



ROLE OF ARTIFICIAL INTELLIGENCE IN DETECTING CANDIDA SPECIES: CURRENT ADVANCES, CHALLENGES AND FUTURE PERSPECTIVES

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ABSTRACT

Candida species are significant opportunistic fungal pathogens which cause superficial, mucosal and life-threatening invasive infections. Given the potential variation in antifungal susceptibility and drug resistance of non-albicans Candida species, it is imperative to be able to identify the species at the earliest so that appropriate antifungal treatment can be administered. While all of the above methods are vital to a diagnosis, they can be limited by time, sensitivity of the test, need for trained staff, and lack of availability in low-resource areas. In this context, the possibilities of Artificial Intelligence (AI), machine learning (ML), deep learning (DL) and computer vision for the rapid and automated detection/identification of Candida are new. AI can be used to process microscopic images, fungal colony morphology, PCR amplification patterns, MALDI-TOF mass spectrometry spectra, outputs from biosensors and antifungal susceptibility data, which may decrease inter-observer variability and enhance the efficiency of the diagnosis. These technologies have the potential to assist in species identification, prediction of resistance, optimizing laboratory workflows, and early epidemiological surveillance. This review explores the new use of AI on the most popular microbiological platforms for the diagnosis of Candida, including the advantages, drawbacks, and clinical implications. It also covers future use of predictive analytics, antifungal susceptibility prediction, multimodal AI, explainable AI, secure data-sharing models, and clinical decision support to enhance the clinical use and accuracy of Candida diagnostics, as well as speed up its delivery.

KEYWORDS: Artificial Intelligence, Candida species, Machine Learning, Deep Learning, PCR, Microscopy, Culture, MALDI-TOF MS, Clinical Mycology.

Introduction

Invasive fungal infections are a significant public health problem in modern era and are emerging as a global problem due to growing population of immunocompromised patients, chemotherapy, immunosuppressive therapy patients, organ transplants, critically ill patients and the patients exposed to broad-spectrum antibiotics. Fungal infections are also

more likely in people with diabetes mellitus, who have medical devices in place, premature babies or elderly people. Candida species are significant fungal pathogens in mucocutaneous infections, candidemia, and invasive candidiasis leading to prolonged hospitalisation, higher cost of healthcare, and high mortality rates especially if diagnosis and treatment are delayed[1].

As an important clinical species, *Candida albicans*, non-*albicans* *Candida* species are becoming more clinically significant, such as *Candida auris*, *Candida glabrata*, *Candida tropicalis*, and *Candida parapsilosis*. Some of these species are also less susceptible to the available antifungal drugs and/or are intrinsically resistant, and therefore species-level identification is crucial for the correct treatment with antifungal drugs. Early and accurate diagnosis, therefore, is not just a factor in selecting appropriate therapy, but also plays a significant role in infection control, drug resistance monitoring, and better clinical results[2].

The classical laboratory diagnosis of *Candida* infections is based on microscopy, culture, biochemical identification and molecular techniques. While these are the basic principles of clinical mycology, turn-around time, specimen quality, fungal burden, the availability of specialized equipment, and reliance on trained personnel may affect the performance. These restrictions have led to the emergence of alternative technologies that can handle complex microbiological data more quickly and accurately.

In the field of clinical microbiology, Artificial Intelligence (AI) has gained a growing interest as a technology that can assist. AI systems can identify patterns in images, phenotypic features, molecular information, mass spectrometry spectra, and other diagnostic results which might not be easy to consistently identify manually. These methods have been investigated in *Candida* diagnostics for microscopic image analysis, for culture interpretation, for PCR data interpretation, for MALDI-TOF mass spectrometry-based detection, for biosensor-based detection, and for prediction of antifungal susceptibility.

Combining AI with traditional microbiological techniques could increase the effectiveness of diagnostics, minimize observer variability, aid in species identification, and aid in the interpretation of complex lab data. The role of AI in the detection and identification of *Candida* species in major microbiological diagnostic platforms is, however, emerging and the present review will focus on that. It also explores the potential benefits, current limitations, clinical applications, and future prospects of AI-driven *Candida* diagnostics, highlighting its potential role in speeding up and improving laboratory decision-making[3].

