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A comprehensive review on variants of SARS-CoVs-2: Challenges, solutions and open issues

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A R T I C L E I N F O

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A B S T R A C T

SARS-CoV-2 is an infected disease caused by one of the variants of Coronavirus which emerged in December 2019. It is declared a pandemic by WHO in March 2020. COVID-19 outbreak has put the world on a halt and is a major threat to the public health system. It has shattered the world with its effects on different areas as the pandemic hit the world in a number of waves with different variants and mutations. Each variant and mutation have different transmission and infection rates in the human population. More than 609 million people have tested positive and more than 6.5 million people have died due to this disease as per 14th September 2022. Despite of numerous efforts, precautions and vaccination the infection has grown rapidly in the world. In this paper, we aim to give a holistic overview of COVID-19 its variants, game theory perspective, effects on the different social and economic areas, diagnostic advancements, treatment methods. A taxonomy is made for the proper insight of the work demonstrated in the paper. Finally, we discuss the open issues associated with COVID-19 in different fields and futuristic research trends in the area. The main aim of the paper is to provide comprehensive literature that covers all the areas and provide an expert understanding of the COVID-19 techniques and potentially be further utilized to combat the outbreak of COVID-19.

1. Introduction

In recent times with the pace of fast growth, many new diseases have emerged with time in the world some of which are fatal or diseases of concern for mankind. Many of these diseases came from Viruses Like Ebola, Zika, Nipah, and Coronavirus (CoVs). Out of which Coronavirus (CoVs) have significant outbreaks at different times. One of the Coronavirus (CoVs) mutation severe acute respiratory syndrome (SARS) outbreak in 2002 and Middle East respiratory syndrome (MERS) outbreak in 2012 has shown the severity of the virus. Another mutation of that Coronavirus (CoVs) Severe Acute Respiratory Syndrome (SARS) caused an outbreak of Coronavirus 2019 commonly called Covid-19 or SARS-CoV-2 which has emerged as a Global Pandemic. Effecting the whole world and emerging as the most fatal disease of modern time causing a global health threat [1].

In recent times with the pace of fast growth, many new diseases have emerged with time in the world some of which are fatal or diseases of concern for mankind. Many of these diseases came from Viruses Like Ebola, Zika, Nipah, and Coronavirus (CoVs). Out of which CoVs have significant outbreaks at different times. One of the CoVs mutation severe acute respiratory syndrome (SARS) outbreak in 2002 and Middle East respiratory syndrome (MERS) outbreak in 2012 has shown the severity of the virus. Another mutation of that Coronavirus (CoVs) Severe Acute Respiratory Syndrome (SARS) caused an outbreak of Coronavirus 2019 commonly called Covid-19 or SARS-CoV-2 which has emerged as a Global Pandemic. Effecting the whole world and emerging as the most fatal disease of modern time causing a global health threat [1].

As compared to previous CoVs Covid-19 has a higher transmission rate due to which the cases increased globally. as compared to the other CoVs they have low to moderate transmissibility. Studies suggest that the new variant of the virus emerged from the bats and then came into humans. The primary patients were found in the South China Seafood market in Wuhan Virus was diagnosed early due to better facilities but now drugs existed in the starting to stop the spread. The primary most common symptoms of the coronavirus are common cold, fever, cough, fatigue, dyspnea, headache, body ache from mind to severe which may become fatal. It is one of the Coronavirus variants which affect humans among the 6 others [3]. This virus belongs to the same CoVs family but is genetically different. The individual with a serious condition admitted to the hospital also suffered from other symptoms like diarrhea, shortness of breath [4].

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Covid-19 is a great threat to the Human community and the global healthcare system. After the rapid emergence of Covid-19 in China and its exuberant transmission on such a high scale not only within the county but all over the world within no time. WHO declared a global emergency on 31 Jan 2020 and then declared it a Pandemic on 11 March 2020. Initially, there was no effective treatment or vaccine which treated covid-19 only preventive measures were applied in the initial strategy of prevention.

This Covid-19 pandemic shut the world down and forced them to get isolated in their space with little or no contact with the outside world if not necessary. It created an atmosphere of fear and the world entered into an economic recession. The new variants of this deadly virus emerging create the emergency of getting everyone vaccinated as soon as possible. As the pathogen is constantly evolving and invading immunity race to vaccinate is needed, which may possibly end the pandemic. The covid-19 vaccine will be able to protect against this deadly virus and also help in new emerging variants. These new mutation variants are a cause of concern as new variants may emerge in the future which may lead to an epidemic rebound [1].

Potential advantage from a performance perspective is early detection of covid-19, its variants and its long or short term side effects will help us in controlling the pandemic and limiting its spread.

In this review, we address features of SARS-COV-2 or Covid-19, Techniques for Covid-19 prediction, Deep Learning Models out there for Covid-19 detection, evaluation techniques for such models, Testing techniques for Covid-19 virus, Variants of Covid-19, Effective Vaccines for disease, Impact of this global pandemic on the World in various fields.

1.1. Paper organization

The paper organization is shown in the Figs. 1 and 2. Fig. 1 explains the flow in the paper and Fig. 2 represents the broad division of topics in the paper. Section 1 gives a brief introduction. Section 2 describe previous related work. Sections 3 and 4 discuss SARS-COV-2 variants and new emerging variants. Section 3.7 has the game theory perspective. Sections 3.4 to 3.6 discuss fungus, different side effects and various impacts. Sections 4 and 5 elaborate the diagnostic methods and treatments respectively. Section 6 state open issues in the field. Section 7 present the conclusion.

1.2. Taxonomy

Paper give the detail elaboration SARS-CoV-2 is given in Fig. 3. Section 3 has SARS-CoV-2 its variants, naming of its variants, reason of formation of various variants. New Emerging Variants, Game theory perspective of covid-19. Fungus, placed where it hit, types of fungus. Side effects of covid-19 Long and short term. Impact on various dynamics global economy, Education, healthcare, tourism, Education, Telecommunication. Diagnosis of covid-19 via testing — molecular test, serological test, PCR testing, Lateral Flow, Deep learning model for diagnosis — CNN, VGG, RESNET, Inception V3, DenseNet, Evaluation Metrics. Treatments — vaccine, preventive measures. Lastly open issues and conclusion are concluded.

2. Related work

We studied many articles that looked into how DL models were used in the diagnosis of SARS-CoV-2 infection using CXR and CT scan images [21]. The great majority of the experiments used publicly accessible CNN architectures trained on the ImageNet dataset for transfer learning. They used publicly available parameters settings for training their model and fine-tuned the existing model on the required dataset. However, many researchers used novel architectural models rather than the old existing techniques [22].

In this section, we will state the main approaches and datasets that were used in various studies. Table 1 shows the classification of papers studied in various category for related survey on COVID-19. There are many ways of covid-19 detection [23], by accessing symptoms, taking antigen test, RTPCR test, Medical Image Diagnosis. In all the diagnosis procedure Image diagnosis help us in early and accurate diagnosis. In the time of the pandemic, we have faced an extreme shortage of medical staff as the number of patients increased drastically and the number of medical staff also decreased as they were also infected by the virus [24]. Therefore, we need some medical assistance techniques so that it is easier for medical persons to process a large amount of data test reports. Convolution Neural Network(CNN) [25] in Neural Network is the basic network that works for image classification, Object detection, CNN takes input and pass it through convolution neural net then apply pooling and softmax function on classifying the image into different categories. Extraction of feature is done in the feature learning layer which is connected to the fully connected layers. whose results are passed to the Classification layer where we apply the softmax function on the features extracted and then classify the input [26]. CNN is pre-trained to the back-propagation in which weights are automatically updated with each iteration in the back-propagation. While we train a CNN from scratch the weights are randomly assigned which are adjusted with each iteration as we train the model, and feed the input gain through back-propagation [27]. Nowadays, transfer learning is a popular strategy for training Deep learning models for new tasks. We use the parameters of previously pre-trained models [28] as an input to our the novel model for the new task in transfer learning. This is where we adjust the settings based on our current model. We employ transfer learning since it cuts down on our training time while also improving our accuracy and model performance. We only utilize transfer learning when our model has a high starting point or a high rate of development [29].
3. SARS-CoV-2 variants

As time passes and the virus is spreading to every part of the globe which is giving it more chances to mutate and form new variants. Mutation in the virus can lead to the formation of a new variant of the virus which is different from the existing one. Most mutations can have little or no impact on the virus. However, some mutations can even change the characteristics of the virus making it more deadly, more or less transmissible, more or less effective, more or less severe, and even changing the vaccine efficiency on the virus.

WHO with the help of other organizations is tracking all the variants and mutations on the virus and informing countries and people about the nature of variants so that the required safety precautions can be taken and the spread of the virus can be prevented. accessing the risk any variants can cause on the global health they are divided into categories of VOIs and VOCs.

