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AN INNOVATIVE REGRESSION-BASED METHOD FOR COVID-19 DETECTION: ENHANCING DIAGNOSTIC PRECISION THROUGH CONTINUOUS PREDICTION

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The emergence of the COVID-19 pandemic has underscored the critical importance of accurate and reliable methods for the early detection and management of cases. Traditional approaches to COVID-19 diagnosis often rely on binary classification methods, which may limit their accuracy and robustness. In this study, we propose a novel approach that leverages chest radiography images for predicting COVID-19 cases. By reframing the classification task as a regression problem, we aim to enhance the accuracy and reliability of our predictive model.

Our method involves several key steps. Firstly, we collected a dataset of chest radiography images from confirmed COVID-19 cases and non-COVID-19 cases. Next, we preprocessed the images and extracted relevant features using advanced image processing techniques. We then framed the prediction task as a regression problem, allowing us to model the continuous variation in disease severity rather than relying on binary classification. The predictive model was trained using machine learning algorithms, and both internal and external validation were performed to assess its performance.

Our method involves converting the classification task into a regression task, which enables improved accuracy and robustness in the model. We performed both internal and external validation, with R^2 train = 0.91, CV-MSE = 0.0253, and Q^2_{cv} = 0.91, indicating high accuracy and reliability in predicting COVID-19 cases. Additionally, we conducted an applicability domain analysis, which showed that 99% of unseen data can be accurately predicted by our model.

Our findings suggest that our method can be a valuable tool in the early detection and management of COVID-19 cases, which can ultimately improve patient outcomes and public health. Further validation and testing in real-world clinical settings are needed to confirm the effectiveness and generalizability of our approach.

Keywords: COVID-19, image processing, feature extraction, image classification, machine learning, deep learning, prediction

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INTRODUCTION

The COVID-19 pandemic has impacted countless individuals worldwide and remains a significant public health concern. A crucial aspect of controlling the spread of the disease is identifying infected individuals quickly and accurately. Chest radiography has become a useful tool in detecting COVID-19 because it can reveal unique features of the disease (1). There are various experimental methods for COVID detection, including PCR, antigen tests, and antibody tests. Although these methods have been useful in detecting and diagnosing COVID-19, they have limitations and challenges. PCR tests are widely used to detect the virus, but they require specialized equipment and trained personnel and can have issues with accuracy (2). Antigen tests are faster and less expensive but may not detect all cases of the disease (3). Antibody tests are helpful in determining past infections but not suitable for diagnosing current ones (4). In silico methods, which involve computer simulations and modeling, have the potential to overcome some of these limitations. For example, they can identify potential drug targets for COVID-19 and predict the effectiveness of the existing drugs. In silico methods can also be used for COVID-19 diagnosis, such as using machine learning algorithms to analyze chest X-rays for the signs of the disease. These approaches are faster and less expensive than traditional PCR tests and could be used for mass screening. While traditional experimental methods are valuable in fighting COVID-19, in silico methods can complement or even replace some of these methods. They offer benefits in terms of speed, cost, and accuracy, and could improve diagnosis and screening and lead to the development of new treatments (5).

Numerous studies have reported high accuracy rates in detecting COVID-19 using in silico-based approaches. For instance, Narayan Das and colleagues developed an automated deep transfer learning-based approach that used the Xception model to detect COVID-19 infection in chest X-rays, achieving a sensitivity of 0.974% and specificity of 0.972% (6). Similarly, Wang and team trained the convolutional neural network (CNN) on a dataset of 13,975 chest radiographs, obtaining a sensitivity of 98.9% for COVID-19 detection (7). Another study by Nasiri et al. employed the deep neural network (DNN) DenseNet169 to extract features from X-ray images of patients' chests, which were then fed to the XGBoost algorithm for classification, yielding 98.23% and 89.70% accuracy (5). Moreover, Hemdan et al. employed the COVIDX-Net network to classify chest radiographs as either COVID-19 positive or negative, achieving an accuracy of 91% (8). Hou et al. developed a diagnosis platform using a DCNN that could assist radiologists in distinguishing COVID-19 pneumonia from non-COVID-19 pneumonia with above 96% accuracy (9). Gao et al. created a deep CNN-based chest X-ray classifier that could detect abnormalities and extract textural features of the altered lung parenchyma related to specific COVID-19 signatures, with an accuracy of 91% (10).

