Review Article



Coronavirus Outbreak- A Pandemic

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Abstract | A global health emergency termed as Corona Virus Disease COVID-19 became an international concern since December 2019. Novel coronavirus (nCoV) is a spherical or pleomorphic enveloped beta virus containing single-(positive-sense) RNA strand with a nucleoprotein surrounded by a capsid comprised of matrix protein. The envelope is surrounded by club-shaped glycoprotein projections. The virus spreads primarily from one person to another, typically through close contact or breathing drops caused when the infected person coughs or sneezes, hence it is necessary to keep away from a sick person more than two meters. Many pharmaceutical companies and testing organizations are therefore rushing to develop more reliable and rapid test kits to detect 19-nCoV among people suspected of being contaminated in only a few minutes and without the need to send samples to central laboratories. Coronavirus (Covid-19) vaccine latest update: with the production of a secure, reliable and accessible Covid-19 vaccine as the cornerstone to controlling the pandemic, research and testing are rising at a rapid pace around the world to find a cure for the current coronavirus.

Keywords: Corona Virus Disease COVID-19, Novel coronavirus (nCoV), Severe acute respiratory syndrome (SARS), Middle East Respiratory Syndrome (MERS), Virus

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INTRODUCTION

Aglobal health emergency termed as Corona Virus Disease COVID-19 became an international concern since December 2019 (World Health Organization. *Coronavirus Disease 2019 (COVID-19) Situation Report 46*, 6 March 2020). This fatal disease is characterized by fever, cough, and fatigue along with mild to severe respiratory complications (Yan et al., 2020). On 11 March, this deadly outbreak of the virus was declared as a pandemic by the World Health Organization (World Health Organization. Coronavirus Disease 2019 (COVID-19) Situation Report 68, 28 March 2020). In 1968 the term "corona virus" was derived from the word crown due to its morphological

similarity with a crown as observed under electron microscope. In 1975, the International Committee on the Taxonomy of Viruses established *coronaviridae* family which was further divided into two subfamilies, the coronaviruses and the toroviruses at the 10th International *nidovirus* Symposium in Colorado Springs, Colo., in June 2005. The *coronaviridae* family, Arteviridae and Roniviridae families are altogether clustered to form the Nidovirales order (Susan et al., 2005). Based on phylogenetic and genomic studies this novel coronavirus belongs to genera *betacoronavirus* and has a diameter of 60–140 nm, which enveloped oval or round and polymorphous virions of strong infectivity and general susceptibility to all people irrespective of age across the entire globe (Addie et al., 2014; Almazan et al., 2000).

Betacoronvirus has a close proximity to the sequences of severe acute respiratory syndrome-related coronaviruses (SARSr-CoV) and also uses ACE2 as the entry receptor-like SARS-CoV (7). The understanding of COVID-19's genetic and phenotypic structure in pathogenesis is critical for drug and vaccine development (Bailey et al., 1949).

As on July, 22nd 1,48,45,978 cases have been confirmed worldwide out of which 6,13,879were death cases however 84,28,427 were the recovered cases. India witnessed a spike of 84, 28,427 confirmed cases among which 7,24,578 had successfully recovered whereas 28,084 deaths have been reported till date. The rate of occurrence was spotted as 849 cases per 1 million people. Maharashtra has emerged as the worst affected state with over 3, 18,695 cases.

DATA RESOURCES

CHARACTERIZATION OF COMPLETE CORONAVIRUS GENOME AND STRUCTURE

Novel coronavirus (nCoV) is a spherical or pleomorphic enveloped beta virus containing single- (positive-sense) RNA strand with a nucleoprotein surrounded by a capsid comprised of matrix protein. The envelope is surrounded by club-shaped glycoprotein projections. Some coronaviruses have also been reported to contain a hem agglutinin-esterase protein (HE) (Woo et al., 2010). It is illustrated through various literatures that among all known RNA viruses Coronaviruses have reported to possess the largest genomes of approx. (26.4–31.7 kb), with G + C contents varying from 32% to 43%. There are varied numbers of small ORFs present between the various set of conserved genes such as (ORF1ab, spike, envelope, membrane and nucleocapsid) as well as downstream to the nucleocapsid gene in diverse coronavirus lineages. The viral genome contains characteristic features, which include a unique N-terminal fragment within the spike protein. Genes encoding major structural proteins in all coronaviruses are found in the 5'-3' order as S, E, M, and N (Boheemen et al., 2012). At least six ORFs are present typically in a CoV. Except for Gamma coronavirus that lacks the first ORFs (OR-F1a/b), approx. two-third of the whole genome length, encodes 16 nsps (nsp1-16). ORF1a and ORF1b contain a frameshift within which two polypeptides are produced: pp1a and pp1ab. These polypeptides are processed by virally encoded chymotrypsin-like protease (3CLpro) or main protease (Mpro) and one or two papain-like protease into 16 nsps. All the structural and accessory proteins are translated from the sgRNAs of CoVs. These polypeptides are processed into 16 nsps by virally encoded protease-like chymotrypsin (3CLpro) or main protease (Mpro) and one or two papain-like protease. Both the structural and accessory protein are derived from the CoV sgRNAs. In addition to these four main structural proteins, different CoVs