Reducing the rate of transmission of the virus is the main concern and the first precaution method suggested for the virus, as well as avoiding the virus to spread into the animal population is the crucial step to reduce its mutations which can prove fatal for the human population and can stumble the public health.

3.1. Reason of variants formation

Any virus which is circulating on a large scale among the human population and causes infections to masses, such virus has more chances to mutate. The more it spread the more by making it replicas the more changes it undergoes and more mutations happen in the virus. A single change in the genetic material of the virus is termed as mutation whereas when a genome of the virus contains one or more mutations then it is called a variant. A variant of a virus is a new strain of the existing virus with a change in RNA structure and Virus behavior.

Slight mutations have little or no impact on the virus characteristics such ability to cause infection. but when the virus genome is muted and a new strain is formed then virus characteristics of spreading infection and severity of infection also change. Any such change can make a new variant less or more severe, can change vaccine effectiveness on the virus, and also social measures taken for it.

All viruses, including SARS-CoV-2, change with time, and as it is announced as the pandemic so WHO with other partners, research institutes, and health organizations have been monitoring the virus mutations since their origin from January 2020. Dividing the variants into two categories Variants of Interest (VOIs) and Variants of Concern
3.2. Naming SARS-CoV-2 variants

The naming of SARS-CoV-2 variants is currently done by GISAD, Nextstrain, and Pango. GISAD is a Global initiative on sharing avian flu data it is established in 2008 and provides access to genomic data of influenza and SARS-Cov-2 virus. It is an initiative taken globally for monitoring and keeping a record of this Covid-19 pandemic. Nextstrain is an organization for real-time tracking of pathogens, their evolution, and their genomic data. Pango Lineage (The Phylogenetic Assignment of Named Global Outbreak) is a software tool used for naming the nomenclature name of SARS-Cov-2 the name given by the organization is called pango nomenclature which is commonly used by the researchers to track the spread of the virus. Tables 2 and 3 shows the different CoV-2 variants and their names given by different naming agencies place and time they are earliest documented.

The scientific name is given by these three organizations but for easy public discussion and understanding WHO Technical Advisory Group on Virus Evolution has come up with simple names for laymen people using the Greek Alphabet. Which are easy to pronounce and discuss for any person with a non-medical background.

3.2.1. Alpha

Alpha strain is one of the variants of SARS-CoV-2 which is originated from the UK (B.1.1.7) on Sep-2020 and formally designated in Dec-2020. This is the first variant that came into the VOCs category. It has increased the number of cases from 3% to 96% over a period from October to February in the UK. It then hit the US because of its characteristics of high transmissibility and high mortality rate which is more than double (40%–80%) as compared to the original virus found in China. As compared to the original virus this variant has 23 mutations in it. Out of which 8 mutations were only found in the S protein. The N501Y mutation allowed the S protein to bind more tightly to the ACE2 receptors [30]. A report in January 2021 states that this variant caused more death than other variants mortality rate was 55% higher than the others [31]. This variant has been found in 82 countries [32].

3.2.2. Beta

Beta strain scientifically known as B.1.351 was identified in South Africa in May 2020 and formally designated in December 2020. This variant affected the younger age group as compared with previous variants. It has 23 mutations with 17 amino acid mutations, its E484K mutation where mutation on S protein made it a deadly strain by increasing its transmissible as it escapes the immune system and caused the third wave in South Africa. It even affected healthy people without any prior disease. this E484K variant even reduced the sensitivity to the vaccine. due to its escape nature. vaccines showed less efficacy to this variant than others. This variant has been found in 80 countries [33].

3.2.3. Gamma

Gamma strain is also known as P.1 variant and scientifically known as B.1.1.28.1. It was identified in Brazil in November 2020. the new variant was twice more transmissible as compared to other previous variants. It has a high mortality rate and caused two waves in Brazil. due to its high transmissible rate about 2.2 times more than other variants, it caused re-infection and affected both young and older populations with the same intensity [34]. The gamma strain P.1 has similar receptors as B.1.351 and hence this new variant is similar to beta the vaccine efficacy on the gamma variant is also less [35].

3.2.4. Delta & delta plus

Delta variant is also famous as a double mutant variant and scientifically called B.1.617.2. It was first identified in India. The virus has two mutations in it hence called a double mutant, this variant was the reason behind the second wave in India and increased the number of cases drastically due to its very high transmissibility. WHO also reported this variant as the fastest and fittest variant to date, due to its high contagiousness this variant affected the people’s vulnerability who have some previous disease and it proved fatal to such individuals. It affects more on the places with low vaccination. It is 60% more transmissible rate as compared to other previous variants [27]. This variant is found in 92 countries now transmitting infection. This variant badly affected US and UK where the number of cases is increasing due to this variant [28]. Delta variant had another mutation in its spike protein which formed a new variant coined as Delta Plus. Delta variant with K417N mutation was stated as VOC on May 2021.

3.2.5. Omicron

Omicron is also scientifically known as B.1.1.529. it was first reported on November 2021 in South Africa. It increased the number of
cases in South Africa after the Delta variant. It has a higher transmissibility rate than delta variants analyzing the data we have it may not be as fatal as Delta but is more transmissible and the number of cases per day is increasing day by day from the virus. Omicron variant was stated as VOC on Nov 2021.

Every new variant not only increases transmissibility and mortality rate but also decreases the efficacy of the existing treatment and vaccine on them. Fig. 5 shows the timeline of the variants of SARS-COVID-19 in detail. It increases the danger of reinfection to the individual. More transmission of virus will cause more chances of mutation and every new mutation in the virus comes with the chance of even more vulnerable variants which can affect global health drastically. So monitoring, early identification, prevention measures, and vaccination are the most important steps for coming out of this pandemic.

3.3. New variants of covid-19

3.3.1. Omicron lineage variant

Compared to prior COVID-19 viral varieties, such as the Delta variant, the Omicron version is easier to disseminate. No matter if they have received a vaccination or exhibit any symptoms, the CDC anticipates that everyone with an Omicron infection can transmit the infection to others. The Omicron variant of concern, which accounts for almost all sequences submitted to GISAID, is currently the predominant variant circulating globally. Omicron consists of a number of sub-lineages, each of which is under the supervision of the WHO and other partners. The most prevalent of them are BA.1, BA.1.1 (also known as Nexstrain clade 21K), and BA.2 (or Nexstrain clade 21L). Globally, the fraction of reported sequences with the BA.2 designation has been rising compared to BA.1 in recent weeks, but it is allegedly decreasing globally across all variants. The genetic sequence of BA.2 differs from BA.1, and the spike protein and other proteins have some different amino acids. Studies have revealed that BA.2 outgrows BA.1 in terms of growth. While research is ongoing to determine the causes of this growth advantage, preliminary findings imply that BA.2 is genetically more highly infectious than BA.1, the Omicron sub-lineage that is now most frequently reported. As opposed to, the variation between BA.1 and Delta, this variation in transmissibility seems to be significantly smaller. Additionally, despite the fact that the fraction of BA.2 sequences compared to the two Omicron sub-lineages (BA.1 and BA.1.1) is growing, there is still a confirmed drop in overall cases globally. BA.2 may produce a more serious illness in hamsters than BA.1 does, according to SARS-CoV-2.

3.3.2. BA.2

The new sub-type’s quick spread raises the possibility that it is much more infectious than the original Omicron variety. In accordance with the UK Health Security Agency (UKHSA), BA.2 is a “variant under monitoring”. In several other nations, including Denmark, the UK, India, and Sweden, a novel variant of the Omicron coronavirus variant is circulating. It is still unknown how exactly the genetic alterations will affect things. Since the first Omicron mutant BA.1 was discovered, we are already aware of how much more contagious it is compared to earlier coronavirus variants. Now, BA.2 has become a sub-type. In the UK, at least 400 people have contracted it in the first 10 days of January. Additionally, it has already been found in more than 40 other nations throughout the world.

3.3.3. BA.4 and BA.5

Two additional Omicron spin-offs variant are on the rise globally after the variant’s BA.2 lineage triggered surges. The newest members of Omicron’s expanding family of coronavirus sub-variants are BA.4 and BA.5, which were identified in South Africa for the first time by researchers in April and are associated with a subsequent increase in cases there. They have been found in numerous nations throughout the world. Due to their ability to spread more quickly than other circulating variations, primarily BA.2, which spiked in cases at the start of the
year, the BA.4 and BA.5 sub-variants are spreading rapidly around the world. However, the most recent Omicron variants appear to be causing fewer hospitalizations and fatalities so far than their older relatives, which is evidence that rising population immunity is tamping down the immediate effects of COVID-19 spikes. The two strains resemble BA.2 more closely than the BA.1 variant that started the Omicron waves in the majority of countries late last year. The infectious spike protein carries alterations known as L452R and F486V in BA.4 and BA.5, which may alter the virus’s capacity to attach to host cells and escape some immune responses [36].

