



ISSN: 0975-833X

Available online at <http://www.journalcra.com>

International Journal of Current Research
Vol. 12, Issue, 09, pp.13605-13611, September, 2020

DOI: <https://doi.org/10.24941/ijcr.39698.09.2020>

INTERNATIONAL JOURNAL
OF CURRENT RESEARCH

REVIEW ARTICLE

CONTRIBUTIONS OF ARTIFICIAL INTELLIGENCE IN THE FIGHT AGAINST THE COVID-19 PANDEMIC

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ARTICLE INFO

Article History:

Received 15th June, 2020
Received in revised form
27th July, 2020
Accepted 04th August, 2020
Published online 30th September, 2020

Key Words:

Artificial Intelligence, SARS-CoV-2, COVID-19, Healthcare, Pandemic Control, Diagnostics, Surveillance, Therapeutics, Epidemiology, Artificial Neural Networks, Convolutional Neural Networks, Natural Language Processing, Machine Learning, Deep Learning, Computer Vision, Vaccine Development.

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Citation: Ms. Sukanya Chakraborty and Mr. Siddhartha Sen, B.E. 2020. "Contributions of Artificial Intelligence in the Fight against the COVID-19 Pandemic", *International Journal of Current Research*, 12, (09), 13605-13611.

INTRODUCTION

The COVID-19 (Coronavirus Disease 2019) pandemic is being widely regarded as the largest of its kind, ever since the Spanish Flu. It has infected almost 11.2 million people worldwide, resulted in 530 thousand deaths (Worldometer) and has led to changes in the socio-economic landscape of the world (Ting *et al.*, 2020). The effects are multidimensional and have affected the lower strata of society significantly. A drastic fall in a country's economy, a rise in the rate of unemployment and a substantial increase in the number of crimes are a few of the many major changes that accompany the pandemic. Controlling the virus spread to halt the loss of human lives and burden to society is imperative. Coronaviruses belong to a family of viruses, namely Coronaviridae, primarily responsible for various other well-known diseases such as Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS) (Yadav, 2020, Kumar *et al.*, 2020).

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The outbreak originated from the Wuhan district, located in the Hubei province of China with a cluster of unexplained pneumonia-like cases in December 2019. The World Health Organization, after a thorough analysis of the pattern of spread, declared this disease as a pandemic in early March 2020. This novel strain was not encountered before, resulting in a surge in research. Several aspects related to mechanism of action and pathogenesis of the virus, spread or epidemiology, diagnostics and therapeutics need to be thoroughly examined in such emergency situations. However, the fundamental requirements are speed and efficiency in all these avenues. This has led many countries to consider solutions using applications of Artificial Intelligence (AI) as this may help to meet the demands within a shorter span of time. Artificial Intelligence refers to the simulation of human intelligence by machines, enabling them to solve problems without manual intervention. It consists of various subclasses such as machine learning, deep learning, natural language processing and computer vision among others, each being immensely wide fields in their own right (Nilsson, 2014; Yadav, 2020). The applications of AI have spanned diverse fields ranging from healthcare to environmental issues. In this review, we have aimed to address how AI and its associated fields help in solving the aforementioned problems specifically related to COVID-19.

BRIEF OVERVIEW OF SARS-CoV-2

The SARS-CoV-2 along with other Coronaviruses, have become the major pathogens of emerging respiratory disease outbreaks. A large family of positive-sense single-stranded RNA viruses, these viruses can be isolated from different animal species (Cascella *et al.*, 2020). Derived from the Latin word, "coronam", essentially meaning crown, these viruses, true to their name, have a crown-like appearance in electron micrographs, due to their spike glycoproteins. Based on data from the initial cases in Wuhan and other investigations, the incubation time varies between 3 to 7 days and up to 2 weeks. This data also showed that this novel epidemic doubled about every seven days, whereas the basic reproduction number (R_0) is 2.2. In other words, on an average, each patient transmits the infection to an additional 2.2 individuals (Kannan *et al.*, 2020; Ruan *et al.*, 2020). This estimate has changed however, with varying patterns of transmission as the pandemic has progressed.