Conventional methods for detecting *Candida*

Laboratory diagnosis of *Candida* infections is traditionally based on microscopy, fungal culture, biochemical identification and molecular diagnostic techniques. The choice of diagnostic method will be determined by the clinical specimen, the suspected site of infection, laboratory facilities and the turnaround time. These methods are routinely combined in clinical microbiology to enhance the reliability of the species identification and the diagnostic interpretation[4].

Microscopic Detection

A microscopic examination of any suspected *Candida* infection will give a quick initial diagnosis. Typical methods used include Gram staining, potassium hydroxide (KOH) preparation, calcofluor white staining and fluorescence microscopy. These techniques allow visualization of yeast cells, budding, pseudohyphae and true hyphae, thus serving as an early indication of fungal infection. Microscopy is relatively simple and inexpensive and can be used to quickly assess clinical specimens. The sensitivity of the method, however, depends on the quality of the specimen, the amount of fungus, staining techniques and the experience of the observer. Moreover, the species-level identification of *Candida* spp. is, in general, not possible based on morphology alone.

Culture-Based Detection

Fungal culture is still a valuable tool for the isolation of live organisms for species identification and susceptibility to antifungal agents. Clinical specimens can be cultured on any selective or differential media including: Sabouraud dextrose agar (SDA), blood culture systems, CHROM agar *Candida*, and corn meal agar. Assessment of the colony colour, texture, morphology, growth characteristics, germ tube formation and biochemical properties like carbohydrate assimilation and fermentation pattern can be used for species differentiation. Automated identification systems can also aid in species identification. But culture-based tests can take up to 24 to 72 hours or more to give the definitive results and can give false negative results if there is low fungal burden or if the patient has already been treated with an antifungal drug.

Molecular Diagnostic Methods

Molecular methods have enhanced *Candida* detection sensitivity, specificity and speed. The species identification can be done directly or indirectly from clinical material via conventional PCR, multiplex PCR, real-time PCR (qPCR), loop-mediated isothermal amplification (LAMP), DNA sequencing or whole genome sequencing. These are especially helpful in the management of invasive candidiasis, mixed infection and the study of genetic markers of antifungal resistance. However, these are difficult to implement in regular practice as they need special equipment, trained staff, standard working practices and fairly high cost, especially in low resource areas[5].

Limitations of Conventional Diagnostic Methods

Although clinical mycology has improved, traditional diagnostic methods still have several limitations in terms of turnaround time, labour, inter-observer variability, sensitivity, infrastructure and cost. Such restrictions have stimulated the growth of other technologies, such as AI that can help in the analysis and interpretation of microbiological diagnostic data.

Artificial Intelligence in Candida Detection

AI is a type of computation that lets systems execute tasks which involve learning, pattern recognition, interpretation and decision-making. In the field of clinical microbiology, AI can be applied to analyse complex laboratory and clinical data, and it includes a range of computational techniques, such as machine learning (ML), deep learning (DL), computer vision, and automated decision-support systems (6).

Machine learning (ML) is one of the areas of AI that involves algorithms analysing data to discover patterns and relationships in order to carry out functions like classification, prediction and decision-making. A subset of ML that uses a multileveled artificial neural network to learn complex representations from large sets of data is called deep learning (DL). One of the major DL architectures is the convolution neural network (CNN) that is well suited for image based applications, and in which the relevant features can be automatically learned from suitable microscopic or culture images without having to define all features manually.

The rapid advancement of digital imaging and computational power, combined with vast microbiological datasets, has opened up new horizons for AI in fungal diagnostics. With the growing accessibility of digital imaging, computational power, and large microbiological data sets, AI presents unprecedented possibilities for diagnostic solutions in fungal diseases. AI can help analyse complex data produced by laboratory procedures and detect patterns in the Candida detection process, which could be harder to pick up on consistently by hand. These systems perform well if the datasets used for development are high quality, large, varied and properly annotated[7].

