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Artificial Intelligence Applications in Medical Mycology: Current and Future

Jemin Kim[1], Jihee Boo[1] and Chang Ook Park[2,3,4†]

[1]Department of Dermatology, Yongin Severance Hospital, Yonsei University College of Medicine, Gyeonggi-do, Korea
[2]Department of Dermatology and Cutaneous Biology Research Institute, Severance Hospital, Yonsei University College of Medicine, Seoul, Korea
[3]Institute for Immunology and Immunological Diseases, Yonsei University College of Medicine, Seoul, Korea
[4]Institute of Allergy, Yonsei University College of Medicine, Seoul, Korea

The application of artificial intelligence (AI) in the medical mycology field represents a new era in the diagnosis and management of fungal infections. AI technologies, particularly machine learning (ML) and deep learning (DL) methods, enhance diagnostic accuracy by leveraging large datasets and complex algorithms. This review examines current applications of AI in laboratory and clinical settings for fungal diagnostics. In the laboratory, AI models analyze microscopic images from potassium hydroxide (KOH) examinations, fungal culture tests, and histopathologic slides, which improves the detection rates of fungal pathogens significantly. In the clinical setting, AI assists the diagnosis of fungal infections using medical images, exhibiting high efficacy in binary classification tasks. However, challenges include small sample sizes, class imbalances, reliance on expert-labeled data, and the black box nature of AI models. Explainable AI offers potential solutions by providing human-comprehensible insights into AI decision-making processes. In addition, human-computer collaboration can enhance diagnostic accuracy, particularly for less experienced clinicians. The development of generative AI models, e.g., large language models and multimodal AI, promises to create extensive datasets and integrate various data sources for comprehensive diagnostics. Addressing these limitations through prospective clinical validation and continuous feedback will be essential for realizing the full potential of AI in medical mycology.

Key Words: Artificial intelligence, Deep learning, Explainable AI, Fungal diagnostics

INTRODUCTION

In medical science, the integration of artificial intelligence (AI) has marked a revolutionary shift, particularly in disease diagnostics and management. AI, which simulates human intelligence processes using machines, especially computer systems, encompasses learning, reasoning, and self-correction processes. Machine learning (ML) and its subset, deep learning (DL), have emerged as pivotal technologies within this broad domain[1]. ML algorithms leverage historical data to predict outcomes with increasing accuracy, and DL techniques enable computers to perform complex tasks by learning from examples and large datasets[2].

The application of AI in clinical medicine has introduced a

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†**Corresponding:** Chang Ook Park, Department of Dermatology and Cutaneous Biology Research Institute, Yonsei University College of Medicine, 50-1 Yonsei Ro, Seodaemun-gu, Seoul 03722, Korea.
Phone: +82-2-2228-2080, **Fax:** +82-2-393-6947, **e-mail:** COPARK@yuhs.ac

paradigm shift, notably in diagnostic accuracy, which now rivals that of specialist clinicians across various fields, including dermatology and ophthalmology. For example, the diagnostic prowess of AI techniques is evident in their ability to identify various conditions, e.g., diabetic retinopathy and skin cancer, frequently matching or exceeding the accuracy of human experts[3,4].

In medical mycology, AI and DL technologies are set to transform how fungal infections are diagnosed and treated. Fungal infections, which can range from superficial skin conditions to invasive diseases affecting internal organs, pose significant diagnostic challenges due to fungi's diverse morphology and genetic makeup[5]. The application of DL in medical mycology primarily focuses on enhancing the accuracy and efficiency of diagnosing fungal infections through advanced image analysis techniques[6], which is critical in settings where rapid and accurate pathogen identification can influence clinical outcomes considerably. For example, recent advancements in AI have shown promise in terms of automating the detection and classification of fungal pathogens in clinical and laboratory settings, thereby making it a valuable tool for both direct patient care and backend laboratory analysis.

The primary objective of this review is to elucidate the current and potential applications of AI in the medical mycology field. This paper explores how AI technologies are applied in laboratory and clinical settings to diagnose fungal infections, and we examine the limitations inherent in current technologies and discuss the prospective advancements that could shape the future of fungal diagnostics.

