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Developing an artificial neural network for detecting COVID-19 disease

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Abstract:

BACKGROUND: From December 2019, atypical pneumonia termed COVID-19 has been increasing exponentially across the world. It poses a great threat and challenge to world health and the economy. Medical specialists face uncertainty in making decisions based on their judgment for COVID-19. Thus, this study aimed to establish an intelligent model based on artificial neural networks (ANNs) for diagnosing COVID-19.

MATERIALS AND METHODS: Using a single-center registry, we studied the records of 250 confirmed COVID-19 and 150 negative cases from February 9, 2020, to October 20, 2020. The correlation coefficient technique was used to determine the most significant variables of the ANN model. The variables at $P < 0.05$ were used for model construction. We applied the back-propagation technique for training a neural network on the dataset. After comparing different neural network configurations, the best configuration of ANN was acquired, then its strength has been evaluated.

RESULTS: After the feature selection process, a total of 18 variables were determined as the most relevant predictors for developing the ANN models. The results indicated that two nested loops' architecture of 9-10-15-2 (10 and 15 neurons used in layer 1 and layer 2, respectively) with the area under the curve of 0.982, the sensitivity of 96.4%, specificity of 90.6%, and accuracy of 94% was introduced as the best configuration model for COVID-19 diagnosis.

CONCLUSION: The proposed ANN-based clinical decision support system could be considered as a suitable computational technique for the frontline practitioner in early detection, effective intervention, and possibly a reduction of mortality in patients with COVID-19.

Keywords:

Artificial intelligent, coronavirus, COVID-19, decision support systems, machine learning, neural network

Introduction

Emerging and new pathogens are major threats to global public health. This is principally true for virus-induced diseases that are extremely contagious due to widespread person-to-person transmission and have asymptomatic infectivity periods.^[1-3] Since December 2019, a new strand of coronavirus named severe acute respiratory syndrome coronavirus-2 (COVID-19) was detected in Wuhan District, China, and the outbreak continues to spreading aggressively worldwide. It is thought that the

SARS-CoV-2 outbreak has animal origins that slipped from animal species into the human population. The complex and highly contagious nature of COVID-19 had led the World Health Organization (WHO) to pronounce this disease a global health crisis.^[4,5]

The WHO and other health officials have recommended some safeguard measures including implementing physical distancing, wearing personal protective equipment, and sanitizing the hands to avoid and reduce the spread of the disease.^[6,7] Despite severe preventive measures and lockdown policies, COVID-19 has now become a pandemic on a global scale, which made a

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tremendous impact on the health and safety of people all over the world, affecting their lives and causing an escalating number of deaths. In addition, many indirectly devastating outcomes are derived from this pandemic leading to psychological distress and socio-economic crises in many societies.^[8-11]

Rapid transmission and high rate of mortality particularly in susceptible populations such as the elderly, and people with underlying medical problems, make it necessary to seek early detection and isolation of positive cases as rapidly and accurately as possible for containing the transmission of the virus, especially for individuals with no sign of symptoms in an early stage.^[12-17] These vulnerabilities emphasize the need for early and accurate diagnosis methods for COVID-19 and prompt confinement of the infected people in the absence of a specific vaccine or treatment.^[18,19] In this situation, many governments and public health authorities across the world have been searching for new and innovative technologies as alternative solutions to screening, monitoring, and tracing infected persons.

Artificial intelligence (AI) may be a unique preparation to take up this challenge.^[20,21] AI is a broad field that refers to the capability of a machine to learn from experience, adjust to new inputs, and simulating human intelligence tasks.^[22] Machine learning is a subset of AI and that it can be fueled with a huge dataset for automatically extracting high-quality models.^[23] Artificial neural network (ANN) is biologically system with an adaptive, self-learning, and computational construction simulating the functions of human neurons.^[24,25] This technique can be trained to recognize and categorize complex patterns of diseases through an iterative learning process. Once proper training is achieved, the ANNs try to forecast with greater accuracy than traditional statistical techniques. Due to its capabilities to identify multifarious nonlinear relations between predictor variables and corresponding outcome variables, it has been effectively applied in clinical decision support system (CDSS) to provide solutions for different numerous problems.^[26-30]

Some studies^[31-36] showed that the ANN-based prediction models using clinical or laboratory data can be significantly helpful in a timely, effective, and economical diagnosis of the disease. It can discriminate the COVID-19 from other similar conditions with better accuracy compared to traditional approaches. The ANNs provide timely screening, identify the disease at early asymptomatic phases, and promptly confinement the infected cases. Some other studies are focusing on the deep/convolutional neural network technique to detect any distinguish features from chest X-ray images of COVID-19 patients for identification of disease.^[37-43] It can also provide an automated medical

diagnostic system to support health-care specialists for enhanced decision-making with the aim of detection and management of COVID-19 disease.

