Exploring Machine Learning contribution in COVID-19 cure and management: Predicting Mortality and Vaccine Efficacy: A survey

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Abstract. The SARS-CoV-2 virus, responsible for the COVID-19 pandemic, has left an indelible mark on a global scale. This illness, exhibiting a spectrum of mild to severe symptoms, has triggered a widespread health crisis. Within this context, Machine Learning has emerged as a versatile tool, playing a pivotal role in pandemic management. It has found applications in predicting virus transmission patterns, analyzing medical imaging data, and exploring potential therapeutic avenues. This comprehensive paper delves into the multifaceted involvement of Machine Learning in COVID-19 research, spanning from data aggregation to vaccine advancement. Furthermore, we delve into the ethical and societal dimensions inherent in leveraging Machine Learning for pandemic-related inquiries. In conclusion, we spotlight promising avenues for future exploration and advancement in this burgeoning field.

1 Introduction

The emergence of SARS-CoV-2, the virus responsible for Covid-19, in Wuhan, China in December 2019, has led to a global health crisis that has affected not only human health but also the economy. As of 24 January 2023, there have been 664,618,938 confirmed cases of COVID-19, including 6,722,949 deaths, reported to WHO [1]. The highly contagious nature of the virus, which primarily spreads through respiratory droplets produced by infected individuals through talking, coughing, or sneezing, as well as through close contact with infected individuals or touching contaminated surfaces or objects, has been a major challenge in controlling its spread. Covid-19 presents with a range of symptoms, from mild to severe, including fever, cough, shortness of breath, loss of taste or smell, and fatigue. To mitigate the spread of the virus, several preventive measures have been implemented, including wearing masks, practicing social distancing, and frequent hand hygiene. Therefore, the World Health Organization (WHO) declared this disease to be a Public Health Emergency of international concern on 30th January 2020 [2]. Additionally, vaccines have been developed and authorized for emergency use, with the aim of slowing the spread of the virus. The current situation has highlighted the importance of data analysis and Machine Learning in understanding and addressing the

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spread of the virus. Machine Learning techniques can play an important role within the framework of the COVID-19 era, encompassing stages ranging from data collection during the pandemic to the development of vaccines. The discourse will encompass a comprehensive exploration of diverse Machine Learning methodologies, encompassing the trifecta of supervised, unsupervised, and semi-supervised approaches. In this article, we will explore the use of various Machine Learning techniques in the context of COVID-19.

In the field of Machine Learning, we encounter a trio of techniques: supervised, unsupervised, and semi-supervised methods. Supervised Machine Learning entails instructing a model using meticulously labeled data, where the expected outcome is already discerned. This method proves valuable in endeavors like forecasting the likelihood of severe symptom progression in patients, leveraging their distinct demographic attributes and medical history. On the other hand, Unsupervised Machine Learning embarks on the uncharted terrain of unlabeled data, excelling in tasks such as categorizing patient groups into clusters founded on shared characteristics. The hybrid amalgam known as Semi-supervised Machine Learning presents an appealing avenue, especially in situations where labeled data is sparse. This holds notable relevance in the context of COVID-19, where certain regions might grapple with limitations in confirmed case data availability. Our discourse not only delves into the potential applications of these Machine Learning techniques within the COVID-19 framework but also casts light on the challenges and limitations they entail.

Moreover, our exploration extends to a panorama of datasets and research undertakings that have harnessed these techniques to dissect and unearth insights from the expansive landscape of COVID-19 data.

This paper thoroughly explores the role of Machine Learning in the COVID-19 pandemic. Section I introduces the pandemic's global impact. Section II highlights the topic's significance and motivation. In Section III, data-driven approaches for COVID-19 management are examined. Section IV unveils innovations in treatment and prevention. Section V addresses challenges and limitations. Lastly, Section VI concludes by emphasizing responsible Machine Learning in pandemic combat.

2 Importance of the topic and motivation for writing

The intersection of Machine Learning and COVID-19 is an important area of study because it highlights the potential for technology to contribute to global health initiatives. In recent years, Machine Learning has made significant advances in a wide range of fields, from computer vision and natural language processing to autonomous systems and decision- making. The ability to process vast amounts of data and identify patterns and relationships that might not be apparent to the human eye make Machine Learning algorithms an attractive tool for solving complex problems in various domains, including public health.