The mechanisms of pathogenesis by SARS-CoV-2 are still under investigation. So far, it is known that the virus, upon reaching the lungs, binds to the ACE2 (Angiotensin Converting Enzyme 2) receptor by the interaction of the spike glycoprotein on its envelope and ACE2 on the alveolar surface (Li *et al.*, 2020; Ou *et al.*, 2020). As a result of this attachment, this complex undergoes fusion and endocytosis into the host cell. The virus, once inside, hijacks the host cell transcriptional machinery to replicate and spread throughout the lung. Consequently, with the disruption of the normal functioning of the ciliated alveolar cells, the airways cannot be cleared, leading to the accumulation of debris and fluids in the lungs, and culminating in acute respiratory distress syndrome. Some of the cases progress to become relatively complex such as in the case where SARS-CoV-2 can cause pneumonia which is fatal among the elderly and for patients with comorbidities. The data available till date seem to indicate that the viral infection is capable of producing an excessive immune reaction in the host. In some cases, a reaction characterized by the release of an overwhelming quantity of circulating immunomodulatory protein factors, or cytokines, takes place, a 'cytokine storm'. The effect: extensive tissue damage. IL-6 (Interleukin-6), one of the key players, is produced by activated WBCs and acts on a large number of cells and tissues, having diverse effects on other immune system cells (Prompetchara *et al.*, 2020; Tortorici *et al.*, 2019). It is this response which mediates disease severity.

High throughput sequencing methods have enabled researchers to understand the SARS-CoV-2 genome. Current detection methods are mainly based on quantitative reverse transcription polymerase chain reaction (qRT-PCR) that amplify the viral genetic material (Yang *et al.*, 2020). Auxiliary serological detection methods that recognize host antibodies (Immunoglobulins G and M) and viral antigens have also been established (Yang *et al.*, 2020; Vashist, 2020). To curb pandemic spread, the approaches of social distancing to break transmission chain and removal of source of infection are crucial. The susceptible population needs to be protected for which mass immunization by vaccines is the most viable option. But vaccine development in tackling this novel virus is a hard task. As of April, 2020, 56 (72%) of the confirmed active vaccine candidates are being developed by private/industry developers, with the remaining 22 (28%) of projects being pioneered by academic, public sector and

other non-profit organizations. Lead developers of active COVID-19 vaccine candidates are distributed across 19 countries, which collectively account for over 75% of the global population (Le *et al.*, 2020). Clinical trials are ongoing but require time to standardize efficacious vaccine candidates (Lurie *et al.*, 2020).

AI IN THE HEALTH SCIENCES: Artificial Intelligence (AI) has been applied in the field of medical applications extensively in order to improve the effectiveness, productivity and consistency of health care (Amisha *et al.*, 2019). An increase in the demand of quality medical services and growth of medical knowledge led to the foundation of the domain "Artificial Intelligence in Medicine" (AIM) in 1982 (Davenport *et al.*, 2019). AI in medicine can be broadly classified into two categories: virtual and physical. The virtual part includes applications such as electronic health record systems and artificial neural network-based guidance in treatment decisions. On the other hand, the physical part consists of functions like robots assisting in performing surgeries and intelligent prostheses for handicapped people, among others (Agah, 2013).

The basic idea behind applying AI to the field of healthcare is using statistical techniques to establish correlations between a new case being studied and existing ones in the database (Jiang *et al.*, 2017). It is useful in finding and understanding patterns between cases. The techniques that computers use to diagnose a patient include flowcharts or a database approach. The former deals with translating the process of history-taking, i.e., asking a series of questions and drawing a conclusion from it. The latter deals with the introduction of sophisticated techniques like deep learning and artificial neural networks for pattern recognition and solving more complex problems.

