



COVID-19 in the Age of Artificial Intelligence: A Comprehensive Review

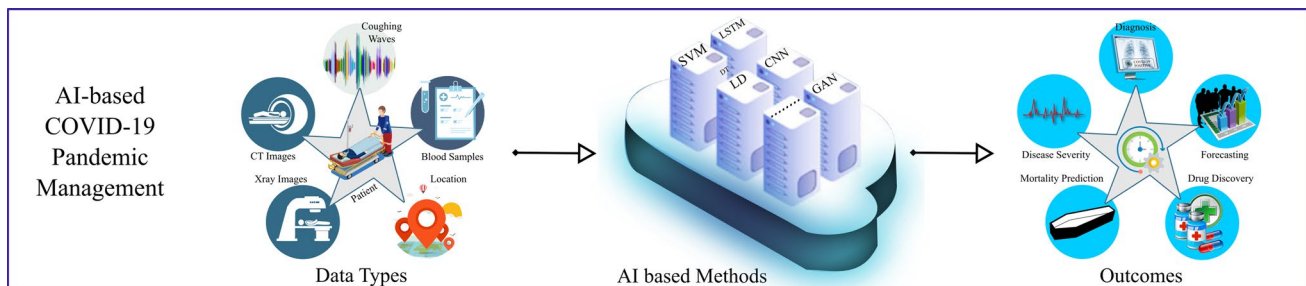
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Abstract

The recent COVID-19 pandemic, which broke at the end of the year 2019 in Wuhan, China, has infected more than 98.52 million people by today (January 23, 2021) with over 2.11 million deaths across the globe. To combat the growing pandemic on urgent basis, there is need to design effective solutions using new techniques that could exploit recent technology, such as machine learning, deep learning, big data, artificial intelligence, Internet of Things, for identification and tracking of COVID-19 cases in near real time. These technologies have offered inexpensive and rapid solution for proper screening, analyzing, prediction and tracking of COVID-19 positive cases. In this paper, a detailed review of the role of AI as a decisive tool for prognosis, analyze, and tracking the COVID-19 cases is performed. We searched various databases including Google Scholar, IEEE Library, Scopus and Web of Science using a combination of different keywords consisting of COVID-19 and AI. We have identified various applications, where AI can help healthcare practitioners in the process of identification and monitoring of COVID-19 cases. A compact summary of the corona virus cases are first highlighted, followed by the application of AI. Finally, we conclude the paper by highlighting new research directions and discuss the research challenges. Even though scientists and researchers have gathered and exchanged sufficient knowledge over last couple of months, but this structured review also examined technological perspectives while encompassing the medical aspect to help the healthcare practitioners, policymakers, decision makers, policymakers, AI scientists and virologists to quell this infectious COVID-19 pandemic outbreak.

Graphic abstract



Keywords COVID-19 · Deep learning · Infectious diseases · Drug discovery · Disease prediction · Machine learning · SARS-CoV-2

Abbreviations

AE Auto-encoders
AI Artificial intelligence
ANFIS Adaptive network-based fuzzy inference system

ANN Artificial neural network
ARIMA Autoregressive integrated moving average
BI-AT-GRU Bidirectional and attentional gated recurrent unit neural network
BI-AT-LSTM Bidirectional and attentional long short-term memory
CNN Convolutional neural networks
CPM-Nets Cross partial multi-view networks

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CRP	C-reactive protein
CT	Computed tomography
CV	Computer vision
CXR	Chest X-rays
DL	Deep learning
DT	Decision trees
DTL	Deep transfer learning
GANs	Generative adversarial networks
GLCM	Gray level co-occurrence matrix
GPU	Graphical processing unit
GRU	Gated recurrent unit
IAVP	Influenza-A viral pneumonia
IoT	Internet of things
KNN	K-nearest neighbor
LD	Linear discriminant
LNR	Linear regression
LSTM	Long short-term memory
LR	Logistic regression
LUS	Lung ultrasound
MAE	Mean absolute error
MAPE	Mean absolute percent error
MCDM	Multi-criteria decision making
MCV	Mean corpuscular volume
MERS-CoV	Middle east respiratory syndrome coronavirus
ML	Machine learning
MLP	Multi-layer perceptron
NPV	Negative predicted value
PCA	Principal component analysis
PDR-NML	Partial derivative regression and non-linear machine learning
PET	Positron emission tomography
PHEIC	Public-health emergency of international concern
PPDLR	Progressive partial derivate linear regression
PPV	Positive predicted value
R-CNN	Region-based convolutional neural networks
RDW	Red cell distribution width
RF	Random forest
RMSE	Root-mean-square error
RNN	Recurrent neural network
RSM	Respiratory stimulated model
RT-PCR	Reverse-transcription polymerase chain reaction
SARS	Severe acute respiratory syndrome
SARS-CoV-2	Severe acute respiratory syndrome—coronavirus 2
SEIR	Susceptible exposed infected recovered
SMILE	Simplified molecule input line entry system
SMOTE	Synthetic minority over-sample technique

SOM	Self-organizing maps
SVM	Support vector machine
TF-IDF	Term frequency–inverse document frequency
VAE	Variational auto-encoder
VGG-X	Visual geometry group
WHO	World Health Organization
XGB	Extreme gradient boosting

1 Introduction

COVID-19 is a highly contagious epidemic disease caused by novel coronavirus (SARS-CoV-2) which has been declared as pandemic by WHO. Researchers across the globe are working round the clock to find solutions and design strategies to control the pandemic and minimize its impact on human health and economy [1]. One of the large family of viruses is called Coronaviruses, which may affect and endanger humans' lives by causing acute ailment [2]. A virus is an infectious microorganism constitutes a specific genome wrapped in a protein layer with the ability to replicate inside living cells. These billions of tiny but powerful viruses, smaller than human cells, can cause viral infection when entered in living creature by hijacking the host cells and forcefully turning those to virus-making factory. This may lead to severe health problems, such as blindness due to smallpox virus or fatal inflammation of the brain or spinal cord by rabies virus [3, 4].

These viruses are either pandemic or epidemic that lasts over a definite duration of time [5]. A pandemic is an occurrence of huge morbidities and mortalities caused by the proliferation of infectious disease at vast geographical area. Contrarily, when a disease is spread in limited region over time [6]. Many epidemics and pandemics occurred over a period, but the mortality rate shows that pandemics had effects that are more devastating in the history of human life. Such as a decade ago, SARS epidemic virus infected around 8096 humans causing deaths of more than 770 humans. Beside such small epidemic, years ago, a famous pandemic known as smallpox affected millions of lives and eventually ended up with 500 million fatalities across the globe [7]. Few of the viruses that caused epidemic and pandemic over last 102 years are depicted in Fig. 1.

The novel Coronavirus is the recent pandemic, officially known as SARS-CoV-2 and member of broader family of infectious viruses, which can affect the respiratory system of humans [8]. In 2002, the first pathogen, SARS emerged in Guangdong (China) that caused mild infection in humans. Another pathogenic member of coronavirus family, known as MERS-CoV, discovered in 2012 around Middle East regions that caused panic due to high infection rate which affected 2494 humans with 858 deaths [9]. Last December

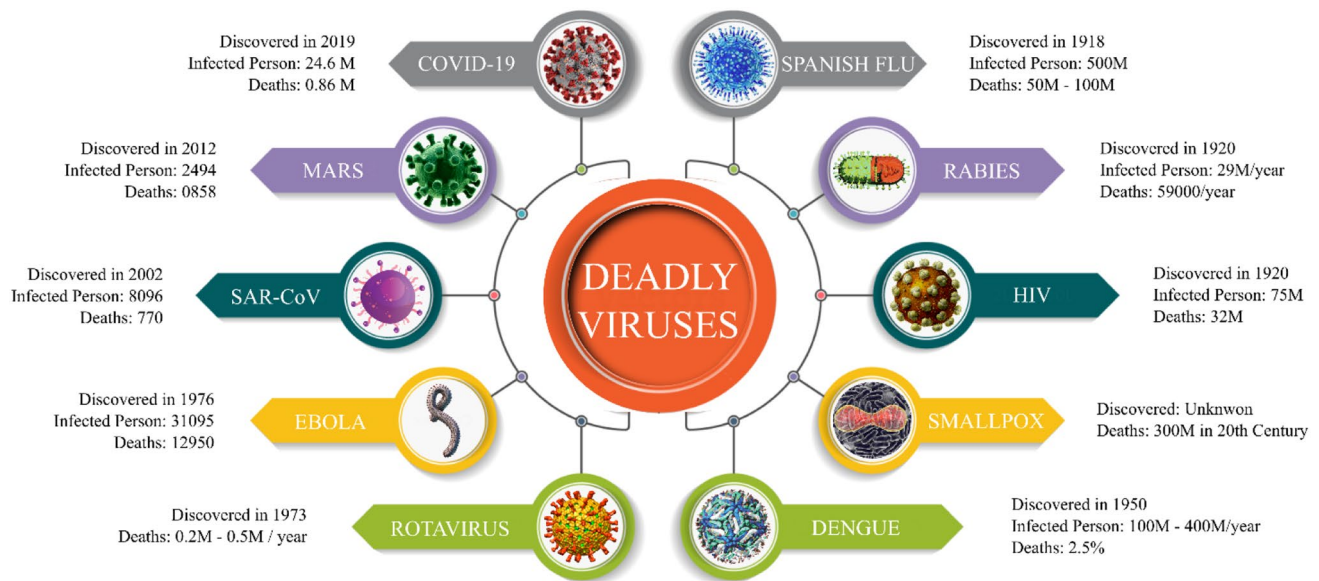


Fig. 1 Deadliest viruses over last 102 years (as of August 28, 2020)