encode unique structural and accessory proteins, such as HE protein, 3a / b protein and 4a / b protein (Fig. 2B, lower panel). These mature proteins are essential for several key aspects in maintaining genomes and replicating viruses (Cascella et al., 2020).

The coronavirus membrane is composed of three or four viral proteins. Membrane (M) glycoprotein is the most dominant structural protein; it crosses the membrane bilayer three times, leaving a short NH2-terminal domain outside the virus and a long lasting COOH (cytoplasmic domain) inside the virion (Woo et al., 2010).

The peplomers are constituted by the spike protein (S) as the type I membrane glycoprotein. In fact, S protein is the principal inducer of neutralizing antibodies. There is a molecular interaction between the envelope proteins with which the formation and composition of the coronaviral membrane is likely determined. M plays a major role in the intracellular formation of virus particles without needing S. In the presence of tunicamycin *coronavirus* grows and produces spikeless, noninfectious virions that contain M but devoid of S (Boheemen et al., 2012, Li et al., 2020).

VIRUS ORIGIN'S STILL A MYSTERY

The virus spreads primarily from one person to another, typically through close contact or breathing drops caused when the infected person coughs or sneezes, which is why it is necessary to keep away from a sick person more than two meters (6 ft. 7 in) (Phan et al., 2020). But the cause of transmission of the coronavirus infection is not just sneezing or coughing. There are other ways of transmitting the virus that include spreading from one person to another through surfaces that the infected person has reached, particularly after studies have shown that the virus remains alive on surfaces for up to 9 days (Riou et al., 2019, Zhou et al., 2020). When people come into contact with these items or structures, they may then develop COVID-19 disease and then touch their eyes, nose or mouth. In addition, research to date suggests that 2019-nCoV is mainly transmitted by interaction with respiratory droplets rather than through air. An individual who suffers from mild cough and not feeling ill may have COVID-19 infections. It is yet another justification to practice good hygiene after using the toilet and before feeding, despite the risks involved. Several uncertainties related to various aspects of coronavirus origin are illustrated in Figure 1.

INFECTIOUS DISEASE TRANSMISSION

We provide a brief overview of available evidence of COVID 19-infected symptomatic, pre-symptomatic and asymptomatic transmission. Figure 2 illustrates three routes of transmission delineated by WHO in one of its situation reports (Maxwell et al., 2017).



wholesale market of Huanan seafood in Wuhan City where live animals are sold, including snakes, marmots, birds, frogs and hedgehogs

Individuals who visited the market developed viral pneumonia due to the new coronavirus.

Fact suggests animals were initially transmitting the virus to humans

However, there were no connections or exposure to the market for people with a more recent diagnosis, confirming that humans can pass the virus on to each other.

2019 novel coronavirus is a zoonotic virus, suggesting these viruses were contracted directly from animals by the first patients who were infected.

Some studies have shown that bat is the potential species of origin of the 2019 novel coronavirus (SARS-CoV-2), since SARS-CoV-2 shows 96 percent full-genome identification with a Rhinolophus affinis bat CoV (BatCoV RATG13) (Zdou et al., 2020).

 $However, SARS-\underline{CoV} \ and \ MERS-\underline{CoV} \ are typically \ transmitted to \ intermediate \ hosts to \ masked palm \ civets \ and \ camels \ before they leap to \ humans \ (Cui \ et \ al., 2019).$

A number of scientists have pointed out that, owing to the similarities of this new virus with SARS-CoV and MERS-CoV, SARS-CoV-2 has probably spread from an unknown intermediate host to humans or directly to people (Zhou et al., 2020).

A Chinese team conducted an analysis as of Jan 17, 2020, and compared the 2019-nCoV genetic sequences with all other known coronaviruses. They suggested that 2019-nCoV will have the most close bias in codon usage with snakes (Ji et al., 2020). Snakes often go wild hunting bats.

Reports suggest that snakes were sold on the local seafood market in Wuhan, raising the likelihood that at the beginning of this coronavirus outbreak the 2019-nCoV may have jumped from the host species, bats, to the snakes and then to humans. But it remains a mystery how the virus could adapt to both cold-blooded and warm-blooded hosts (Ji et al., 2020).