### 3.3.4. NeoCov

Researchers from around the world are warning that it is still unknown how dangerous the coronavirus strain NeoCov could be for humans at this time. However, there are no conversations about the rise of a new coronavirus which is ready to vigorously spread in the human population. This comes after a team of scientists from Wuhan, China, raised concerns about a coronavirus strain that is potentially dangerous than the previous variants. Experts have highlighted hazards that need more research. It was noted that NeoCov, a virus related to the Middle East Respiratory Syndrome (MERS-CoV), was found in a South African bat colony and is now exclusively affecting animals [37]. The virus however, have the latent ability to evolve and infect the human population. Scientists assert that all it takes for the virus to enter human cells is one mutation. Scientists had also noted that SARS-CoV-2 or MERS-CoV antibodies could not cross-neutralize NeoCov infection.

### 3.3.5. Deltacron

In January 2022, the Deltacron variant was found for the first time. It was found by Leondios Kostrikis, who is the head of the Cypriot Laboratory of Biotechnology and Molecular Virology and a professor at the University of Cyprus. He found the variant in 25 people with COVID. But this variant was different because it was made up of viral genetic material from two different variants. Dr. Kostrikis called it “Deltacron” because it was like both Delta and Omicron [38].

### 3.3.6. Recombinants

WHO has warned people against the recombinant virus. The presence of three hybrid COVID-19 types, XD, XF, and XE, was also validated in a recent study conducted by the UK Health Security Agency (UKHSA). In the case of the SARS-CoV-2 virus, the recombinant strain contains genetic material from two strains, which are Omicron and Delta in the case of currently circulating hybrid versions. As both the two variants Omicron and Delta are deadly and have high transmissibility so experts are keeping eye on the recombinant viruses.

Recombinants are expected is widespread among humans and many animal species now. Testing, surveillance (including ILI & SAR), sequencing & data sharing still important to keep track of the pandemic & take early action when new variants emerge.

The World Health Organization (WHO) recently issued a warning regarding the XE recombinant virus, claiming that its infection incidence is around 10% greater than the BA.2 (Omicron sub-lineage) variety. Humans and many animal species are now exposed to recombinants, as expected. All the three variants are kept under observation and assigned as variants under monitoring (VUMs). A recombinant virus is an amalgamation between two different strains of the same virus. It can be formed naturally or through the use of recombinant DNA technology to combine strands of DNA.

### 3.3.7. XE

The XE recombinant, which is a combination of BA.1 and BA.2 Omicron sub-lineage, was first detected in the UK on January 19 and less than 600 sequences have been reported and confirmed so far, as per the UK Health Security Agency report. It contains the spike and structural proteins from BA.2 but comprises a fifth of the genome of BA.1. According to WHO, Early-day estimates indicate a community growth rate advantage of 10% as compared to BA.2, however, this finding requires further confirmation.

### 3.3.8. XD & XF

The recombinant variants XD and XF share genetic material of the previous strains of Delta and BA.1 Omicron variant of COVID-19. Both contain several 10 s of sequences currently. While XD has been detected in France, Denmark and Belgium, XF has been widely identified in the UK.

Experts have no confirmation on the severity of the hybrid variants. However, depending on one’s vaccination status, established immunity and history of past infections, symptoms could vary from person to person. The most common symptoms to look out for are fever, sore/scratchy throat, cough, runny nose, sneezing, fatigue, body pain, rashes and discoloration, gastrointestinal problems and in certain cases loss of sense of smell and taste, which was less prevalent during the Omicron wave. Severe symptoms include shortness of breath, heart palpitations, chest pain, low blood oxygen levels. In light of these symptoms, call for medical assistance immediately.

### 3.4. Fungus

The second covid-19 wave in India affected the county much drastically with the infection many people also encountered with a fungal infection. This fungal infection is more commonly called Black fungus as it affected the skin tissue and turned it black. This fungal infection is known as Mucormycosis which happened due to the use of immunosuppressant for the treatment of Covid 19. Any patient who has some previous history of hyperglycemia, ketoacidosis, bone marrow transplant, Liver cirrhosis, and then infected by this Covid-19 virus has more chances of getting this fungal infection mucormycosis. India has reported total cases of 51,775 cases till November 29, 2021. This is one of the rarest types of infection which resulted as a side effect of treatment of Covid-19. This mucormycetes mould mainly occurs in soil, leaves, dead and decay work, etc. The use of steroids for the treatment of covid-19 is the main reason for the spreading of this infection. It has a high mortality rate of about 50% with the side effects of the blackening of infected tissues. In many cases, it has affected the eyes where the outcomes are poor causing potential blindness or brain defect or headaches or even seizures, and to stop the spread of the infection only removal of the infected part was the solution making it more vulnerable. Fig. 6 shows the chances of fungal infection in different scenario in different combination. To treat Mucormycosis for major factors are the early diagnosis of symptoms, removal of predisposing factors, anti-fungal therapy on time before the infection spread too much, and adjunctive therapies.

#### 3.4.1. Places where fungus hit

As Mucormycosis is a side effect of Covid 19. It is mostly spread in many countries affection some very badly. India has a very large number of covid 19 cases, so if any person has any history of disease like diabetes is very much prone to get this fungus infection. Post covid 19 our body immunity decrease and it is easy for any fungal infection to attach us. Whereas India is affected by this pandemic in pandemic.
disease more badly than other cold countries as the temperature, heat, and humidity in the country make it easier for the fungus to spread and attack. Mucormycosis cases are seen in countries like the UK, US, Australia, Chile, Uruguay, Egypt, Iraq, South America, India. It has been documented that about 70% of the total cases are reported from India itself. A recent study demonstrates people who got affected by the fungus 94% of them suffered from diabetes. Which could also be a triggering point in India with the atmospheric conditions.

3.4.2. Types of fungus

Table 4 shows the summary of different types of fungal infection, their visible symptoms, curability, any pre-medical conditions and the affected area. It is further elaborated in the given section.

| S. No. | Fungus type | Visible patched | Curable | Pre-medical condition | Affected areas |
|-------|-------------|-----------------|---------|-----------------------|---------------|
| 1     | Black       | Yes - black in color | Yes | Diabetes | eyes, brain, lungs, sinuses |
| 2     | White       | Yes - white in color | Yes | Diabetes | body, skin, tongue, brain, Digestive system, Kidney, and genitals |
| 3     | Yellow      | No               | Yes - if diagnosed early else fatal | Diabetes | Internal body organs |
| 4     | Green       | No               | Yes - easy to cure | Diabetes | lungs |

3.5. Side effects of covid-19

The novel coronavirus has impacted our lives in various ways. Not only have we battled mild to severe symptoms, but we have also outlived a series of deadly and infectious variants. Furthermore, the long-term effects of SARS-CoV-2 virus is something that has left many of us drained and exhausted. Almost 10 percent of COVID-19 patients are estimated to be impacted by long COVID following 12 weeks of initial infection. The symptoms could persist for up to 6 months.

3.5.1. Long term

Long COVID is a condition that occurs in people who have caught the SARS-CoV-2 virus in the past. However, the patients continue to experience the symptoms long after their recovery. Most common symptoms include cough, fatigue, body ache, loss of smell and taste and brain fog. However, recent study suggests that it could also have certain psychological implications in patients [39].

- A severe case of COVID-19 can cause scarring and other irreversible issues in the lungs, but even minor infections can cause recurrent shortness of breath and the inability to sustain even light activity without becoming exhausted. Lung healing following COVID-19 is achievable but time-consuming.
- Some individuals infected with SARS-CoV-2 may have heart issues, involving inflammation of the heart tissue. In fact, one study revealed that sixty percent of individuals who recovered from COVID-19 exhibited signs of persistent cardiac inflammation, which may result in the classic symptoms of breathing difficulties, palpitations, and rapid heartbeat. This inflammation emerged even in patients with a moderate form of COVID-19 and no preexisting medical conditions.
• Coronavirus infection produced kidney damage, the risk of chronic renal disease and the requirement for dialysis may increase.
• Because the coronavirus can impact receptors in the nose, acquiring COVID-19 might cause altered or lost perceptions of smell and taste. Before and after being ill with COVID-19, individuals may completely lose their sense of smell or taste, or find that familiar items smell or taste unpleasant, weird, or unfamiliar. About a quarter of COVID-19 patients with one or more of these symptoms get resolution within a two weeks. For most, though, these symptoms continue. Though not life-threatening, persistent distortion of these senses can be debilitating, leading to loss of appetite, anxiety, and despair. Some studies indicate that there is a 60% to 80% likelihood that these individuals may experience a recovery in their sense of taste and smell within a year.
• Following COVID infection, some persons have moderate to long-term symptoms, such as brain fog, lethargy, headaches, and vertigo. The etiology of these symptoms is unknown, although inquiry is ongoing.
• The most common psychological [40] symptoms experienced by those suffering from long COVID are as follows:
  - Anxiety
  - Depression
  - Poor sleep
  - Stress

3.5.2. Short term

The majority of patients infected with COVID-19 exhibit little or no symptoms, however those with mild symptoms have reported breathlessness, fever, cough, lethargy (fatigue), and body aches. In more severe situations, short-term effects may also include respiratory (breathing) difficulties, confusion or other cognitive issues, and kidney or heart damage caused by a lack of oxygen or blood clots, which can sometimes lead to long-term complications. The severity of COVID-19 symptoms correlates with the likelihood of unfavorable organ effects [40].