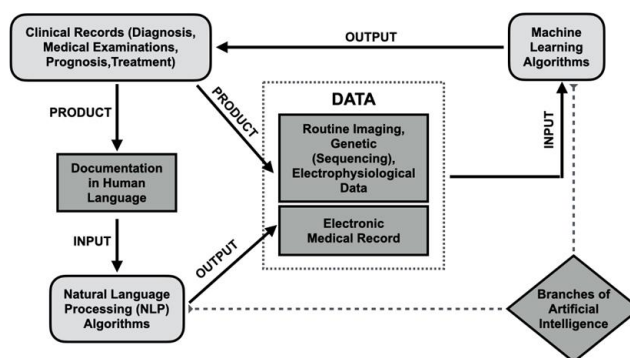


Fig 1. Schematic of AI workflow in Healthcare. Algorithms based on different aspects of AI such as Natural Language Processing, Machine Learning and Deep Learning are used to analyse clinical data and yield predictions for diagnostics, prognosis and treatment regimens.

On several occasions, AI has been used to tackle major diseases pertaining to cardiology, neurology and oncology. Convolutional Neural Networks (CNNs) have been used to analyse clinical images for identification of skin cancer subtypes (Khosravi *et al.*, 2018). AI systems have been developed to restore the control of movement in patients having quadriplegia (paralysis of all four limbs) (Chaudhury *et al.*, 2016). CNNs have also been used to analyse the risk of heart diseases from cardiac images. Start-ups such as Atomwise and Deep Genomics have made considerable progress in the aforementioned fields (Davenport *et al.*, 2019).

In order to maximize the scope of AI in the health sciences, multiple domains such as Natural Language Processing (NLP), Machine Learning, Image Processing and several others need to work concurrently (Datta *et al.*, 2019).

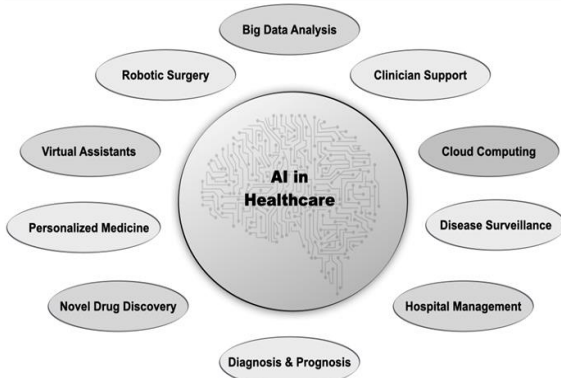


Fig 2. Branches of Healthcare in which AI finds potential applications

APPLICATIONS IN COVID-19

We have summarized the recent aspects in which AI has found applications to tackle the COVID-19 pandemic.

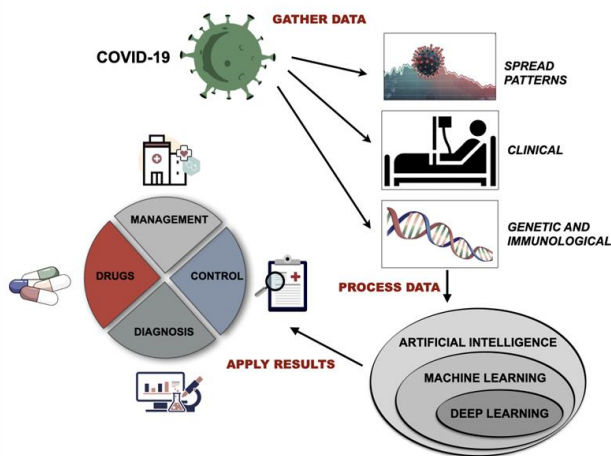


Fig 3. Summary of AI based usage in COVID-19. Epidemiological, clinical and genetic data from patients are fed into AI programs to obtain trends for downstream real-life applications

EPIDEMIOLOGY

During the rapid spread of infectious diseases, one key feature is being able to trace the transmission. Contact tracing includes following the pathogen from a patient to other susceptible people. This process requires a huge amount of manpower to support the large population, especially in developing countries. As a solution, countries like South Korea, Taiwan and China have initiated the use of applications to track location data. These can be installed on smartphones, enabling users to update their movement information to a central database. This is in turn being analysed by AI based tools to predict disease spread. Similar applications have also been deployed in Singapore to keep a record of proximity contacts so that if an individual gets infected it would effectively return the data of all the people he came in contact with (McCall, 2020). However, making this technology accessible to all is a major challenge.