(2019), the deadly COVID-19, the seventh strain of coronavirus, originated in Huanan Seafood Market, Wuhan state of Hubei province, China, that quickly gained global attention due to fast transmission among species and caused respiratory problems [10, 11]. COVID-19 being an infectious disease has high transmission rate among humans as respiratory droplets of infected patient are inhaled by humans around [12]. Tiredness, cough, fever, and loss of smell are considered as most common symptoms, while headache, aches, rash on skin, diarrhea and sore throat are less common symptoms observed in patients affected by COVID-19. Besides these normal looking symptoms, it can cause severe respiratory problems that can damage several human organs, which eventually causes death [13, 14].

On January 30, 2020, due to high horizontal transmission rate among humans of 18 different countries, WHO announced it a PHEIC [15]. Keeping in view the sharp incline of COVID-19 cases around the world in succeeding 2 months, health organizations stated it as global pandemic due to its hazardous effect on human life [16]. Since the first outbreak of highly pathogenic in China, the pandemic has affected 213 countries and territories around the world according to figures compiled by Worldometer [17]. As reported by John Hopkins University this particular virus has infected more than 98,529,820 humans around the globe, while the tally of confirmed deaths is over 2,116,101 [18], thus becoming the greatest pandemic of all time. As per John Hopkins data, a total number of infections and deaths in top 10 disease burden countries are shown in Fig. 2.

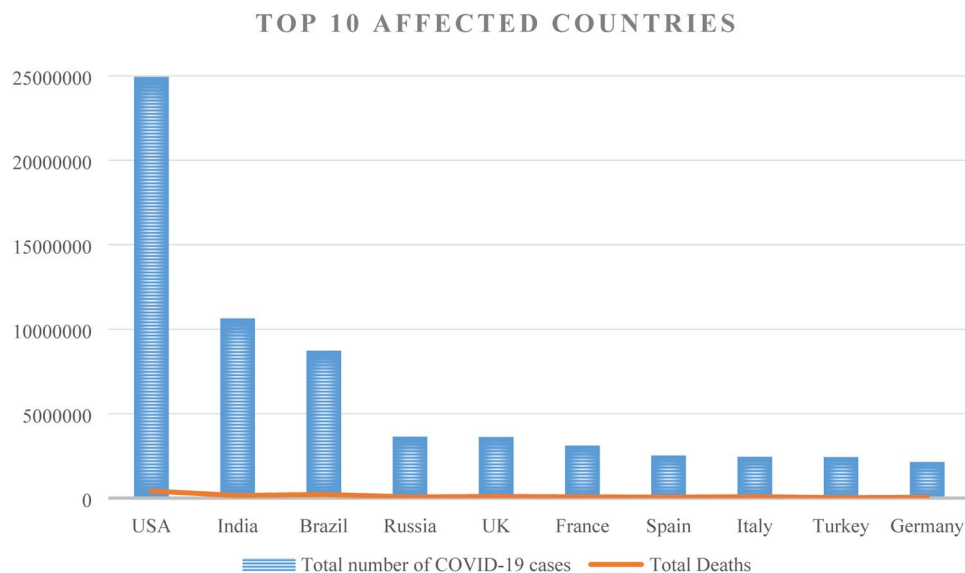
The early identification of COVID-19 cases is momentous as it not only helps start treatment of the cases immediately, but also facilitates containing the virus by isolating

the patient from other humans. Presently, RT-PCR is considered as the established procedure to identify the positive cases of COVID-19. To further speed up the identification operations, there is still room for the advancement of better auxiliary alternative diagnostic tools to enhance the identification and tracking at earliest and start the cure right away [19, 20]. As this deadly pathogen is spreading sustainably, easily, and exponentially among mankind, the healthcare workers and medical staff to quell this are severely limited. Due to this scarcity, radiologists are overwhelmed and in severe need of digital tools to take the workload off them. AI experts have suggested a more feasible solution to keep pace in battling this disease by developing ML and DL techniques. Such systems are founded on predicting and diagnosing pneumonia image modalities and scans of the chest thus aiding physicians.

AI-based techniques have shown promising results for various CV tasks, such as image classification, speech recognition, machine translation, object recognition etc. The recent progress in AI techniques is driven by advent of deeper network architectures, availability of powerful computation platforms and accessibility to large scale benchmark data sets [21]. The DL methods have produced more promising results for various complex CV tasks compared to traditional ML approaches due to their capabilities to learn and represent features automatically. This eliminates the need to manually engineer features based on human expertise and hence obtain higher accuracies for different classification and regression tasks.

Although DL-based methods have been successful in solving various problems, yet they suffer from two main problems: (1) they are extremely difficult to train, and (2)

Fig. 2 Top 10 most affected countries by COVID-19



they require large amount of training data. The first problem is usually solved by implementing and running highly optimal code on powerful GPU-based computers. The later problem can also be alleviated by using data generation techniques, such as GANs. The main objective of GAN is to generate additional data that is similar as much as possible to the original training data. This data along with original data is then used to train the DL networks.

Motivated from CV community, the AI methods have also been adopted for medical image analysis.

In addition to the known established procedure to detect COVID-19-infected humans, there is urgency to develop auxiliary tools that can be exploited for identification and monitoring of positive cases. The availability of CT and CXR images of lungs provide certain characteristics linked with COVID-19 [22, 23]. The DL algorithms, such as CNN, incrementally learn the patterns in such images by passing the input data through a sequence of convolutional layers. Initial layers of the network capture low-level features, such as edges, lines, corners etc. while the later layers derive highly abstract features, which can help to capture the most prominent feature that can distinguish between COVID-19 and other cases.

Practicing AI systems for investigation, prediction and analysis of diseases is long-established. The first-ever adoption of such program was fashioned in 1976 called MYCIN which operated and prescribed antibiotics for a bacterial illness [24]. Many healthcare experts have been employing such methods not only to identify diseases but also for formulating drugs, analyzing medical images collected for clinical trials and pandemic prediction.

Many examples of ML and AI medical tools for diagnosis of non-infectious (diabetic, cancer, Parkinson's, heart diseases etc.) [25–29] and contagious diseases (HIV, Ebola,

SARS, and COVID-19) [30–33] were developed. In a recent series, ML methods have been successfully used for Ebola outbreak estimation. The purpose of obtaining a better outcome was achieved by conducting experiments on ten distinctive classifiers giving accuracy results of approximately 90.95% with 5.39% MAE and 42.41% RMSE value [34].

1.1 Comparisons to Similar Surveys

The COVID-19 pandemic have turned the center of research activities as scientists and researchers are focusing more to mitigate this disease by proposing various methods in AI-based domain. Meanwhile, experts have presented various review and survey articles based on role of AI in COVID-19 to help policy makers and medical practitioners. These peer reviewed published surveys can be categorized into two inculcation; problem-based AI solutions, and AI-frameworks applied on different COVID-19 problems. Such as Pham et al. and Rasheed et al. [35, 36] presented a survey that categorizes the tasks in respond to COVID-19 pandemic by outlining the applications of big data and AI but mostly investigated the papers that have not been peer-reviewed. Moreover, the open research challenges are neither mentioned nor discussed. Similarly, Bansal et al. [37] briefly outlined the role of AI approaches used for identification, prediction and management of COVID-19. However, it did not cover all aspects, such as death rate and severity assessment. In addition, Kumar et al. [38] succinctly generalized the role of DL- and ML-based networks to quell COVID-19 though it did not inspect the papers based on COVID-19 diagnosis through clinical data or respiratory waves. Besides, Lalmuanawma et al. [39] analyzed AI-based applications from various aspects but inspected few papers.