3.6. Impact

This pandemic has hit the world in the most extreme ways about 26.4 Crore people were affected by the virus out of which 52.2 L people died as of 2nd December due to covid-19. As the world was unaware and unprepared for the virus it has impacted the sectors of life. Fig. 7 shows the impact in the various fields unforeseen challenges in Heath, Economy, Education, Food System, Personal life, Mental health. This economic and social disorder has devastating effects in almost all sectors. The pandemic has had a terrible impact on the economy and society. The number of undernourished persons is expected to rise to as high as 132 million by the end of the year from its current estimate of about 690 million. An existential threat is looming over millions of businesses worldwide. Of the world’s 3.3 billion workers, over half could be out of work soon. Workers in the informal economy are especially at risk because most of them lack social protection, access to proper health care, and have had their possessions seized or otherwise confiscated. Many people cannot afford to eat because they cannot work and bring in money during lockdowns. When people lose their jobs, they often lose access to food or are forced to eat less healthy options.

The pandemic has demonstrated the susceptibility of the worldwide food supply system. Due to border closures, trade restrictions, and confinement measures, farmers have been unable to obtain raw materials and sell their goods, and agricultural workers have been unable to harvest crops, thereby disrupting domestic and international food supply chains and limiting access to nutritious, safe, and diverse diets. It is safe to state that the outbreak has endangered the jobs of millions of individuals. Food production and nutrition are jeopardized for millions of women and men as breadwinners lose their jobs, become ill, or die. Those in low-income countries, particularly small-scale farmers and indigenous populations, are among the hardest afflicted.

3.6.1. Economy

Due to the absence of a concrete treatment approach and the daily appearance of new strains, there is no 100% effective short-term defense strategy against covid-19. Based on the amount of lockdowns and restrictions implemented by governments in various parts of the world at various times. As a result of changing the entire, the global economy has taken a significant hit. All non-essential services have been ordered to shut down, generating massive supply chain disruptions across nearly all industrial sectors and placing billions of people at risk of losing their jobs. In addition, the rapid spread of COVID-19 has compelled countries to restrict the trade of the vast majority of products across international boundaries, threatening the viability of international trade flows. According to JPMorgan Chase & Co.’s estimations, the COVID-19 pandemic has the ability to cripple the world economy, with a projected loss of even more than 5.5 trillion US dollars over the next 18 to 24 months.

In this section, we analyze the impact of the COVID-19 pandemic on the overall economy by thoroughly dissecting its impact on different economic sectors.

In an effort to contain the epidemic, numerous governments have enacted rigorous lock-down measures, which have caused significant manufacturing disruptions in the automobile sector. As social separation is imposed and people are expected to remain in their houses, automobile utilization, both public & private transportation, has decreased globally. Currently, only vehicles affiliated with critical services are in operation.

Following the emergence of COVID-19, the tourism sector is one of the businesses hardest hit. 10% of the world’s gross domestic product is comprised of tourism-related revenues. Therefore, any difficulty affecting the tourism industry has the potential to adversely impact the world economy.

As a result of the COVID-19 epidemic, present construction projects are likely to be severely disrupted and delayed. Due to the inability of the bulk of the workers to work as a result of strict self-quarantine regulations, the majority of construction companies will be obliged to suspend all non-essential services until the epidemic is contained. This will certainly lead to a massive rescheduling of existing projects, which could result in significant losses for the industry.

3.6.2. Education

During the lockdown period, schools were forced to close because to the pandemic, and students and teachers were forced to adapt to online
teaching and learning. In India, over 250 million pupils were impacted by the shutdown of schools at the commencement of the lockdown caused by COVID-19. The epidemic offered a number of issues for public and private schools, including an anticipated increase in dropout rates, learning losses, and a widening digital gap. The epidemic also put into question the preparedness of the systems, including teachers, and the viability of private schools to respond to such a catastrophe. COVID-19 worked as a catalyst for the implementation of digital technologies in classroom education. With schools reopening in a number of states, it is crucial to devise a comprehensive plan to ease the transition of children starting school after more than 15 months of home-based education. This shift must also take a futuristic perspective to develop a resilient system that can resist any future shocks, taking into account the learning losses that occurred over the preceding year [41].

3.6.3. Healthcare/medical

The global healthcare system has been severely impacted by the COVID-19 epidemic. While lock-downs and travel bans have had a chilling effect on the economies of most manufacturing sectors, the healthcare sector has seen anything but a standoff. Ventilators, critical care units, and personal protective equipment (PPE) to treat patients with COVID-19 are in insufficient supply at hospitals around the world. The exponential growth of the COVID-19 patient population has put the healthcare systems of even the world’s most affluent countries on the verge of collapse.

3.6.4. Tourism

Following the emergence of COVID-19, the tourism industry has been one of the businesses hardest hit. 10% of the world’s gross domestic product is comprised of tourism-related revenues. Therefore, any difficulty affecting the tourism industry has the potential to adversely impact the world economy. According to estimates by the World Travel & Tourism Council (WTTC), the COVID-19 pandemic might result in the global layoff of over 50 million tourism industry workers. According to data released by the United Nations World Tourism Organization (UNWTO), international tourist arrivals could decline by as much as 30% in 2020, resulting in a loss of 300–450 billion in international tourism revenues (ITRs).

3.6.5. Telecommunication

The pandemic of COVID-19 has had scattered effects on the telecommunication sector. Multiple telecommunications service providers (TSPs) and internet service providers (ISPs) [42] have reported a dramatic rise in traffic. Large-scale network bandwidth consumption has been attributed to government lockdown initiatives, which have compelled educational institutions to use online teaching platforms and businesses to permit employees to work from home [43]. The COVID-19 pandemic has not, however, spared the telecommunications industry. Similar to other industrial firms, the bulk of TSPs & ISPs have experienced a precipitous decline in their share values during the previous few months. According to GlobalData's examination of the share prices of some of the world's leading TSPs, the share prices of AT&T, China Telecom, and Telefonica fell by more than 20 percent from 1 January and 25 March 2020. The large-scale effects of the COVID-19 outbreak on the world economy can be traced to the inadequate response strategy that was implemented after its initial outbreak [44]. Despite the fact that the response to the COVID-19 outbreak has been better structured than to earlier epidemics and pandemics, there are still a few problems with the present epidemic/pandemic response system [45].

3.7. Game theory perspective

3.7.1. Supply chain

The current global pandemic of COVID-19 is a healthcare calamity that is neither period nor place specific. In response to the COVID-19 pandemic, the academic and professional groups have pooled their knowledge and used operations research and associated analytical tools to great effect. It has sparked further studies, as well as advancements in modeling and methodology, to aid in gaining more nuanced understanding, making more informed decisions, and advising policymakers. There have been several interesting developments and new uses of game theory that have been sparked by the COVID-19 outbreak [46]. Brief introduction to variational inequality theory, the underlying methodology for the construction, qualitative analysis, and solution of the models discussed. The models presented here are relatively new; they capture, in order, the incorporation of labor into supply chain networks, allowing for a quantitative assessment of labor disruptions; the intense competition between entities for pandemic medical supplies, from PPE to vaccines; and, finally, the calculation of the potential synergy associated with teaming, i.e., cooperation, among organizations [17].