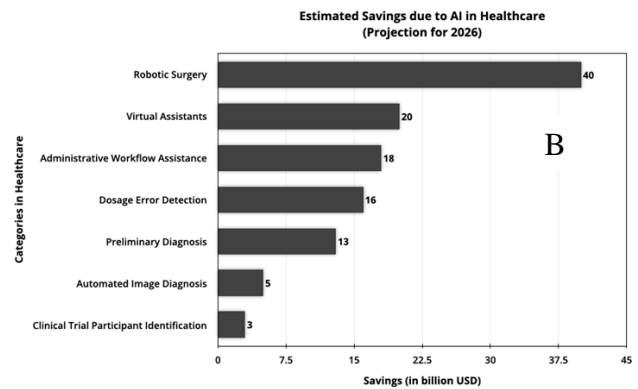
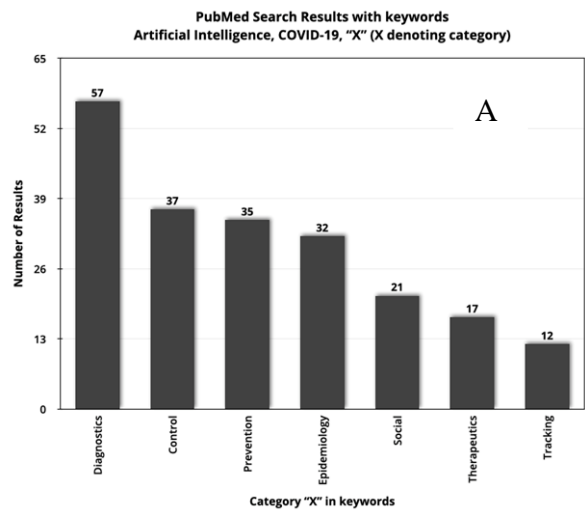


Fig 4. (A) Search of AI Literature in PubMed Database for Applications in COVID-19, as conducted on 21.06.20. Categories in COVID-19 specific healthcare are indicated on X-Axis and number of studies in 2020 on Y-Axis. (B) Estimated Savings offered by AI incorporation into Healthcare. Projection for 2026. Accenture Analysis 2017

In another recent study from India, scientists used the dataset available from WHO regarding spread of the disease in India and developed a program to predict the disease transmission pattern for the subsequent 7 days. The model is based on concepts of regression analysis that enables one to forecast values of outcome variables based on one or more predictor variables. A linear relation between the two variable sets is assumed. By training and testing the model the researchers were able to yield the number of predicted COVID-19 cases that were a very close estimate to the original (Yadav, 2020). Such results can help governments prepare in advance for pandemic control.

Mathematical models such as the Susceptible-Infected-Recovered (SIR) Model and its modifications (such as those which also factor exposed, E individuals) are widely used for disease modelling. A recent trend has emerged in which these are endorsed by training neural networks to confirm the results. In one of the initial studies from China, during March 2020 such a study was performed in which the group of researchers initially utilized the SEIR model to mark epidemic peaks and dips. Later they also trained a recurrent neural network-based model using available data of confirmed cases. The disease parameters specific to COVID-19 such as its R_0 value, incubation and recovery period were incorporated to optimize it. It yielded promising results for long-term prediction in disease statistics (Yang *et al.*, 2020).

