ORIGINAL ARTICLE

Developing an Intelligent System for Diagnosis of COVID-19 Based on Artificial Neural Network

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Abstract- An outbreak of atypical pneumonia termed coronavirus disease 2019 (COVID-19) has spread worldwide since the beginning of 2020. It poses a significant threat to the global health and the economy. Physicians face ambiguity in their decision-making for COVID-19 diagnosis and treatment. In this respect, designing an intelligent system for early diagnosis of the disease is critical for mitigating virus spread and resource optimization. This study aimed to establish an artificial neural network (ANNs)-based clinical model to diagnose COVID-19. The retrospective dataset used in this study consisted of 400 COVID-19 case records (250 positives vs. 150 negatives) and 18 columns for the diagnostic features. The backpropagation technique was used to train a neural network. After designing multiple neural network configurations, the area under the receiver-operating characteristic curve (AUC), accuracy, sensitivity, and specificity values were calculated to measure the model performance. The two nested loops architecture of 9-10-15-2 (10 and 15 neurons used in layer one and layer two, respectively) with the ROC of 98.2%, sensitivity of 96.4%, specificity of 90.6%, and accuracy of 94 % were introduced as the best configuration model for COVID-19 diagnosis. ANN is valuable as a decision-support tool for clinicians to improve the COVID-19 diagnosis. It is promising to implement the ANN model to improve the accuracy and speed of the COVID-19 diagnosis for timely screening, treatment, and careful monitoring. Further studies are warranted for verifying and improving the current ANN model.

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Keywords: Coronavirus disease 2019 (COVID-19); Artificial neural network; Intelligent system

Introduction

New emerging pathogens are serious threats for the worldwide public health. This is mainly true for virus-originated illnesses that are highly transmissible due to extensive human-to-human spread and have symptomless contagion periods (1,2). In December 2019, a novel strand of Coronavirus termed SARS-CoV-2 (COVID-19) emerged in Wuhan Region, China, and still remains to scatter violently global. The multifaceted and highly infectious nature of COVID-19 had led World Health Organization (WHO) to declare this epidemic a public health emergency (3,4). Despite severe protective measures and lockdown strategies, COVID-19 has now become a global pandemic, causing a tremendous influence on the wellbeing and safety of populations all over the world, affecting their lives and causing an escalating number of losses. There are also other induced dangerous conditions as secondary influences of this epidemic, such as mental distress economic catastrophes that might lead to severe challenges and threats in many societies (5-8).

Rapid transmission and high-rate death, mostly in vulnerable people such as the aged persons and those who have underlying diseases, require pursuing early identification and separation of the infected persons as

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quickly and accurately as possible to limit the spread of the infection, particularly for individuals with no sign or symptom in the early stage (9-14). These susceptibilities highlight the need for timely and reliable diagnosis techniques for COVID-19 and rapidly quarantining the infected individuals in the absence of a licensed vaccine or drug (15,16). In this critical situation, many countries and health policymakers around the world are looking for new and advanced technologies as alternative solutions for screening, monitoring and tracking infected people.

Artificial intelligence (AI) may be a unique way for tackling this major challenge (17,18). It is a wide field that refers to a machine's ability to learn from previous experiences, adjust to new inputs and mimic human astuteness behaviors (19). Machine learning (ML) is a subset of AI and can be valuable in extracting high quality prediction models from large datasets (20). ANN is a subset of ML with an adaptive, tutorial and computational structure that mimics the structure and behavior of neurons in the human brain (21,22). This technique can be trained to discriminate and classify intricate patterns of diseases through an iterative learning process. Once proper training is executed, the ANNs can predict with higher accuracy than traditional statistical models. Due to its ability to detect multifaceted nonlinear relations amid predictors and outcomes has been effectively applied in clinical decision support systems (CDSS) (23-27). Thus, the current study aimed to establish an intelligent system based on ANN for the diagnosis of COVID-19 by training on a retrospectively collected dataset.