3.7.2. Federated learning

Collaborative learning in FL has expanded into many fields thanks to its new cutting-edge capabilities, particularly in the field of intelligent IoT. The host data stays within the local nodes while FL techniques are used to transfer the local model parameters throughout the network. This lessens the likelihood of data leaks and improves privacy. Furthermore, FL’s generalization capability is improved by training networks on a variety of data. The transmission cost is further decreased because only gradients are uploaded rather than entire datasets. FL has taken these measures to ensure that big IoT networks use their bandwidth effectively and do not become congested. Despite this, FL provides a fresh setting in which IoT networks can be used productively. Unfortunately, FL has some security flaws that cannot be ignored [47]. There are a number of privacy-related challenges with IoT, however their adoption can be aided by FL. For instance, information from IoT devices’ local models feeds into the global model, which in turn updates itself. The attacker can launch a successful assault and obtain sensitive user data by employing a construction attack. Another way an opponent can figure out what kind of information is being sent is through an inference attack carried out by a hostile user. Possible examples of such information include blood samples, disease classifications, and clinical notes. Further, information about intrusion assaults can be found in the. Therefore, the nature of IoT assaults must be taken into account before any privacy solution can be developed [48]. A large amount of collected data can be utilized for diagnosis or diagnosis model development with the aid of numerous devices. However, the potential disclosure of patient data will potentially raise privacy and security concerns during the contact period. To address these challenges, we offer DEEP-FEL, a decentralized, efficient, and privacy-enhanced federated edge learning system that enables medical devices from various institutions to jointly train a global model without exchanging raw data [50]. To alleviate the centralization of the standard training framework, we first build a hierarchical ring topology and present the ring building as an optimization problem that can be solved by an optimal heuristic approach. In order to develop a new global model, we create an effective parameter aggregation algorithm for dispersed medical institutions [51].

3.7.3. Tourism economy

The evolutionary game theory derives from the concept of evolutionary processes and is frequently applied to several domains, including economics and the social sciences [52]. In contrast to the premise of “perfect rationality” in classical game theory, the assumption of “limited rationality” in evolutionary game theory makes the dynamic system more suitable for predicting the behavior of game participants. Thus, evolutionary game theory is applicable to the present circumstance. Due to its applicability to stakeholders, evolutionary game theory is frequently employed to examine the interrelationships amongst stakeholders.

Over time, players contact other players, and their steps are influenced by the decisions of other players. The evolutionary game
4. Diagnosis of Covid-19

4.1. Testing

The fast spread of SARS-CoV-2 requires the construction of sensitive and specific diagnostic tools. There are currently two distinct types of COVID-19 tests:

4.1.1. Molecular tests

The most widely used method for diagnosing SARS-CoV-2 infection is the Nucleic Acid Amplification Test (NAAT), which has been endorsed by the World Health Organization. To conduct these analyses, a nasopharyngeal swab is used to collect a mucus and saliva sample from the patient's upper respiratory tract (the back of the throat). However, the WHO suggests collecting samples from the lower respiratory tract as well in case the individual being tested has severe respiratory problems.

These samples are then analyzed in a specialist facility utilizing a real-time Reverse-Transcription Polymerase Chain Reaction (rRT-PCR) assay to determine the presence of viral RNA. A COVID-19 diagnosis is only confirmed if the test identifies either (i) the existence of two discriminatory forms of the SARS-CoV-2 genome, one of which is ideally explicit to the SARS-CoV-2, or (ii) the presence of beta coronavirus followed by the identification of SARS-CoV-2 using partial or complete virus genome sequencing. The target sequence must be longer than the amplicon used for the NAAT assay. The viral genes targeted by Nucleic Acid Amplification Tests (NAATs) are the N, E, S, and RdRp genes. A single gene identified in the NAAT necessitates a repeat test for the patient. The WHO suggests using a different specimen from that used in the initial testing if required.

4.1.3. PCR testing

PCR tests are used to effectively detect the existence of viral RNA, which is detectable in the body prior to the formation of antibodies or the onset of disease symptoms. This indicates that the tests can detect the presence of the virus relatively early on in the illness. During laboratory Covid-19 PCR testing, reverse transcriptase or DNA polymerase is introduced to a nasopharyngeal sample. These chemicals function to multiply any viral RNA which may be present. This is done so that sufficient replicas of the RNA are generated to show a positive result, since primers and probes latch themselves to regions of the genetic sequence of the virus to indicate the presence of a pathogen.

PCR provides a reliable indicator of who is affected. Those individuals could be isolated and anyone with whom they have been in contact can also be quarantined, for preventing the further spread of the disease. This is the fundamental benefit of the current primary diagnostic tests; we can break the transmission chain and obtain a clearer idea of what is occurring. By scaling PCR tests to screen large bands of nasopharyngeal swab samples within the population, health authorities can better understand the epidemic of diseases such as Covid-19.

However, there are still some caveats with PCR. These types of Covid-19 tests should be sent to the lab for analysis. That is, it can take several days for people to know the results. False-negative results can occur with a probability of up to 30% in various PCR tests. In other words, it helps confirm the presence of the infection rather than giving the patient true results. It is also so sensitive to detecting a dead inactivated virus that is still present in the body of a person who has recovered from Covid-19 can give a positive result, which can lead to false positives.

4.1.4. Lateral flow

LFTs are comparable to PCR testing in that they are both antigen tests designed to detect active Covid-19 infection instead of disease-specific antibodies. A Covid-19 LFT involves placing a nasopharyngeal sample on a small absorbent pad, which is subsequently dragged along the pad via a capillary tube to a strip coated in antibodies that bind to SARS-Cov-2 proteins. If certain proteins are present, a colored line will appear on the test to indicate infection. The primary advantage of LFTs over PCR is that they might not require validation and produce results in 15 to 30 min. They gain speed, however, they lose accuracy. Various research studies all around the world revealed that the accuracy of different LFT brands varied significantly. The research also indicated that these tests were significantly better at finding Covid-19 in symptomatic individuals than in those without symptoms. The sensitivity of LFTs in symptomatic individuals ranged from 34% to 88%, with an overall accuracy of 72%. LFTs successfully detected an average of 58 percent of asymptomatic individuals who were infected. In nations such as the United Kingdom, the use of LFTs for widespread asymptomatic testing has been recommended, but experts have thrown doubt on the usefulness of these Covid-19 tests in this context.

4.2. Deep learning algorithm for CAD

Artificial intelligence is a branch of computer science concerned with making smart machines capable of performing actions that typically require human intelligence. It tries to mimic the human brain into a machine by some algorithm and make them do the task as humans. Advancements in the field of machine learning and deep learning are creating a paradigm shift in almost every sector.

Image diagnosis in medical science is one of the emerging ways where AI and ML are being used extensively nowadays. Due to poor
conditions of the healthcare sector low number of healthcare experts and the high number of health issues have created a high imbalance in the system. Where Image diagnosis is a type of non-invasive method used to diagnose the human body or part to find the injury or illness or any lesion. Image diagnosis helps the experts for faster and precise processing to diagnose any disease from high-quality different type images.

Area of Image recognition has improved exponentially over the period, due to the availability of large-scale datasets and Deep CNN models. But there is no large-scale dataset present for the medical field as data acquisition is difficult and a costly process. In this paper, the authors have done an exhaustive digging into major techniques that used CNN or medical image classification. Tables 5 and 6 shows the comparative analysis of different latest techniques their merits and De-merits. It also representing how will the system behave when we train a CNN from scratch secondly, using pre-trained CNN models, and thirdly pre-training a model on natural image and then fine-tuning on a medical dataset using Deep learning models [55].

Fig. 8 shows a general CAD architecture, when a patient goes to doctor he prescribes some text for proper detection of disease such as X-ray or CT-Scan the data is stored in a database and used for training the model. Initially features are extracted from the dataset which are passed to the deep learning model for training, after training the model it used for classification and prediction and the accuracy of the model is checked by using various accuracy metrics.

For Feature Extraction various techniques are used for extracting and selecting features depending upon the model we are using. Encoder and Decoder are the most commonly used feature extraction techniques in CNN models. Dataset is divided into three categories training, validation and testing. 60% to 70% of the data is used for testing and 10% of data is used for validation and 20% to 30% of the data is used in testing.

Transfer learning is a technique used widely in training Deep learning models for new tasks nowadays. In this transfer Learning, we use the knowledge and training of previously pre-trained models as the base model of the new task. Where we fine-tune the parameters according to our current model. The major reason we use transfer learning is it reduces our training time and improves our accuracy and model performance. We use transfer Learning only when we have a high start of our model or a high rate of improvement of the model [56].

4.2.1. CNN

Convolution Neural Network(CNN) in Neural Network is the basic network that works for image classification Fig. 9 shows the flow of CNN Architecture. In object detection CNN takes input and pass it through convolution neural net then apply pooling and softmax function on classifying the image into different categories. Convolution Neural Network(CNN) in Neural Network is the basic network that works for image classification, Object detection, CNN takes input and pass it through convolution neural net then apply pooling and softmax function on classifying the image into different categories [69].

Extraction of feature is done in the feature learning layer which is connected to the fully connected layers. whose results are passed to the Classification layer where we apply the softmax function on the features extracted and then classify the input. CNN is pre-trained to the back-propagation in which weights are automatically updated with each iteration in the back-propagation. While we train a CNN from scratch the weights are randomly assigned which are adjusted with each iteration as we train the model, and feed the input gain through back-propagation.

