. Using powerful logical inference and automatic learning capabilities, 3D printing technology enables the design of the most suitable drug size, shape, and combinations of different pharmaceutical components (36).

This technology has most recently been used for COVID-19 drug design and research, and more than 80 drugs have been discovered (37). Utilizing a deep learning-based model called Molecule Transformer-Drug Target Interaction (MT-DTI), which is one of the AI applications, research has been conducted to identify drugs among commercially available existing drugs that could be effective on the viral proteins of

SARS-CoV-2. Drugs such as atazanavir, remdesivir, efavirenz, ritonavir, and dolutegravir have been investigated, and it has been found that they have inhibitory potency against SARS-CoV-2 (38). By employing AI approaches such as fingerprint vectors, neural network models, and automatic descriptors, a deep neural network training has been completed to design new molecules with antibacterial activity. The c-Jun N-terminal kinase inhibitor SU3327 (Halicin) molecule, which exhibits bactericidal activity against many pathogens including carbapenem-resistant Enterobacteriaceae and Mycobacterium tuberculosis, was designed. Pan drug resistant Acinetobacter baumannii and Clostridioides difficile infections were treated in mouse strains with the designed molecule (38,39). In another study, oxidative damage caused by many drugs or nutritional supplements to human body cell components was tried to be prevented by hydrogen atom transfer and a model was created using machine learning to evaluate the results. In this way, the process and costs were reduced (40).

Despite the advantages provided by AI technologies in the development of anti-infective drugs, there are glaring problems in their application to drug discovery. One of the major challenges is that it is unclear how well ML models generalise to unexplored biomolecular domains. Another major challenge is the need for advanced mechanical models to complement phenotypic approaches. Although drug-target interactions can be designed in AI models, more research is needed to accurately predict them (41).

AI applications have been used in vaccine development efforts during the COVID-19 pandemic. AI prediction models provided benefits to create vaccine design combinations, thereby reducing R&D costs and time (42). Throughout the COVID-19 pandemic, numerous vaccine studies have been conducted using AI technologies. ML models have provided utility in vaccine development efforts. However, low data quality, limited data availability and generalisability, and complex testing procedures are challenges encountered in this process. Furthermore, validation of vaccine candidates can be time-consuming and expensive. An adequate level of immunogenicity must be ensured by analyzing the level of the vaccine. Standardizing the quality of vaccine-related data could enhance the predictive power of next-generation machine learning approaches in vaccine development (41).

In the future, AI and ML will be used in new vaccine development researches and in the identification of existing or new chemical structures with antimicrobial activity. It offers predictions in the process of vaccine and anti-infective drug development. With the models created, the results become transparent and interpretable. In this way, the future environment of trust may encourage the adoption and acceptance of systems based on AI and ML (43).

Conclusion

With the advancement of science and technology, AI applications are a necessity of the age. The use of AI technologies in infectious diseases can provide significant advantages in the diagnosis and treatment of diseases. However, the ethical and legal challenges of these applications should not be ignored. In particular, it is crucial to establish and enforce the ethical and legal framework for AI-supported diagnosis and treatment applications to safeguard the safety and privacy of patients in medical practices. The rapid development and utilization of technologies such as artificial intelligence and machine learning during extraordinary situations such as pandemics can offer more effective and faster solutions in medical interventions. Therefore, it is essential to continue to researching on the role and impact of technology in healthcare. Effective management and implementation of these technologies is vital to achieve better outcomes in the healthcare system.

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