In addition, there is no reliable evidence to suggest that coronaviruses live in hosts other than mammals and birds (Bassetti et al., 2020). So there is likely to be an intermediate mammal host for 2019-nCoV (Zhang et al., 2020a).

A published article on March 19, 2020 showed that, with SARS-CoV-2 and BatCoV RaTG13, the Pangolin-CoV genome exhibited 91 per cent and 90.6 per cent nucleotide identity. Coronaviruses are usually well known to have multiple intermediate hosts for animals.

Studies in 2003 showed that the main intermediate host of SARS-CoV is the palm civet (Paguma larvata), but other studies also indicate that the raccoon dog (Nyctereutes procyonoides) and the ferrite badger (Melogale moschata) play a similar function as intermediate hosts (Guan et al., 2003).

Figure 1: Uncertainty related to various aspects of coronavirus origin

*(20)-Zhou et al 2020, (21)-Cui et al 2019, (22)-Ji et al 2020, (23)-Zhang et al 2020(a), (24)-Guan et al 2003

POTENTIAL EFFECTS OF VIRUS ON PREGNANCY

At this period very little is known about the impact of 2019-nCoV on pregnant women and infants and there are currently no clear guidelines about the disease for pregnant women. The CDC has no evidence to suggest the incidence of adverse outcomes of pregnancy for pregnant women with COVID-19 while two of the other SARS-CoV and MERS-CoV coronaviruses were associated with more serious illnesses and higher mortality in pregnant women (Assiri et al., 2016, Chen et al., 2020). Figure 3 illustrate the impact of this deadly virus on pregnant women.

POTENTIAL EFFECTS OF VIRUS ON CHILDREN

Notwithstanding 2019-nCoV's rapid diffusion, it appears that children usually tolerate the virus with few complications (COVID-19 in Children, 2020). This trend is substantially similar to previous CoV outbreaks, such as SARS-CoV and MERS-CoV, the symptoms of which did not occur widely in children. Figure 4 illustrates the effects of corona virus on children.

The routes of transmission from COVID-19 patients

Symptomatic transmission

Symptomatic transmission refers to transmission from a person while they are experiencing symptoms.

Data from published epidemiology and virology studies show that COVID-19 is transferred primarily from symptomatic people to others who are in close contact through respiratory droplets, through immediate contact with the diseased Persons, or infected objects and surfaces.

Clinical observation and virological studies that have obtained repeated biological samples from identified patients indicate that COVID-19 virus shedding is the strongest in the upper respiratory tract (nose and throat) at an early stage of the disease. That is to say, within the first 3 days of the initiation of symptoms.

Pre-symptomatic transmission

The incubation period for COVID-19, which is the time between virus exposure (becoming infected) and onset of symptoms, is 5-6 days on average, but can be as long as 14 days. Any infected persons may become infectious during this time, also known as the "presymptomatic" phase. So transmission from a presymptomatic case may occur before the onset of

symptoms.

Pre-symptomatic

transmission was reported by contact tracing efforts enhanced analysis of confirmed cases.12-17 This supported by evidence indicating that certain individuals that test positive for COVID-19 from 1-3 days before symptoms develop.6,16

Thus, humans infected with COVID-19 may be able to transmit the virus before severe symptoms emerge. It is necessary to note that presymptomatic transmission often involves infectious droplets or infected surfaces to transmit thevirus.

Asymptomatic transmission

An asymptomatic case confirmed by the laboratory is a person who is infected with COVID-19 and who does not develop symptoms. Asymptomatic transmission refers to a person transmitting the virus, but does not develop symptoms.

There are several findings of laboratory-confirmed cases that are truly asymptomatic, and as yet no asymptomatic transmission has been documented. In some countries, asymptomatic cases were identified as part of contact tracing efforts.

Figure 2: The patterns of transmission from COVID-19 patients according to WHO

A report published in mid-February 2020 by the China-WHO Joint Mission found that in 147 pregnant women infected with 2019-nCoV, 8% of cases were considered serious and 1% were critical (Chen et al., 2020b). These figures appear similar to cases of non-pregnant infections.