CURRENT APPLICATIONS: LABORATORY DIAGNOSIS OF FUNGAL INFECTION

Multiple AI-based and ML-based models have been developed to assist at various stages of laboratory diagnostics for fungal infections. These technologies are employed to analyze datasets derived from microscopic images of specimens obtained through potassium hydroxide (KOH) examinations, fungal culture tests, or histopathologic slides from human samples[7-13]. AI and ML can utilize four basic approaches, i.e., supervised, unsupervised, semisupervised, and reinforcement learning; however, most AI research on fungal diagnostics relies on supervised learning techniques. In this approach, researchers provide algorithms with labeled training data and a smaller dataset for validation. The algorithms are trained iteratively to learn the dynamics of the data and the relationship between the inputs and outputs, and then the corresponding models are evaluated on a test set to determine how accurately they match the gold labels[14]. Gold labels are frequently determined by expert interpretation of microscopic slide images or are validated through results from other confirmation tests, e.g., PCR analysis.

Recent studies on DL methods for laboratory diagnosis of fungal infections are summarized in Table 1. Koo et al.[8] developed a model using the YOLO-v4 network to detect hyphal structures in video images processed with KOH staining. They converted the videos into frame-by-frame images, and they annotated the fungal hyphae locations for training. The model was validated on datasets (Dataset-100, Dataset-40, and Dataset-all) comprising different optical magnification ratios. Here, two methods were employed for detection, i.e., image classification and object determination. In image classification, the presence of hyphae results in a positive outcome. In contrast, the object determination method identifies and analyzes hyphae-like objects for more detailed insights into their location and size. This method achieved ROC AUC values of 0.9987 for the Dataset-40 model and 0.9966 for the Dataset-100 model, highlighting its accuracy and reliability for the hyphae detection task.

Zieliński et al.[13] introduced a method that utilizes deep neural networks and a bag-of-words method to classify various fungi species from microscopic images, thereby eliminating the need for costly biochemical identification process. Their multistep algorithm generates robust image features and classifies them using a support vector machine, which reduced diagnosis time by two to three days and lowered costs. This method focuses on morphologically similar species by refining various visual parameters, e.g., size, shape, and color, to realize improved accuracy in identification. In addition, Decroos et al.[7] employed a CNN (similar to VGG-13) for the histopathological diagnosis of onychomycosis using whole slide images of PAS-stained nail clippings. This model was trained on data annotated by experts and refined through self-supervised learning to avoid overfitting, and it achieved an AUC value of 0.981. This method demonstrates noninferiority to human dermatopathologists and offers significant benefits, e.g., time savings and reduced misdiagnosis, particularly under high workloads or time pressures.

CURRENT APPLICATIONS: CLINICAL DIAGNOSIS USING MEDICAL IMAGES

In addition to laboratory tests, numerous reports have highlighted the use of AI models to diagnose fungal infections

Table 1. Recent studies in laboratory diagnosis of fungal infection using AI

Study	Objectives and key findings	Algorithm	Sample size
Koo et al. (2021)[8]	To detect fungal hyphae from potassium hydroxide (KOH) examination images at 40-fold and 100-fold magnifications. ROC AUC of 0.9987 for 40X model and 0.9966 for 100X model.	Regional CNN (YOLOv4)	3,707 images from 38 samples
Yilmaz et al. (2022)[12]	KOH examination to detect onychomycosis from microscopic images. These networks demonstrated superior diagnostic performance compared to dermatologists, with mean accuracy rates of 88.10% for InceptionV3 and 88.78% for VGG16.	VGG16, Inception V3	457 images - Fungi: 160 images (1,835 patches) - Keratin: 297 images (5,238 patches)
Tochigi et al. (2022)[11]	To distinguish *Aspergillus* from *Mucorales* in GMS stain images using hyphal angle and tortuosity as key features, demonstrating effectiveness with a threshold curve generated by 2D plots of the data.	Custom AI algorithm	214 images - Aspergillosis: 147 - Mucormycosis: 67
Rahman et al. (2023)[10]	Classified 89 different fungal genera from culture images using DL models, with DenseNet providing the highest accuracy. Achieved a top-1 accuracy of 65.35% and top-3 accuracy of 75.19%.	DenseNet, Xception, Inception-ResNet, InceptionV3, ResNet50, VCG16, VCG19	1,079 images
Milanović et al. (2024)[9]	For the presumptive determination of nondermatophyte molds. The software utilizes the EfficientNet-B2 architecture to classify nine nondermatophyte mold genera from permanent slide images with an accuracy of 93.73%.	EfficientNet-B2	8,138 images from 920 samples
Zieliński et al. (2020)[13]	Developed an ML approach using deep neural networks and bag-of-words to classify microscopic images of nine fungus species. Accuracy from 51.1% to 93.9% depending on the models.	Multiple CNNs, Bag-of-Words, Fisher Vector SVM, Random Forest	180 images
Decroos et al. (2021)[7]	For histopathological diagnosis of onychomycosis using PAS-stained sections of nail clippings. The AI model demonstrated noninferiority to human dermatopathologists with an AUC of 0.981.	CNN similar to VGG-13	727 images