AI-aided diagnostic methodologies are thus being explored as adjuncts to current microbiological processes. They do not aim to replace traditional diagnostic approaches and microbiological knowledge, but rather to help interpret data, recognize patterns and provide support for decision making. The uses of AI depend on the diagnostic platform and are explored in the next sections, from microscopic analysis, through to culture interpretation, PCR-based diagnosis, MALDI-TOF mass spectrometry, biosensor-based detection, to antifungal susceptibility prediction.

AI Applications in Various Diagnostic Techniques

AI is proving to be a useful solution to improve the detection and identification of Candida species in several microbiological diagnostic platforms. AI-based methods can help with complex microbiological data analysis, such as pattern recognition, automated data interpretation, and diagnostic decision support. These applications include microscopic image analysis, culture interpretation, molecular

diagnostics, MALDI-TOF mass spectrometry, and biosensor based detection. There are several key applications of AI in Candida diagnosis, which are outlined below.

AI in Microscopic Detection

With the help of developments in digital microscopy and computer vision, AI models have been developed that are able to recognise fungal structures in microscopic images automatically. The labelled image datasets can be utilized for training CNNs or other deep learning models to identify fungal cells and differentiate them from background material and other microorganisms. Convolution networks like ResNet, DenseNet and EfficientNet have been shown to be capable of detecting morphological features like cell size, shape, budding patterns, cellular arrangement and filamentous structures[8].

Using AI to help with image segmentation can also aid in the diagnostic interpretation process by distinguishing fungal cells from host cells and debris. Automated systems can count the cells, estimate the level of fungal burden, measure cell size and detect distinct morphological patterns. These features can help screen many clinical specimens in a short period of time and minimize inter-observer variation and tedious manual specimen examination.

Although these benefits have been noted, AI-powered microscopy is not intended to replace the role of the practicing microbiologist in interpreting the results of a specimen. Before widespread use in diagnostic laboratories, large well annotated image sets, external validation and prospective clinical evaluation are required for routine clinical application[9].

AI in Culture-based Detection

Automated analysis of fungal cultures has been opened up to new possibilities thanks to artificial intelligence and computer vision technologies. The images captured on Sabouraud Dextrose Agar (SDA), CHRO Magar Candida and other selective media can be used to assess the colour, texture, diameter, pigmentation, surface characteristics, edge morphology and growth patterns of colonies by using machine learning algorithms.

AI models can analyse multiple phenotypic traits at once and detect patterns linked to the various Candida species, which may help with distinguishing between similar species. Sequential images of colony growth can also be taken on automated incubation systems with digital imaging. These changes over time can be analysed and machine learning algorithms can determine the identity of organisms earlier than traditional visual inspection.

The use of AI tools for the culture interpretation could enhance the standardization of the process, minimize inter-observer variability, and facilitate laboratory workflow management by tracking specimens, preliminary identification, and prioritizing results. But the interpretations made by AI

should always be verified by known microbiological and biochemical techniques before definite species identification is reported[10].

AI in PCR-Based Diagnosis

Artificial Intelligence has demonstrated promising applications in the processing of the molecular diagnostic assays applied to the detection of *Candida*. Molecular methods like conventional PCR, multiplex PCR, qPCR and LAMP produce intricate data, including amplification curves, fluorescence signals, cycle threshold values (Ct), melting curve and multiplex reaction patterns.

Validated amplification profiles can be used to train machine learning algorithms to identify *Candida* species' molecular signatures. Random Forest (RF), Support Vector Machine (SVM), Artificial Neural Networks (ANNs) and Gradient Boosting algorithms are methods that can help classify amplification patterns and interpret complex and borderline cases. Nonlinear relationships in large molecular datasets can also be identified with the help of deep learning methods[11].

AI-backed molecular analysis can also aid in the identification of mixed infections, atypical amplification profiles and genetic markers linked to antifungal resistance. Moreover, automated quality-control devices can detect abnormal amplification curves, technical artefacts, and inconsistent fluorescent signals, which further minimize interpretation errors and enhance diagnostic uniformity. However, AI based interpretation should be used in conjunction with molecular diagnostic techniques that have been validated and not as a substitute for validated techniques, and needs to be thoroughly analysed and clinically validated before being used in routine practice.