Furthermore, Alqahtani et al. proposed a COV-Net model to learn COVID-specific patterns from chest X-rays, which attained high accuracy (99.23%) in multi-class and binary classification of COVID-19 and pneumonia (11). Carlile and colleagues deployed a previously validated deep-learning AI algorithm for assisted interpretation of chest radiographs, which was easy to use and influenced clinical decision-making for 20% of the respondents (12).

Farooq and Hafeez presented a multi-stage fine-tuning scheme for pre-trained ResNet-50 architecture named COVIDResNet, achieving an accuracy of 96.23% (13). Similarly, Abbas et al. developed the DeTrac CNN model to distinguish COVID-19 symptoms using chest X-rays, reaching 95.12% accuracy and 97.91% sensitivity (14).

Convolutional neural networks (CNNs) have shown potential in identifying COVID-19 in chest radiography images by recognizing unique disease features through convolutional and pooling layers (15). In this study, we applied CNN to extract features from COVID-19 X-ray images, which were then fed to a feedforward neural network for binary regression. A value of one indicated a positive COVID-19 case, and a value of zero denoted a healthy X-ray chest radiography. We trained and tested the model on a COVID-19 X-ray image dataset, obtaining high accuracy in detecting COVID-19 cases. This approach offers the benefits of leveraging the powerful feature extraction capabilities of CNNs while using the flexibility and interpretability of feedforward neural networks, showing promise in improving the accuracy and speed of COVID-19 diagnosis from chest radiography images. The main objective of this research is to investigate the feasibility of framing COVID-19 detection as a regression problem by combining CNN-based feature extraction with a feedforward neural network, thereby enabling a more flexible and interpretable diagnostic output than traditional classification approaches.

METHODS

Our approach comprised several crucial steps, which are depicted in Figure 1. To begin with, we procured a dataset of chest x-ray images from a Kaggle database (16). Subsequently, we fine-tuned a pre-existing AlexNet model to extract pertinent features from the images in the dataset. We then utilized these extracted features as inputs to a feedforward network, which we trained to predict the probability of a patient having COVID-19. For this purpose, we set the output of the feedforward network to 0 for negative COVID-19 images and 1 for positive COVID-19 images. Finally, we evaluated the accuracy and effectiveness of our model by analyzing its results.

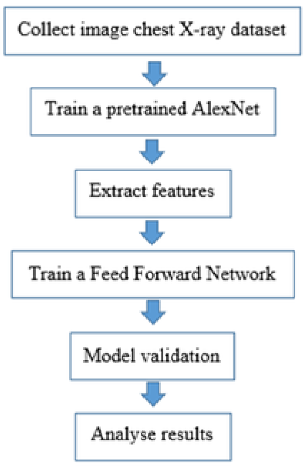

Figure 1. *Flowchart of the method used in the study*

Collection of chest X-ray dataset

In this scientific research, we collected a dataset of 1,000 chest radiography images related to COVID-19. The dataset was obtained from the Kaggle database (16) and contained 500 images of positive COVID-19 cases and 500 images of negative COVID-19 cases. The images were reviewed by a team of experienced radiologists to ensure their accuracy and authenticity. Our dataset of COVID-19 chest radiography images provides a valuable resource for researchers in the development of artificial intelligence-based tools for the early detection of COVID-19. The availability of such datasets is essential for training robust models and enabling their reliable deployment in clinical settings.

Feature extraction

In this research paper, we used transfer learning to extract features from COVID-19 chest radiography images. Specifically, we utilize the AlexNet deep learning architecture, pre-trained on the ImageNet dataset, to extract relevant features from our COVID-19 chest radiography dataset. Transfer learning is a powerful technique that allows us to leverage the knowledge learned from a source domain (e.g., ImageNet) to improve performance in a target domain (e.g., COVID-19 chest radiography) (17). In our experiments, we fine-tuned the last six layers of AlexNet with new ones designed for our target task. Table 1 summarizes the list of the new layers. We also set the dimension of the extracted features to be ten, which was chosen based on a trade-off between model complexity and performance.