Other applications of ANNs in the management of the COVID-19 epidemic include prognosis, prediction, and risk assessment of individuals for disease outcomes (individual level),^[33,34,44-50] the ANNs also can be used in the prediction of disease outbreak trends at the macrolevel (community),^[51-53] and finally, it also employed to predict the hospital resources utilization (bed occupancy, length of stay, etc.).^[54,55]

The present study aimed to establish an intelligent system based on back-propagation ANN for earlier diagnosis of COVID-19 by training on a retrospectively collected dataset (clinical and laboratory data) specifically for frontline practitioners.

Materials and Methods

Study design

This retrospective study was conducted in 2020, consisted of four sequential steps as follows.

Data collection and preprocessing

This retrospective and the single-center study was conducted in Ayatollah Taleghani Hospital, which is the focal center for COVID-19 special care and treatment in South West of Khuzestan, Iran. The experimentation is ethic compliant and has been approved a certificate of ethics (code: IR.ABADANUMS.REC.1400.008) by the Ethics Committee board of the Abadan University of Medical Sciences. A total of 4369 supposed COVID-19 cases were referred to this center, February 9, 2020, to October 20, 2020. Of those, 2814 cases were identified as suspicious. By applying the predefined exclusion criteria, 435 cases remained. After a quantitative analysis of medical records, 35 incomplete records that had a lot of missing data (more than 70% missing) were excluded from the analysis; and 400 records have remained. After the test, 250 and 150 cases were confirmed as positive and negative reverse transcription-polymerase chain reaction respectively. A flowchart to represent the patient selection methodology is given in Figure 1.

Feature selection

It is effective in reducing the input number for processing, or finding the most meaningful inputs to reduce the dimensions of the dataset for increasing the data mining performance and its calculation capabilities. In our study, we had the 38 independent variables including different criteria for COVID-19 diagnosis such as demographic (age, sex, and body mass index), clinical findings (respiratory rate, body temperature,

fever, cough, weakness, dyspnea, disability, chest pain, throat pain, rhinorrhea, headache, rhinophyma, tremor, digestive sign, loss of sensation, lung lesion existence, lung lesion appearance, and statue and pulmonary infection), epidemiological factors (job risk, travel to high-risk regions, contact history, contact type, contact number, exposure time, geographic living, and contact with susceptible people), and medical and personal history (history of drinking alcohol, in taking Vitamin D, smoking, in taking blocker, history of acute respiratory distress syndrome, and history of pregnancy) and oxygen saturation in the blood. Considering the qualitative variables that existed in the research database, the phi coefficient correlation has been used to investigating the meaningful relationship between the inputs (diagnostic criteria) and outputs (negative or positive COVID-19) variables, statistically. $P < 0.05$ was considered for a statistically meaningful level. IBM SPSS Statistics V25.0 (Armonk, NY: IBM Corp., USA) was used for this purpose.

Selecting the artificial neural network model

Selecting the ANN characteristics and efficient model is the key prerequisite to improving model performance. The ANN model used in this research was a standard feed-forward, back-propagation neural network (BPNN) with three input, intermediate (hidden), and output layers. The BPNN is a deep learning method in ANN with more than one hidden layer (multi-layered perceptrons [MLP]).^[56,57] BPNN is the best technique for training in MLP of ANN. This method is often done by optimizing the learning algorithm and the weight of neurons by calculating the decreasing gradient of the cost function. It is a kind of multilayer feed-forward neural network which uses supervised learning technique for diseases prediction.^[58-60]

All data were entered into the MLP as a new and the most common design tool for layered feed-forward neural networks [Figure 2]. An MLP architecture includes