AI using MALDI-TOF Mass Spectrometry

Rapid microbial identification is achieved globally through the use of matrix-assisted laser desorption/ionisation time-of-flight mass spectrometry (MALDI-TOF MS) using proteins as the 'fingerprints' of the microbes. Advancements in AI and machine learning have sharpened MALDI-TOF MS's analytical power, allowing it to detect intricate spectral patterns that go beyond traditional database matching methods.

Machine learning models can process thousands of spectral variables and be used to determine the peak combinations that correspond to certain *Candida* species. These methods can help to better distinguish between closely related species, and can be helpful in identifying new species when reference databases are incomplete. Deep learning techniques can also detect small, difficult-to-detect differences in spectrum[12].

AI-driven MALDI-TOF analysis has a special significance for clinically relevant species like *Candida albicans*, *Candida glabrata*, *Candida tropicalis*, *Candida parapsilosis*, and *Candida auris*. In addition to species identification, machine learning models are currently being investigated

for susceptibility and resistance patterns to antifungal. But the accuracy of these systems is highly dependent on the quality of the reference databases, instrument calibration, and data pre-processing and external validation. AI should thus be regarded as an analytical tool in addition to the existing MALDI-TOF identification workflows.

AI-Based Biosensors and Point-of-Care Diagnostics

Another innovation is the use of biosensors as tools for *Candida* diagnosis combined with AI. Fungal cells, nucleic acids, proteins, metabolites and other fungal infection markers can be detected by biosensors. AI systems can help to analyse complex sensor data and filter out abnormal readings from normal ones.

Machine learning analysis can lead to real time pattern recognition and enhance the sensitivity and specificity of biosensor-based detection systems, especially at low target concentrations. Furthermore, AI can address sensor performance differences and environmental factors, enhancing the accuracy of the diagnosis.

The micro fluidic, imaging, wireless communication and computational analysis capability of portable diagnostic platforms may enable the rapid diagnosis of infections away from the traditional microbiology laboratory. These technologies could be especially beneficial in emergency departments, intensive care units, rural healthcare facilities, and other places where rapid diagnostic support is needed[13].

Although AI-powered biosensor systems have immense potential, there are several challenges involved with standardising devices, reproducing results, validating analytical performance, ensuring data security, approval from regulatory bodies, and integrating the systems into existing laboratory workflows. Extensive clinical validation and technological development is needed before mass clinical use is possible[14].

Advantages of AI-Based Detection

When combined with traditional microbiological techniques, AI-based methods can provide several benefits in the detection and identification of *Candida* species. The advantages are that it can process large quantities of diagnostic data quickly and reliably. Automated analysis can help in the interpretation of complex images, molecular results, spectral data and other laboratory outputs, which cuts down on the time spent carrying out repetitive manual work.

AI also can help minimize observer-dependent variability by using the same analytical criteria across diagnostic datasets. This could help to make laboratory interpretation more reproducible and helpful to the microbiologist in prioritizing samples which may need a more detailed expert evaluation. AI-driven systems can assist with streamlined laboratory processes, optimized staff utilization, and quicker

dissemination of clinically significant results by automating repetitive tasks.

One more benefit is the capacity of AI algorithms to spot complex patterns that can be challenging to spot using conventional manual analysis. This ability could aid in the identification of more species or help identify new or rare species of *Candida*, including those that are associated with antifungal resistance. The combination of AI tools and various sources of laboratory data could further enhance the interpretation of complex diagnostic results.

The potential applications of AI in antifungal susceptibility prediction, risk assessment, epidemiology surveillance, and clinical decision support are additional possibilities. These applications, if properly validated, can help in more targeted antifungal therapy and better antimicrobial stewardship. The advantages, however, rely on the quality of the datasets, the proper validation of models, and the careful implementation of AI systems into existing clinical laboratory workflows[15].

Challenges

AI has a great promise in the field of clinical mycology; however, there are many challenges that need to be overcome before AI diagnostics systems can be adopted on a regular basis. The major constraint is the availability of data sets that are large, diverse and well annotated for modelling and validation. Laboratory to laboratory variation is possible in diagnostic information such as micro images, culture images, molecular results, and MALDI-TOF spectra due to differences in equipment, staining, culture, and specimen quality and data acquisition. This variability may impact model performance and restrict the applicability of AI systems in various clinical scenarios.