Training a Feed Forward Network

To predict the likelihood of COVID-19 infection, we utilized a feed-forward neural network that took the extracted features as input. To enable a continuous output, we transformed the classification task into a regression task by setting a value of one for a positive COVID-19 chest radiography and zero for a negative COVID-19 chest radiography in the output layer of the network. This approach provided a more nuanced understanding of the relationship between input and output variables. Changing a classification problem to a regression problem in a neural network has several benefits, including continuous output that is useful when the target variable has a natural ordering or is a continuous variable. Moreover, regression models can be more effective in some cases than classification models as they are more sensitive to the magnitude of the errors and can be more robust to imbalanced or noisy data. By converting a classification problem to a regression problem, we were able to use a wide range of regression techniques and architectures, which provided greater flexibility and customization of the model. In addition, regression problems allow the use of a wider range of loss functions such as mean squared error or mean absolute error, which can be more effective for some types of problems than the cross-entropy loss function typically used in classification problems. Finally, regression models are often more effective at generalizing to new data than classification models, as they can capture the underlying structure of the data rather than simply classifying it into discrete categories (18). We designed

Table 1. *The twenty layers of our ALEXNET transfer learning architecture*

N	Abbreviation	Layer's name	Properties
1	'data'	Input	227x227x3 matrices with 'zero center' normalization
2	'conv1'	Convolution	96 11x11x3 convolutions with stride [4 4] and padding [0 0 0 0]
3	'relu1'	ReLU	ReLU
4	'norm1'	Cross channel normalization	cross channel normalization with 5 channels per element
5	'pool1'	Max pooling	3x3 max pooling with stride [2 2] and padding [0 0 0 0]
6	'conv2'	Grouped convolution	Two groups of 128 5x5x48 convolutions with stride [1 1] and padding [2 2 2 2]
7	'relu2'	ReLU	ReLU
8	'norm2'	Cross channel normalization	cross channel normalization with 5 channels per element
9	'pool2'	Max pooling	3x3 max pooling with stride [2 2] and padding [0 0 0 0]
10	'conv3'	Convolution	384 3x3x256 convolutions with stride [1 1] and padding [1 1 1 1]
11	'relu3'	ReLU	ReLU
12	'conv4'	Grouped convolution	Two groups of 192 3x3x192 convolutions with stride [1 1] and padding [1 1 1 1]
13	'relu4'	ReLU	ReLU
14	'conv5	Grouped convolution	Two groups of 128 3x3x192 convolutions with stride [1 1] and padding [1 1 1 1]
15	'relu5'	ReLU	ReLU
16	'pool5'	Max pooling	3x3 max pooling with stride [2 2] and padding [0 0 0 0]
17	'fc6'	Fully connected	4096 fully connected layer
18	'relu6'	ReLU	ReLU
19	'drop6'	Dropout	50% dropout
20	'fc7'	Fully connected	10 fully connected layer

a Feedforward Neural Network (FFNN) with multiple hidden layers and trained it using the backpropagation algorithm with gradient descent and momentum optimization. The network was trained on a dataset of 1,000 chest radiography images, of which 70% were randomly selected for training. To assess model performance during training, we used 5-fold cross-validation, a form of internal validation where the training data is split into five parts: four used for training and one for validation, iteratively. In addition to this, we reserved 15% of the entire dataset as an external validation set, a separate subset not used during training or cross-validation, to evaluate the model's generalization ability on unseen data. The remaining 15% was allocated for assessing the model's applicability domain, helping to define the boundaries within which the model's predictions can be considered reliable.

Choosing a size of 10 for the fully connected layer of the CNN can have several benefits (19):

1. It can help reduce overfitting: By reducing the number of parameters, we are simplifying the model and making it less prone to overfitting on the training data.
2. It can make training faster: With fewer parameters, the model will require less computation during training, which can speed up the training process.
3. It can improve generalization: By compressing the feature representation, we may be removing some noise and irrelevant information from the input, which can improve the model's ability to generalize to new, unseen data.