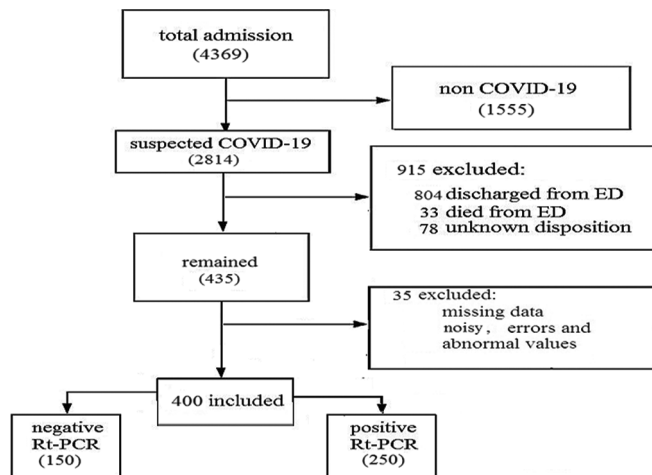


Figure 1: Flowchart describing patient selection

three layers (an input layer, a hidden layer, and an output layer). Each node in MLP or generally in every ANN uses a stimulating method for communicating to other nodes that this process can be simulated with nonlinear stimulating function in the ANNs. MLP uses a supervised learning technique called repetition for training.^[61-63] This training algorithm stabilizes the weights of the neurons according to the error that existed between the features of the real and target class to make a suitable relationship between the input and output classes by the nonlinear connection between neurons.^[64] Furthermore, the Levenberg–Marquardt was used in this research because of its popularity in error reduction and increasing the efficiency in the calculation process.^[57] The MLP activation function (tansig function) was implemented in the MATLAB 2013a that was used in this study as an ANN activation method and physiologic connection between ANN’s neurons like human’s NN.^[60]

Developing artificial neural network architecture

In this study, to determine the best configuration of the ANN, we used the different types of the ANNs configuration by different hidden layers with the number of the neurons that existed in them for data processing and performance evaluation based on different evaluation criteria such as sensitivity, specificity, and accuracy. In this step, the datasets were split into both training and testing. About 70% of cases were for training and 30% for the testing process. Finally, the final architecture of ANN for COVID-19 diagnosis was acquired based on measuring and comparing the sensitivity, specificity, and accuracy of different ANN configuration types. Our conditional threshold in ANN’s COVID-19 diagnosis was the 0.5 value; the uninfected people was considered <0.5 ($0.5 \leq x$) and positive outputs were classified more than 0.5 ($0.5 > x$).

Results

The result of determining the most important diagnostic criteria based on the phi coefficient at $P < 0.05$ is demonstrated in Table 1.