The COVID-19 pandemic has underscored the urgency of innovative solutions for this global crisis. Machine Learning has been extensively applied to address a range of COVID-19 challenges, encompassing early detection, diagnosis, predictive modeling, and treatment development, offering potential insights and guidance for future endeavors in this field and broader global health initiatives. However, integrating Machine Learning into COVID-19 research presents challenges, including technical limitations such as data quality and ethical considerations like privacy and data security, emphasizing the need for ongoing research, responsible implementation, and transparent utilization of Machine Learning algorithms in public health contexts. As technological advancements continue to

accelerate, Machine Learning algorithms are set to evolve in sophistication and capability, underscoring the significance of comprehending their potential and constraints in the context of public health crises like COVID-19. Through illuminating the role of Machine Learning in COVID-19 research, this paper spans the spectrum of applications, from initial data collection and diagnosis to advanced prediction techniques and pivotal contributions to vaccine development (Fig.1).

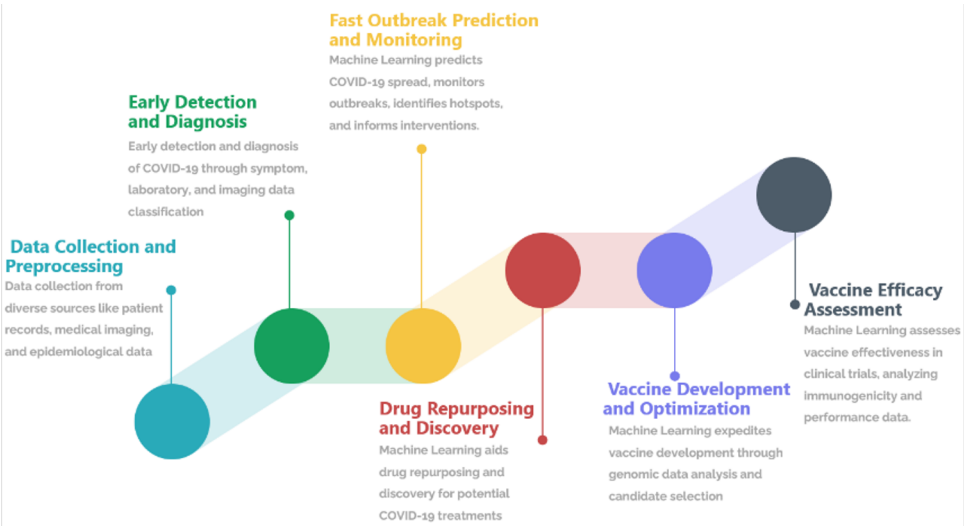

Fig. 1. Machine Learning contribution to combat COVID -19 pandemic

3 Data-driven approaches in covid-19 context

3.1 Data Collection and Preprocessing

During the COVID-19 pandemic, Data Collection in Machine Learning played a crucial role in understanding and managing the virus. Various sources like healthcare records, epidemiological data, genomic sequencing, social media, and contact tracing apps provided essential information. This data aided in predicting the virus's spread, identifying high-risk groups, tracking mutations, and assessing public compliance.

The authors in [3] presents an insightful exploration of various initiatives aimed at collecting and disseminating medical imaging data for COVID-19 analysis. The authors emphasize the significance of data aggregation and distribution in combating the pandemic and highlight the role of advanced data processing techniques and algorithms in enhancing diagnosis and therapeutic advancements. One notable initiative discussed is the establishment of a global COVID-19 open radiology database by the Radiological Society of North America. This database is crucial for consolidating medical imaging data and can potentially serve as an alternative or supplementary method to Reverse Transcriptase Polymerase Chain Reaction (RT-PCR) testing, which has limitations in terms of false negative rates. Moreover, the authors underscore the National Institutes of Health's employment of AI for COVID-19 diagnosis, treatment, and monitoring, underscoring the growing importance of imaging data in clinical decision-making.

In another investigation, other researchers employed public Chest X-Ray (CXR) Datasets, including the JSRT Dataset and the NLM Dataset, to contrast COVID-19 cases with those of normal and various lung conditions. The comprehensive use of diverse sources contributes to a comprehensive understanding of COVID-19's radiological manifestations. Notably, the inclusion of the U.S. National Library of Medicine (USNLM) Montgomery County (MC) Dataset for cross-database validation enhances the robustness of the study's findings. Addressing potential bias stemming from database limitations, the authors applied a universal preprocessing step involving data normalization across the entire dataset [4].

Another article highlights a deep learning-based variational autoencoder model introduced for COVID-19 detection and classification [5]. The integration of adaptive Wiener filtering in image preprocessing and the utilization of Inception v4 with Adagrad for feature extraction contribute to the model's remarkable accuracy rates, particularly in binary and multiple class scenarios.