AUC: area under the curve; CNN: convolutional neural network; GMS: Grocott's methenamine silver; KOH: potassium hydroxide; PAS: periodic acid-Schiff; ROC: receiver operating characteristic; VGG: visual geometry group

from medical images obtained in clinical settings. Studies leveraging large databases of medical images typically fall into two categories, i.e., those that focus exclusively on fungal infections[15-17] and those that include a subset of fungal-related conditions within a broader range of disease presentations[18-20]. Most image labeling is based on the clinical assessment of specialists, and some studies have utilized diagnostic results from concurrent fungal cultures or incorporated other clinical information[17,19].

Table 2 summarizes recent studies that have utilized DL methods to analyze medical images in clinical settings to aid the diagnosis of fungal infections. Han et al.[15] developed an AI system to diagnose onychomycosis using a large dataset of 49,567 nail images. Their model combined ResNet-152 and VGG-19, and it achieved an AUC value of 0.98. This AI-based method outperformed most of the 42 dermatologists who participated in the study, with a sensitivity/specificity of 96.0/94.7 for the primary dataset. The Youden index, which reflects diagnostic accuracy, was significantly higher for the AI system than the dermatologists, thereby demonstrating its potential in clinical diagnosis. In addition, Pangti et al.[20] reported the development of a mobile health application based on DenseNet-161 to diagnose 40 common skin diseases. The algorithm trained by datasets including five categories

Table 2. Recent studies in clinical diagnosis of fungal infection using AI

Study	Objectives and key findings	Algorithm	Sample size
Han et al. (2018)[15]	Classified onychomycosis in nail images with an AUC of 0.98.	Ensemble model combining ResNet-152 and VGG-19 models	49,567 images
Nigat et al. (2023)[16]	Used CNN to classify four common fungal skin diseases (tinea pedis, capitis, corporis, and unguium) with a classification accuracy of 93.3%.	CNN based model	407 images
Liu et al. (2020)[18]	Identified 26 common skin conditions in adult cases referred for teledermatology consultation, including various dermatitides and tinea infections. Achieved a top-1 accuracy of 66% and top-3 accuracy of 90% across these conditions.	Inception-v4	16,114 images (tinea: 299 images)
Pangti et al. (2021)[20]	To diagnose 40 common skin diseases, including specific types of tinea (tinea capitis, tinea cruris, corporis or faciei, tinea manuum, tinea pedis, and tinea unguium). Overall top-1 accuracy of 75.07% and mean AUC of 0.90 for detecting these conditions.	DenseNet-161	15,418 images from 5,014 patients (tinea: 3,086 images)
Muhaba et al. (2022)[19]	To diagnose five common skin diseases (including onychomycosis and tinea capitis). Multiclass classification accuracy of 97.5%, sensitivity of 97.7%, and precision of 97.7%.	MobileNet-v2	1,880 images
Tang et al. (2023)[17]	To classify pathogenic fungal genera in fungal keratitis using IVCM. Demonstrated an AUC of 0.887 and accuracy of 81.7% for identifying Fusarium, with an AUC of 0.827 and accuracy of 75.7% for identifying *Aspergillus*.	Inception-ResNet V2, LightGBM	3,364 images from 100 patients

AUC: area under the curve; CNN: convolutional neural network; GBM: gradient boosting machine; VGG: visual geometry group

of superficial fungal infections (tinea capitis, tinea cruris, tinea corporis or faciei, tinea manuum, tinea pedis, and tinea unguium), which comprised 20% of the total dataset by image count. The application was validated on 5,014 patients, achieving an overall top-1 accuracy of 75.07% and a mean AUC value of 0.90 for detecting these conditions. Tang et al.[17] developed an AI model to classify pathogenic fungal genera in fungal keratitis using 3,364 *in vivo* confocal microscopy (IVCM) images. The model demonstrated an AUC of 0.887 and an accuracy of 81.7% for identifying Fusarium, and an AUC of 0.827 and an accuracy of 75.7% for identifying *Aspergillus*, showcasing the potential of deep learning in the clinical management of fungal keratitis.