Another 7 March 2020 article revealed clinical data from nine pregnant women in China with confirmed COVID-19 pneumonia. Such patients with COVID-19 infection during pregnancy had a similar physical appearance to that of COVID-19 non-pregnant adults. Neither patient developed or died from serious pneumonia (Chen et al., 2020b)

No children have been diagnosed with the virus in the small number of possible cases in which newborns were born from mothers with 2019-nCoV. Further, though in the uterus, the virus did not appear in amniotic fluid samples surrounding the fetus. In addition, 2019-nCoV will not cross the placenta (Schwartz and Graham, 2020)

No experimental research were performed on breast milk and the 2019-nCoV. A new born baby in London has tested positive for 2019-nCoV, just minutes after being born to a mother who has also been exposed to the virus, according to news reports. This is not the first case since the Chinese authorities have confirmed that, a child in Wuhan, China, had tested positive for the 2019-nCoV 30 hrs after birth

Figure 3: Reports which suggest impact of COVID19 on pregnancy

*(28)-Chen et al 2020b, (29)-Schwartz and Graham 2020

SIGNS AND SYMPTOMS OF DIABETES

If someone has the nCoV19 infection, the first symptoms usually appear after five to six days, according to reports

from the WHO (Phan et al., 2020). However, there are individual cases where the virus' incubation period with a median incubation period of 14 days will last for up to 40 days (Zhang et al., 2020). The time of incubation for serious cases can vary from the mild cases and depend on the patient's age and immune response. Among patients > 70 years (11.5 days) this period tended to be shorter than those aged < 70 years (20 days) (Zhang et al., 2020). COVID-19 symptoms are typically close to normal cold and influenza, and do not get serious. For people suffering from underlying diseases such as diabetes, heart, lung and other diseases, however, it is different. In this situation, the disease may take severe forms that sometimes lead to death. Some individuals do not experience any symptoms (mild pneumonia). According to a recent WHO study on over 70,000 cases in China, the most frequent symptoms of COVID-19 are: fever (in 88% of cases), dry cough and sore throat (68%), weakness (38%) and diarrhea (4%), similar to SARS-CoV and MERS-CoV (33,34.). In addition, extreme shortness of breath occurred in about 20 percent of cases, and about 13 percent had severe headache or sore throat. 19-nCoV is commonly a member of the family of coronaviruses, which typically target the respiratory system. Many patients are prone to various complications including acute respiratory distress syndrome, acute heart injury and secondary bacterial infection (Schwartz et al., 2020). Figure 5 and 6 highlight the recent symptoms and mechanism of immune system in to response the viral entry.

No child died during the SARS-CoV epidemic in 2003 with the majority of the 800 deaths in people over the age of 45 years (Kliegman et al., 2007).

It is also not alarming that these viruses only progress to mild inflammation in children and more severe adult diseases. In history, the most notable examples of this are smallpox, which had a mild impact on children but was devastating in adults (Lee et al., 2020; Zheng et al., 2020).

Children recover rapidly and in general while serious complications include the outcome of death in adults (Ludvigsson, 2020). Adults may be more vulnerable to the virus because they're more likely to get infected with other diseases, such as diabetes, high blood pressure or heart disease, which diminishes their ability to resist infection

Children today tend to be the least affected by the impact of the disease and the number of infected children (under 19 years of age) has not reached 2% of all infected people in the world and there are no deaths under 9 years of age (Zheng et al., 2020)

Scientists are unable to completely understand this phenomenon but some medical theories can understand it. In addition, contrary to the general belief, the immune system of a child is more effective than that of an adult. For example, adults are 25 times more likely more children to die from chickenpox and seasonal influenza (Zhou et al., n.d.), respectively.

Figure 4: Reports which suggest impact of COVID19 on children

*(30)-Kliengman et al 2007, (17)-Lee et al et al 2020, (31)-Zheng et al et al 2020 (32)-Ludvigsson et al et al 2020, (20)-Zhou et al et al 2020

Lung SARS pathology was connected with diffuse alveolar damage, proliferation of epithelial cells and a raise in macrophages. Multinucleate giant-cell infiltrates of macrophage or epithelial origin have been linked with putative syncytial development typical of many infections with coronavirus. Table 1 shows stepwise progression of the symptoms in human.

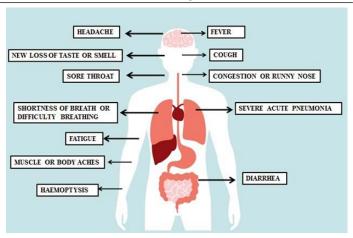


Figure 5: Symptoms of coronavirus-an update

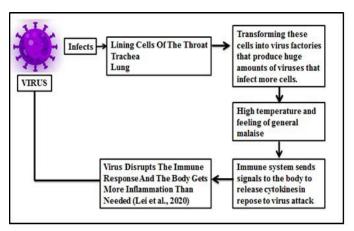


Figure 6: Role of immune system in viral infectivity

CASES OVERVIEW

The first two patients, who died in Wuhan, appeared to be in good health although they had been smoking for a long time and this resulted in their lungs weakening. On arrival at hospital, the first 61-year-old patient had acute pneumonia. Despite the use of a respirator, he had acute respiratory distress syndrome, his lungs failed and his heart just stopped.