DIAGNOSTICS

Diagnosis of any disease is an important step in halting its spread. For non-transmissible diseases like cancer, an early diagnosis results in a more effective treatment procedure. Similarly, in the case of transmissible diseases like COVID-19, the suspected patients need to be diagnosed as soon as possible, as it simultaneously improves the efficiency of the treatment (Ganasegeran *et al.*, 2019), and prevents the further spread through that patient, by placing him in quarantine. Prognosis, on the other hand involves the prediction of a medical condition, which in this case, is the person being infected by the virus. It tries to answer questions related to the stability of symptoms over time, recovery rate, mortality rate and others. To a certain extent, accurate prognosis means being better prepared and thus, it helps in building and improving medical infrastructure accordingly. With the rapid increase in population, the amount of medical information in terms of records, documents, images and others available to us is considerably more than the situation a few decades ago. The simultaneous increase in computational power and advancement in technology has naturally led us to question whether AI can be used for medical diagnosis. The answer is, unsurprisingly, yes. Especially in case of pandemics like the ongoing one, AI can help save lives by early recognition of the disease.

Rather than the suspected patient having to wait for 72 hours for his RT-PCR test report, chest CT scans have been used for a faster, equally reliable AI-based diagnosis (Mei *et al.*, 2020). The CT scan, along with a certain amount of clinical history like travel record, absolute and relative counts of certain types of white blood cells, age, sex among others generate a sufficiently reliable database. It has been observed that suspected patients whose RT-PCR report turn out to be positive, have some common imaging patterns on their chest CTs. A CNN has been used for the detection of similar patterns in images. A database has been formed from such images, and this dataset has been used to train the network (Sethy *et al.*, 2020). Predictions are accordingly made on new cases. Another method has gained considerable popularity: it is the idea of a mobile application to predict COVID-19 infection, by comparing the user's symptoms with the results of traditional COVID tests. For the same, a mathematical model may be generated that helps make fairly accurate predictions with the help of the available dataset. An AI agent can train itself to identify patterns amongst data that even experienced doctors fail to recognize. For example, the fact that loss of taste and smell can be an important symptom for the early detection of COVID-19 was overlooked until fairly recently (Nguyen *et al.*, 2020). Other methods, although not widely used, may still be applied. For example, diagnosing a patient using unsupervised learning for pattern recognition, or using supervised learning to classify a patient into a class of a pandemic are other challenging ideas (Wynants *et al.*, 2020).

SURVEILLANCE

Until an effective drug has been tested and released for worldwide use, the only alternative we have in order to ensure our safety is to socially distance ourselves from others and use protective gear. Despite guidelines in place, proper implementation remains a challenge. Given the size of the population under consideration, in developing countries,

manual supervision is not a realistic option. Solutions have been devised which incorporate AI (Calvo *et al.*, 2020). A very promising concept has been the proposed idea of AI based surveillance cameras. Sophisticated fields of study like Computer Vision helps us understand how computers understand and process visual data. Rather than having surveillance cameras with manual monitoring, with the introduction of certain algorithms similar to ones that help in facial recognition, it is possible to check whether a person is wearing a mask or not. Similarly, existing techniques suggest the inclusion of a similar idea in checking whether social distancing norms are being followed, which will be a more efficient and rapid process compared to manual surveillance (Calvo *et al.*, 2020; Allam *et al.*, 2020). Training on a large dataset is mandatory for smooth functioning of the system. Such datasets involving crowd movements are abundant, which makes this particular approach highly feasible. High risk areas can be observed, and interventions issued where required based on the outputs from the AI system.