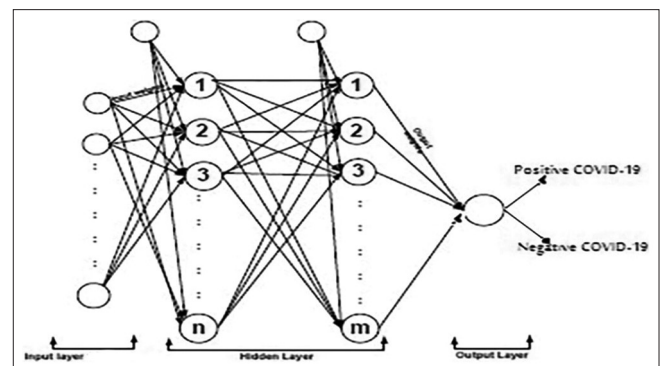


Figure 2: The schema of an artificial neural network used in diagnosing COVID-19

Table 1: The key diagnostic criteria at $P < 0.05$

Input variable	Variable type	Variable features with frequency	Correlation coefficient	P
Respiratory rate	Binominal	≤24 (128) >24 (272)	0.245	0.000265
Body temperature	Polynomial	<37.3 (199) 37.3-38 (116) 38-39 (40) >39 (45)	0.554	0.005405
SPO ₂	Polynomial	>95% (274) 85%-95% (86) <0.85% (40)	0.327	0.0093105
Shortness of breathing	Binominal	Haven't (285) Have (115)	0.198	0.00124
Fever	Binominal	Haven't (244) Have (156)	0.545	0.00512
Cough	Binominal	Haven't (229) Have (171)	0.621	0.00405
Digestive sign (diarrhea)	Binominal	Haven't (296) Have (104)	0.114	0.0269847
Chest pain	Binominal	Haven't (285) Have (115)	0.074	0.0301
Weakness	Binominal	Haven't (280) Have (120)	0.138	0.002515
Contact type	Polynomial	Haven't (272) Person-the person (62) Contaminated surface-the person (24) Water/food consumption (12) Air-breathing (8) Other (22)	-0.479	0.007755
Contact number	Binominal	Complete (100) Relative (45) Haven't (255)	-0.411	0.00695
Contact history	Binominal	Haven't (276) Have (124)	0.172	0.019
History of respiratory failure	Nominal	Haven't (262) Have (138)	0.3	0.0159
History of taking the blocker drugs	Nominal	Haven't (301) Have (99)	0.130	0.0219
Pulmonary lesion existence	Nominal	Haven't (235) Have (165)	0.6	0.00258
Pulmonary infection	Nominal	Haven't (288) Have (112)	0.146	0.000125
History of traveling to high-risk COVID-19 occurrence	Nominal	Haven't (302) Have (98)	0.130	0.0212
Age	Polynomial	Young (<45) (125) Middle-aged (45-55) (143) Adult (>55) (132)	0.110	0.0105

SPO₂=Oxygen saturation in the blood rate

Based on the information provided in Table 1, the cough ($\phi = 0.621$) ($P = 0.00405$), fever ($\phi = 0.545$) ($P = 0.00512$), lung lesion existence ($\phi = 0.6$) ($P = 0.00258$), and body temperature ($\phi = 0.554$) ($P = 0.005405$) had obtained the most amount of correlation coefficient at $P < 0.05$; therefore, in this research, they were considered as the most important diagnostic for diagnosing the COVID-19. In general, the 18 diagnostic criteria acquired the determined correlation coefficient at $P < 0.05$.

After comparing different configurations of ANNs by evaluating the three mentioned comparison criteria [Table 2], the most common architecture of ANN was obtained [Figure 3]. Indeed, the architecture of 18-28-20-2 (28 and 20 neurons in hidden layer 1 and hidden layer 2, respectively) had been gotten as the best configuration for designing the ANN for diagnosing the COVID-19 disease.

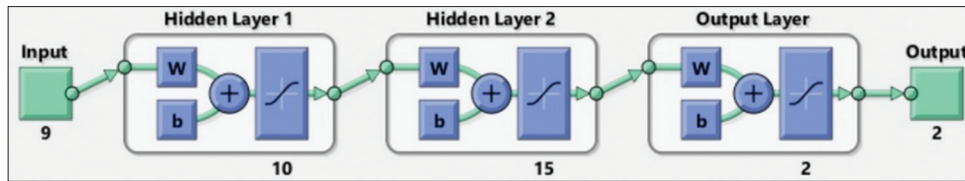


Figure 3: Final artificial neural network architecture used for COVID-19 diagnosis with the best performance

This ANN was trained by 24 iterations (Epochs), and the results of evaluating the ANNs by mean squared error (MSE) [Figure 4] have demonstrated that in the 18th epoch of the ANN training, the ANN's error rate had been reached to the least amount (MSE = 0.04). In fact, in the six steps prior (in the 12th step), this ANN model had obtained the best performance to diagnose the COVID-19.

The result of the sample classification based on the confusion matrix for all processes of developing the ANN such as training, validating, and testing the ANN is demonstrated in Figures 5 and 6. We considered the total cases (total confusion matrix [TCM]) for evaluating the performance of the ANN, in this research. Based on the TCM, the 241 positive COVID-19 cases (96%) were classified as positive out of 250 positive cases (true positive [TP] = 241), 136 non-COVID-19 samples (91%) were classified truly as negative (true negative [TN] = 136) by ANNs, also about the misclassified cases, the ANNs falsely classified 14 non-COVID-19 cases (9%) as positive (false positive [FP] = 14), and classified 9 records (4%) about the positive people as negative (false negative [FN] = 9). Based on the TCM, the sensitivity, specificity, and accuracy of the ANN have been obtained 96.4%, 90.6%, and 94%, respectively.

