INFORMATION BRIEF (RAPID REVIEW)

USING ARTIFICIAL INTELLIGENCE (AI) APPLICATION FOR LEPROSY DETECTION

Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
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Rapid Review
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TITLE: USING ARTIFICIAL INTELLIGENCE (AI) APPLICATION FOR LEPROSY DETECTION

PURPOSE

To review the effectiveness, safety and cost-effectiveness of Artificial Intelligence (AI) Application for Leprosy Detection based on request from the Deputy Director of Disease Control Section (Communicable Disease), Disease Control Division, Ministry of Health Malaysia.

BACKGROUND

Leprosy, also known as Hansen's disease, is a chronic infectious disease caused by *Mycobacterium leprae*. The disease mainly affects the skin, the peripheral nerves, mucosal surfaces of the upper respiratory tract and the eyes. Leprosy is known to occur at all ages ranging from early infancy to very old age. Leprosy is curable and treatment in the early stages can prevent disability. Leprosy is likely transmitted via droplets, from the nose and mouth, during close and frequent contact with untreated cases.[1]

At the end of the year 2020, the global prevalence was 129 389 cases on treatment and prevalence rate corresponds to 16.7 per million population.[2] Leprosy is endemic in Malaysia but the incidence is low.[3]

The World Health Organization (WHO) guidelines on leprosy recommended no additional tests in addition to standard methods for diagnosis of leprosy: the diagnosis of leprosy remains based on the presence of at least one of three cardinal signs: (i) definite loss of sensation in a pale (hypopigmented) or reddish skin patch; (ii) thickened or enlarged peripheral nerve with loss of sensation and/or weakness of the muscles supplied by that nerve; or (iii) presence of acid-fast bacilli in a slit-skin smear. The clinical diagnosis of early leprosy and paucibacillary (PB) leprosy can be a challenge. Therefore, a number of serological and other laboratory assays have been developed to supplement clinical diagnostic methods. However, enzyme-linked immunosorbent assays (ELISA) and lateral flow assays are associated with low diagnostic accuracy for PB leprosy. Although some polymerase chain reaction (PCR)-based assays are associated with higher diagnostic accuracy, they are lacking in standardisation, are not commercially available, and would be difficult to perform in most primary health-care settings. The WHO also does not recommend any test for the diagnosis of leprosy in

asymptomatic contacts. The predictive accuracy of diagnostic tests for identifying persons who will develop leprosy is low, with poor positive predictive values.[4]

Artificial intelligence is a field, which combines computer science and robust datasets, to enable problem-solving. It also encompasses sub-fields of machine learning and deep learning, which are frequently mentioned in conjunction with artificial intelligence. These disciplines are comprised of AI algorithms which seek to create expert systems which make predictions or classifications based on input data. [5] The AI research is already being conducted in numerous medical fields, including dermatology. In the last decade, AI is gradually finding its relevance in different fields of dermatology including skin cancer, eczema, and psoriasis.[6]

EVIDENCE SUMMARY

There were 9 articles retrieved on the AI technology for leprosy from the scientific databases such as Medline, EBM reviews, Pubmed and from the general search engines [Google Scholar and US Food and Drug Administration (USFDA)] using the search term *hansen's disease, leprosy, leprosy paucibacillary, leprosy multibacillary. artificial intelligence, computational intelligence, computer reasoning, computer vision system and machine intelligence.* Last search was conducted on 22th September 2022. A total of three studies were included in this review, consisted of three pilot studies on AI application for leprosy detection.

EFFICACY/ EFFECTIVENESS

Barbieri RR et al. conducted a pilot study to create the first open source image and databank for leprosy and AI model for suspected leprosy cases. They described the accuracy of an AI-enabled image-based diagnosis assistant for leprosy (AI_4leprosy). It used combination of skin images and clinical data which were collected following a standardised process. A total of 222 patients with leprosy or other dermatological conditions from Brazilian leprosy national centre were included. They used the dataset to test whether convolution neural networks (CNN)-based AI algorithm could contribute to leprosy diagnosis. All the three AI models, testing images and metadata were employed both independently and in combination. Two-step patient-level models were developed, first to predict the probability of leprosy based on the skin lesion image [Model 1 using ResNet-50 and Inception-v4] or the metadata [Model 2 using Elastic-net Regression (LR), XGBoost (XGB) and Random Forest (RF)]. Each model produced a probability of leprosy for each image or set of metadata. Given that patients could have multiple lesions or metadata records, they combined outputs from both models per

patient in a histogram, to represent the predicted probabilities. Lastly, [Model 3 using Elastic-net Regression (LR), XGBoost (XGB) and Random Forest (RF)] was trained to combine analysis made in the first step, with the patient information. That step established the overall probability by combining the histograms from Model 1 and 2, with patient information.[7]