Determining the optimal number of hidden neurons in a modeling task is a challenging task with no clear answer. To address this issue, we followed the approach outlined by Khaouane et al. in their study to determine the appropriate number of neurons in the hidden layer. This approach has been detailed in various reviews and is widely used in the literature (20).

The mathematical equation of the model for the prediction of COVID-19 cases is shown below.

Model validation

Validation of models is a critical step in ensuring their reliability and accuracy in predicting new COVID-19 cases. The performance of the model on an independent set is evaluated using the best model, based on its performance on the cross-validation folds. The external set must be independent of the dataset used for training and cross-validation, ensuring that the evaluation is unbiased and represents the model's true performance on new data.

$$f = \sum_{j=1}^{k} w2j \left(\frac{exp\,(\sum_{i=1}^{p} xi + wij + bj) - exp\,(-\sum_{i=1}^{p} xi + wij + bj)}{exp\,(\sum_{i=1}^{p} xi + wij + bj) + exp\,(-\sum_{i=1}^{p} xi + wij + bj)} \right) + b \qquad (1)$$

x i (I = 1…p) represents the input corresponding to the number of data included in the training of the FFNN, where i ranges from 1 to 10, wij (i = 1…p, j = 1…k) are the weights connecting the input to hidden layer, b j (j= 1…k) are the biases of the neurons in the hidden layer, w2j (j = 1…k) are the weights connecting the hidden layer to the output layer, b is the bias of the output neuron, and f is the output.

Analogous to QSAR models, our model uses both internal and external parameters to assess performance. Internal parameters such as correlation coefficient (R), determination coefficient (Q2), and mean square error (MSE) measure the accuracy of the model's predictions on the data used for model building. External parameters such as Tropsha parameters assess the model's ability to predict the COVID-19 cases of new chest x-ray images not included in the original dataset. Therefore, combining internal and external parameters is essential to validate models and ensure their reliability in predicting COVID detection from new chest radiography images (21).

Table 2. *Selected criteria of the obtained different feed-forward neural networks*

Number of hidden neurons	train R^2	Q^2_{cv}	CV- MSE
1	0.91	0.91	0.025
3	0.88	0.92	0.029
5	0.91	0.91	0.029
7	0.91	0.88	0.035
10	0.88	0.86	0.034
13	0.88	0.92	0.034
15	0.86	0.91	0.038
17	0.88	0.88	0.041
20	0.88	0.88	0.037

RESULTS

The suitability of the 10 structural features generated with CNN for the modeling task was determined based on their correlation coefficient R. The results indicated an acceptable level of multicol-linearity, with an absolute value of R below 0.75 (20). A heatmap (Figure 2) was created to provide a more comprehensive view of the correlation structure among the features. To specify the number of hidden neurons required, the procedure detailed above was followed. Using multiple evaluation criteria can help ensure that the chosen model is accurate. R^2train, Q^2_{cv}, and CV-MSE criteria were employed for the evaluation of the accuracy of

The mathematical equation of the model for the prediction of COVID-19 cases is shown below:

$$R = \frac{\sum_{i=1}^{n}(\hat{y}_i - \bar{\hat{y}}_i)(y_i - \bar{y})}{\sqrt{\sum_{i=1}^{n}(\hat{y}_i - \bar{\hat{y}}_i)^2 \sum_{i=1}^{n}(y_i - \bar{y})^2}} \qquad (2)$$

$$R^2 = 1 - \frac{\sum_{i=1}^{n}(y_i - \hat{y})^2}{\sum_{i=1}^{n}(y_i - \bar{y})^2} \qquad (3)$$

$$Q^2_{cv} = 1 - \frac{\sum_{i=1}^{n}(y_{exp(app)} - \hat{y}_{app})^2}{\sum_{i=1}^{n}(y_{exp(app)} - \bar{y}_{app})^2} \qquad (4)$$

$$MSE = \sum_{i=1}^{n} \frac{(\hat{y}_i - y_i)^2}{n} \qquad (5)$$

$$CV - MSE = (1/5)\sum_{i=1}^{5} MSE \qquad (6)$$

$$(r^2 - r_0^2) < 0.3 \qquad (7)$$

$$(r^2 - r_0^2)/r^2 < 0.1 \qquad (8)$$

$$0.85 < k < 1.15 \qquad (9)$$

$$(r^2 - r'^2_0)/r^2 < 0.1 \qquad (10)$$

$$0.85 < k' < 1.15 \qquad (11)$$

R_0^2 and r_0^2 are the squared correlation coefficients between the observed and predicted values with and without intercept, respectively. The parameter r'^2_0 has the same meaning but uses the reversed axes.