Contrarily, Hussain et al. [40] overviewed basic AI-based frameworks and Big Data applications applied to combat COVID-19. It elaborated various AI classified learning techniques with cursory details of COVID-19 clinical data analysis and results. Similarly, Swapnarekha et al. [41] categorized the review into type of DL, ML and statistical models to quell COVID-19-related issues. The survey covered vast area, from origin of COVID-19 virus to AI-based models, but focused less on comparative analysis of implemented techniques. A very short survey on COVID-19 detection and prediction is presented in Ref. [42] by analyzing work of only 10 articles.

Beside these, Jamshidi et al. [43] only examined the publication based on advanced DL methods, such as GAN, Extreme Learning Machine, RNN and LSTM for COVID-19 diagnosis and treatment. It just presented the implemented models without comparative analysis. Likewise, Shinde et al. [44] delineates statistical and AI-based forecasting models only, whereas Albahri et al. and Ahmad et al. [45, 46] reviewed only ML and data mining techniques for detection of COVID-19. Similarly, Monshi et al. [47] mainly focused on taxonomy of advanced DL-based methods for generating radiology reports. Some articles reviewed only specific type of data set, such as Jalaber et al. [48] set forth with role of CT images to handle COVID-19 suspected patients at large, severity signs and presentation of lesions, and in the end inspected five articles to describe the role of AI for COVID-19 diagnosis. Shaikh et al. [49] investigated AI approaches and landscape of radiographic imaging modalities (CXR, CT and PET) in few articles with limited information about obtained results. Likewise, Dong et al. [50] mainly highlighted CT and PET-CT imaging characteristics presented in different articles and later compared the AI techniques implemented for COVID-19 detection, while Shi et al. [51] accentuated AI approaches to diagnose COVID-19 that segments CXR and CT images. Articles like Refs. [52, 53] discussed the aspects of IoT and biosensors in COVID-19 management.

The study shows that most of above mentioned review articles either focused on single aspect of COVID-19 management or delineated one type of data set. In addition, majority of these surveys presented little comparative analysis and investigated less than fifty articles, which includes high number of papers that have not been peer-reviewed. Our paper mostly covers peer-reviewed articles that presented AI techniques to accomplish tasks, such as COVID-19 diagnosis, prediction, survival assessment and disease prediction, pandemic outbreak forecasting, and drug discovery. Following are the points, which differentiate this study from aforementioned review and survey papers.

- Covers majority of aspects and problems to manage COVID-19 pandemic, such as diagnosis, prediction,

disease severity and survival assessment, outbreak forecasting, protein sequence formation and drug discovery.

- Focuses on both ML- as well DL-based models and frameworks.
- Incorporates all types of data, such as radiographic images (CXR, CT, and ultrasound images), clinical blood samples data, respiratory and coughing waves, time series and other textual data.
- Detail comparative performance analysis of various AI-based techniques implemented to combat COVID-19.
- A comprehensive analysis mostly based on peer-reviewed articles (90% are peer-reviewed published papers).

1.2 Scope and Contribution of the Survey

The primary aim of this comprehensive study revolves around the in-depth analysis of AI-based approaches and models used to quell and combat COVID-19 pandemic by mitigating the virus in various prospects, such as prognosis and diagnosis, drug discovery and molecular structural formation. This review will provide a meaningful and compact knowledge both for medical computer scientist and experts to further broaden the research direction to deal with this deadly virus. The main contributions of this study are as follows:

- The short summary of history, patterns, and characteristics of infectious viruses including COVID-19 are presented.
- AI techniques and tools adopted to mitigate COVID-19 pandemic in various prospects, such as prognosis and diagnosis of SARS-CoV-2 disease, drug discovery and molecular structural formation, are highlighted
- An extensive information regarding approaches to diagnose COVID-19 using radiography images, breathing and coughing wave samples, and clinical blood samples are described in details.
- A comprehensive summary on issues and recommendations to overcome this infectious virus is provided that can timely facilitate effective decision making.
- A detailed discussion on open research challenges regarding COVID-19 is also provided.

The remaining paper is managed as follows. Section 2 focuses on the novel ML and DL techniques that are in practice for diagnosis through various modes. Furthermore, it explores the potential ML- and DL-based tools to predict survival and mortality rate, discover vaccine and forecast the COVID-19 pandemic outbreak. Section 3 presents the issues and recommendation to overcome virus, while Sect. 4 outlines the open research challenges regarding COVID-19 and presents counter-measures to layout a firm groundwork

for further research. Finally, the conclusion to summarize the overview of this review is presented in Sect. 5.

2 AI-Based Applications to Quell COVID-19

The inevitable infectious pandemics are unpredictable and can inflict huge agonies and mortalities across the world. The newly emerged SARS-CoV-2 virus may just be a small capsid but too powerful that requires great efforts and better countermeasures by society to mitigate its negative impact. At the time of this COVID-19-related global emergency, AI researchers had responded the threat by strategically applying various ML and DL techniques in a wide range of applications that not only detect and classify the COVID-19 cases but also forecast the outbreak, tracks the transmission pattern, discovers the effective drugs, predicts the mortality rate and assess the disease's severity.

AI is a wide-ranging scientific area concerned with mimicking human intellectual processes by smart devices. ML is sub-domain of AI that uses statistical models to learn from examples (also known as instances) in data to predict future outcomes without prior knowledge and explicit programming [54]. Whereas, DL is the most tangible manifestation of ML that exploits artificial neural networks for classification or detection task by discovering useful representations from raw data within the predefined space of possibilities. As COVID-19 pandemic is under the spotlight in medical research and AI-based technologies are one of panacea, this section encompasses various novel applications established on ML and DL methods to combat ongoing SARS-Cov-2 pandemic crisis. Figure 3 unfolds the general approach used

to incorporate AI techniques that requires clinical blood samples and radiography images for identification, classification and diagnosis of COVID-19. Various repository are built to store and share data sets regarding COVID-19. Later on, besides data mining, various pre-processing techniques, such as noise removal, data cleaning, feature extraction, segmentation and feature analysis, are mostly employed to enhance the data set and transform it to more meaningful and effective representation. Finally, AI-based techniques and tools are defined to utilize the data sets for COVID-19 segregate COVID-19 affected patients from others.

2.1 Radiography Image-Based COVID-19 Diagnostic Tools

Saving precious lives is the topmost priority in emergencies, but that requires early detection of disease. The outbreak of this pandemic created a new landscape and requirements of rapid diagnostic tools for early disease detection. Early ailment detection leads to immediate treatment, which can save many lives and helps in halting the pandemic spread. The standard RT-PCR technique limits the early detection of COVID-19 due to low sensitivity and high procedural and experimental time. Contrarily, AI-based health care systems provide outstanding support for efficient screening, early identification and fast diagnosis by analyzing Clinical blood sample data and radiology images, such as CT and CXR, thus providing a sigh of relief for radiologists.

Researchers and scientists effectively adopted several ML approaches and techniques to curb the COVID-19 ailment, such as Sethy et al. [55], developed automatic tool that predicts COVID-19 infection in CXR images by employing