He died after being hospitalized for 11 days. A 69-year-old man, the second patient, had acute respiratory distress syndrome. He died of a septicemia and acute pneumonia (Tarek et al., 2020). The causes of these symptoms need to be further researched.

TESTINGS DONE FOR COVID19

Many pharmaceutical companies and testing organizations are therefore rushing to develop more reliable and **rapid test kits** to detect 19-nCoV among people suspected of being contaminated in only a few minutes and without the need to send samples to central laboratories. The ELISA -- enzyme-linked immunosorbent assay -- antibody test is a kind of blood test. These are similar to rapid antibody tests, which detect antibodies in the blood to identify the infected individual with in case of COVID-19. Through

Table 1: Step wise progression of the symptoms in human

S. No.	First step	Second step	Third step
	Oxygen flows to the blood within the lungs but in the case of serious pneumonia	The alveoli tend to fill with water which may cause shortness of breath.	Cough with sputum(a thick mucus that contains lung cells killed by the 19-nCoV)
	nCoV19 infecting digestive system	Appetite loss, diarrhea, vomiting and major disorders of the digestive system.	Destroys the gastrointestinal bacteria (Fan et al 2020).
	High expression of ACE2 found in the lungs membrane,, kidneys cells and seminiferous ductal cells of the testis.	Affect renal tubular cells and testicular cells	nCoV19 binds directly to such ACE2 bearing cells and deteriorates the kidney and testicular tissue of patients. (Huang et al, 2020).

latest updates it has been known to us that "National Institute of Virology, Pune, has successfully developed the 1st indigenous anti-SARS-CoV-2 human IgG ELISA test kit for antibody detection of COVID-19. This reliable test will be critical in monitoring proportion of the population exposed to SARSCoV2 infection. The test kit is named as "COVID KAVACH ELISA" and its first batch released by Zydus-Cadila is approved by Indian Council of Medical Research (ICMR). This kit will be helpful in "SE-RO-SURVEY", which means it could detect prevalence of antibodies that appear after the patient has recovered. According to researchers the SARS-CoV-2 viral antigens produce antibodies via stimulating the body's immune system which can be detected with IgM and IgG antibody tests. IgM is produced during early onset of the disease and is detectable. Later IgG is produced which is maintained for long-term immunity. ERBA Mannheim's kit, called ErbaLisa® COVID-19 ELISA kits, can detect both antibodies (Mousavizadeh et al., 2020). Clinical diagnosis of COVID-19 is illustrated in Figure 7.

Mechanisms of viral pathogenicity

Lymphopenia and sustained inflammation have been found to be dominating in majority of cases of severe disease and death.

The biological mechanisms behind the epidemiological anomaly of severe acute respiratory syndrome (SARS) and COVID-19 is observed somewhat similar (Lei et al., 2020). Some comorbidities related to the disease are mentioned in Figure 8.

OVERVIEW OF THERAPEUTICS AND AVAILABLE TREATMENT

Currently there are no different COVID-19 vaccines or drugs available at this time. Treatments are being explored, and will be examined in clinical trials.

TRIALS DONE THROUGH PLASMA TREATMENT

The FDA approves the utilization of blood plasma from persons who have recovered from COVID-19 with a high

neutralizing antibody titer, which could be a reliable donor source of convalescent plasma (CP) (Cheng et al., 2005). Clinical and vaccine trials have been summarized in Table 2 and Table 3.

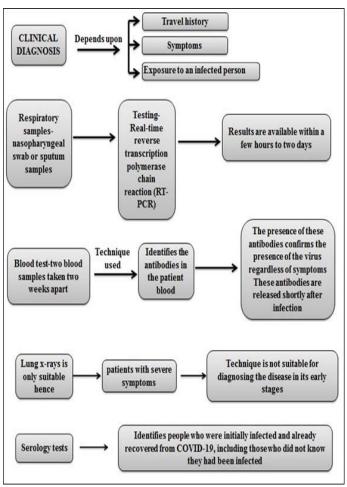


Figure 7: Clinical diagnosis of COVID19 through various modes (37)

CP is a classic adaptive immunotherapy, implemented for more than a century to the management and cure of many infectious diseases. This plasma therapy can be more successful if COVID-19 patients are administered early to remove the virus before it does significant damage to their lungs.

