Engineering Applications of Artificial Intelligence 133 (2024) 108529

Contents lists available at ScienceDirect

Engineering Applications of Artificial Intelligence

journal homepage: www.elsevier.com/locate/engappai

Machine and deep learning methods in identifying malaria through microscopic blood smear: A systematic review

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ARTICLE INFO

Keywords:
Malaria
Machine learning
Conventional machine learning
Deep learning
Convolutional neural network
Transfer learning

ABSTRACT

Despite the persistency of World Health Organization to eliminate malaria since 1987, malaria disease continues to pose a significant threat to global health. As the severity of malaria persists over the years, there is a critical need for an automated diagnosis system for more efficient diagnosis and effective treatment administration. To mitigate the increase in mosquito-borne diseases, there has been a heightened interest in the application of Artificial intelligence (AI), specifically deep learning. With the assistance of the Preferred Reporting Items for Systematic Review and Meta-Analyses (PRISMA) framework, an extensive review of current state of automated malaria diagnosis systems utilizing machine learning and deep learning approaches was performed across eight scientific databases, with 50 articles shortlisted from the years 2015–2023. Besides, identifying the research gaps, we synthesise the existing literature, analyse the outcomes, and explore the critical parameters that influence model performance. From the review, the prevailing models primarily focus on binary classification while disregarding cross-dataset validations and multi-stage classification. This gap challenges the delivering effective treatments, especially considering potential drug resistance. Established protocols and classification models are needed to anticipate the specific malaria species. The keywords in automated malaria diagnosis that we identified include machine learning, deep learning, transfer learning, and convolutional neural networks. Through examinations of the constraints in current methodologies, we provide valuable suggestions that could propel the field of automated malaria diagnosis. This systematic review provides a comprehensive overview, critical insights, and a roadmap for future research endeavours in this vital domain of healthcare.

1. Introduction

Malaria is a severe and sometimes fatal disease caused by a *Plasmodium* parasite that commonly infects the Anopheles mosquito, feeding on humans. Malaria eradication is a long-standing goal of the World Health Organization; however, the number of cases and deaths being reported globally is still concerning to date. Since 2018, the number of cases has been significantly increasing, with an estimated 249,000 million cases and 608,000 deaths globally in 2022 compared to 244 million cases and 610,000 deaths in 2021 (Fig. 1). The malaria mortality rate halved between 2000 and 2015 from 30.1 to 15.0 per population at risk before decreasing slightly to 14.3 in 2022. Most deaths are among children under the age of five. Malaria is a significant drain on many national economies. Since many countries with malaria are already among the low socio-economic nations, the condition maintains a vicious cycle of illnesses and poverty. Malaria prevention, diagnosis, and treatment services are disrupted during the Covid-19 pandemic, exacerbating the situation. It is estimated that treatment disruptions caused approximately two-thirds (i.e., 47,000) of these additional deaths during the Covid-19 pandemic (WHO, 2021).

Abbreviations: AI, Artificial Intelligence; ML, Machine learning; CML, Conventional machine learning; DL, Deep learning; TL, Transfer learning; CNN, Convolutional Neural Network); NIH, National Library of Medicine.

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https://doi.org/10.1016/j.engappai.2024.108529
Received 19 June 2022; Received in revised form 7 April 2024; Accepted 27 April 2024

There are two categories of malaria parasites: the human plasmodium species and zoonotic malaria species. The human plasmodium species consists of *Plasmodium falciparum, P. vivax, P. ovale, and P. malariae*. Whereas the zoonotic malaria species consists *of P. knowlesi*. The first species cause the most infections with more severity, death, and drug-resistance infections worldwide (Capela et al., 2019; Gitta and Killian, 2019; Mace et al., 2021; Tuteja, 2007). Malaria parasites undergo several phases during their life cycle, each resulting in a distinct characteristic that can be observed and differentiated under a microscope. These stages are the ring, trophozoite, schizont, and gametocyte (Poostchi et al., 2018). Factors contributing to this severity are parasite species, the patient's health history, acquired or protective immunity, and, most significantly, the time it took to discover the disease and initiate appropriate treatment (Capela et al., 2019).

According to the World Malaria Report 2023 by the World Health Organization (WHO), most global malaria burdens are accounted for by countries with moderate to high transmission rates in sub-Saharan Africa. The African Region accounted for 93.6% of cases and 95.4% of deaths in 2022. Between 2019 and 2020, estimated malaria cases increased from 218 million to 230 million, and deaths from 552,000 to 604,000 in this region. Besides that, in 2022, the Southeast Asia region contributed to 2% of malaria cases globally, with 5.2 million cases. In the WHO Eastern Mediterranean region, cases steadily increased to 8.3 million in 2022, about 92% from 2015 (WHO, 2023).