Materials and Methods

Study design

This developmental and applied study aimed to design the CDSS based on the ANN for early COVID-19 prognosis and included four steps as follows:

Dataset delineating and pre-processing

Research deputy of Abadan University of Medical Sciences confirmed this study with the ethical code of IR.ABADANUMS.REC.1400.097. In this work, we used the data of Ayatollah Taleghani Hospital in Khuzestan Province affiliated to Abadan University of Medical Sciences for COVID-19 diagnosis investigation as the research community. After the quantitative analysis of the dataset, we excluded 35 incomplete case records with many missing data (more than 70% lost) from the study. Finally, 400 samples remained (250 and 150 cases related to the positive and negative cases, respectively).

Feature selection

This technique reduced the size of the dataset to facilitate the calculation process and increase the data mining performance. Our study had 40 independent variables that included different qualitative or quantitative criteria for COVID-19 diagnosis. We used the *IBM SPSS Statistics V25*.0 to rank and select the essential attributes. Moreover, we applied the independence Chi-square test to determine the best factors associated with the COVID-19 diagnosis. Finally, to investigate the combined effect of all the crucial variables regarding the two-valued output class in COVID-19 diagnosis, we used binary logistics regression (BLR) along with forward logistic regression (FLR) methods. We obtained the best variables through the IF-term removed table and log-likelihood criteria. In this method, we used one constant with the specified log-likelihood rate in the initial regression model to create the model. By adding a variable in the next steps of creating the model, the rate of the log-likelihood should be reduced. Therefore, that variable can be considered an essential diagnostic criterion in the regression model. In other words, by adding an influential variable in diagnosing COVID-19, concurrently reducing the amount of log-likelihood, the efficiency of the regression model is increased in that situation.

Development of the ANN model

Selecting the ANN characteristics and efficient model is critical for improving model performance. The ANN model used in this research was a standard feed-forward, backpropagation neural network (BPNN) with three inputs, intermediate (hidden) and output layers. The BPNN is a deep learning method in ANN with more than one hidden layer (multi-layered preceptors (MLP)) (28,29). BPNN is the best technique for training in the 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. This supervised data mining technique is the BPNN type to efficiently model disease knowledge and efficiently predict the output classes (30-32).

We entered all the data into the MLP as a new and the most common design tool for layered feed-forward neural networks (Figure 1). The ANN algorithm based on the MLP has the structure including the input, hidden or calculation and output layers with activation function for connecting each neuron in these layers (33-35). This training algorithm stabilizes the neurons' weights according to the error between the natural and target class features to make a harmonious relationship between the input and output classes by the nonlinear connection between neurons (36). Furthermore, the Levenberg-Marquardt (LM) was used in this research because of its popularity in error reduction and increasing the efficiency in the calculation process (37). The MLP activation function (tansig function) implemented in MATLAB 2013a was used in this study as an ANN activation method and customized user interface (UI) (32).

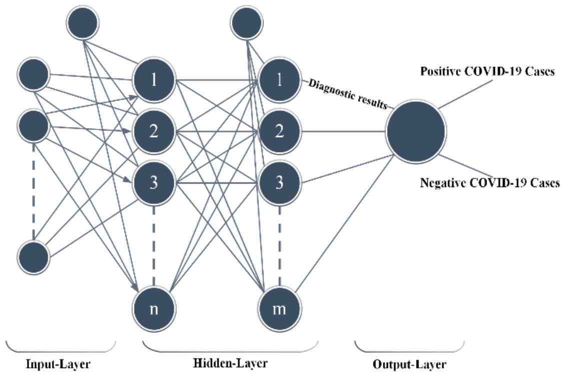

Figure 1. MLP network

Adjusting artificial neural network parameters

The MLP activation *function* (tansig) was implemented in Visual Studio-2018 software to generate the best diagnosis output. In this study, we used different configurations of ANNs by different hidden layers. The number of neurons existed in them for data processing and performance evaluation by other evaluation criteria to get the best configuration of the ANN. We split the datasets into training and testing and used 70% of the data to train and 30% to test the ANN. Finally, we implemented the best architecture of ANN for COVID-19 diagnosis based on the sensitivity, specificity and accuracy measures.

Developing artificial neural network

We trained different configurations of ANNs on a retrospectively collected dataset by exclusive hidden layers for data processing and performance evaluation by other evaluation criteria. We split the datasets into training and testing and used 70% of the data for training and 30% for testing. Then, we implemented the best architecture of ANN for COVID-19 diagnosis based on the sensitivity, specificity, accuracy and receiver characteristics operator (ROC) measures. Finally, the MLP activation *function* (tansig) was implemented in Visual Studio-2018 software to generate the best diagnosis output for COVID-19.