An additional noteworthy study outlined in [6] introduces a hybrid Deep Learning framework for unsupervised anomaly detection in multivariate spatiotemporal COVID-19 data. The approach leverages unlabeled data and reconstruction error, effectively identifying early indications of COVID-19 outbreaks. The application of Principal Component Analysis (PCA) and K-means to analyze a COVID-19 dataset reveals valuable trends, regional impacts, and variations at the country level, showcasing the utility of these techniques for a broad spectrum of stakeholders, including researchers, policymakers, and health managers [7].

These studies underscore the vital role of advanced data processing and Machine Learning in enhancing COVID-19 diagnosis, monitoring, and anomaly detection. The highlighted initiatives emphasize data aggregation's significance and showcase innovative models for radiological analysis. These efforts offer powerful tools for informed decision-making, heralding a data-driven approach to combatting the pandemic and informing effective interventions across diverse stakeholders.

3.2 Early Detection and Outbreak Monitoring

Having discussed data collection and preprocessing as a foundation, this section focuses on pivotal studies that exemplify the influence of Machine Learning. These works encompass predicting disease progression, diagnosing COVID-19 through medical images, classifying severity levels, and identifying face masks. The applications extend to global risk assessment, sentiment analysis, patient grouping, and prediction. These investigations collectively underscore the extensive reach of Machine Learning, illuminating its role in comprehending, addressing, and anticipating COVID-19 challenges. In [8], a feature dataset obtained through preprocessing effectively predicts Covid-19 progression using supervised Machine Learning models, with LWL, K*, Naive Bayes, and KNN achieving high accuracy rates and AUC values for detecting severe and mild cases. Hasoon et al. [9] employs X-Ray images and Machine Learning, achieving diagnosis accuracies up to 98.66% with the LBP-KNN model. In [10], the authors test ML classification models, finding Random Forest best predicts COVID-19 severity. The authors in [11] create supervised ML models, with decision trees excelling in accuracy, SVM in sensitivity, and Naive Bayes in specificity.Regarding Deep Learning approaches for COVID-19 detection from X-Rays, this paper employs CNNs for segmentation with 94% accuracy [12]. "nCOVnet" introduced in [13] offers rapid COVID-19 detection with 97.62% true positive

rate, aiding patient management. VGG19 in [14] achieves 95% accuracy in multiclass classification, demonstrating COVID-19's importance and deep learning's health role.

In the context of managing outbreaks Amidst the global COVID-19 crisis, face masks have become a pivotal preventive measure. A hybrid model, combining deep learning (ResNet50) with classical algorithms, demonstrates robust face mask detection, achieving remarkable accuracy rates with SVM in various datasets [15]. Machine Learning's (ML) far-reaching impact during the pandemic spans diverse domains such as imaging, forecasting, and drug development. CNNs, LSTM, and more are commonly employed, addressing challenges, and revealing gaps in pandemic management. Keras stands out as a prevalent ML library (24.4%), with medical imaging accounting for a significant portion (20.4%) [16]. In [17], Elastic Net predicts COVID-19 outbreak risk globally, while in [18] the authors analyze positive sentiment about outbreaks on Twitter. A Gaussian mixture model is introduced for patient clustering, predicting severity and length of stay, providing valuable decision support for medical staff [19].

4 Innovations in treatment and prevention strategies

4.1 Drug Discovery and Repurposing

Innovative applications of Machine Learning extend beyond diagnostics and outbreak prediction, venturing into the realm of drug discovery and repurposing to combat the COVID-19 pandemic.
The Multimodal Restricted Boltzmann Machine (MM-RBM) approach is explored for drug repurposing, combining chemical structure data and gene expression perturbations to identify potential COVID-19 treatments with antiviral properties. Validation through in vitro or in vivo tests is required, but MM-RBM holds promise for efficient drug discovery [20].

A mechanism-driven Neural Network, DeepCE, is introduced for phenotype-based chemical compound screening, utilizing a graph Neural Network and multihead attention to model chemical-gene associations. DeepCE outperforms existing methods, incorporating a novel data augmentation technique for enhanced predictions. It showcases accuracy in downstream tasks and proves effective in COVID-19 drug repurposing, offering robust compound screening through omics data integration [21].
Machine Learning's role in accelerating drug repurposing, particularly in the context of the COVID-19 pandemic, is discussed. The article provides guidelines on employing Machine Learning for precision medicine and exemplifies how these approaches can expedite COVID-19 drug repurposing, emphasizing its relevance in pandemic response [22]. Addressing the urgency of COVID-19 treatment discovery, the study establishes a COVID-19-related biological network to identify essential proteins linked to disease disruption. Five drug clusters are formed based on drug-target interactions and protein-protein interactions, suggesting potential treatments. The approach bridges the gap between preclinical and clinical stages, expediting treatment strategies by leveraging network-based informative features [23].

