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Current treatment of Corona (SARS-CoV-2): A Review.

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ABSTRACT

In the current scenario the world is suffering due the SARS-Cov-2 or corona virus. It was first originated in Wuhan, China in 31st December 2019 and spread all over the world with a very short time. It killed more than eight lakh ninety six thousand people in all over the world where as affected two crore seventy five lakh people within this period. Till now there is no potential approved vaccine or medicine is not available in the world. However, some drugs are indicating a potential against the deadly virus. This review is aiming to identify those drugs which are potential against the SARS- CoV2. As per research papers and several reports there are 4 classes of drugs which will be effective against the Corona virus, they are i) Anti-viral drugs and anti-inflammatory drugs ii) Anti H.I.V drugs iii) Anti-malarial drugs iv) Traditional Chinese dugs and other types of drugs. Though these drugs may be partially effective against the Corona virus but the research should continue to find some new molecule or new vaccine to cure this disease.

Keywords: Corona Virus, SARS-CoV-2, Different classes of effective drugs, Vaccine

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INTRODUCTION

In current situation COVID-19 or SARS-CoV-2 is a night mare for all over the world. This virus was first originated at Wuhan, China in December 2019[1]. It was observed that several patients were admitted in hospital mostly with cough, sneeze, fever and shortness of breath. Most of the cases were transformed to severe pneumonia[2]. Within a very short time it was spread more than 140 countries, and infected lots and lots of people with a mortality rate more than 6%. W.H.O declared it as a health emergency and pandemic[3]. More than 27.5 million people were infected and a huge number 8.96 lakh people were died due to the SARS-CoV-2 infection[4]. The primary symptoms are very simple like sore throat, fever, sneezing, and cough. But time to time it increases and turns in to a severe pneumonia. In the first phase it was established that the disease was spread from the Wuhan market. It was reported in some peer reviewed journal that the disease was caused due to some illegally sold animal in Wuhan market. So, there may be an invisible bridge between the SARS-CoV-2 and the Wuhan market. After 7th January China confirmed about the new SARS-CoV-2 virus, which has a resemble with SARS-CoV virus and MERS–CoV virus[5]. But this new strain is really powerful than the other two. In first phase W.H.O also thought that it was a traveler's disease. But within 15 days it was proved wrong. Primarily it was spread through the passengers specially coming from China. And accordingly, it infected all over the world. It was observed that the international flights from different countries are the sources. So, after a while W. H.O declared to stop the international flight for time being to control this contagious deadly disease. China was first started the restrict life style and 'lock down' for seven weeks for control this infection. Accordingly, most of the countries also followed this. In India the lock down is continuing till now. People are maintaining the restrict life and also the social distancing. A group of scientists were found that this SARS-CoV-2 virus has very similar structures like the bat coronavirus RaTG13[6]. But after sometime this was rejected. Only in China more than eighty thousand people were infected and more than three thousand five hundred people were died. It was also affected U.S.A, Italy, Spain, Britain, France, and Germany badly. In India more than fifty thousand people were infected whereas more than one thousand five hundred people were died[7]. Till now there is no established treatment is available. And till now no vaccine was invented. In some of the countries they are claiming that hydroxychloroquine and Azithromycin combination are working[8]. Some of the patients were also treated with this combination and they cured from SARS-CoV-2. But there is also some evidence where these combinations are not working. Some anti-retroviral combinations (Lopinavir/ritonavir) are also showing a posetive way of treatment[9]. Recently a group of researchers claimed that Remdesivir monophosphoramidate prodrug of an adenosine analog which was used in the time of Ebola it has a good effect in the treatment of SARS-CoV-2[10]. It was used for the clinical trial in U.S.A, already some good positive results were found. There are a lot of drugs are in the pipe line and also in clinical trial stage. Some of the pharmaceutical industries are claiming that they are very hopeful for inventing the vaccine within a year. Some are already in clinical trial function. But all are in pipeline to be honestly the situation in all over the world becomes horrible. In U.S.A more than ten lakh people were affected. There is a tremendous shortage of ventilation unit even in rich countries like, U.S.A, Italy, UK. The doctors, nurses, health staff are working day night for treatment of COVID-19 patients. Till date all over the world the emergency situation is continuing. Several countries are in 'lock down' situation. It also affects in the world economy. But with the using of social distancing and proper sanitization in China the patients number become decrease[11]. However, it is still a challenge for the scientists and health personal specially doctors. This article further describes the epidemiology and present treatments of COVID-19.