A second challenge is that there are no standardized validation procedures for AI based systems for fungal diagnosis. There are numerous published models, most of which have been developed and tested on a single-institution, retrospective data set, and there are few prospective and multi-institutionally validated models available. Additionally, algorithmic bias can form when training data sets are not representative of various patient populations, specimen types, disease states, or laboratory settings. Therefore models trained with a small set of data may not work well on a population or setting that is different from the one they were trained on.

The clinical implementation should also take note of regulatory approval, data privacy, cyber security, interoperability with the current laboratory information systems, infrastructure costs and implementation costs. Furthermore, it is critical that the results of AI algorithms can be interpreted, as microbiologists and clinicians must understand and critically assess an AI's suggestions before they can accept it and use it for their diagnostic decision-making.

So, before AI-driven diagnostic systems can be used in the regular microbiology laboratory, they must be thoroughly tested and evaluated outside the lab and be subject to ongoing performance monitoring. Their reliability and clinical usefulness will need to be validated through standardized assessment tools, representative data sets and prospective multicentre studies. Furthermore, close collaboration between microbiologists, clinicians, computational scientists, laboratory personnel and the regulatory authorities will also be necessary to implement the successful application[16].

Future Perspectives

One of the key future challenges for AI in clinical mycology is the integration of various data sources, including clinical and diagnostic data, into comprehensive analytical platforms. The ability to integrate microscopic, fungal culture, PCR, MALDI-TOF MS, genome sequencing, and antifungal susceptibility data with relevant clinical parameters would allow for a more thorough evaluation of *Candida* infections. These multimodal procedures can help to expedite species identification and assist with tailored treatments[17].

New technologies like explainable AI, federated learning, foundation models, and cloud-based platforms for computational tasks could enhance the scalability, transparency, and clinical effectiveness of AI systems. Explainable AI could assist microbiologists in understanding what features are behind automated diagnostics predictions, adding to the confidence in AI-assisted diagnostics. Federated learning may allow each lab to participate in creating the model but without having to share patient data at the individual level between labs.

Another key future focus will be to create AI models to predict antifungal susceptibility and resistance. These systems can be used to identify patients who are at greater risk for resistant *Candida* infections such as *Candida auris* and facilitate earlier infection containment measures. AI-enabled surveillance systems could also help identify that there is an unusual increase in *Candida* infection in a healthcare setting, helping to advance the investigation and response of outbreaks[18].

In the longer-term, the inclusion of rapid species identification, resistance prediction, epidemiological surveillance, and patient-specific clinical information could help to provide a more individualized approach to antifungal management. The clinical relevance of these new technologies, however, will rely on comprehensive validation and adequate representation of the data sets, interoperability, and integration with current clinical and laboratory procedures.

Conclusion

The use of AI is proving to be potentially useful as an adjunctive approach to the diagnosis and identification of *Candida* species in a clinical microbiology laboratory.

Its use in microscopic analysis and culture interpretation, PCR-based detection and diagnosis, MALDI-TOF mass spectrometry, and biosensor-based detection illustrates its ability to aid quicker, more consistent, and efficient interpretation of complex diagnostic information. AI can help minimize observer variability and aid microbiologists in managing the growing diagnostic burden by helping with repetitive analytical activities and pattern recognition.

While this progress has been made, the clinical application of AI must take into account the quality of the data sets, bias, standardization, external validation, regulatory considerations, and existing laboratory workflows. Prospective and multicentre evaluation will be an especially critical step in assessing whether successful research models can be consistently successful in a variety of clinical and laboratory environments.

The use of AI should be seen as a tool to complement and support the traditional microbiological and experiential approaches, not a substitute for them. With proper development and validation, AI can be a valuable tool for early and accurate identification of *Candida*, resistance identification, monitoring of *Candida*, and better clinical treatment decisions. Effective implementation, careful validation and ongoing cooperation between microbiologists, clinicians, computational scientists and regulators will be essential to its successful adoption.

Conflict of Interest

The authors do not have any conflicts of interest.

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