4.2 Vaccine Development and Optimization

In the joint effort to combat the SARS-CoV-2 virus, significant progress has been achieved in the field of vaccine development through the integration of Machine Learning

methods. Noteworthy advancements include the creation of Vaxign-ML by Ong et al., employing XGBoost-based Machine Learning to prioritize non-structural proteins as potential vaccine candidates for SARS-CoV-2. The study indicates that nsp3, the largest non-structural protein within the "Coronaviridae" family, exhibits strong potential as a COVID-19 vaccine candidate, outperforming the S protein in protective antigenicity. Similarly, Prachar et al. employed a feed-forward Neural Network to identify 174 stable SARS-CoV-2 epitopes that bind effectively to 11 HLA allotypes. These findings, highlighting stable peptide-HLA interactions, suggest promising avenues for vaccine development against SARS-CoV-2. Another approach, proposed by Yang et al., introduces DeepVacPred, a deep neural network-based methodology for predicting and designing a multi-epitope vaccine. DeepVacPred constructs a 694aa multi-epitope vaccine comprising 16 B-cell epitopes, 82 CTL epitopes, and 89 HTL epitopes, with consideration for SARS-CoV-2 RNA mutations to ensure vaccine efficacy [24]. In the pursuit of effective and safe COVID-19 vaccines, the utilization of Machine Learning tools such as Vaxign and Vaxign-ML has become crucial. These tools contribute to the practice of reverse vaccinology, addressing the limitations of traditional vaccine candidates targeting whole virus structures and specific proteins [25].

4.3 Assessing Vaccine Efficacy and Population Immunity

Continuing our exploration of the multifaceted landscape of COVID-19 research, we now turn our attention to an essential realm: Assessing Vaccine Efficacy and Population Immunity. This segment delves into the innovative integration of Machine Learning techniques, shedding light on their pivotal role in understanding vaccine effectiveness, population immunity dynamics, and their collective impact on pandemic response.

Machine Learning and Natural Language processing are employed to detect COVID-19 vaccine adverse events from Twitter data, validating social media's suitability for monitoring adverse events and emphasizing the importance of diverse data for a comprehensive understanding of public perspectives [26]. The authors assess COVID-19 vaccination impact on fatality rates across 192 countries, revealing significant reductions due to vaccination efforts, offering insights for pandemic management [27]. Enhancing vaccine safety, some studies identify common factors contributing to adverse reactions, utilizing statistical analyses and Machine Learning to classify individuals at risk, providing profiles for tailored monitoring and mitigation [28]. By leveraging Machine Learning modeling, the researchers in [29] enhances the utility of Vaccine Adverse Event Reporting System (VAERS) data, identifying reporting disparities and improving vaccine safety assessment. Analyzing side effects and perceptions post-vaccination, this study predicts severity using statistical and Machine Learning tools, confirming safety, and showcasing predictive analytics' potential [30]. Addressing COVID-19 challenges, this research establishes a metric for global vaccination uptake and socio-economic influences, promoting universal access and global cooperation [31]. In an observational study, modifiable factors influencing mRNA COVID-19 vaccine side effects are identified, suggesting further randomized controlled trials for a deeper impact assessment [32].

In the midst of these remarkable efforts, Figure 2 offers a panoramic perspective of Machine Learning's pivotal role across the pandemic's distinct phases. This illustrative graph magnificently displays the wide spectrum of data types harnessed at every juncture - spanning from the commencement of data collection, through the realm of prediction, and culminating in the critical sphere of vaccine development. Concurrently, Table 1 provides an all-encompassing synopsis of studies conducted within the context of COVID-19 research and the application of Machine Learning. This compilation underscores the

indispensable contributions made by Machine Learning in harnessing data to effectively combat the multifaceted challenges posed by the Covid-19 pandemic.