A total of 1229 skin images were collected and 585 sets of metadata were stored in an open source dataset. They reported that AI modelling indicated that the most important clinical signs were thermal sensitivity loss, nodules and papules, feet paraesthesia, number of lesions and gender. Scaling surface and pruritus were negatively associated with leprosy. The probability models were able to recognize leprosy with classification accuracy (90%) and AUC (96.46%) when combining Elastic-net Regression model 2 outputs and patient information. It also was reported to be simpler and more interpretable than XGBoost or Random Forest. [7]

De Souza MLM conducted a pilot study to develop a cross-platform application for leprosy screening based on AI. Leprosy data such as age, gender, race, education, grade of disability, operational classification, bacilloscopy index, number of affected nerves, clinical form, municipality ID, number of household contacts, and the number of skin lesions were extracted from National Notifiable Diseases Information System (SINAN) database, Brazil. The AI decision models were based on the random forest algorithm to predict operational classification in paucibacillary or multibacillary leprosy. They used Phyton programming language to extract and clean the data, and R programming language to train and test the AI model via cross-validation. They deployed the final random forest classification model in a web application via shinyApp using data available from the Brazilian Institute of Geography and Statistic and the Department of Informatics of the Unified Health System for a broad access. They mapped the dispersion of leprosy incidence in Brazil from 2014 to 2018 and diagnostic accuracy of AI model applied to the differential diagnosis of paucibacillary and multibacillary leprosy in 26,546 cases as shown in Table 1.[8]

Table 1: Diagnostic accuracy of the artificial intelligence model applied to the differential diagnosis of paucibacillary and multibacillary leprosy.

Quality parameter	Mato Grosso model	Rio Grande do Sul model	Paraná model
Accuracy	0.970	0.812	0.929
Sensitivity	0.926	0.977	0.877
Specificity	0.812	0.218	0.919
PPV[a]	0.936	0.803	0.972
NPV[b]	0.786	0.740	0.698

Another pilot study was conducted by Gama RS et al. to test the integration of molecular and serological methods using AI by random forest algorithm to better diagnose and predict new cases of leprosy. The study was developed in Brazil and included new cases diagnosed in 2011 and their respective household contacts were followed in 2011, 2012, and 2016. All contacts were evaluated by clinicians from Reference Center for Endemic Diseases (CRE-DEN-PES) before being classified as asymptomatic. Samples of slit skin smears (SSS) from the earlobe of the patients and household contacts were collected for quantitative polymerase chain reaction (qPCR) of 16S rRNA, and peripheral blood samples were collected for ELISA assays to detect leprosy immune diagnostic 1 (LID-1) and natural disaccharide octyl leprosy immune diagnostic (ND-O-LID).[9]

The receiver operating characteristic (ROC) curve was employed for the ELISA and qPCR tests to analyse sensitivity, specificity, accuracy, likelihood ratio, and cut-off point associated with the least number of erroneous test results. Meanwhile, the artificial intelligence-based classification model was applied using the random forest (RF) package in the R program. Random forest is a combination of tree predictors, where each tree depends on the values of a random vector sampled independently and with the same distribution for all trees in the forest. Three models for predicting the disease were evaluated: Madrid classification, operational classification, and dichotomous status (Sick/Healthy). For each of these models, a set of explanatory variables was used: age, gender, treatment time, qPCR (level of *M.Laprae* DNA), serological level of IgG/IgM, and bacilloscopy index. Each decision tree of the RF models was obtained from the fit of 70% of the total number of leprosy cases and endemic control from the database. The remaining 30% of cases and endemic control were included to define a prediction.[9]

The statistical analysis of the tests revealed sensitivity for anti-LID-1 (63.2%), anti-ND-O-LID (57.9%), qPCR SSS (36.8%), and smear microscopy (30.2%). Using the dichotomous model of Sick/Healthy, they compared the performance of random forest

relation to bacilloscopy, qPCR/SSS, and ND-O-LID and LID-1 tests for the diagnosis of leprosy. It was shown that random forest increased frequency in diagnosis of multibacillary leprosy (90.5%) and paucibacillary leprosy (70.6%) as shown in Table 2.[9]

Table 2. Frequency of positive results using various methods for diagnosis of PB and MB leprosy.

Operational Classification	N	BacilloscopyN (%)	qPCR SSS N (%)	ND-O-LID N (%)	LID-1 N (%)	Random Forest N (%)
PB	17	0 (0.0)	3 (17.7)	7(41.2)	9(57.9)	12(70.6)
MB	21	11 (52.4)	11(52.4)	15(72.4)	15(72.4)	19(90.5)
Total	38	11 (28.92)	14 (36.8)	22(57.9)	24(63.2)	31(81.6)

N: number of individuals; qPCR SSS: qPCR slit skin smears; PB: paucibacillary; MB: multibacillary.

SAFETY

There was no evidence retrieved on the safety.

COST-EFFECTIVENESS

There was no evidence retrieved on the cost-effectiveness of AI technology for leprosy. The estimated cost for the AI application was also not retrieved.

CONCLUSION

There was very limited evidence retrieved on artificial intelligence application for leprosy detection. All the studies use different input data and evaluate the different system. Hence, more pilot study with sufficient data to train the AI system is needed to ascertain its benefit for leprosy screening.

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