Results

We presented the results of determining the correlation of the most important diagnostic criteria with the output class (1: positive cases and 0: negative cases) in Table 1. By analyzing the variables using the IBM SPSS Statistics software V25.0 tool and spearman correlation coefficient technique at the level of $P<0.05$, we obtained 18 crucial diagnostic criteria for supporting the COVID-19 diagnosis. In Table 1, we portrayed all the essential variables for COVID-19 diagnosis.

The BLR was performed in nine steps and resulted in essential COVID-19 diagnostic criteria in model IF-term removed using SPSS software V25.0 in the last step (Figure 2).

By evaluating different structures of the ANN using the mentioned performance indicators (Figure 3), we obtained the best configuration of the ANN with 9-10-15-2 (10 and 15 sigmoid nodes used in the first and second hidden layers). In reality, the ANN with two hidden layers with 25 sigmoid nodes was the best structure for COVID-19 diagnosis, as shown in (Figure 4).

We trained the ANN by 24 epochs (repetition); evaluating the ANN performance using the mean squared error (MSE) (Figure 5) demonstrated that in the 18th iteration of the ANN training process, the error rate reached the minuscule amount (0.048297 value for validation performance).

We also evaluated the ANN using the total confusion matrix, including the training, validating and testing modes (Figure 6). We observed that the ANN with sensitivity=96.4%, specificity=90.6% and accuracy=94% in this structure was the best among the configurations.

The ROC of the selected ANN is demonstrated in (Figure 7) (the vertical and horizontal vertices are true positive rate (TPR) and the false positive rate (FPR), respectively). It could be found this ANN classification was closer to the true positive rate (TPR) than the false positive rate (FPR); so, the ANN had the common capability for classifying the positive and negative cases. This curve was also the best in performance than other ANN configurations (ROC of 98.2%).

We developed the clinical decision support system user interface (CDSSUI) for COVID-19 diagnosis by Visual Studio-2018 software (Figure 8). The CDSS users, such as physicians, can feed the CDSS using the information of Suspicious COVID-19 people information and the system would suggest the best diagnostic results about the COVID-19 disease.

Table 1. The critical diagnostic criteria at the P level

No	Input Variable	Variable type	Variable content	Correlation coefficient	Significant difference
1	**Respiratory rate**	Numeric		0.245	<0.01
2	**Body temperature**	Numeric		0.554	<0.01
3	**oxygen saturation in the blood rate (SPO_2)**	Numeric		0.327	<0.01
4	**Shortness of breathing**	Nominal	Haven't Have	0.198	<0.01
5	**Fever**	Nominal	Haven't Have	0.545	0.01
6	**Cough**	Nominal	Haven't Have	0.621	<0.01
7	**Digestive sign**	Nominal	Haven't Have	0.114	0.02
8	**Chest pain**	Nominal	Haven't Have	0.074	0.02
9	**Weakness**	Nominal	Haven't Have	0.138	<0.01
10	**Contact type**	Nominal	Person - person Contaminated surface –person Water/food consumption Air-breathing Other	-0.579	<0.01
11	**Contact number**	Nominal	Complete Relative	-0.411	<0.01
12	**Contact history**	Nominal	Haven't Have	0.172	0.01
13	**History of respiratory failure**	Nominal	Haven't Have	0.3	0.015
14	**History of taking blocker**	Nominal	Haven't Have	0.130	0.02
15	**History of Pulmonary lesion**	Nominal	Haven't Have	0.6	<0.01
16	**History of infection**	Nominal	Haven't Have	0.146	<0.01
17	**History of travelling**	Nominal	Haven't Have	0.130	0.02
18	**History of tobacco using**	Nominal	Haven't Have	0.110	0.01