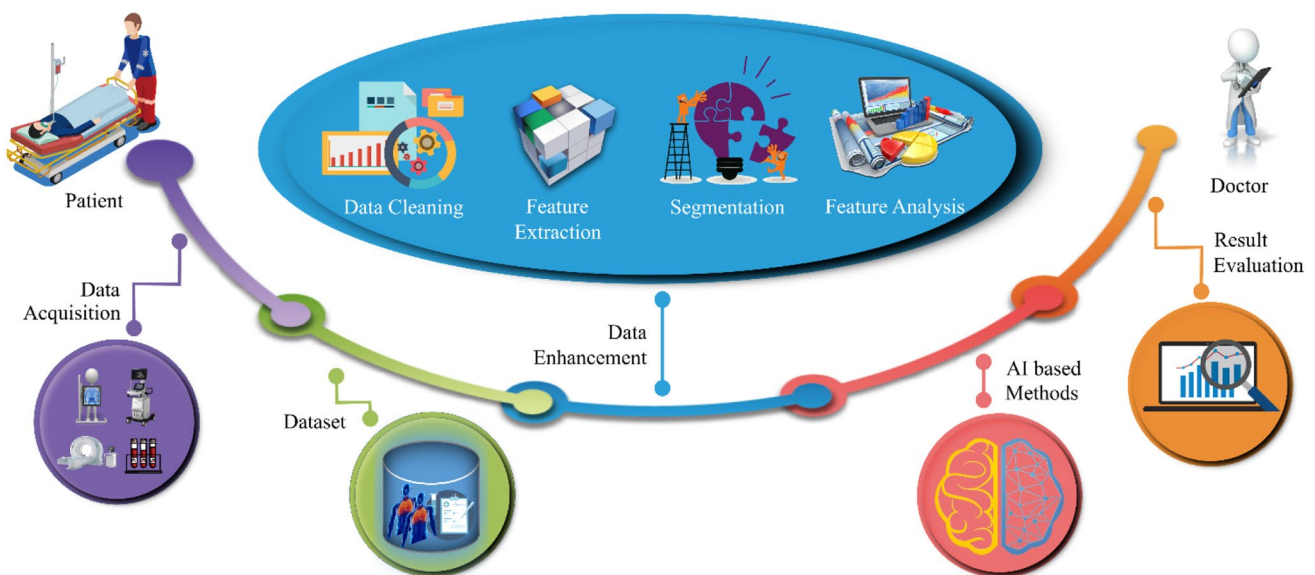


Fig. 3 Illustration of computer vision and AI based model for COVID-19 diagnosis and prediction

SVM. To segregate the patients affected by COVID-19 among normal and other pneumonia affected patients, they exercised thirteen different pre-trained state-of-the-art models (VGG19, VGG16, AlexNet etc.) to extract features from 381 CXR. Each class/label (normal, COVID-19, bacterial pneumonia) has 127 CXR to balance the data set. Later, SVM classified COVID-19-infected patients by exploiting the extracted deep features. By comparative analysis, author demonstrated that SVM with ResNet50 model achieved 95.33% average accuracy with a data split ratio of 80:20% while training and testing, respectively. Moreover, it also accomplished better performance in terms of F1-score and sensitivity of 95.34% and 95.33%, respectively. A combination of data over-sampling, image augmentation techniques with ML-based classifier has been introduced in Ref. [56]. The researcher first extracted the features by GLCM and its variants, and then used SMOTE for balancing class distribution. The model consists of SVM classifier with stacked AE and PCA to exhibit an accuracy of 94.23%, precision of 96.73%, sensitivity of 91.88%, F1-score of 93.99%, and specificity of 98.54% on CXR.

An alternative technique has been proposed by Ref. [57] to show the effectiveness of multi-view representation learning that transform original features into latent representation of class space for COVID-19 diagnosis. In pre-processing step, V-Net model [58] extracted pulmonary segments and lung lobes from CT images to segment the infected lesions. They further divided the obtained 189-dimensional features into two radiomic features (Gray, and Texture) using GLCM and its variants, and five handcrafted features (histogram, number, intensity, volume, and surface). The CPM-Nets [59] learnt the later features. Later, they trained Latent-representation Regressor model followed by several ML-based classifier models (LNR, SVM, Gaussian Naïve Bayes, KNN, and logistic regression) for COVID-19 prediction. With the incorporation of proposed model, the model achieved an overall accuracy, specificity and sensitivity of 95.5%, 93.2% and 96.6%, respectively, on 2522 CT images, among which 1495 samples belong to patients affected by COVID-19). Table 1 represents ML-based approaches and classifiers, such as DT, KNN, LNR, and LD used to screen and detect COVID-19 cases by analyzing medical radiology images.

Table 1 Adopting radiography images for COVID-19 diagnostic applications based on machine-learning approaches

Ref	Name of algorithm/model	Problem/assignment	Type of data	Classes	P	Sp	Se	A
[55]	ResNet50 for deep feature extraction and SVM as classifier	COVID-19 detection	CXR	3	–	–	95.3	95.3
[56]	SMOTE for feature oversampling, stacked Auto-encoders and Principal Component Analysis for feature extraction and SVM for classification	Classification of COVID-19	CXR	6	96.7	98.5	91.8	94.2
[57]	Multi-view representation learning technique with ML-based classifiers (LNR, SVM, KNN, NN, and Gaussian Naïve Bayes)	COVID-19 screening	CT	2	–	93.2	96.6	95.5
[60]	Adaptive Feature Selection guided Deep Forest based on Random Forest	Classification of COVID-19 from other community acquired pneumonia by extraction location specific features	CT	2	93.1	89.9	93.0	91.7
[61]	Majority voting-based classifier ensemble of SVM, KNN, Decision Tree, Naïve Bayes, ANN, and Binary Gray Wolf Optimization	COVID-19 screen by extracting radiomic texture descriptors	CXR	2	99.7	99.5	99.8	99.6
[62]	Decision Tree based on CNN	Detection of COVID-19	CXR	2	94.0	93.0	97.0	95.0
[63]	SVM for classification with Social Mimic Optimization, SqueezeNet and MobileNetV2	Detection of COVID-19	CXR	2	98.8*	99.6*	98.3*	99.2*
[64]	Various ML classifiers including kNN, DT, RF, SVM and MLP with Clus-HMC	Identifying COVID-19 in multiclass and hierarchical schemes	CXR	7	–	89.0	–	–
[65]	Five ML classification algorithms with IRF-based ResExLBP for feature extraction/selection	Diagnosis of COVID-19	CXR	2	–	100	98.8	99.6
[66]	DT, kNN, SVM, kNN, ensemble and three-naïve Bayes as classifiers	Identification of COVID-19	CT	2	90.6	90.3	93.5	91.9

P precision, Sp specificity, Se sensitivity, F1 f1-measure, A accuracy, CXR chest X-ray images, CT computed tomography images

*Values related to classification of COVID-19 class only

The costly RT-PCR tests kits are short in supply; therefore, AI scientists have proposed various cost-effective solutions by attempting various DL models in prediction, diagnosis and prognosis of SARS-CoV-2 due to outstanding performance in handling and processing complex biological and medical data. Such as Apostolopoulos and Mpesiana [67] exploited transfer learning technique with various state-of-the-art CNN-based frameworks including Inception, Inception ResNet v2, MobileNet v2, VGG19 and Xception to isolate SARS-CoV-2-infected patients among 1427 CXRs images. The analyzing, author concludes that MobileNet v2 surpassed other frameworks by securing sensitivity of 99.10%, specificity of 97.09%, accuracy of 97.04% on two-class problem, while on three-class classification task, it achieved an accuracy of 92.85%. Moreover, they tested the implemented models on second data set that contains 224 COVID-19-infected cases images, 714 CXRs of patients with viral pneumonia, and 504 CXRs of healthy person. On this data set, for three-class problem, MobileNet v2 attained accuracy of 94.72%, while for two-class problem, it secured 98.66% sensitivity, 96.46% specificity, 96.78% accuracy. Similarly, Brunese et al. [68] implemented DTL approach with fine-tuned DL-based customized VGG16 framework to differentiate between pulmonary diseases patients and health person (model-1), and then figures out COVID-19-infected patients among discovered pulmonary diseases patients (model-2). The suggested model uses 6523 CXRs, among which 250 CXRs correspond to COVID-19-infected patients, 2753 CXRs belong to pulmonary diseases patients and 3520 images of healthy patients to diagnose COVID-19 while highlighting the potential-infected region due to SARS-CoV-2 virus. Model-1 accomplished a sensitivity, f1-score, specificity, and accuracy, of 96%, 94%, 98%, and 96%, respectively. The experimental finding yields that second model, disease classification model, attained sensitivity, specificity, accuracy and f1-score of 87%, 94%, 98%, and 89%, respectively. Apart from using the DTL approaches and pre-trained models, authors of Ref. [69] designed and trained a CNN-based network that utilizes features extracted through PCA. The authors further proposed a GAN model to eliminate the class imbalance issue and enhance the data set. The incorporation of PCA not only significantly reduced the computational time but also improved the accuracy to its maximum extent.

Besides CXRs, researchers also focused on CT images, such as Xu et al. [70], designed a 3-D CNN-based framework to isolate patients affected by COVID-19 among healthy and IAVP in timely manner. They segmented 219 COVID-19-infected CT images, 224 IAVP CT images, and 175 normal cases CT images and extracted meaningful features by incorporating ResNet model. Finally, location-attention classification framework achieved an overall prediction accuracy of 86.7%. Jaiswal et al. [71] presented an

alternate state-of-the-art CNN-based model to distinguish COVID-19-infected humans using chest CT images. It employed pre-trained DenseNet201 with DTL approach to analyze 1230 CT images of patients other than COVID-19, while 1262 CT images are of SARS-CoV-2 positive cases. The proposed model achieved precision, sensitivity, specificity, accuracy and f1-score of 96.29%, 96.29%, 96.21%, 96.25%, and 96.29%, respectively. Table 2 lists performance details of COVID-19 diagnostic tools and applications based on DL-guided methods that may aid concerned personnel while selecting an appropriate architecture for SARS-CoV-2-infected patient's identification.