the best model. Table 2 shows 09 network models developed and evaluated using R^2 train, Q^2_{cv}, and CV- MSE criteria. The best model was chosen based on the maximum R^2 train = 0.91, Q^2_{cv} = 0.91, and the minimum CV-MSE = 0.025. The best performance of the model had a topology of 10-[1]-1, with 10 input nodes, one hidden layer with 01 node using the hyperbolic tangent as a transfer function, and one output layer with an identity transfer function. The neural networks were implemented using a MATLAB program developed by the team. Figure 3 depicts the comparison between the true and predicted COVID x-ray chest radiography images indicating the presence of infection or not for both the training and testing sets of the best fold. The results demonstrate a significant level of correlation between the predicted and original infection or not COVID x-ray chest radiography images, affirming the model's accuracy in detecting the presence of COVID.

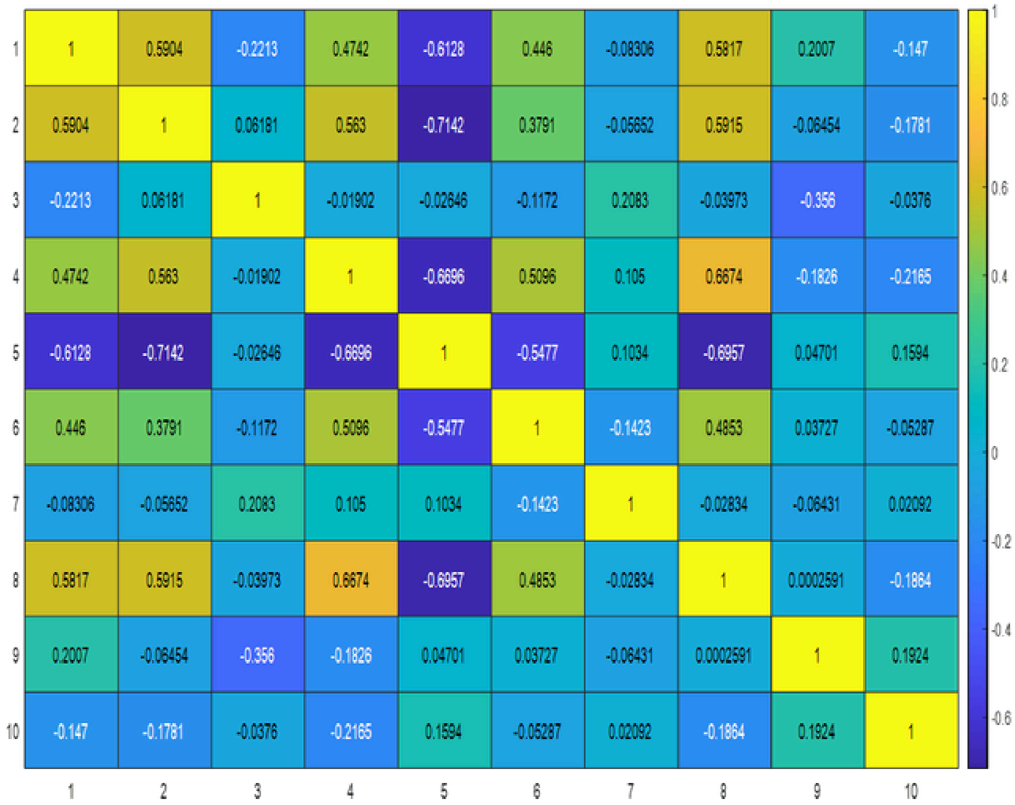

Figure 2. *Heatmap of the 10 structural features generated with CNN*

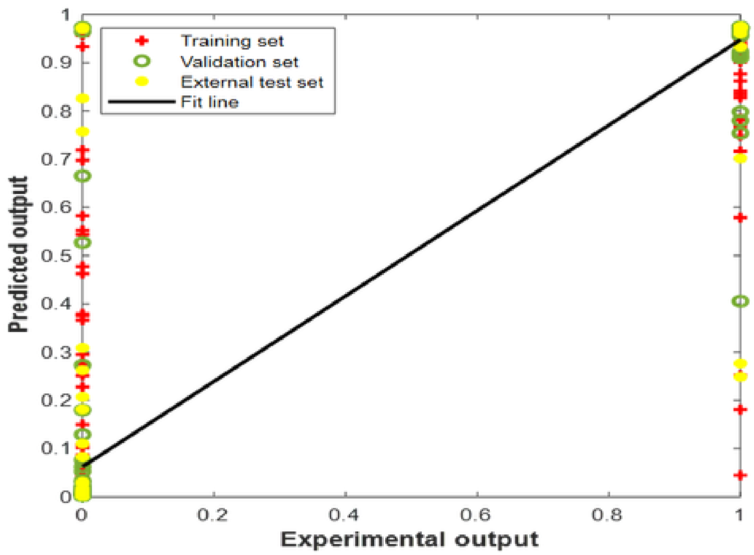

Figure 3. *Comparison between the true and predicted COVID x-ray chest radiography images indicating the presence of infection or not for training, validation, and external testing sets using the best fold.*

Table 3. *External and internal validation criteria*

Internal validation criteria for the best fold		
R	0.95164	
$trainR^2$	0.91	> 0.6
Q^2_{cv}	0.91	> 0.5
$CV\text{-} MSE$	0.0253	
External validation criteria for the best fold		
R	0.93596	
Q^2	0.88	> 0.6