The receiver operating characteristic (ROC) plot of the ANN is depicted in Figure 5, and the result of calculating the area under the curve (AUC) demonstrated that these ANNs had an efficient classification strength (AUC = 0.982) in diagnosing the COVID-19 and non-COVID-19 cases with being closed the curve to the true positive rate (perfect classifier than the random type); on the other hand, the AUC plot indicated that the ANN diagnosing model had a high diagnostic power with the high TP and TN rate and low FN and FP rate. This curve also was the best in terms of efficiency among all the ANN configurations.

In Figure 7, the Clinical Decision Support System User Interface for COVID-19 diagnosis was designed by MATLAB v 2013a software (The MathWorks, Inc., Natick, Massachusetts, USA), in which, the users such as a physician could enter the data about their patients, then the system suggests the best recommendation about having COVID-19 disease or not.

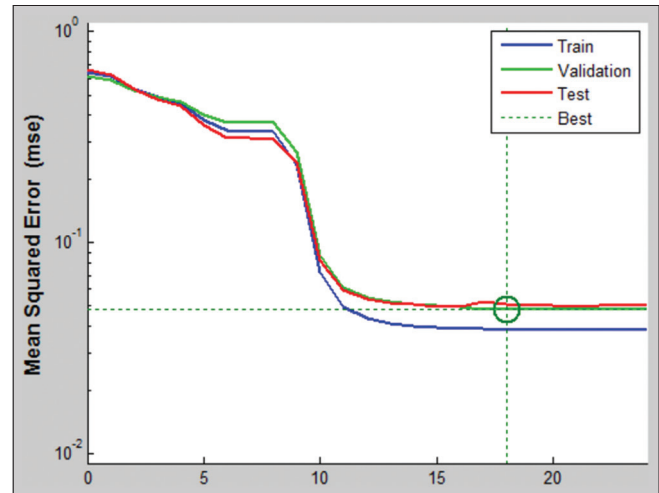


Figure 4: The artificial neural networks mean squared error for error rate evaluation

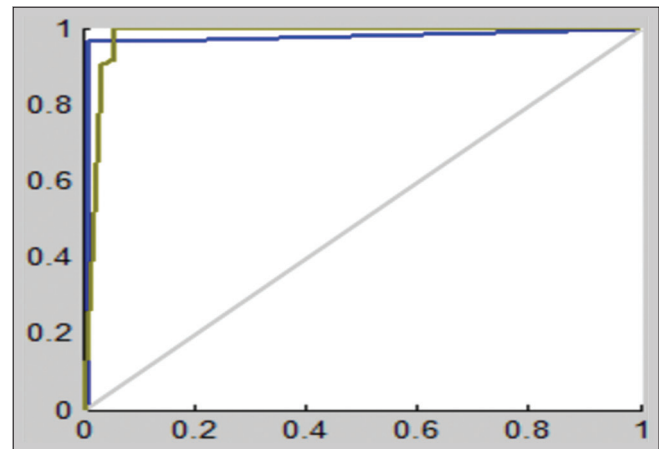


Figure 5: The receiver operating characteristic of artificial neural networks in diagnosing COVID-19

Discussion

The high risk of infection, vague characteristics, the uncertainty of nature, long incubation period, vigorous progression, and difficulties for conduct laboratory tests make COVID-19 a critical public health issue that raised intense attention internationally.^[65] In this situation, a timely and accurate diagnosis can provide a better plan for health policymakers and clinicians to mitigate disease outbreaks and improve patient survival probability.^[56] To this end, developing intelligent models for COVID-19 diagnosis is very crucial in determining their likely new cases at an early