4.2.2. VGG

VGG is a typical design for deep Convolutional Neural Networks (CNNs) with several layers. Deep refers to the number of convolutional
layers, with VGG-16 and VGG-19 including 16 and 19 convolutional layers, respectively. The VGG architecture serves as the foundation for innovative object recognition models. Designed as a deep neural network, the VGGNet outperforms benchmarks on numerous tasks and datasets outside ImageNet. In addition, it remains one of the most prominent image recognition architectures.

The VGG architecture: The VGG Net accepts an input image size of 224 by 224 pixels. To maintain an uniform input size for the ImageNet competition, the designers of the model clipped out the 224x224 patch in the center of each image. Convolution Layers In addition, there are 11 convolution filters that operate as linear input transformations. Following this is a ReLU unit. ReLU, which stands for rectified linear unit activation function, is a piece-wise linear function that outputs the input if it is positive and returns zero otherwise. The convolution stride is fixed at 1 pixel in order to maintain the spatial resolution after the convolution stride is the number of pixels shifted across the input matrix. Hidden Layers: ReLU is utilized by all hidden nodes in the VGG network. Fully Connected Layers: Model VGGNet contains three layers that are all fully connected. The first two are equipped with 4096 channels apiece, while the third has 1000 channels, one for each class.

4.2.3. ResNET

Residual neural networks and the most well-known ResNets, such as ResNet-34, ResNet-50, and ResNet-101. ResNet-50 is a popular convolutional neural network (CNN) with fifty layers. ResNet is a type of artificial neural network (ANN) in which residual blocks are stacked on top of one another to build a network. ResNet was developed with the specific intent of addressing this issue. Deep residual nets makes use of residual blocks to increase the accuracy of the prediction. The concept of “skip connections”, which sits at the heart of residual blocks, is the foundation of this neural network type. These skip connections function in two manners. In the first place, they address the issue of vanishing gradient by creating an alternative shortcut for the gradient to pass through. Additionally, they allow the model to discover an identity function. This ensures that the model’s higher levels do not execute any function. Following this is a ReLU unit. ReLU, which stands for rectified linear unit activation function, is a piece-wise linear function that outputs the input if it is positive and returns zero otherwise. The convolution stride is fixed at 1 pixel in order to maintain the spatial resolution after the convolution stride is the number of pixels shifted across the input matrix. Hidden Layers: ReLU is utilized by all hidden nodes in the VGG network. Fully Connected Layers: Model VGGNet contains three layers that are all fully connected. The first two are equipped with 4096 channels apiece, while the third has 1000 channels, one for each class.

4.2.4. Inception V3

Deep Learning Model Inception V3 is implemented using Keras. The model employs the pre-trained ImageNet weights. In Inception V3, there are 48 layers. It is a variation of the Deep learning model developed by Google. In Inception, we use Global average pooling in the feature learning layer to reduce the size of the feature map, which is then fully coupled to the Softmax layer in the classification layer,
which provides the model's final classification. Pooling parameters on an average basis minimizes the number of parameters, resulting in less over-fitting at the inception stage and a consequent increase in accuracy.

4.2.5. DenseNet

DenseNet is a Deep Learning Model we develop using Keras. The model employs pre-trained ImageNet weights. DenseNet169 is an upgraded version of previous DenseNet versions; the model has 169 layers of depth. DenseNet’s primary characteristic is that it mitigates the vanishing gradient and reduces the number of parameters. All layers in DenseNet are coupled in a feed-forward method. In which the output of each layer serves as input for the remaining layers.

4.3. Evaluation

The quality of a statistical or machine learning model is measured using evaluation metrics. It is vital to evaluate machine learning models and algorithms for every project. There are numerous sorts of assessment metrics that can be used to evaluate a model. Among these metrics that can be used to evaluate a model. Among these are classification precision, logarithmic loss, the confusion matrix, and many others. Classification accuracy is the ratio of the number of right predictions to the total number of input samples. Typically, the term accuracy refers to this ratio. Logarithmic loss, often known as log loss, penalizes incorrect classifications. The output of a confusion matrix is a matrix that describes the overall performance of a model. There exist additional evaluation indicators which have not been included. Using an amalgamation of these specific evaluation metrics to assess a model or algorithm constitutes evaluation metrics. It is crucial to employ several evaluation measures while evaluating your model. This is because a model may perform well with some evaluation metric, but poorly with another measurement from a different evaluation metric. It is vital to evaluate machine learning models and algorithms for every project. There are numerous sorts of assessment metrics that can be used to evaluate a model. Among these are classification precision, logarithmic loss, the confusion matrix, and many others. Classification accuracy is the ratio of the number of right predictions to the total number of input samples. Typically, the term accuracy refers to this ratio. Logarithmic loss, often known as log loss, penalizes incorrect classifications. The output of a confusion matrix is a matrix that describes the overall performance of a model. There exist additional evaluation indicators which have not been included. Using an amalgamation of these specific evaluation metrics to assess a model or algorithm constitutes evaluation metrics. It is crucial to employ several evaluation measures while evaluating your model. This is because a model may perform well with some evaluation metric, but poorly with another measurement from a different evaluation metric. Utilizing evaluation metrics is essential for ensuring that our model is running optimally.

4.3.1. Accuracy

The accuracy score is the most easy and widely used metric for evaluating classification ability. Accuracy is computed as the ratio of correct predictions to total prediction.

\[
\text{Accuracy} = \frac{\text{Number of correct predictions}}{\text{Total number of predictions}}
\]

| S. No. | Paper | Year | Problem targeted | Technique used | Merits | De-merits |
|--------|-------|------|------------------|----------------|--------|-----------|
| 1      | [65]  | Jun-20 | How to use AI-based approaches in Covid 19 | RNN, LSTM, GAN, and ELM | Can work on large scale data; Different techniques for different problem are proposed | NO measure of effectiveness of the models |
| 2      | [11]  | Feb-21 | Studying deep learning techniques using CT and X-ray | Listed different Deep Learning Techniques | †systematically review of deep learning techniques; †the proposed architecture for diagnosis, and the performance evaluation metrics ; †explained the taxonomy of the reviewed literature | †Did not analyzed MRI, PET images; †image data are incomplete, noisy, ambiguous, and inaccurately labeled; †Data shortage due to small dataset; †Over-fitting and under-fitting of the models |
| 3      | [66]  | Jan-21 | Study focuses on X-ray images using CNN and DL models | DL and CNN models | †Explainable Deep Learning models are explained; †CNN-based transfer learning models were used | †Class imbalance problem ; †data samples overlap ; †did not dive into deep training models |
| 4      | [8]   | Sep-21 | At home testing techniques | CRISPR diagnostics, immunoassays for | †At-home test for covid-19 ; †fast in detection; †help in pandemic management | †limited scope as critical condition and drug metabolism are not covered. ; †at home test are not user friendly and completely robust; †not able to detect the initial stage; †no need for sample collection from outside |
| 5      | [5]   | May-20 | Paper evaluate the role of IOT, AI, drone, Blockchain and 5G how can we minimize the impact of covid19 using them and impact on global economy | State the impact of covid 19 in different are | †elaborated the effect of covid 19 on our economy ; †impact on automotive, aviation, tourism, oil, construction, food, healthcare and telecom | †telem has faced very high demand and emerging 5G technology do not have infrastructure to support the demand.; †Healthcare need more and more assisting tools which are not available |
| 6      | [67]  | Jan-21 | It is a Multivocal Literature Review (MLR) which elaborate the cyber-attacks during pandemic. | Used SLM, SLR, | †state of the art MLR survey; †used MLR that bridge gap between industry expert and researchers; † phishing is the most common threat; †used both formal and grey literature | †Limited Scope; †Limited search keywords used; †only three search engines for data collection |
| 7      | [68]  | Sep-21 | Model that analyze CT for covid-19 classification | UNet, DeCoVNet | †0.959 ROC AUC and 0.976 PR AUC; †time taken 1.93 s for a single patient’s CT; †Large CT dataset used; †Fast and accurate model | †Weak Labeling of dataset; †only work on CT images; †Black box algorithm; †Explainable AI not used |
4.3.2. Contingency table

The concept of the contingency table is fundamental to all scores for binary classification performance. A contingency table is a four-cell table that displays the number of occurrences that meet specific parameters. For the layout of the contingency table, we consider (1,1) two binary classes, negative and positive respectively.

4.3.3. Recall

The recall or true positive rate estimates the proportion of positive examples properly identified as positive out of all positive examples. Using the table of contingencies. In situations involving anomaly detection or defect detection, when the positive class represents anomalous instances, the recall score is also called as sensitivity. In the detection scenario, recall intuitively evaluates the model’s sensitivity in recognizing abnormalities or defects among samples of normal functioning.