$r^2 - r_0^2$	0.02	< 0.3
k	0.89	0.85< k<1.15
k'	0.99	0.85< k'< 1.15
$/r^2\ (r^2 - r_0^2)$	-0.02	< 0.1
$/r^2\ (r^2 - r_0'^2)$	-0.1	< 0.1

Validation of the model

The statistical evaluation presented in Table 3 shows that the developed FFNN model has high performance and quality of predictions. The internal validation statistical coefficients, such as R2 train, Q2cv, and CV- MSE are all acceptable and satisfactory, indicating that this model is robust. The model was also evaluated in terms of external validation criteria, and the value of Q2 was found to be greater than 0.6, which is considered excellent. Therefore, the model has excellent predictive power. Furthermore, the difference between R^2 train and Q^2 was found to be equal to 0.03, which did not exceed 0.3. This indicates that the model is robust and not overfitting the training data (20).

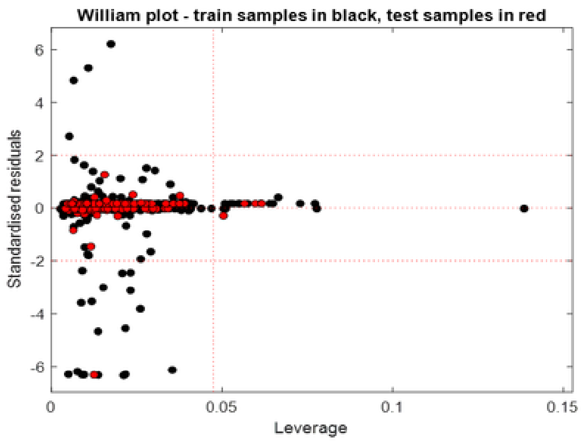

Figure 4. *Plot of residuals for the true and predicted COVID x-ray chest radiography images indicating the presence of infection or not in the training set and applicability domain set*

Applicability domain

When utilizing machine learning models for prediction tasks, it is critical to consider the concept of applicability domain, which determines the range of inputs for which a model can generate accurate predictions. Applying a model beyond its applicability domain may result in unreliable or meaningless predictions. There are various methods for determining the applicability domain of a machine learning model, such as distance-based, leverage-based, and model-based techniques (22).