As a tropical country, Malaysia has also been affected by this disease. Malaysia has maintained its status as the primary source of the simian parasite *P. knowlesi* despite reporting zero malaria cases caused by human *Plasmodium* species for five consecutive years beginning in 2018, according to the World Malaria Report 2023 (Fig. 2). Between 2008 and 2018, indigenous malaria cases caused by human parasites decreased from 6071 to 0, while *P. knowlesi* cases increased from 376 to 4131 (Chin et al., 2020; Hussin et al., 2020). In 2020 and 2021, *P. knowlesi* cases increased from 2609 to 3575, respectively, resulting in five and thirteen deaths in 2020 and 2021(WHO, 2022). In 2023, Malaysia reported 2505 *P. knowlesi* (WHO, 2023) cases, and 99% were classified as indigenous (originated locally). Since 2017, there have been a total of 17,125 *P. knowlesi* cases and 48 deaths reported in Malaysia. Malaysia Borneo contributes to the most malaria cases caused by this zoonotic malaria parasite. Sabah state has had the highest number of cases since 2013, followed by Sarawak (Hussin et al., 2020). As the number of cases of *P. knowlesi* malaria in Malaysia continues to rise, current approaches to preventing the spread of the parasite should be reconsidered. Additional control and preventive measures are due to the rising trend of zoonotic *P. knowlesi* malaria and preventive surveillance.

Malaria diagnosis plays a huge role in providing timely treatment and eradicating malaria infections. Early diagnosis enables one to fight the disease effectively. The current gold standard for malaria diagnosis is the microscopic examination. This technique examines hundreds and thousands of blood films annually under the microscope. Typically, two types of blood smear images are analysed: thin and thick. Microscopic visualisation of thin blood smear images allows the identification of the plasmodium species and the stages of infections. At the same time, the thick blood smear images reveal the presence of parasites in the blood. The effectiveness of microscopic examination heavily relies on the microscopist's abilities, resources, and diagnostic quality. Therefore, the results are prone to producing more false-negative and false-positive findings. In a non-endemic country where the disease is rarely seen, the expertise level in malaria diagnosis may not be maintained or well-trained over the years, causing the healthcare personnel to be unfamiliar with the disease and fail to detect the parasite during blood smear examination. In malaria-endemic countries, the lack of resources is a significant barrier to a reliable and timely diagnosis. Healthcare personnel often need to be more trained and equipped and pay divided attention to other severe infectious diseases (Capela et al., 2019; Tangpukdee et al., 2009). Besides detecting the presence of the parasite, identifying the specific species and stages of infections is also important, as knowledge of the infecting parasite can provide information on the likelihood of its drug resistance and enable the treating clinician to choose an appropriate drug or drug combination for treatment (Poostchi et al., 2018). As a result, new developments in artificial intelligence (AI) in healthcare have shown to be beneficial to medical professionals in diagnosing and treating a wide range of diseases (Gudigar et al., 2021; Khalil et al., 2021; Ramli et al., 2021)

AI is poised to play a prominent role in medicine and healthcare due to advances in computing power, learning algorithms, and the availability of large datasets from medical records. The practice of medicine is changing with the growth of new artificial intelligence and machine learning algorithms. With rapid advances in computer processing, these

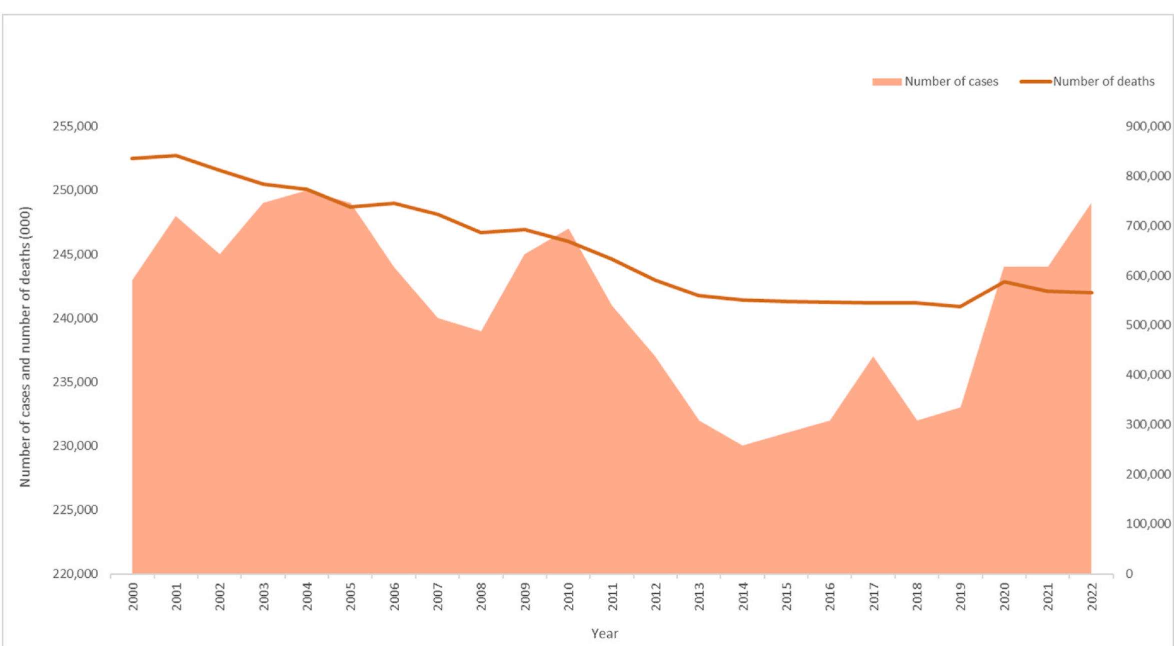

Fig. 1. Global malaria cases and death from 2000 to 2020 (Source: Data acquired from WHO, 2021).