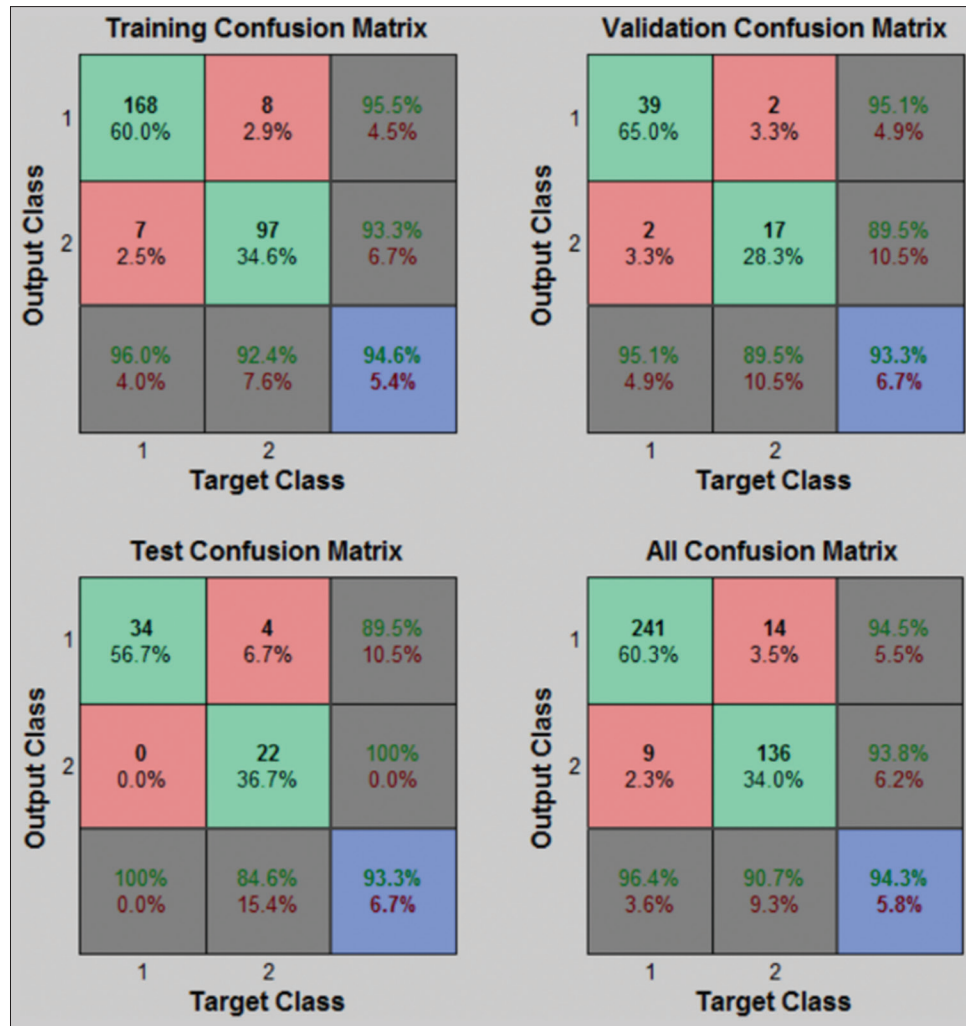


Figure 6: All situations of the artificial neural networks confusion matrix

Shortness of breathing	<input type="text" value="Haven't"/>	Fever	<input type="text" value="Haven't"/>	Contact History	<input type="text" value="Haven't"/>
Age	<input type="text" value="<45"/>	Digestive Signs	<input type="text" value="Have"/>	Resp failure Hist	<input type="text" value="Haven't"/>
Cough	<input type="text" value="Haven't"/>	Chest Pain	<input type="text" value="Haven't"/>	Taking Block Hist	<input type="text" value="Haven't"/>
Respiratory Rate	<input type="text" value=">24"/>	Weakness	<input type="text" value="Haven't"/>	Pulmonary Inf	<input type="text" value="Haven't"/>
Body temprate	<input type="text" value="<37.3"/>	Contact type	<input type="text" value="Haven't"/>	Pulmonary Lesion	<input type="text" value="Haven't"/>
SPO2	<input type="text" value="85%-95%"/>	Contact Number	<input type="text" value="0"/>	Travel Hist	<input type="text" value="Haven't"/>

You have not COVID-19 !

Figure 7: The Clinical Decision Support System User Interface is based on artificial neural networks for COVID-19 diagnosis

stage.^[23,66] The purpose of this study was to develop an intelligent model for detecting the presence or absence of COVID-19 based on ANN techniques.