The recall is computed as
\[
\text{Recall} = \frac{TP}{TP+FN}
\]

4.3.4. Precision

The precision score evaluates the accuracy with which the classifier detects positive examples by minimizing the mistaken identification of negative cases as positive. Thus, the precision score is determined as the proportion of positive examples that were accurately predicted among all positive examples that were predicted (correctly or incorrectly).

The precision score is calculated as
\[
\text{Precision} = \frac{TP}{TP+FP}
\]

4.3.5. Specificity

The goal of both recall and precision is to increase the proportion of true positives. When evaluating the model from negative class perspective, we compute specificity also called true negative rate.

Specificity = \[
\frac{TN}{TN+FP}
\]

For fair analysis of the model we evaluate any model we need to evaluate both specificity and sensitivity (recall).

4.3.6. F1 score

F1-score represents the harmonic mean of accuracy and recall. Using the following formula, it combines accuracy and recall into a single number. F1-score takes both precision and recall into consideration, which means that both FPs and FNs are accounted for. The F1 score is higher the greater the precision and recall. The F1-score is between 0 and 1. The closer the value is to 1, the superior the model.

\[
\text{F1 Score} = 2 \times \frac{\text{Precision} \times \text{Recall}}{\text{Precision} + \text{Recall}}
\]

4.3.7. Receiver operating characteristic (ROC) curve

Numerous classifiers can be designed to operate based on a threshold. For instance, in anomaly detection, when any anomaly score is generated by the predictive model for particular observations above a given threshold, we may consider such data to be abnormal. In the context of threshold-based classifiers, a single precision/recall value may not provide the full performance profile. For a given assignment of examples to positive and negative classes, precision and recall are computed. Changing the threshold will result in new assignments. The receiver operating characteristic (ROC) curve permits examination of the model’s comprehensive performance profile.

The ROC curve is a depiction of the true positive rate (also known as recall) vs the true negative rate (also known as specificity) for varying values of the thresholds. We calculate the recall and specificity for every potential value of the threshold, ranging from the highest possible value to the lowest possible value. In this exercise, you will be provided with a list of matched recall and specificity values, which, when plotted, will result in the ROC curve.

For the maximum threshold value, all cases are categorized as negative. The actual negative rate is therefore 1.00 while the actual positive rate is 0.00. In contrast, with the lowest threshold value, all instances are classified as positive. The actual negative rate is therefore 0.00 and the true positive rate is 1.0.

The ROC curve is not only utilized as a tool for evaluation, but it is also put to use in the process of finding the best thresholds. The point along the ROC curve that is deemed to be a good threshold is the point that is closest to the coordinate (1,0) when recall and specificity are both given the same amount of weighting in the analysis.

4.3.8. Area under the curve (AUC)

The ROC curve takes into account everything. We need to reduce it to a single number so that it can be compared quantitatively. This will make it easier to analyze. The area under the curve, also known as AUC, is the same thing as the area under the ROC curve; however, it is expressed as a single value. A better classifier is indicated by a higher value of the area under the curve (AUC).

5. Treatment

5.1. Vaccine

Developing vaccinations for viral infections is especially difficult due to their potential to mutate from one individual to the next. To put an end to the COVID-19 epidemic, however, only the creation of dependable and effective immunizations is a possible option. Various medical organizations, independent laboratories, and scientists have been seeking to develop a vaccine against SARS-CoV-2 since the outbreak. As of 26 April 2020, according to the WHO, approximately 82 candidate vaccines are in the pre-clinical stage, while 7 have already begun clinical testing.

SARS-CoV-2 has been present in the human population for more than a year, producing severe sickness in some individuals and culminating in a pandemic that continues to place a tremendous burden on global economies and healthcare infrastructures. In the United Kingdom, emergency use authorization has been granted for the first three vaccines, and a nationwide roll out is currently underway. Vaccination programs on a massive scale are also being implemented in a number of other nations. This vaccine expresses the spike glyco-protein, the primary target of neutralizing antibodies during a natural infection. Vaccines provide protection against disease, and preliminary findings imply that disease transmission declines following vaccination (see Fig. 10). The following are examples of some of the most significant attempts now being undertaken toward the development of a vaccine against COVID-19:

5.2. Types of vaccines

5.2.1. BNT162 vaccine by Pfizer and BioNTech

The United Kingdom was the first country to approve the COVID-19 vaccine BNT162 developed by Pfizer and BioNTech via the EUA on December 2, 2020. In phase III clinical trials, BNT162 revealed a 95 percent efficacy rate in disease prevention [70]. On December 11, 2020, the US Food and Drug Administration (FDA) approved the first EUA for the drug. Canada and Mexico subsequently approved BNT162 under their respective EUA processes. WHO authorized the BNT162 vaccine candidate for emergency use on December 31, 2020, making it much easier to manufacture and sell this vaccine worldwide. Initially, four possibilities were created, including two nucleoside modified mRNA (modRNA), one mRNA containing uridine (uRNA), and one self-activating mRNA (saRNA). In the pre-clinical study, modRNA BNT162b2 demonstrated protective antiviral effects in Rhesus macaques, as well as enhanced neutralizing antibody titers and a Th-1 biased cellular response in both Rhesus macaques and mice. This vaccine has a storage temperature requirement of 80° to 60 °C, which could provide logistical issues [71].
5.2.2. Covishield (AstraZeneca’s vaccine manufactured by Serum Institute of India)

The Oxford–AstraZeneca COVID-19 vaccine, available under the brand names Covishield and Vaxzevria, is a viral vector vaccine used to prevent COVID-19. Developed in the United Kingdom by Oxford University and the Anglo-Swedish pharmaceutical corporation AstraZeneca utilizing the modified chimpanzee adenovirus ChAdOx1 as a vector. The vaccine is administered intramuscularly. Covishield is a recombinant, replication-deficient adenovirus vector derived from chimpanzees that encodes the SARS-CoV-2 Spike (S) glycoprotein. Following delivery, the corona virus's genetic material is expressed, eliciting an immunological response. Studies conducted in 2020 demonstrated that the vaccine is 76.0% effective in preventing symptomatic COVID-19 commencing 22 days after the first dose and 81.3% effective after the second dose. According to a research conducted in Scotland, the vaccine is 81 percent effective against the Alpha variant (lineage B.1.1.7) and 61 percent effective against the Delta variation for symptomatic COVID-19 infection after the second dose (lineage B.1.617.2) [5]. This vaccination necessitates refrigeration (2–8 °C), which could be problematic in low-income nations [71].

5.2.3. Covaxin (manufactured by Bharat Biotech Limited)

Bharat Biotech has developed COVAXIN, India’s indigenous COVID-19 vaccine, in conjunction with the Indian Council of Medical Research — National Institute of Virology (NIV). India authorized Covaxin, an inactivated vaccine produced by Bharat Biotech and India’s National Institute of Virology, on January 2, 2021 [70]. The vaccine is created using platform technology derived from Whole-Virion Inactivated Vero Cells. Vaccines that have been inactivated do not multiply and thus are unlikely to reverse and induce pathological effects. They include inactive virus that is incapable of infecting humans but can nevertheless educate the immune system to generate a defensive response to an infection. A two-dose regimen delivered to Rhesusmacaques resulted in a rise in SARS-CoV-2-specific IgG and neutralizing antibodies, as well as a reduction in viral replication in the nasal passage, throat, and lungs. According to the primary investigator of the trial, the preliminary results from the first few volunteers who received the vaccination are promising. According to Bharat Biotech, the trial’s first two phases did not reveal any significant side effects. The projected delivery date for this vaccine is February 2021, according to a Reuters interview with a scientist from the ICMR [72].

5.2.4. Sputnik vaccine is developed by Moscow’s Gamaleya Institute

Russia has approved the Sputnik V CVC, formerly known as Gam-COVID-Vac. In a Phase 3 clinical trial, the Gamaleya Research Institute in Russia and the Health Ministry of the Russian Federation are evaluating its non-replicating viral vector vaccine, Sputnik V. ‘To yet, however, no study data are available. This led to criticism, as the vaccine was licensed despite a lack of data on its safety and efficacy [73]. Two Phase 1/2 trials involving a total of 38 individuals were conducted (NCT04436471, NCT04437875). Sputnik V is also being tested in a Phase 2 trial with 110 participants over the age of 60. (NCT04587219). A Phase 3 experiment with around 40,000 people is also now underway (NCT04530396). Sputnik V is being tested in Belarus (NCT04564716) and the United Arab Emirates in addition to Russia. The Phase 1/2 clinical trials demonstrated the vaccine’s safety and immunogenicity. In addition, the Russian Direct Investment Fund revealed that Sputnik V is 92 percent effective based on intermediate trial data from 20 participants [74]. In addition, a first preliminary submission of the vaccine has been suggested in Brazil.