Model if Term Removed

Variable		Model Log Likelihood	Change in -2 Log Likelihood	df	Sig. of the Change
Step 9	Tobbaco using	-7.265	4.337	1	.037
	Pulmonary-Lesion	-15.466	20.739	1	.000
	ARDS	-5.333	.473	1	.492
	Contact-Number	-6.704	3.216	1	.073
	Contact-Type	-13.075	15.957	1	.000
	Cough	-5.687	1.181	1	.277
	Fever	-11.598	13.003	1	.000
	Dyspnea	-5.806	1.420	1	.233
	Digestive-Sign	-6.421	2.650	1	.104

Figure 2. Final diagnostic criteria analyzed by BLR

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

Figure 3. Comparing different ANN configuration performance

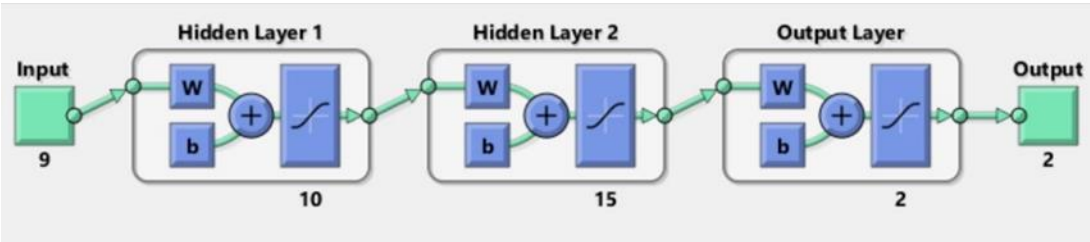

Figure 4. Final ANN architecture used for COVID-19 diagnosis

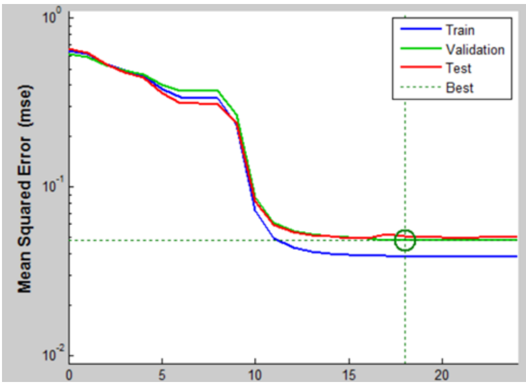

Figure 5. ANN's MSE for error rate evaluation

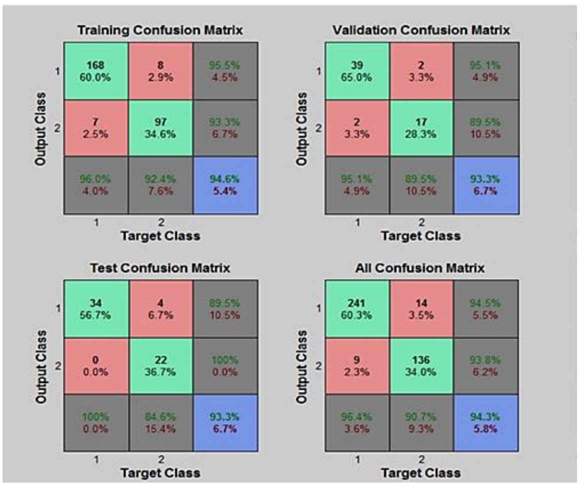

Figure 6. ANN's confusion matrix

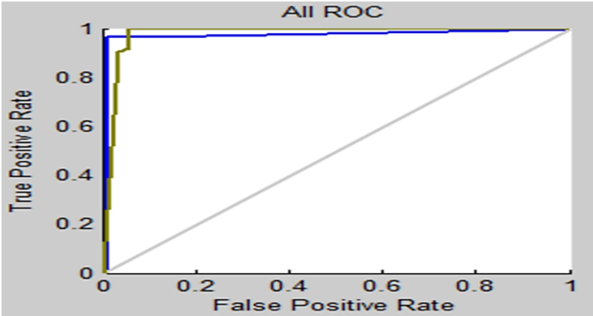

Figure 7. ROC of ANN for COVID-19 diagnosis

Figure 8. The CDSSUI is based on Visual Studio 2018 for COVID-19 diagnosis

Discussion

High risk of being contagious, ambiguous features, the unknown nature, long incubation period, rapid deterioration, financial constraints and limited resources to performing COVID tests make COVID-19 a serious public health problem that has captured intense consideration globally (33). In these circumstances, timely and reliable diagnosis can inform health policy-makers and clinicians with a better plan to lessen disease spread and increase patients' survival likelihood. For this purpose, it is crucial to build an intelligent model for COVID-19 diagnosis (20,34). Our study aims to develop an intelligent decision support system for detecting COVID-19 using the ANN method. The ANN model has strong error tolerance; so, it can be widely applied in prediction and analysis tasks (35). Moreover, DSS-based ANN may help caregivers to make better decisions about COVID-19. Although standard statistical approaches (e.g., logistic regression) need different modeling processes, the ANN technique does not require distributional assumptions (36).