Epidemiology of COVID-19:

COVID-19 or SARS-CoV-2 was first originated Wuhan China in December 31st Dec 2019[5]. A group of people were suffering in fever, cough and sneeze. After that it turned into severe Pneumonia, and most of the cases patients died. In China till date around eighty-five thousand people were diagnosed with COVID-19 positive whereas more than three thousand five hundred people were died[6]. Mostly this disease is spreading through human transmission with the droplet of infected persons to others **[Fig-1].**

In U.S.A the situation is very critical more 6.41 million people were affected and 192000 had died till date[7]. In Italy more than thirty thousand people were already died with COVID-19 infection. In Britain also more than thirty thousand people were died. In India more than seventy thousand people were affected and more than 2,200 were died already. All over the world total infected numbers are huge 4.38 million. Already two lakh eighty thousand people were died. So, world health organization announced it as global pandemic[8]. For SARS-CoV-2, mean incubation period is 5.2 days (95% Confidence Interval). This virus is very contagious with a reproductive number R_0 ranging between 1.4-3.5[9]. As per the W.H.O report it was mentioned the R_0 is ranging

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between 1.4-2.5[10][10]. Some preliminary case was found where the R_0 level was much higher. (2.24-3.58[32]). Normally the mortality rate is nearly 4%. The mortality rate was first higher in China around 2.1 to 4% but now mortality is almost touched 5 to 6 % in all over the world[2]. U.S.A is in more danger position more than 6% mortality rate is found as per report. In India 1.70 % is the mortality rate. The mortality rate is also higher in Italy it is more than 13% as per the report. These viruses were mutated so fast and at least 60 times the virus was mutated. So, that it is really difficult to predict all about COVID-19. The incubation period of SARS- CoV2 can be compared with the SARS CoV and MERS. In case of both of the diseases the incubation period is [2-7 days] and [2-14] days[11]. SARS- CoV and MERS has resembled with Corona or COVID-19. Whereas COVID-19 is more powerful and infected more and more people at a time[12]. The mortality rate is high in case elderly patients specially diagnosed with diabetes, asthma, cardiac problem and cancers. A report is showing of around 88 cases where the incubation period is 6.4[9]. Most of the cases are attached with travel history. Already COVID-19 spread more than 130 countries as per the latest report. But still there are lots of unknown facts of SARS-CoV-2 which could not find. The stability of the virus is still unpredictable in the environment. Still unknown facts are continuing regarding the fomites of transmission of this virus.

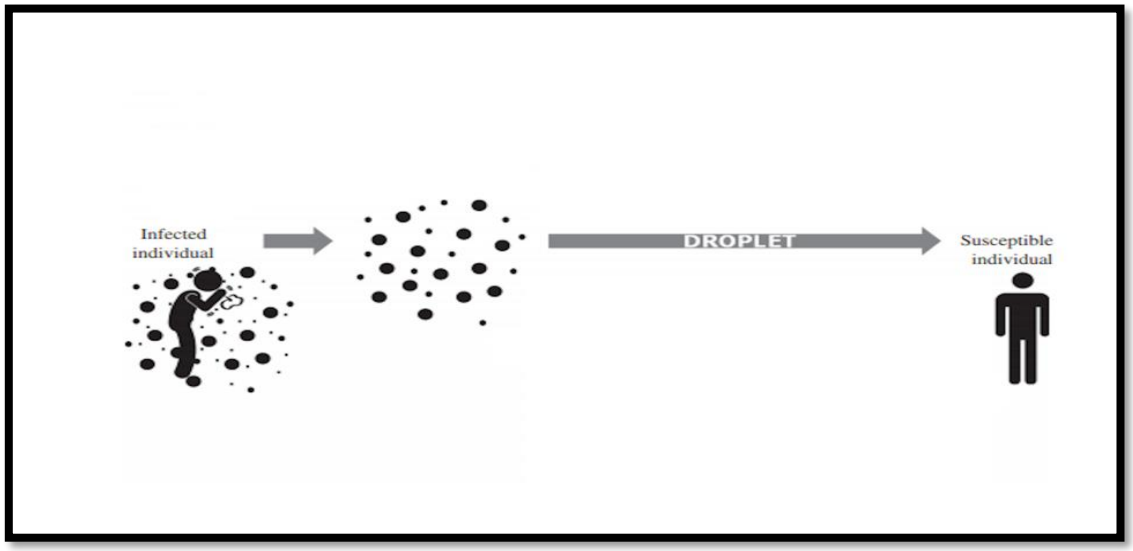

Figure 1: Transmission of corona virus through human droplets.

Diagnosis of COVID-19:

Patients those who got travel history specially from china, Wuhan they diagnosed primarily with the reverse transcription (RT)-PCR test with a COVID-19 positive result or a patient came in contact with an infected person he or she may be COVID-19 positive with the reverse transcription (RT)-PCR test[12]. But these were performed when there was a way to do the regular test. Now the time is different because a huge number of people are affected throughout the world. It is nearly impossible to perform test each and every one or cluster wise. So still there are a plenty of asymptomatic cases are in the world. There are three types of tests available across the globe for diagnosis of COVID-19 they are i) RT- PCR (Reverse-transcription polymerase chain reaction) ii) rRT- PCR (Real time RT- PCR iii) RT- LAMP (reverse transcription loop-mediated isothermal amplification)[13]. The last one RT- LAMP is very sensitive and it can detect easily the MERS-COV. Nasopharyngeal and oropharyngeal swab tests are the two-basic method for the diagnosis of COVID-19 still[14]. The sample after collection with saline it should be in a sterile container. Serum samples should be collected in a vial (simple vial) with anti-clotting agent but the sample should be collected in acute phase of the illness as well as convalescent phase[15]. For the transportation of the swab to the laboratory it should be kept separately in a viral transport medium. As per the guidelines from W.H.O and I.C.M.R the samples should be covered with triple packaging[16].