LIMITATIONS

Despite AI's promising applications in fungal diagnostics, several limitations must be acknowledged. First, sample sizes across studies vary significantly, often under 5,000 images, which results in substantial class imbalances and selection bias. Many studies utilize closed, in-house datasets, thereby hindering cross-validation and broader applicability[21].

Second, various models have shown high performance in binary classification tasks at consistent backgrounds, e.g., detecting onychomycosis presence in the nail plate[6]; however, their efficacy in multilabel classification tasks or when the background environment varies is inconsistent. This variability can limit the utility of AI in more complex diagnostic scenarios, where the model must differentiate between multiple conditions or adapt to diverse imaging settings.

Third, the performance of these algorithms is heavily dependent on the quality of the provided images and the accuracy of the gold labels, which are frequently based on the assessments of a few clinical experts. This reliance is particularly problematic for tests like KOH, where interobserver variability can affect algorithm training and outcomes.

Furthermore, ML models struggle to distinguish diagnostically meaningful structures from background or artifacts, even though algorithms have been developed to facilitate the object detection of relevant fungal structures[8,22]. The black box nature of DL algorithms raises concerns about the transparency and interpretability of these decision-making processes, which is critical in terms of establishing and maintaining clinical trust and justification.

Finally, most studies have been retrospective and validated in silico rather than in real-world clinical settings. Prospective validation is crucial to ensure these algorithms perform reliably in uncontrolled, high-stakes environments, address ethical concerns, and minimize selection bias[23].

FUTURE PERSPECTIVES

As AI methods continue to evolve, overcoming the black box nature of DL models has become increasingly important. Explainable AI is gaining traction, particularly in medical fields, to elucidate how neural networks arrive at their decisions. Most attempts to produce human-comprehensible explanations for decisions acquired using ML methods focus on post-hoc explainability, aiming to dissect the model's decision-making process[24]. Techniques like heat maps (or saliency maps) highlight the image's most crucial areas for diagnosis. In contrast, other methods, e.g., locally interpretable model-agnostic explanations and Shapley values, permute input examples to identify which local features most influence the model's decisions[25]. These approaches can help identify AI-induced image biomarkers that significantly affect the identification of specific fungal species.

Another promising development is the application of human-computer collaboration and augmented decision-making processes, which are becoming increasingly prominent in image-based AI fields. Research has demonstrate that AI assistance can improve the diagnostic accuracy of nonexpert physicians significantly for various skin conditions[26]. Less experienced clinicians derive the most significant benefit from AI support[27], which suggests that AI could be particularly valuable in settings requiring more specialized personnel to diagnose fungal infections. However, there is a risk of over-reliance on AI, which could lead to adherence to incorrect AI diagnoses, and continuous feedback and iterative testing in clinical environments are essential to mitigate this issue.

Finally, leveraging large-scale generative AI models, e.g., the Chat Generative Pretrained Transformer model, represents a novel approach. In addition, generative adversarial networks can create extensive datasets from small sample sizes or generate images with specific phenotypes[28]. Further, combining medical images, electronic health records, molecular analysis related to fungal infections[29], and existing literature through multimodal self-supervised training can develop generalist medical AI (GMAI)[30], which could make decisions in a manner that is similar to human clinicians. The advent of GMAI promises revolutionary advancements in medical mycology, and it offers comprehensive and integrated diagnostic capabilities.

CONCLUSION

In conclusion, the integration of AI in medical mycology holds immense potential to revolutionize fungal diagnostics. Despite the limitations related to sample size variability, class imbalance, and the black box nature of DL models, ongoing advancements in explainable AI, human-computer collaboration, and generative AI models promise significant improvements. By addressing these challenges and harnessing the power of AI effectively and efficiently, we can enhance diagnostic accuracy, reduce misdiagnosis, and optimize clinical outcomes. Future research and prospective clinical validation will be crucial to fully realizing the transformative impact of AI in the medical mycology field.

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CONFLICT OF INTEREST

In relation to this article, we declare that there is no conflict of interest.

ORCID

Jemin Kim: 0000-0001-6628-3507
Jihee Boo: 0009-0004-4576-2030
Chang Ook Park: 0000-0003-3856-1201

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