 Table 2: Clinical trials done for COVID19

Favilavir (Developed by Toyama Chemical)	An antiviral drug approved by Japan in 2014 to treat influenza.	To treat nose and throat infections. (But not currently approved by the	(Holshue et al
D 1		U.S. Food and Drug Administration (FDA) (Li and De Clercq, 2020)	2020)
Remdesivir	Developed by Gilead Sciences to target Ebola. Showed efficacy by resisting two viruses similar to Covid-19, SARS-CoV and MERS-CoV, in animals (Wang et al., 2020b) It terminates RNA transcription thereby inhibiting viral replication (Li et al., n.d.).	On January 19, 2020, remdesiver was given to a 35-year-old man in Washington State who has recovered from COVID-19 (Holshue et al., 2020). However, the efficacy and safety of this drug still needs validation in patients with 2019-through further clinical studies.	(Dong et al,2020)
Chloroquine and Hydroxy-chloroquine	It is used to treat malaria, chemoprophylaxis and certain inflammatory conditions which include rheumatoid arthritis, lupus and the blood disorder porphyria cutanea tarda	Approved by the FDA to be tested against COVID-19 In vitro activity against SARS-CoV and SARS-CoV-2 is seen for both the drugs (hydroxychloroquine has relatively higher potency against SARS-CoV-2) Hence both these drugs are recommended for treatment of COVID-19 patients in several countries, including in the U S. A In a chinese study showed that when chloroquine was tested on more than 100 patients, it showed superior results to control drug inhibiting pneumonia, improving lung-imaging, promoting a virus negative conversion and shortening the disease course. Side effects - worsening vision, nausea, digestive disorders and heart failure. *A man in Arizona died and his wife was in critical condition after taking chloroquine prophylactically to pre-	(Gao et al, 2020) (Cao et al 2020)
	droxy-	Showed efficacy by resisting two viruses similar to Covid-19, SARS-CoV and MERS-CoV, in animals (Wang et al., 2020b) It terminates RNA transcription thereby inhibiting viral replication (Li et al., n.d.). Chloroquine and Hydroxy-chloroquine It is used to treat malaria, chemoprophylaxis and certain inflammatory conditions which include rheumatoid arthritis, lupus and the blood disorder porphyria	Showed efficacy by resisting two viruses similar to Covid-19, SARS-CoV and MERS-CoV, in animals (Wang et al., 2020b) It terminates RNA transcription thereby inhibiting viral replication (Li et al., n.d.). Chloroquine and Hydroxy—divided and his wife was in critical condition animals (Wang et al., 2020b) It is used to treat malaria, chemoprophylaxis and certain inflammatory conditions which include rheumatoid arthritis, lupus and the blood disorder porphyria cutanea tarda Approved by the FDA to be tested against COVID-19 In vitro activity against SARS-CoV and SARS-CoV-2 is seen for both the drugs (hydroxychloroquine has relatively higher potency against SARS-CoV-2) Hence both these drugs are recommended for treatment of COVID-19 patients in several countries, including in the U S. A In a chinese study showed that when chloroquine was tested on more than 100 patients, it showed superior results to control drug inhibiting pneumonia, improving lung-imaging, promoting a virus negative conversion and shortening the disease course. Side effects - worsening vision, nausea, digestive disorders and heart failure. *A man in Arizona died and his wife was in critical condition after taking

4	Lopinavir/ritonavir (anti-retroviral drugs)	Sold under the name Kaletra by AbbVie and are designed to treat HIV (AIDS).	99 positive patients were treated No benefit was observed compare to standard care In South Korea, a 54-year-old man showed significant and substantial decrease in the levels of the β-coronavirus	(Lim et al 2020) (Elfiky et al 2020)
			According to the WHO, there may be of using it with other drugs such as interferon-β, oseltamivir or ribavirin	(Caly et al, 2020)
5	Tocilizumab	Marketed as Actemra, used to treat patients with moderate to severe rheumatoid arthritis to lower inflammation.	An initial clinical trial was done in China on 20 acute COVID-19 patients. Nineteen patients (95%) were cured and discharged from hospital within two weeks. The FDA has officially approved its phase 3 trial of in severe COVID-19 patients.	
6	Darunavir (anti-retroviral HIV-1 protease inhibitor)		In February 2020, it significantly inhibited SARS-CoV-2 replication and its inhibition efficacy was 280-fold more than that in the untreated group	
7	Ivermectin (anti-parasitic drug)		Effective against the SARS-CoV-2 virus as studied by researchers in an in-vitro at Monash University in Melbourne, Australia. Although, clinical trials are still needed to confirm the effectiveness of the drug in humans with COVID-19	(Chen et al, 2005)