2.2 Routine Clinical Data-Based Diagnostic Tools

Due to expensive radiographic imaging machines, several developing countries and states lacks in CT, CXR and ultrasound machines but has basic blood testing facilities. Keeping in view such scenarios, scientists and programmers have developed AI-based applications and tools to screen COVID-19 positive case using Clinical blood reports. Batista et al. [119] implemented five various ML classifiers, such as RF, NN, LR, SVM, and gradient boosting trees to segregate COVID-19-infected patients by collecting a 235 adult patients blood sample data from hospital in Brazil. The collected data set contains 125 samples of COVID-19 negative patients, while 110 samples belong to COVID-19-infected patients. Each data instance had 15 attributes that includes CRP, mean corpuscular hemoglobin, MCV, mean corpuscular hemoglobin concentration, age, gender, hemoglobin, RDW, red blood cells, leukocytes, monocytes, platelets, lymphocytes, basophils, and eosinophils. From experimental findings, it is noted that SVM outperformed other ML approaches by securing a sensitivity, specificity, accuracy, F1-score, NPV, PPV and brier score of 67.7%, 85.0%, 84.7%, 72.4%, 77.3%, 77.8% and 16.0%, respectively, when tested and trained under tenfold cross validation. Table 3 lists COVID-19 diagnostic applications empowered by various AI approaches, which analyzes data related to routine clinical blood samples.

2.3 Coughing Waves and Respiratory Pattern-Based Diagnostic Tools

Beside diagnostic applications for COVID-19 based on radiography images or clinical blood samples data, Wang et al. [124] presented a classification network (BI-AT-GRU) which effectively utilizes the respiratory patterns of patients [125]. In addition to the stimulated data, it adequately uses real-world data. The framework discovers and differentiates the respiratory pattern known as Tachypnea (an occurrence of more speedy respiration) among six other patterns of viral infections. Due to scarcity of respiratory data, authors used

Table 2 Adopting radiography images for COVID-19 diagnostic applications based on deep-learning approaches

References	Name of algorithm/model	Problem/assignment	Type of DATA	Classes	P	Sp	Se	A
[72]	Deep transfer learning-based model (ResNet18, ResNet50, ResNet101, and SqueezeNet)	COVID-19 detection and abnormality localization	CT	2	99.0	98.6	100	99.4
[73]	DL-based transfer models (VGG16, ResNET50, and InceptionV3) with Haralick texture feature extractor	COVID-19 detection using already available model	CXR+CT	2	93.0	–	93.0	93.0
[74]	Customized InceptionV3 network with Generalized Extreme Value (GEV) activation function	COVID-19 diagnosis using highly unbalanced data	CT CXR	2	–	65.1	62.8	–
[75]	Inf-Net framework (CNN-based model connected with parallel decoder and reverse attention modules)	COVID-19 identification by generating global maps and learning edge features to detect infected region using CT slices	CT	2	–	77.8	79.8	–
[76]	3D-U-Net architecture for lobe segmentation, and 3D-ResNet-based Prior-Attention Residual Learning (PARL) blocks	COVID-19 diagnosis using highly unbalanced data	CT	3	–	66.9	72.6	–
[77]	Semi-supervised CNN-based ResNext+ model with Bi-directional LSTM for spatial feature transformation	COVID-19 identification by generating global maps and learning edge features to detect infected region using CT slices	CT	2	–	72.0	96.0	–
[78]	3D ResNet34 with attention module and VB-Net toolkit for infectious region segmentation	COVID-19 lesion region detection by learning discriminative representations	CT	3	–	95.5	87.6	93.3
[79]	Weakly supervised learning framework with deep multiple instances learning, attention mechanism and deep 3D instances generator (AD3D-MIL)	COVID-19 screening by extracting spatial, axial, and temporal features using lung segmentation mask, attention aware mechanism for volume level prediction	CT	2	100	100	100	100
[80]	AH-Net for segmentation and Densenet-121 for classification	COVID-19 classification using lung-infected region segmentation	CT	2	–	95.4	95.4	95.4
[81]	Tailored ResNet50 framework	COVID-19 screening by solving 3D spatial complexity of CT images	CT	2	97.9	–	97.9	97.9
[82]	Multi-scale spatial pyramid (MSSP)-based multi-scale convolutional neural network (MSCNN)	COVID-19 classification using multi-national data set	CT	3	95.9	–	90.5	94.3
[83]	Kapur's entropy thresholding (for segmenting) with ML-based classifiers (k-NN, Random Forest, Decision Tree, and SVM with Radial Basis Function)	COVID-19 classification using multi-national data set	CT	2	–	93.0	84.0	90.8
[84]	DenseNet121-FPN and COVID-19Net	Detection of COVID-19 among different classes	CT	3	–	90.29	92.1	91.0
[85]	3D U-Net for pulmonary lobe segmentation and lesion detection while MVP-Net and 3D U-Net for COVID-19 lesion segmentation	Automatic distinction between common pneumonia and COVID-19-infected person by analyzing ground-glass opacities at slice level and scan level images	CT	2	–	95.6	99.5	97.7
[86]	Three dimensional CNN framework	COVID-19 screening and infectious region segmentation	CT	2	86.8	86.5	89.0	87.7
[87]	Combination of MLP (RF and SVM) and CNN	Diagnosis and prognosis of COVID-19	CT	2	–	76.6	80.3	78.3
[88]	CNN network with ResNet-32	Characterize COVID-19 pneumonia disease on per-patient and per-lung lobe basis	External Validation. set 2 CT	2	–	81.1	79.3	80.1
		Diagnosing COVID-19 by identifying infiltrative biomarkers	CT	2	–	–	–	–
		Diagnosing COVID-19	CT+CD	2	81.9	82.8	84.3	83.5
		Classification of COVID-19	CT	2	95.1	94.7	91.4	93.0

Table 2 (continued)

References	Name of algorithm/model	Problem/assignment	Type of DATA	Classes	P	Sp	Se	A
[89]	Three dimensional ResNet-18 classification framework along with DeepLabv3, FCN, DRUNET, SegNet and U-net for segmentation	COVID-19 diagnosis and severity detection	CT + MD	3	–	91.1	94.9	92.4
[90]	CNN-based ResNet50 framework	Identifying COVID-19 patients among other pneumonia-infected patients	CT	2	–	61.5	81.1	76.0
[91]	FCN with EfficientNet B4	Classification of COVID-19	CT	2		96.0	95.0	96.0
[92]	Three dimensional DL frameworks	Identification of infected areas in lungs for detection of COVID-19	External data set CT	2		86.0	89.0	87.0
[93]	AlexNet and Inception-V4	COVID-19 prognosis and diagnosis	CT	2	–	87.4	87.3	94.7
[94]	Customized CNN network based on multi objective differential evolution	Evaluation and classification of COVID-19	CT	2	–	91.0	91.0	93.5
[95]	Stack Hybrid Classification (RF, SVM and CNN) using CHFS feature selection approach	Recurrences prediction of SARS and COVID-19	CT	2	96.1	–	96.1	96.0
[96]	Customized CovNet	Detecting COVID-19 among CA-pneumonia/non-pneumonia cases	CT	3	–	92.0	87.0	–
[97]	CAPSNET based on CNN	Diagnosing COVID-19	CXR	2	97.0	97.0	97.4	97.2
[98]	EfficientNet-B0 with two dimensional curvelet transform-CSSA	Detecting COVID-19	CXR	3	84.6	91.7	84.2	84.2
[99]	Customized and tailored transfer learning frameworks	Detecting COVID-19	CXR	3	99.6	99.8	99.4	99.6
[100]	Several pre-trained state-of-the-art frameworks with image augmentation approach	Detecting COVID-19	CXR	2	–	97.2	97.0	97.4
[101]	Faster Regions-CNN	Detecting COVID-19	CXR	2	99.7	99.5	99.7	99.7
[102]	Fast-track COVID-19 Classification Network (FCONet) based on 2D DL frameworks (Inception-v3, ResNet-50, VGG16, and Xception)	Detecting COVID-19 based on single chest X-ray	CXR	3	97.9	97.9	97.9	97.9
[103]	Truncated InceptionNet	Screening of COVID-19	CXR	2	99.2	–	97.6	97.3
[104]	Hybrid DL framework consisting VGG, data augmentation and spatial transformer network with CNN	Detecting COVID-19 based on single chest X-ray	CXR	2	–	100	99.5	99.8
[105]	Fine-tuned pre-trained VGG16 with transfer learning approach	Detecting COVID-19 lung disease prediction	External Data set	2	–	–	–	96.9
[106]	Customized CNN-based CoroNet using pre-trained Xception model	COVID-19 detection	CXR	2	99.0	99.0	95.0	98.7
[107]	CovXNet using transferable multireceptive feature optimization technique	COVID-19 among several other pneumonia cases	CXR	13	69.0	–	63.0	73.0
		COVID-19 detection	CXR	2	–	97.2	92.6	96.0
		Detecting COVID-19	CXR	3		95.1	86.7	92.5
		Detecting COVID-19	CXR	2	98.3	98.6	99.3	99.0
		Detecting COVID-19	CXR	3	95.0	97.5	96.9	95.0
		Detecting COVID-19 among several other pneumonia cases	CXR	4	90.0	96.4	89.9	89.6
		Detecting COVID-19 among several other pneumonia cases	CXR	2	98.0	97.9	98.5	98.1
		Detecting COVID-19 among several other pneumonia cases	CXR	3	94.9	94.3	96.1	95.1
		Detecting COVID-19 among several other pneumonia cases	CXR	4	92.9	93.6	92.0	91.7