So far, several types of research have been focused on applying and evaluating the ANN techniques in COVID-19 early prognosis, risk assessment, and trend

Table 2: The performance of some artificial neural network configuration

Network type	Layer 1	Layer 2	Sensitivity	Specificity	Accuracy
1	1	0	0.212	0.91	0.6125
2	2	0	0.532	0.9	0.6725
3	3	0	0.996	0.02	0.63
4	4	0	0.992	0.02	0.6275
5	5	0	0.74	0.33	0.5875
6	6	0	0.996	0	0.6225
7	7	0	0.884	0.12	0.6
8	8	0	0.804	0.42	0.66
9	9	0	0.42	0.8	0.565
10	10	0	1	0.02	0.635

estimation. Abdulaal *et al.* in their study developed an ANN model for COVID-19 mortality risk prediction that yielded a sensitivity, specificity, and ROC of 87.5%, 85.94%, and 90.12%, respectively.^[67] Toraman *et al.* proposed a novel ANN (Convolutional CapsNet) for detecting COVID-19. Their suggested technique attained an accuracy of 97.24% and 84.22% for twofold and multiclass, respectively.^[68] Chowdhury *et al.* showed that the convolutional neural networks (CNNs) for COVID-19 screening had accuracy, precision, sensitivity, and specificity of 99.7%, 99.7%, 99.7%, and 99.5%, respectively.^[69] Hassantabar *et al.* in their study showed that the CNN method with an accuracy of 93.2% and sensitivity of 96.1% is the better model for diagnosis and detection of COVID-19 when compared to the deep neural network (DNN) method with an accuracy of 83.4% and sensitivity of 86%.^[70] Alakus *et al.* compared the predictive performance of selected deep learning algorithms including ANN, CNN, LSTM, RNN, CNNLSTM, and CNNRNN for COVID-19 diagnosis. Finally, LSTM deep learning model was recognized as the best model with an accuracy of 86.66%, recall of 99.42%, and AUC score of 62.50. Torrealba-Rodriguez *et al.*^[11] and Moftakhar *et al.*,^[71] compared the prediction performance of statistical (regression) and computational (ANN) models in COVID-19 diagnosis, and finally, the ANN exhibits better performance than the regression model.

The results of the current study illustrated that the designed ANN model can appropriately identify the COVID-19 cases using parameters that are readily available in clinical practice. To that end, the data were balanced and then used as contributor predictors for the ANNs. Later, the models were developed and their performance was evaluated. The key findings of our study, first, identify the most important clinical predictors using logistic regression, and then a promising performance level with an AUC of 0.982. In the first step, we identified 18 significant predictors [Table 1] which were independently associated with COVID-19. However, the sensitivity, specificity, and accuracy were 96.4%, 90.6%, and 94%, respectively.

The ANN model has robust error tolerance; thus, it can be extensively used in the fields of prediction and analysis.^[72] Furthermore, leveraging the potential of an ANN-based CDSS would assist health-care providers to make better decisions concerning COVID-19 (diagnosis, classification, etc.). Despite standard statistical approaches (e.g., logistic regression) that need further modeling processes, ANNs do not necessitate distributional assumptions.^[73] In addition, contrasting to traditional statistical-based prediction methods, this study offers a new technique for modeling complex nonlinear relationships in spatial epidemiology. Such a prediction model can be employed even for analyzing noisy, imbalanced, and inadequate datasets.

Several limitations need to be addressed. First, the dataset was obtained from a single center that limits the external validity of the results; thus, future multi-central datasets and external validation possibly will improve the developed model. Second, only the data of 400 patients were included to devise the model. It is considered a small population and the probability of an overfitting problem. To overcome these limitations and improve the results, we recommend prospective, multicenter teamwork, with a great dataset.

In this research, by introducing a scientific and noninvasive evidence-based method, we will be able to propose the best ANN configuration for COVID-19 detection based on the most effective diagnostic criteria. The proposed configuration appears to have a higher performance than the conventional evaluation approaches, and also can be used by physicians to improve their diagnostic performance.

We rely on that, in future, an ANN-based CDSS risk assessment will be existing for use in the health-care facilities, which will be straightforward for clinicians to use. We anticipate that this technique may apply to wider fields of medicine, facilitating the complex and nonlinear information processing about patients, and leading to the establishment of personalized risk profiles.

Conclusion

We have created and tested an ANN model for COVID-19 diagnosis based merely on patient history and exposure parameters commonly available in inpatient medical records. Our results reveal that ANN can offer high specificity and good sensitivity for the diagnosis of COVID-19. The results also disclosed that ANN could discriminate COVID-19 from other viral pneumonia and flu-like diseases with high accuracy. While our neural network could be potentially used as a clinical tool for COVID-19 diagnosis, further development with more clinical variables included and

more evaluation would be required. This study could develop other diseases to help the health-care system respond more effectively during the present and even future pandemics.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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