Table 3: Draft Landscape of Candidate Vaccines

S.NO.	Company name	Production	Mechanism for COVID19	Ref
1.	Entos Pharmaceuticals	DNA vaccine (Fusogenix naomedicine) proteo-lipid vehicle (PLV)	It contains plasmid DNA encoding multiple antigens from key SARS-CoV-2 proteins to promote maximum protection.	(Roldao et al., 2010)
2.	Airway Therapeutics	AT-100 human surfactant protein-D (rhSP-D)	Effective in reducing inflammation and infection in the lungs in preclinical trials. Generating an immune response against various respiratory diseases	(Shimabukuro et al., 2018)
3.	Canada's Medicago	Virus-Like Particle (VLP)	Stimulates cellular immunity with the aim of responding to the virus without the risk of infection	(Rayner et al,. 2020)
4	Biopharma	I-Mab (TJM2, a neutralizing antibody)	Used in treatment for cytokine release syndrome common in patients suffering from a severe infection of SARS-CoV-2 TJM2 targets the human granulocyte-macrophage colony stimulating factor (GM-CSF), responsible for acute and chronic inflammation.	(Alharbi et al., 2017)

5	Tiziana Life Sciences	TZLS-501 human anti-interleukin-6 receptor antibody	Prevents lung damage and raised levels of IL-6 during the disease. Through various tests it is depicted that this treatment rapidly depletes circulating levels of IL-6 in the blood	(Alharbi et al., 2017)
6	The University of Oxford's Jenner Institute and Italian pharmaceutical manufacturer Advent Srl	ChAdOx1 (viral vector)	Attenuated adenovirus which is capable of producing the spike (S) protein of SARS-CoV-2, which allows formation of endogenous antibodies against these proteins and, consequently, against SARS-CoV-2 (Alharbi et al., 2017).	(Alharbi et al., 2017)

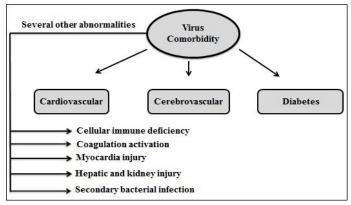


Figure 8: Comorbidities related to COVID19

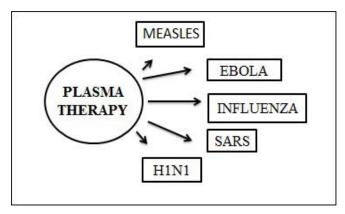


Figure 9: Plasma treatment used for earlier epidemics (Van Griensven et al., 2016; Cheng et al., 2005)

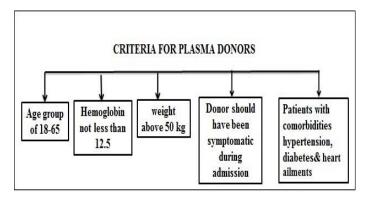


Figure 10: Guidelines standardized for plasma donor (52)

During the SARS epidemic in 2003, a research conducted on 80 patients in Hong Kong revealed that patients given CP therapy, recovered within two weeks of symptoms following as compared to other patients (Jawhara et al., 2020).

After studies conducted in China to measure the effectiveness of CP therapy New York hospitals also used the plasma blood as a potential antidote to the disease (MacLenam et al., 2006).

However, a small risk is associated with the use of CP therapy as it could also transmit blood-borne pathogen which includes human immunodeficiency virus (HIV), hepatitis B virus (HBV), or hepatitis C virus (HCV) (51).

Figure 9 and 10 illustrate plasma treatment used earlier for epidemics and standardized guidelines for plasma donor.

VACCINE TRIALS

Coronavirus (Covid-19) vaccine latest update: with the production of a secure, reliable and accessible Covid-19 vaccine as the cornerstone to controlling the pandemic, research and testing are rising at a rapid pace around the world to find a cure for the current coronavirus. In current events, US firm Moderna Inc, one of the front leaders in the vaccine race, has said it had begun dosing patients in a mid-stage study while Russian scientists intend to launch clinical trials within two weeks. There are about 120 vaccines at work worldwide, of which at least 10 are undergoing clinical trials, even as cases around the globe crossed the 61 lakh mark, including 372,566 deaths. Large pharmaceutical companies such as Gilead Sciences, Pfizer, Moderna, among others, are racing to find a successful vaccine. In India, Ramdev's Patanjali has also joined the race to develop coronavirus vaccine.

China's CanSino adenovirus vaccine, Oxford University's adenovirus vaccine, Moderna's mRNA vaccine and Novavax have surfaced as the most hopeful Covid-19 vaccine candidates to date (Crouch et al., 2000).

A Chinese vaccine, co - developed by Beijing Institute of Biological Products and China National Biotec Group Co, has finished Phase II evaluation and may be ready for market in late end of this year or slightly earlier next year, according to a report issued by the State-owned Assets Supervision and Administration Commission (Crouch et al., 2000).