5.2.5. Moderna’s mRNA-1273

Moderna, a biotechnology company based in the United States, and the National Institute of Allergy and Infectious Diseases have developed a vaccine candidate (NIAID). Moderna’s strategy is centered on the injection of mRNA, a genetic form of the virus’ genome, into human cells to enable the production of antiviral proteins. Unlike conventional vaccine approaches, this method does not require the virus to be grown in vast quantities [75]. This vaccine’s storage temperature requirement of 25° to 15 °C could be a possible issue [71].

5.2.6. Johnson & Johnson’s COVID-19 lead vaccine

Johnson & Johnson and the Biomedical Advanced Research and Development Authority (BARDA), a subsidiary of the United States Department of Health and Human Services (HSS), have committed to invest more than $1 billion in the research and development of COVID-19 vaccines. Johnson & Johnson announced on 30 March 2020 that, following three months of extensive research on many vaccine candidates in partnership with the Beth Israel Deaconess Medical Center, a subsidiary of the Harvard Medical School, it has discovered their leading candidate vaccine [76]. Johnson & Johnson aims to commence the clinical trials of its leading candidate vaccination no later than September 2020. This vaccine must be stored between 2 and 8 degrees Celsius [71].

5.2.7. BBIBP-CorV by Sinopharm

BBIBP-CorV is an inactivated CVC created by Sinopharm and Beijing Institute of Biological Products in China. First China and then United Arab Emirates (UAE) granted EUA approval for the vaccination [77]. Currently, BBIBP-CorV is being evaluated in Phase 2 (ChiCTR2000032459) and Phase 3 (ChiCTR2000034780) trials in China, as well as a Phase 3 trial in Argentina (NCT04560881). BBIBP-CorV has been proven to be highly effective against SARS-CoV-2 in preventing illness in Rhesus macaques. Phase 1 data demonstrated that BBIBP-CorV was safe and well tolerated at all dose levels, with all individuals developing an antibody response after 42 days [78]. The United Arab Emirates announced that the vaccine is 86% effective.
5.3. Prevention measures

The COVID-19 virus travels most frequently from person to person and does so in the following ways:

- It is able to propagate through very minute liquid particles. When an infected person coughs, sneezes, speaks, sings, or breathes, they generate a variety of particles, ranging from larger respiratory droplets to tiny aerosols.
- It is more likely to spread among persons who are in close proximity to one another, often within a distance of one meter.
- Additionally, it can spread in interior environments that lack adequate ventilation and/or that are very crowded and in which aerosols remain suspended in the air or move further than one meter.
- It is also possible for the virus to spread when a person contacts a surface that has already been infected with it.

There are numerous obligatory recommendations and suggestions supplied as guidelines to all of the people throughout the world to limit the transmission of COVID-19. The goal of these recommendations and suggestions is to prevent the spread of COVID-19. To guarantee that people adhere to all of the laws, norms, and regulations, the authorities have implemented checks and even monetary penalties [79]. Given guidelines are as follows:

- Even if the people around you do not appear to be ill, you should still keep a safe distance from them (at least one meter).
- Always wear a mask in public, but especially inside and in situations where moving away physically is not an option. Put on a mask that offers the optimal level of comfort, fit, and protection for you.
- Stay away from crowded areas and rooms with poor ventilation. Prefer open, well-ventilated spaces to closed ones wherever possible. If you are indoors, you should try to bring in some fresh air by opening the windows and doors if you can. You should avoid busy areas and indoor settings that do not have fresh air from the outdoors if you are at an increased risk of being very sick from COVID-19.
- Regular hand washing is required. You can use soap and water, or you can use a hand rub that contains alcohol.
- When it is your turn, you should be vaccinated. Regarding vaccinations, heed the advice of local authorities. Vaccines against COVID-19 are proven to be a successful means of warding off illness. Vaccines against COVID-19 are extremely efficient at preventing serious disease, hospitalization, and death.
- When you cough or sneeze, bring your elbow up to your chest and cover your nose and mouth with a tissue or your bent elbow.
- Stay home if you feel unwell.
- When you travel, make sure to use all precaution methods.
- In the case of isolation, follow the suggestions. If you have symptoms or a positive test for COVID-19, you should follow the advice for isolating yourself.
- Obey the guidelines provided for the quarantine. In the event that you have close contact with someone who is infected with COVID-19.

Seek medical treatment if you have a fever, a cough, and difficulty breathing all at the same time. Make sure to give your healthcare practitioner plenty of notice so that they can point you in the direction of the appropriate health facility. This shields you against harm and stops the spread of illnesses caused by viruses and other pathogens. **Masks** Masks that fit properly can prevent the spread of the infection from the individual wearing it to others. Masks alone are insufficient protection against COVID-19; physical separation and hand cleanliness are also required. Follow the recommendations of the local health authority.

5.4. Case study

“How sewage can help countries get ahead of COVID-19 variants”

In areas with limited testing capabilities, environmental monitoring of wastewater and surface water may provide early warnings of epidemics. Considering that both symptomatic and asymptomatic individuals shed SARS-CoV-2 in their faces, environmental surveillance (also known as sewage water epidemiology) could be an effective tool to help countries and healthcare system control COVID-19, particularly in countries with limited capacity for laboratory trials and contact tracing. Since virus “shedding” begins shortly after an infection, sewage and wastewater provide an authentic snapshot of infection trends in the community. As a supplement to clinical testing, environmental monitoring can rapidly provide information into the circulation of SARS-CoV-2, perhaps identifying newly imported variations and forecasting peaks. W-SPHERE is a research cooperation between Michigan State University, KWR Water Research Institute, UC Merced, and Veristat Technologies that uses data visualization tools to display sample sites, the presence of SARS-COV-2, and temporal patterns. Researchers doing investigations on ways to identify the existence of SARS-CoV-2 and forecasting studies to estimate the probability of COVID-19 infections have public access to these datasets.

6. Open issues

- Public, exhaustive, and diversified databases must be compiled. The datasets should be confirmed by specialists and labeled with the respective lung disease lesions. Incorporating the identification of indicators into classification output would improve both the accuracy of predictions and the transparency of the models.
- As the medical research to define the primary characteristics of COVID-19 is still underway, it is crucial to use more extracted qualities based on the advice of medical professionals. Given the limited number of accessible CXR COVID-19 datasets, adding domain knowledge would aid in the development of diagnostic models that replicate the diagnostic patterns of human experts and emphasize the indications or regions they pay special attention to. However, relevant domain expertise must be determined first. To achieve the necessary performance, the trade-off between dynamically acquired deep features and retrieved domain knowledge features must be handled.
- It is essential to quantify the degree of discrepancy across radiologists in order to construct a baseline for the evaluation of deep learning models’ prediction capabilities.
- We believe semi-supervised learning has yet to reach its full potential, given that clinicians frequently rely on similar cases from the past to make accurate diagnosis decisions. The training set for semi-supervised algorithms consists of few labeled samples and much unlabeled data. Not only may semi-supervised modeling lower the cost of data augmentation, but it can also help uncover hidden patterns and relationships in the data.
- We can look for some more authentic data augmentation techniques for augmentation of the data due to the unavailability of the required datasets such as covid positive CXR and CT images for training models.
- To further quantify these false positive rates, it will be necessary to do additional research on deep learning explain-ability approaches on normal X-rays to see how often the methods indicate abnormal areas which radiologists considered normal. Answering this question will help to further characterize the effectiveness of explain-ability methodologies when used to differentiate between normal and subsequently abnormal radiography.
7. Conclusion

COVID-19 remains an ongoing pandemic, creating new records daily for cumulative global infection numbers and death tolls. It is important to understand all the aspects of covid-19 and its direct and indirect effects on our lives. In this paper, different SARS-CoV-2 is explored from a holistic perspective where we analyzed it in different sections. The survey is divided into 12 section and four major parts. The first part of the survey discussed Covid-19 variants, all new emerging variants and a game theory perspective of covid-19 in detail. The second part of the survey discussed the side effects of covid-19, fungus as a major side effect after covid, region it effected most and its types, and impacts on various domain. The third part of the paper discussed various diagnosis and treatments of SARS-CoV-2. The comparative analysis of the existing techniques are shown in the form of table. Finally, the open issues and challenges of the area are discussed which can be further explored by the authors. implementing more XAI models for the clinical acceptance of the methods, optimizing the models and hyper parameter tuning for increasing the accuracy of the model.

CRediT authorship contribution statement

Deepanshi: Data collection, analysis. Ishan Budhiraja: Data collection, Analysis. Deepak Garg: Comparative analysis. Neeraj Kumar: Editing, Proof reading and overall structure. Rohit Sharma: Literature analysis.

Declaration of competing 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.

Data availability

Data will be made available on request.

Acknowledgment

All the authors agreed on the submission of the paper at this venue.

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