THERAPEUTICS

At present there is no known vaccine or drug found to be effective against SARS-CoV-2 infection. One major approach is drug repurposing - using drugs or antivirals clinically approved for other diseases. Owing to similarities in viral pathogenesis mechanisms or host immune responses certain drugs may yield results in the context of COVID-19. The other alternative is the discovery and design of new pharmaceuticals, which is a tedious process. Both approaches can be addressed using AI. Machine learning based tools have been developed to reposition drugs, combined with statistical analysis. This framework identified an anti-tumour inhibitor of the enzyme PolyADP ribose polymerase as a potential therapeutic for COVID-19, substantiated by wet-lab experimentation (Ge *et al.*, 2020). In another collaborative study by Insilico Medicine and Nanome Inc. an AI-driven generative chemistry perspective was used for novel drug design. Deep learning has received significant attention in recent years for molecular docking and optimization experiments. This has reduced the resources required in traditional approaches for downstream synthesis of novel molecules. This particular study yielded 10 possible structures that can be used as potential inhibitors for the SARS-CoV-2 protease enzyme and are in the process of validation (Zhavoronkov *et al.*, 2020). Google DeepMind created a deep learning system called AlphaFold for protein structure prediction. This neural net has produced structures for SARS-CoV-2 viral proteins which were not experimentally possible. These have revealed docking sites that hold promise in novel drug discovery, reducing several months of effort. Investigations are underway in using these for vaccine design as well (Jumper *et al.*, 2020). Since AI has already found success in disease prognosis for COVID-19 (Awwalu *et al.*, 2015) the current focus is on the betterment of personalized medicine. An integrated approach consisting of inputs by medical personnel and AI-based predictions for hospitalization and extent of therapeutics can be successful in addressing the extensive disease burden of SARS-CoV-2.

DISCUSSION

The COVID-19 emergency has led to unprecedented changes in the world spanning multiple aspects. Although the disease burden has started declining in most developed nations,

South-east Asia and the USA are struggling to bring the pandemic situation into control. A lesson for the healthcare community has been the need for prompt response to a surge in cases. It is crucial to design and implement a medical service system that satisfies mainly three aspects. These include ease of access to healthcare, particularly in low-resource regions, optimizing the quality of care with focus on personalized treatment regimens, and an effective cost containing principle (Bullock *et al.*, 2020). All these can be achieved if methods are used to support the medical workforce at every step. AI can augment the efficacy of handling such situations if applied in a constructive manner.

The rapid advancement in science and technology, in particular, fields such as robotics, AI, data analytics and bioinformatics can be used to create a foundation for strengthening the healthcare system. Triaging of patients, as evident from the current situation can be simplified by incorporating AI prediction systems (Agrebi *et al.*, 2020). This would ensure delivery of appropriate care at the point of need, while minimizing redundancies in treatment (Jiang *et al.*, 2017). Since SARS-CoV-2 infection presents mostly as mildly symptomatic or asymptomatic in a large fraction of the population, reducing the need to consult doctors at every stage is essential. This can very well be achieved through access to applications that gauge severity of symptoms remotely (Gugnani, 2020). Automated solutions are being explored for analysis of CT and MRI scans to speed up the diagnosis and prognosis processes. Real time support to radiologists and clinicians could be helpful to reduce burden on hospitals (Di Gennaro *et al.*, 2020; Naudé, 2020). The AI Oncology Suite of Arterys Inc., a US based provider of cloud-based medical imaging software solutions has received FDA clearance and is achieving promising success.

The inclusion of AI in primary healthcare is in initial stages and needs to undergo significant validation (Bashshur *et al.*, 2020). The basis of using AI to maneuver the pressing issues lies in the collection and analysis of a significant amount of patient records and databases. This is used to develop and build operational programs and software for mainstream application (Vaishya *et al.*, 2020; Wang *et al.*, 2019). A growing concern is that these approaches could impinge on data privacy. Protection of patient records from external threats is an important feature to be guaranteed by medical practitioners (Noorbaksh-Sabet *et al.*, 2019). Any shortfall in justifying the need to collect data to the public can have long-lasting setbacks. The innovations in AI that have accompanied the urgency of the pandemic need to be kept under strict jurisdiction, while also ensuring rapid incorporation into practical usage.