Fig. 2. Machine Learning Data Usage Across Pandemic Phases

Table1. Machine Learning techniques applied in the review: supervised and unsupervised methods

Application Area	Key contributions	References
Diagnostic and prognostic insights	Prediction of COVOD-19 progression using ML	[8][9][10][11]
	X-Ray image detection with Deep Learning	[12][13][14]
	Face mask detection using hybrid mode	[15]
Outbreak Monitoring	Global outbreak risk prediction with Elastic Net and Twitter sentiment analysis	[17][18]
	Unsupervised anomaly detection for early outbreak identification using hybrid Deep Learning	[6]
	Patient clustering and severity prediction using Gaussian Mixture Model	[19]
	Identification of potential drug candidates	[20][21]
Therapeutic Approaches	Identification of vaccine candidates through Vaxign-ML and Neural Networks	[24]
	Mechanism-driven Neural Network for compound screening and drug repurposing	[21]
	Insights into vaccine efficacy and population immunity through various ML approaches	[26][27][28] [29][30]
	Global vaccination uptake and socio-economic influences	[31]
Societal Impacts	Identification of modifiable factors influencing vaccine side effects	[32]

5 Challenges and limitations

The utilization of Machine Learning in addressing the COVID-19 pandemic encounters several obstacles and constraints. Technical limitations, including the availability of quality data, potential bias in data, model intricacy, and computational resource restrictions, can compromise the accuracy of Machine Learning algorithms. Moreover, ethical concerns such as privacy and data security must be meticulously weighed when applying Machine Learning to public health data. Despite these challenges, Machine Learning offers substantial potential to enhance our comprehension of the pandemic and facilitate its control and management endeavors. Consequently, acknowledging these limitations becomes pivotal, urging us to surmount them for the full realization of this technology's benefits. The necessity for ongoing research and development, coupled with a transparent and responsible application of Machine Learning algorithms in public health, underscores the significance of triumphing over these challenges and limitations.
Furthermore, the lasting impact of vaccination efforts adds another layer of complexity to the situation. While vaccines have demonstrated their effectiveness in curbing the immediate effects of the pandemic, it's important to recognize that the broader effects and benefits might extend over generations. The challenge lies in understanding the long-term implications of vaccination, including potential changes in disease dynamics, immunity patterns, and the emergence of new variants. This requires continuous monitoring, research, and adaptation of strategies, emphasizing the need for sustained commitment in the face of uncertainty.

Machine Learning, encompassing supervised, unsupervised, and semi-supervised learning, has gained prominence in the management of COVID-19. Yet, criticisms regarding its application in this context persist. Numerous studies rely on small, restricted datasets, which can lead to overfitting and poor generalizability. Additionally, these datasets might not accurately represent the wider population, introducing biases into results. The use of medical images like CT scans and chest radiographs for COVID-19 detection might not be feasible for all patients, especially in resource-limited settings. Some studies focus solely on specific regions, impeding the extension of their findings to other areas. The ethical and privacy ramifications of employing patient data for Machine Learning are not always adequately addressed. In spite of these limitations, Machine Learning holds potential as a valuable tool in comprehending and managing COVID-19, provided it is used in conjunction with other methodologies and expertise, such as clinical judgment and epidemiological analysis. Supervised learning, reliant on labeled data, suits tasks like predicting COVID-19 severity or detecting the disease in X-ray images. Nonetheless, its efficacy hinges on the quality of labeled data and its adaptability to novel or unforeseen data patterns. Unsupervised learning, functioning without explicit guidance, proves beneficial in scenarios with scarce or unavailable labeled data, though its interpretability can be challenging, and it may not capture the intricate data distribution. Semi-supervised learning integrates labeled and unlabeled data, contingent on a sufficient amount of labeled data, yet its performance is heavily influenced by labeled data quality. Striking a balance between labeled and unlabeled data remains intricate. Additionally, these techniques might lack robustness against shifts in data distribution and might struggle to generalize across diverse populations or regions.

6 Conclusion

This review has extensively explored the utilization of Machine Learning techniques in the fight against COVID-19. The review has highlighted the numerous ways in which Machine Learning has been employed to tackle the pandemic, including the prediction of the spread of the virus, identification of high-risk individuals and areas, and support in the

development of treatments and vaccines. The potential of Machine Learning to mitigate the impact of the pandemic cannot be overstated, as evidenced by its successful use in predictive modeling, Natural Language processing, computer vision, and many other applications.

However, it is essential to acknowledge that the use of Machine Learning in COVID-19 research and response should be approached with caution. The results generated by these techniques must be transparent, interpretable, and fair, to ensure that they are unbiased and do not discriminate against any particular group of people. It is crucial that Machine Learning is utilized in an ethical and responsible manner, to avoid any potential negative consequences.

In conclusion, the review has emphasized the importance of Machine Learning in COVID-19 research and response and the need for caution in its utilization. By providing an overview of the current state of Machine Learning in this field, the review has aimed to highlight the immense potential of Machine Learning to tackle the pandemic and support the development of effective solutions. These exploits can be extrapolated to combat other viral and highly contagious infections to limit its extension and development to reach the pandemic stage.

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