In this study, we employed a leverage approach, analogous to QSAR models, to analyze the applicability domain. The Williams plot (Figure 4) revealed that one of the test samples was outside the applicability domain, indicating that the model can predict approximately 99% of new, untested chest radiography images related to COVID-19. Our method complies with the third principle of the OECD used in QSAR models, ensuring the robustness and reliability of our findings (23).

Comparison with literature

We have developed a method that aims to enhance the precision and efficiency of COVID-19 diagnosis through chest radiography images. In order to evaluate the effectiveness of our approach, we conducted a comparative analysis with various other methods that have been previously reported in the literature. The findings of our analysis are presented in Table 4, which provides a comprehensive overview of the comparison between our method and the ones reported in the literature. Table 4 illustrates that our method has achieved a commendable accuracy of 91% on the training data, indicating its effectiveness in detecting COVID-19 cases. It is important to note, however, that making direct comparisons between different methods can be challenging due to variations in dataset and data size.

Additionally, our method stands out as it has been validated on three external sets, including a validation set, an external test set, and an applicability domain set, which other methods did not perform. This proves that our model can perform well on a wide range of external datasets, enhancing the reliability of our results. Our novel approach of converting the classification task into a regression task has enabled us to achieve better accuracy and robustness in our model.

Furthermore, our approach has been thoroughly validated both internally and externally, providing empirical evidence of its effectiveness in detecting COVID-19 cases in chest radiographs. Based on our findings, we strongly believe that our approach has the potential to significantly improve the accuracy and reliability of COVID-19 diagnosis through chest radiography.

Table 4. *Comparison of our method with others from literature*

Method	Accuracy
Our method	91 %
Abbas et al. (14)	95.12%
Farooq et al. (13)	96.23 %
Ali Alqahtani et al. (11)	99.23 %
Terry Gao et al. (10)	91 %
Jie Hou et al. (9)	96%
Hemdan et al. (8)	91%

DISCUSSION

In this study, we presented a deep learning approach for COVID-19 chest radiography detection, using the AlexNet deep learning model for feature extraction and a feedforward network for prediction. Our method involves converting the classification task into a regression task, which enables improved accuracy and robustness in the model. We performed both internal and external validation, with R^2 train = 0.91, CV-MSE = 0.0253, and Q^2_{cv} = 0.91, indicating high accuracy and reliability in predicting COVID-19 cases from chest radiography images. Additionally, we conducted an applicability domain analysis, which showed that 99% of unseen data can be accurately predicted by our model. Overall, our study provides promising evidence for the potential of deep learning models in COVID-19 diagnosis through chest radiography, with high accuracy, robustness, and applicability to new data. The use of deep learning models for COVID-19 detection has the potential to significantly improve the speed and accuracy of diagnosis, especially in resource-limited settings where access to medical experts may be limited.

However, it is important to note that our study has some limitations, including the relatively small size of the dataset used in this study. Future studies could benefit from larger datasets to improve the generalizability of our findings. Overall, our study provides promising evidence for the use of deep learning models in COVID-19 diagnosis through chest radiography, and highlights the potential of machine learning in advancing medical diagnosis and treatment.

In terms of practical applications, the strong internal and external validation results suggest that our model could be integrated into clinical decision-support systems to assist radiologists in rapidly screening suspected COVID-19 cases. In settings with limited access to PCR testing or specialized personnel, the model may provide an efficient, lowcost triage tool. Additionally, the regression-based prediction output could offer clinicians an interpretable, continuous score reflecting the likelihood of infection, which may aid in prioritizing patients for further testing or treatment.

In conclusion, our study presents a novel approach for COVID-19 case prediction using chest radiography images. By converting the classification task into a regression task, our method achieved improved accuracy and robustness in the model. Our internal and external validation results demonstrated high accuracy and reliability, with R^2 train = 0.91, CV-MSE = 0.0253, and Q^2_{cv} = 0.91.

Furthermore, the applicability domain analysis indicated that our model can accurately predict 99% of unseen data. Our findings suggest that our method can be a valuable tool in the early detection and management of COVID-19 cases, which can ultimately improve patient outcomes and public health. Future studies can build on our findings and further validate the effectiveness and generalizability of our method in real-world clinical settings.

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Competing Interest

The authors declare no relevant conflicts of interest.

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