Several studies have focused on applying and evaluating ANN techniques in COVID-19 early prognosis, risk assessment and trend estimation. Betancur *et al*., (2021) compared thirty-two ANN architectures for COVID-19 diagnosis. In their study, the Resnext101_32x8d configuration with the sensitivity, specificity, F1-score, G_mean, IBA and training time of 97.75%, 96.40%, 97.75%, 97.06%, 94.34% and 76.98, respectively, gained the best performance than others (37). Similarly, in Kiri¸sci’s (2021) study, the efficiency of several back propagation ANN techniques including conjugate gradient, Levenberg Marquardt and Bayesian regularization neural networks were compared for the COVID-19 prognosis. It is concluded that the Bayesian regularization model gained the highest accuracy (>90%) (38). Goel *et al*., (2021) compared the performance of the selected ANN models for the automatic detection of COVID-19. Finally, the best performance was yielded by the CNN algorithm with the accuracy of 97.78%, sensitivity of 97.75%, specificity of 96.25%, precision of 92.88% and F1 score values of 95.25% (39). Accordingly, Lad *et al*. (2020) compared the predictive performance of the selected ANN architectures, including sequential bi-layered CNN, VGG-16 CNN and MobileNetV2 CNN architectures, for the COVID-19 diagnosis. Finally, the best meaningful results were observed from MobileNetV2 with 99.2% accuracy (40). Lessage *et al*., (2022) assessed the performance of the selected ANN architecture in the COVID-19 diagnosis. Eventually, the MobileNet architecture provided the highest performance with 99.3% accuracy and 99.3% sensitivity (40). Biradar *et al*., (2020) displayed ResNet architecture with the accuracy of 93.2% was outperforming ANN architecture in the COVID-19 diagnose and detection (41).

Our study suggested that the ANN model could correctly detect the COVID-19 cases using readily available parameters. For this purpose, the data were standardized and, then, used as inputs for the ANNs. Later, classification was carried out and the models' performance was measured. The key findings of our study were, first, identifying the most clinical features using logistic regression that provided insights about the diagnostic process used by current clinical practice and, then, promising performance levels with the ROC of 98.2%. We identified 18 significant predictors (see Table 1) in the first step, independently related to COVID-19. However, sensitivity, specificity and accuracy were 0.964%, 0.906% and 0.94%, respectively.

Limitations

There are several limitations necessary to be addressed. First, we obtained the data from a single hospital that bounds the external validity generalization of the results. Thus, upcoming multi-central datasets and external validation will increase the model performance. Second, we only used information of 400 patients to train the model. It is considered a small sample size and chances of an overfitting problem. To overcome these limitations and generate more strong results, we recommend multi-center partnerships to increase the power of such studies.

Future Implications

In the future, a web-based risk assessment tool will be available for use in the clinic, which will be straightforward for clinicians to use and which will be powered by a neural-network-based algorithm. We expect this method to be applied to other fields of medicine, enabling the synthesis of complex information about patients and leading to the development of individualized risk profiles.

We developed and validated a multi-parameterized ANN for COVID-19 risk prediction based merely on patient history and exposure parameters commonly available in the patients' medical records. Our results revealed that ANN could provide high specificity and good sensitivity for the COVID-19 diagnosis. The results also revealed that ANN could accurately distinguish COVID-19 from other atypical and respiratory pneumonia diseases. The ANN is a cheap, non-invasive and easy to implement method. While our developed model could potentially be used as a clinical tool for COVID-19 risk classification, its performance can be enhanced using more risk factors and more clinical testing. This study could develop other health domains to aid the healthcare system respond more successfully in the current and future epidemics.

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