From a realistic viewpoint, a major delimiter in the inclusion of AI in primary healthcare, especially in developing countries, is the availability of state-of-the-art technology. For modern technology to be incorporated into primary healthcare, the available budget will be a significant concern (Shachar *et al.*, 2020). In times when the economy has taken such a hit, the question of whether people will be willing to invest in AI naturally arises. Another aspect to be considered is the loss of livelihood as a result of the pandemic. Under the current circumstances, thousands of employees have lost their jobs with unemployment becoming a very serious problem. Will governments agree to use AI and risk further

loss of livelihood in exchange for improved and more efficient systems? That remains to be seen.

FUTURE PROSPECTS

The future is unpredictable. A study from the World Economic Forum has shown that 65% of tomorrow's workers, i.e., the future generation, will have jobs and work on technologies that do not exist today. That is the rapid rate at which technological advancement is taking place. Given the unpredictability surrounding future technology, it can be said with some confidence that AI is here to stay, and it is very likely that with time, the inclusion of AI in fields such as primary healthcare is bound to increase. Completely eliminating the need for a doctor in the near future is questionable. However, AI based "doctor-like" applications for medical diagnosis and the introduction of robots into the field of medical surgery are two of the many ways AI has been included to not only improve healthcare, but also be used as a substitute for doctors (Altman, 1999). Probabilistically speaking, the ideal opportunities for the inclusion of AI in healthcare in the near future are hybrid models, where the doctors are supported in diagnosis, treatment planning, identifying risk factors as well as performing surgeries, but retain overall responsibility for the patient's care. By doing so, healthcare providers will also be keen on adopting the modern technology into their systems because of the various advantages it has to offer, while at the same time, retaining control over the entire system too.

CONCLUSION

In this review, the concepts of Artificial Intelligence in tackling COVID-19 has been elaborated. We have tried to show how and why AI has been introduced to the field of healthcare and looked at specific instances where AI has helped in tackling a medical condition. We would like to conclude by stating that although the advantages of incorporating AI into fields like healthcare outweigh the disadvantages, the practical implementation depends upon several factors, as mentioned previously. In the long run, the ideal solution would be human intelligence and artificial intelligence working hand in hand in order to improve our lives.

IMPORTANT HIGHLIGHTS OF THE MANUSCRIPT:

- This review article primarily focuses on the vast potential and applications of Artificial Intelligence in Healthcare.
- The critical aspects of the SARS-CoV-2 Virus, responsible for causing the Coronavirus Disease 2019 and its important characteristics are elaborated upon.
- The review highlights the workflow of AI in gathering and processing clinical records of infectious diseases, particularly, COVID-19, while emphasizing the significance of AI in rapid combat of the pandemic.
- It also specifies the general advantages conferred by AI in hospital and patient management and clinician support.
- The article discusses the recent developments in incorporation of AI Algorithms in the Diagnostics, Epidemiological tracking, Therapeutic development and Surveillance measures for COVID-19.
- The main focus of the article is the importance of monitored and structured AI incorporation in Healthcare on a global scale and more so in developing nations to

enable efficacious control in low-resource and heavily populated regions.

- Lastly, the paper discusses the future scope, applications and limitations of these developments and possible strategies for better implementation in light of the current pandemic.

LIST OF ABBREVIATIONS

ACE2 - Angiotensin Converting Enzyme 2
 ADP – Adenosine Di Phosphate
 AI – Artificial Intelligence
 CNN – Convolutional Neural Networks
 COVID-19 – Coronavirus Disease 2019
 CT – Computed Tomography
 IL-6 – Interleukin 6
 MERS - Middle East Respiratory Syndrome
 ML – Machine Learning
 MRI – Magnetic Resonance Imaging
 NLP – Natural Language Processing
 qRT-PCR – Quantitative Reverse Transcription Polymerase Chain Reaction
 SARS - Severe Acute Respiratory Syndrome
 SARS-CoV-2 - Severe Acute Respiratory Syndrome Coronavirus 2
 SIR – Susceptible-Infected-Recovered
 WBCs – White Blood Cells
 WHO – World Health Organization

FINANCIAL SUPPORT

This review does not have any external source of funding or financial support. No support is available for bearing cost of publications and is entirely self-funded by the authors.

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