Another Chinese biopharmaceutical company Sinovac Biotech, dubbed CoronaVac, has stuck hope on its inactivated vaccine and said it is 99 percent sure of its effectiveness. According to a report from Sky News, Sinovac researcher Luo Baishan said, "It has to be successful ... 99 per cent sure (Crouch et al., 2000).

US Company Moderna Inc. reported recently that it had started dosing patients with its experimental coronavirus vaccine in a mid-stage study and ultimately plans to enroll 600 patients in the trial. The step suggests that the firm's mRNA vaccine passed its initial safety tests. Reuters announced that Moderna plans to start late-stage trials in July (Crouch et al., 2000).

Russia, which has the third-highest Covid-19 toll in the world after the United States and Brazil, has stated that it plans to set up clinical trials on a vaccine within two weeks. In addition, authorities also accepted the country's first anti-Covid-19 drug, according to a Reuters report (Crouch et al., 2000).

The US pharmaceutical giant Pfizer has said that a Covid-19 vaccine may be ready by the end of October 2020, that is being developed in partnership with the German firm Biontech (Crouch et al., 2000).

DISCUSSION

Viral diseases continue to arise, and pose a significant public health problem, according to the World Health Organization (WHO). Several viral epidemics, such as the extreme acute respiratory coronavirus syndrome (SARS-CoV) in 2002 to 2003 and H1N1 influenza in 2009, have been reported in the last twenty years. Recently the Middle East coronavirus respiratory syndrome (MERS-CoV) was first reported in 2012 in Saudi Arabia. An outbreak of cases of unidentified low respiratory infections found in Wuhan, the largest metropolitan area in China's Hubei province, was first identified to China's WHO Country Office on December 31, 2019, in a timeline that reaches the present day. Available literature can date the emergence of symptomatic people back to early December 2019. These first cases were labeled as "pneumonia of unknown etiology" because they were unable to classify the causative agent. An expansive outbreak response plan was initiated by the Chinese Center for Disease Control and Prevention (CDC) and local CDCs. The etiology of this disease was ascribed to a novel coronavirus (CoV) family virus. The new virus tends to be very infectious, and has spread rapidly worldwide.

The epidemic was declared a Public Health Emergency of International Concern (PHEIC) by the WHO at a meeting on 30 January 2020 according to the International Health Regulations (IHR, 2005), as it had spread to 18 countries with four countries reporting human-to - human transmission. An additional milestone occurred on 26 February 2020, when the first case of the disease was reported in the United States (US), not imported from China. The CoVs have been the main pathogens of new outbreaks of respiratory illness. These viruses can cross species boundaries for reasons yet to be established, and can cause disease ranging from common cold to more serious diseases such as MERS and SARS in humans. Interestingly, these latter viruses originally originated in bats and then spread to other mammalian hosts — the SARS-CoV Himalayan palm civet, and the MERS-CoV dromedary camel — before moving to humans. SARS-Cov-2 dynamics are currently unclear, although there is evidence that it is also of animal origin. World authorities are trying to put in place countermeasures to prevent their catastrophic consequences. Health organizations are organizing knowledge flows and issues guidelines and recommendations to help minimize the effects. Around the same time, scientists around the world are working relentlessly, and knowledge about the mechanisms of transmission, the clinical spectrum of illness, new treatments, and preventive and therapeutic approaches are evolving rapidly. There are still several uncertainties with regard to both the virus-host relationship and the evolution of the pandemic, with specific reference to the times when it would hit its peak. The therapeutic approaches for coping with the infection are currently only supportive, and prevention aimed at minimizing social transmission is our best tool. Aggressive efforts to isolate China have led to a gradual decline in incidents. In Italy, in northern regional areas, initially, and progressively around the peninsula, political and health authorities are making extraordinary efforts to control a shock wave that is seriously challenging the health care system.

CONCLUSION

There's no particular treatment currently available for COVID-19. Given the high rate of human-to-pandemic transmission of this virus, it is important to identify the basis of its replication, structure, and pathogenicity for discovering a way to specific treatment or prevention. Because of the virus' high similarity to its families, efforts have been made to provide COVID-19 drugs and vaccines. Differences in spike length as is longer in COVID-19 are likely to play a significant role in pathogenesis and treatment of this virus. Identifying the specific molecular details of the virus is however helpful in achieving treatment objectives.



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CONFLICT OF INTEREST

There is no conflict of interest.

AUTHORS CONTRIBUTION

SS designed and planned the research. NRG has written the manuscript. STR revised the manuscript and RS,SS and PS collected the data samples for the study.

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