Table 2 (continued)

References	Name of algorithm/model	Problem/assignment	Type of DATA	Classes	P	Sp	Se	A
[108]	Tailored pre-trained frameworks (trained on ImageNet) with customized CNN model	Screening of COVID-19 cases using modality-specific features	CXR	3	99.0	–	99.0	99.0
[109]	CovidGAN (CNN-based model with Auxiliary Classifier Generative Adversarial Network)	To enhance COVID-19 detection by data augmentation	CXR	2	–	97.0	90.0	95.0
[110]	MobileNetV2	Biomarkers detection for identification of pulmonary diseases	CXR	2	–	99.4	97.36	99.1
[111]	Combination of ResNet50 v2 with Xception	Identification of COVID-19 among pneumonia-infected and normal patients	CXR	7	72.8	94.2	87.3	87.6
[112]	Several DL networks using weakly labeled data augmentation approach	Detecting COVID-19	CXR	3	–	–	–	91.4
[113]	Customized InceptionV3	Screening of COVID-19 cases	CXR	2	–	91.8	93.0	99.2
[114]	Various transfer learning networks (Resnet18, Googlenet, and Alexnet) with GAN	Detecting COVID-19	CXR	4	100	–	100	76
[115]	DarkCovidNet architect based on CNN	Classification of COVID-19	CXR	3	85.2	–	85.2	85.2
[116]	COVIDdiagnosisNet based on fine-tuned Bayes-SqueezeNet with data augmentation approach	Diagnosis of COVID-19	CXR	4	84.2	–	80.6	80.6
[117]	Combination of ConvLSTM-based networks with CNN and GAN	Detecting COVID-19	CXR	3	98.0	95.3	95.1	98.0
[118]	CAD based on commercialized deep-learning model	Identification of COVID-19	CXR+CT	3	–	99.1	–	98.2
				2	97.7	97.8	100	99.0
				2	–	66.7	68.8	–
				2	–	72.3	81.5	–
				2	–	100	90.0	94.1

P precision, *Sp* specificity, *Se* sensitivity, *A* accuracy, *CXR* chest X-ray images, *CT* computed tomography images, *CD* clinical data, *MD* metadata, *CD* community acquired

Table 3 Artificial intelligence-based diagnostic tools for COVID-19 using data related to clinical blood samples

References	Name of algorithm/model	Problem/assignment	Type of data	Classes	P	Sp	Se	A
[120]	Several machine learning classifiers (DT, SVM, kNN, RF, LR, and Naïve Bayes)	Diagnosis of COVID-19 diagnosis using hemato-chemical values obtained from blood examination	Text	2	83.0	65.0	92.0	82.0
[121]	Various machine learning-based models (LR, RF, DT, and Gradient-boosted DT)	Diagnosing COVID-19 by considering regular laboratory tests	Text	2	–	80.8	76.1	–
[122]	Feature engineering using TF-IDF with seven different supervised machine learning classifiers (DT, Stochastic Gradient Boosting, LR, RF, Adaboost, SVM, and Multinomial Naïve Bayes)	Classifying COVID-19 cases among various viral pneumonia with the use of use of clinical reports	Text	4	94.0	–	96.0	96.2
[119]	LR, RF, and SVM	COVID-19 diagnosis	Text	2	77.8	85.0	67.7	84.7
[123]	Random Forest	Identifying COVID-19 cases by considering 49 different parameters of clinical data	Text	4	–	96.9	95.1	95.9

P precision, *Sp* specificity, *Se* sensitivity, *A* accuracy

RSM to generate stimulated breathing patterns. From discussion, it concludes that BI-AT-GRU framework outperformed other state-of-the-art models, such as GRU, LSTM, and BI-AT-LSTM by accomplishing a precision of 94.4%, recall of 95.1%, accuracy of 94.5%, and f1-measure of 94.8% when tested on real-world data obtained from depth camera. Table 4 illustrates various ML- and DL-based COVID-19 diagnostic tools and applications that uses coughing or respiratory data.

2.4 Disease Severity and Survival-Mortality Assessment Models

The timely knowledge about the severity of disease facilitates the attending staff in dealing patients priority wise and utilizing the hospital facilities accordingly. A very rare work has been observed on lung's ultrasound

data, such as Carrer et al. [129], proposed a unsupervised method based on Viterbi algorithm and Hidden Markov model for localization and detection of pleural line in LUS data. Later it evaluates the severity level of patient using SVM. From results, it is observed that pleura detection model achieved an accuracy of 94% and 84% for linear and convex probes, while SVM classifier evaluated the severity with an accuracy of 94% and 88% for linear and convex probes. Zhou et al. [130] proposed machine-agnostic quantification and segmentation technique to cater 3D segmentation problem in CT images for severity identification of COVID-19-infected regions. The proposed simulator decreases the model parameters by using symmetry properties of lungs and tissues that decomposes 3D segmentation into three 2D ones (along $y-z$, $x-y$, and $x-z$ planes) thus reduces time complexity. The three independent 2D U-Nets segmented infectious

Table 4 Artificial intelligence-based diagnostic tools for COVID-19 using respiratory data

References	Name of algorithm/model	Problem/assignment	Data-type/modality	Classes	P	Sp	Se	A
[126]	Deep Transfer-Learning-based Multiclass classifier (DTL-MC)	Analyzing irregularities of pathomorphological mutation in respiratory process to diagnosis COVID-19	Sound waves/coughing	2 4	91.4 89.9*	91.1 96.6*	94.5 89.1*	92.8 92.6*
[127]	Feature extraction using VGGish with LR and SVM for classification	Analyzing coughing samples to diagnose COVID-19	Sound waves/coughing and breathing	2	80.0	–	72.0	–
[128]	Bi-AT-GRU	Identifying COVID-19 cases by examining RBG and thermal videos	Thermal videos/breathing	2	–	76.3	90.2	83.6
[124]	BI-AT-GRU	Detecting positive COVID-19 cases	Patterns of breathing	2	94.4	–	95.1	94.5

P precision, *Sp* specificity, *Se* sensitivity, *A* accuracy

*Values related to classification of COVID-19 class only

regions along three orthogonal directions and later integrated these entire masks together with Mask R-CNN to produce final segmentation. The tool achieved an average dice of 76.4%, 82.3% and 87.5% on early, progressive and severe cases for segmentation problem, while it attains a 96.7% Pearson correlation coefficient for quantification task.

Bai et al. [131] proposed a hybrid DL-based network with multivariate LR classifier to predict COVID-19 malignant progression. The model converts statistical instances (75 clinical data characteristics) to 40-D feature vector using MLP. Finally, it predicts high-risk patients using quantitative CT sequences, obtained at different time interval, along with these transformed multi-dimensional feature vectors with the help of LSTM. The proposed severity assessment tool secured an AUC of 95.4% and overall accuracy of 89.1% when evaluated on data set of 133 patients under fivefold cross-validation. Similarly, an ML-based MCDM has been proposed in Ref. [132] to optimize the treatment strategy. The network detects the severely infected SARS-CoV-2 patients and prioritized them for relevant convalescent plasma transfusion. Table 5 shows the severity and fatality assessment models based on conventional ML and advanced DL techniques.

2.5 COVID-19 Outbreak Forecasting Models

The widespread of COVID-19 outbreak has created panic as a human community is still at risk, while hospitals are full, people are facing financial issues as governments are struggling to pass critical decisions, mortality rate is increasing exponentially, whereas social activities are halted. In this high uncertainty, experts have applied various DL and ML techniques to design outbreak-forecasting models that would help decision makers to recommend new preventive strategies and develop critical measures for future possibilities. Such as Carrillo-Larco and Castillo-Cara [144] suggested an unsupervised ML-based model that uses *k*-means clustering algorithm to classify the countries sharing same number of confirmed COVID-19 cases. In this study, researchers considered different attributes, such as prevalence of tuberculosis and HIV/AIDS diseases in 156 countries, social-economic parameters, such as gross domestic production as social-economic parameters and other health system metric, such as air quality along with COVID-19 prevalence data (confirmed cases, death etc.). It concludes that the integration of PCA with *k*-means-based model successfully stratify countries into five and six groups. The researchers conclude that model works well for countries stratification based on confirmed SARS-CoV-2 cases but not able to classify in terms of SARS-CoV-2 fatality cases.

Table 5 Mortality and survival rate prediction with disease severity assessment of patients using artificial intelligence-based application

References	Name of algorithm/model	Problem/assignment	Type of data
[133]	2 stage 3D U-Net for lobe segmentation and 3D-inflated modified variant of Inception for COVID-19 Reporting and Data System (CO-RADS) score prediction	Severity assessment of COVID-19-infected patients by automatic segmentation of pulmonary lobes of lung	CT
[134]	3D CNN-based network with VB-Net	COVID-19 quantification and detection	CT
[135]	Deep neural network based on six dense layers	Mortality prediction in COVID-19 patients using clinical data	Text
[136]	VGG16	Analyzing and assessing severity of COVID-19 infection in lungs	Radiography images
[137]	Various machine learning classifiers (Elastic Net, RF, Adaboost Regressor, DT, SVM, and Huber Regression etc.)	Analyzing COVID-19 transmission by examining the humidity and atmospheric temperature	Textual and TS
[138]	Customized CNN framework with fractal techniques for feature extraction	Assessing COVID-19 disease severity	CXR
[139]	DenseNet model	To find the severity of COVID-19 lung and the degree of opacity in lung	CXR
[140]	Fine-tuned RF with AdaBoost	Predicting disease severity to highlight chances of death or recovery	Text
[141]	Various LNR models	Diagnosing COVID-19 cases and predicting its volume and severity	CT and CD
[142]	SVM	Predicting recovery cases	Text
[143]	SVM	Critical cases detection among patients with mild symptom	Text

CXR chest X-ray images, CT computed tomography images, CD clinical data, TS time series

To assist policymaker, Kavadi et al. [145] presented a PDR-NML framework that predicts SARS-CoV-2 transmission patterns in India. The proposed statistical model, PDDL, normalizes it by searching the best features, which are then fed to a support Kuhn–Tucker-based nonlinear global pandemic ML model to forecast the future outbreak of COVID-19 pandemic cases. The presented model outperformed LNR and other famous AI-base models by securing 99.7% accuracy. Hu et al. [146] attempted modified AE that uses real-time data for pandemic outbreak forecasting in large geographical area by considering the interventions and measures to curb the pandemic. The framework use data of confirmed COVID-19 cases happened between January 20, 2020 to March 16, 2020 in 152 countries to forecast future cases, as well as pandemic peak and end time. It consists of 2 single AEs each comprised of 3 feed-forward NN layers that performed well while estimating the daily new cases in China as compared to SEIR model. The model attained error of 0.00134 and recommended that early precautionary measures would eliminate 99.4% of potential cases.

Other than the conventional ML algorithm, experts also used advanced DL techniques to determine the unseen forthcoming cases. Authors in Ref. [147] forecasted global pandemic outbreak by using multivariate spatiotemporal model based on convolutional LSTM framework. They used the data of Italy and USA, and transformed spatial features into clusters. The proposed forecasting tool predicted number of potential cases for the next 5 days with an MAPE of 5.57% and 0.3% for USA and Italy, respectively. Table 6 illustrates more AI-based applications/tools to assess the risk and predict the pandemic outbreak.

2.6 COVID-19 Protein Sequence Formation and Drug Discovery Models

In this panic-stricken era of COVID-19, rapid drug discovery in accordance with the exact virus genome is crucial to saving thousands of lives. Still many genomes and peptides of this noxious virus are being identified on a regular basis. To bring the effective drug-making process up to speed,

Table 6 COVID-19 outbreak prediction and risk assessment using artificial intelligence-based applications

References	Name of algorithm/model	Problem/assignment	Type of data
[148]	Several ML-based classifiers (DT, LR, SVM and RF)	Forecast COVID-19 spreading patterns in 42 countries	Text
[149]	ARIMA, Bi-LSTM, LSTM, and SVM	Forecast death, recovery rate and potential cases in major countries	TS
[150]	ARIMA and Least square-SVM	Estimate COVID-19 cases for the next month	TS
[151]	RNN, Bi-LSTM, LSTM, GRU, LSTM, and VAE	Predict (on short term) the new contaminated and recovered patients	TS
[152]	FbProphet	COVID-19 epidemic trend prediction	TS
[1]	ANN-based adaptive incremental network	Monitor and analyze the disease's growth stimulation for forecasting and population Compartmentalization based on its risk	TS
[153]	Polynomial Regression, LNR, and SVM	Predict the migration type, growth and transmission rate	Text
[154]	LNR, MLP and Vector autoregression method	COVID-19 spread prediction in India	TS
[155]	Various ML-based models (SVM, LNR, Exponential Smoothing, and Least Absolute Shrinkage and Selection Operator)	Forecast cases, deaths and recoveries due/from COVID-19 in the next 10 days	TS
[156]	Unsupervised-SOM	Spatially cluster the countries having similar COVID-19 cases	TS
[157]	Cloud computing with ML-based approach	Predict the growth and analyze potential threat related to COVID-19	TS
[158]	LSTM with LNR	Forecast COVID-19 outbreak trends in Iran	TS
[159]	Wavelet transform approach with Regression tree	COVID-19 outbreak prediction/forecasting in various countries and assessing the risk	TS
[160]	Fuzzy rule induction with Composite Monte Carlo	Future possibilities prediction	TS
[161]	LSTM with Curve fitting	Analyze the effect of social distancing and lockdown on predicting COVID-19 cases	TS
[162]	SEIR	Examine the effect of control measures while predicting COVID-19 outbreak	TS
[163]	Customized SEIR with LSTM	Analyze and predict COVID-19 pandemic curve for China	TS

TS time series

many ML models are in process to master the viral structural analysis. In the interest of seeking probable vaccine possibilities for SARS-CoV-2, Ong et al. [164] established a machine learning-based Vaxign-ML reverse vaccinology system. Their research based on a system equipped with five conventional ML algorithms (XGB, SVM, RF, kNN and logistic regression) applied on extracted protein data set, subsequent to fivefold cross-validation, defined further with biological and physicochemical characteristics. From findings, it can be noted that XGB model indicated an F1-measure of 94%. The results of the system indicated conservancy of SARS-CoV-2 N protein sequence with SARS-CoV and MERS-CoV only. While discussing the crucial matters of virus attacking and attaching itself to the host, the responsible adhesions proteins found were the S protein along with non-structural proteins; nsp3, 3CL-pro, and nsp8-10. Moreover, high protective antigenicity causing inferred by the designed Vaxign-ML system was attributed to three proteins namely S, nsp3, and nsp8 as potential vaccine candidate based on high proteogenicity score. This particularly tailored vaccine aptitudes for designing a reliable and competent COVID-19 vaccine.

Magar et al. [165] founded a machine learning idea envisioned to identify synthetic COVID-19 inhibitory antibodies. The ML strategies segregated the data of virus-antibody sequences via graphical diagrams and reported 8 stable antibodies with the ability to perform as COVID-19 inhibitors. The way that led the COVID-19 antibody identification starts with gathering and maintaining the data for the devised system. Then comes the featurization, embedding and benchmarking ML designs and screening for the best model available. Later on, a hypothetical antibody group is assembled and ML screening is done for obliteration. Lastly, the validity of the suggested antibodies is evaluated. Such generalized flowchart makes fast and facile screening of probable antibodies having an immense potential to defeat COVID-19. Table 7 depicts other AI-empowered applications used to detect protein sequence and discover to tackle COVID-19 pandemic.

3 Discussion

In this survey, we not only presented an analysis of clinically utilized AI tools providing assistance against COVID-19 but also presented a detailed historical account of the virus and related family. The detailed investigation reveals several ML and DL approaches so far lending help to a great extent, initiating from image diagnostics and going up to the presentation of prospective models for methodical anticipation of the epidemics outbreaks. Therefore, this study can facilitate healthcare and research operatives to efficiently and effectively cope the COVID-19 pandemic. With timely and precise analysis, approach at hand for the desired solution an immediate response against the disease can be lead. This survey concentrates mainly on the obstacles faced so far while executing AI and ML-based arrangements for COVID-19 prognosis. Moreover, some suggested plans and quick fixes to resolve those issues are also covered.

The foremost inaccuracy fails to arise from not constituting diagnostic programs, which segregates on the basis of symptoms. Thus, to have robust and well-generalized predicting tools, various other ailments (liver, heart, diabetes, etc.) and patient's information (gender, age, etc.) must be considered. In comparison with known community acquired and viral pneumonia, these aspects (patient's information and ailments) have significantly influences the severity of COVID-19 disease in a human. Thus, leading to an instantaneous identification of the virus. An enormous amount of data is laid out there by several countries severely hit by the pandemic. If those statistics are attained in the right way, schemes for the prediction can efficiently generate smart and uncomplicated results.

Then, there comes the issue of urgency. Since the government needs statistics right away to regulate quarantine laws for constraining the disease expansion. Therefore, the scientific data sets are constructed on hasty calculations. Thus, providing ineffective and non-reproducible structures. In pursuance of productive and quick implementation of policy models, the data set must be fixed and generate reproducible

Table 7 Protein sequence detection and drug discovery using artificial intelligence-based applications

References	Name of algorithm/model	Problem/assignment
[164]	DTL-based Vaxign-machine-learning reverse vaccinology tool	Candidate vaccine prediction for SARS-CoV-2 virus
[166]	LSTM and semi-supervised VAE	Discover drug by detecting SMILE fingerprint of molecules
[167]	GAN	Designing the drug compound (non-CoV)
[168]	A pre-trained network based on AI approach, called Molecule-Transformer-Drug-Target-Interaction	Determine the availability of antiviral drug to tackle SARS-COV-2
[165]	SVM, RF, MLP, LR, and XGBoost	Potential antibodies discovery for COVID-19
[169]	MLP and ANFIS	Detect nucleic acid based on CRISPR
[170]	GAN	Develop formation of drug compound for COVID-19

outcomes and solve the urgent problem as well. In designing the analysis applications based on statistical approach, one of the most important and challenging task is availability of high-quality samples at real time. In circumstances, where data are rapidly changing at faster pace, the reliability of produced tools are minimized. Therefore, to tackle this problem, regular updating the data based on region-specific values are decisive.

For planning any systems for prediction studies, attaining large data is the crucial requirement that needs to be fulfilled. Deep learning-based systemization needs big data sets of clinical images and statistical numerals. A large amount of data can be produced for better training of deep learning approaches if obtained sets are not divided on the basis of geography. Regulation of data sources needs to be addressed as well while handling massive data to avoid misunderstandings. Yet, another challenge that arises while training and designing such AI systems is due to little or almost no association of researchers with medical experts. While assessing the medical data, such as X-ray or scans relatable medical personnel, must be present to make a definitive opinion.

A better and definitive estimation of potential patients and the number of deaths that are going to happen in future is a top priority in the current situation. This can be achieved by gathering and structuring the data of heavily affected countries and utilizing it with accurate and robust AI-based models as better equipment against an upcoming alarming situation.

4 Open Research Challenges

The COVID-19 pandemic has unequivocally affected both individuals and economies everywhere in the world. This led to various systemic challenges in various field, such as health, governance, trade, education, technology etc. This section highlights some of the challenges to combat the current pandemic.

4.1 Research Collaboration and Data Sharing

The COVID-19 is a family of viruses that has various forms and has different behavior on people living in various regions around the globe. This requires a cross examination of the cases in multi-folded perspectives. There must be some agreements reached among various entities including civil society, private and public sectors to share data and conduct research to expedite the process for finding an ultimate solution. This envisions the authorities about expected abiding transformations, and motivates them to revamp the condition of the world by taking advantages of this moments.

It is critical for combating the disease to do research collaboration to accelerate the process towards normalizing the life and overcome the pandemic. This requires high-level decision making to remove obstacles in free flow of research ideas and make availability of research data for more critical decision making. Infrastructure should be developed to share and collaborate the research data globally, which is still a challenging task. This also requires policy to be defined for integrity of the patient data by introducing some defined set of rules and measures, interoperability and co-ordination, in conjunction with quality and interpretation of data.

4.2 Lack of Technology Infrastructure

Availability of IT infrastructure is crucial for early detection, tracking and monitoring of the patients. In China, ubiquitous availability of IT infrastructure help finding hotspots and crowd gathering, thus assisted the administrators to take faster decision making and implementation. Developing countries are suffering from serious lack of infrastructures to fully utilize the ability of AI for both detection and previous strategies.

4.3 Development of Vaccines

AI is inevitable in almost all fields of life. Multidisciplinary research should be conducted for development of vaccine for COVID-19. The use of AI for drug delivery, design, development and efficacy will eventually speed up the drug testing in real time. Policies should be designed to take advantage of this.

4.4 Increased Pressure on Hospitals

There has been sharp increase of patient admissions in hospitals across the globe that overwhelmed the healthcare professionals due to high workload. To increase the efficiency and properly managing the critical patients, AI should be used from patients' admission, testing and monitoring. This will reduce the pressure and workload for medical staff.

4.5 Adopting Models from Developed Countries

Some countries, such as South Korea, flattened the curve of COVID-19 by adopting digital technology and combining it with other strategies, such as early detection, free treatment, and isolation of COVID-19 cases. No severe lockdowns were placed; however, they used technology to monitor trends and hotspots to take early action. In addition, the public awareness and participation was very good. Adopting such model in the developing countries need these three important components: digital infrastructure, healthcare infrastructure, and public awareness.

4.6 Transparent Disclosing all Information

Accurate information sharing is crucial for public safety and crucial decision making. Governments should develop strategies for sharing the accurate information about the COVID-19 cases, through press briefing, to make awareness among mankind about ways to minimize the transmission of virus, and the impact of the social distancing.

Finally, the developing countries must cautiously and gently relaxes the restrictions related to immigration and quarantine keeping in view the global transmission rate of disease and corresponding healthcare situation/facilities of the country. Countries should also aim for assistance and capacity building in communal institutions. International associations and societies must collaborate and join the developing countries to cope with this pandemic.

4.7 Lesson Learning from this Pandemic

This may not be the last pandemic, as world has witnessed many similar challenges in the past. Learning some lessons from current pandemics and preparing for future challenges is a crucial step now. The models and preparedness should be done keeping future perspective in mind. Creating awareness among people and balanced distribution of wealth can highly reduce the risks of spread of such diseases.

5 Conclusion

The recent advancements in AI techniques have played an important role in biomedical sciences providing a handy role in diagnosis and monitoring of various diseases. For COVID-19 pandemic, it is essential to detect it as early as possible by collecting and analyzing related information to predict, where this virus will affect in the future. In this paper, we report the recent active role of AI for combating the COVID-19 and highlighted new research directions and main challenges in adopting a robust solution for this pandemic. The paper spans over two main domains, medical and technological. In the first domain, this review covered the global transmission patterns of COVID-19 and brief history of various other viruses. Then, it described the advances in AI tools to diagnose, assess the severity of disease, predict the mortality rate, and discover the drug compounds. Furthermore, an analysis of recently applied techniques for various biological and computing approaches have been presented. This work will help decision makers to better understand the role of AI for combating COVID-19, so that better decisions can be taken to properly handle and take precautionary steps by designing instructions in pandemic

stricken regions. Subsequently, computer-aided platforms are in operation for smart utilization of medical facilities on a priority basis.

Declarations

Conflict of interest The authors declare that they have no conflict of interest. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Informed Consent For this type of study, formal consent is not required.

Statement of Human and Animal Rights This paper does not contain any studies with human participants or animals performed by any of the authors.

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