As per the guideline when sample to be collected from a patient the data should be filled in a form and it is mandatory and very vital. The filled form should contain regarding the patient's history, mostly travel history, time, site of sample collection, date, risk factors, requirement of tests. A particular number should be mentioned in the biological sample category B that is UN3373[17]. As per the recommendation of W.H.O the virus culture should be carry out in biosafety levels 3 lab. The biosafety levels 2 lab is applicable for the test (RT- PCR)[18].

Precaution should be taken when the sample will be handling specially it will be applicable for the health staff. Real time RT- PCR was first developed by Charité Berlin, Germany[19]. This test actually identifies the presence of three important genes they are Glycoprotein E, *RdRp* and glycoprotein-N[20]. This identification follows steps. In Wuhan hospital the positive case rate was nearly 40 % with RT- PCR according to nearly 5000 cases of SARS-CcV2 infected. As per the PCR technique in oropharyngeal swabs the positive case rate was nearly 54%[21]. In case of RT- PCR technique the positive result may come after a long day naturally within 2-8 days. An accurate result with a less time can be performed by using the cobas 6800. It is actually the molecular assay to find out the presence of SARS-CoV-2[22].

Though there are some prescribed test but all are time consuming. Some of the tests are also very expensive. It may be a drawback for the diagnosis of this disease People those who are suffering from fever, cough, sneezing, dyspepsia, shortness of breath they have a tendency for a positive CT (chest computerized tomography) result in spite of negative RT-PCR detection[23]. In China more than 80% patients were got CT positive result whereas the RT-PCR was showing only 60 % positive. But there are still to overcome for the diagnosis purpose of this disease. Most of the research institution and some renounced universities are working on it. Still there is hope to get an accurate and fast diagnostic kit within a short time.

Mortality rate of COVID-19 as per W.H.O:

After the detection of this virus in Wuhan China, in December 2019, it declared pandemic by W.H. O with in January 2020. Till now it has spread more than 130 countries[24]. The transmission is mostly form infected human to human through the droplets. Still there is no sign of airborneness of this virus. This virus was first struck to China, Wuhan. In china total 84597 people were affected with this deadly virus and 4650 were reported death[25]. The mortality rate was nearly 6%. In USA the situation become worst 1,783,638 people were infected with reported death of 104,247. The mortality rate is around 6%[26]. A survey reported that COVID-19 hunts elderly patients more rather than the young[27]. Italy was badly affected by COVID-19, 233,197 people were infected and 33475 reported death. Mortality rate is quite higher 14.35%[28]. There are also countries which are affected badly like Germany, Russia, India, Iran etc. In India the mortality rate is lower around 3%. Whereas a huge number of people are infected. **[In Table 1]** the mortality rate is described with the badly affected countries.

Table 1: Mortality rate of COVID-19 in different countries till 2nd June 2020 [29]-[30]

Sl. No.	Country name	Total Infected	Death	Mortality rate (%)
1	USA	6410000	192000	2.99
2	China	84597	4645	5.49
3	Russia	100000	17332	1.19
4	Germany	182028	8522	4.68
5	Italy	233197	33475	14.35
6	Spain	240010	29858	12.44
7	United Kingdom	276336	39045	14.13
8	Iran	393000	22600	5.75
9	India	4400000	75000	1.70
10	Pakistan	76398	1621	2.12
11	Bangladesh	49534	672	1.35
12	Brazil	4170000	128000	3.1%
13	Japan	16930	895	5.28
14	France	148775	28776	19.34

From the **table 1** it is confirmed that most of the countries mortality rate is within 6% except Italy, Spain, U.K and France. The highest mortality rate was found in France it is more than 19%. Though all over the world the infected people number is huge 6194533 people found positive result with the COVID-19 infection and 376320 people were reported death as per W.H.O report. Global mortality rate is also more than 6%. Still now there is no marketed vaccine or medicine is available globally. So, as a result the mortality rate becomes more in some countries. Also, there is an age-related issue. Aged people mostly more than 60 are in a high risk.

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The infant is comparatively lower risk in this infection. Still the transmission is continuing through the infected human droplets. According to W.H.O in 1st june there was 124139 new cases were confirmed. [**Fig 2]** describes about the highest mortality countries with a comparative global mortality rate. In this figure we use those countries whose mortality rate was already recorded in higher range.

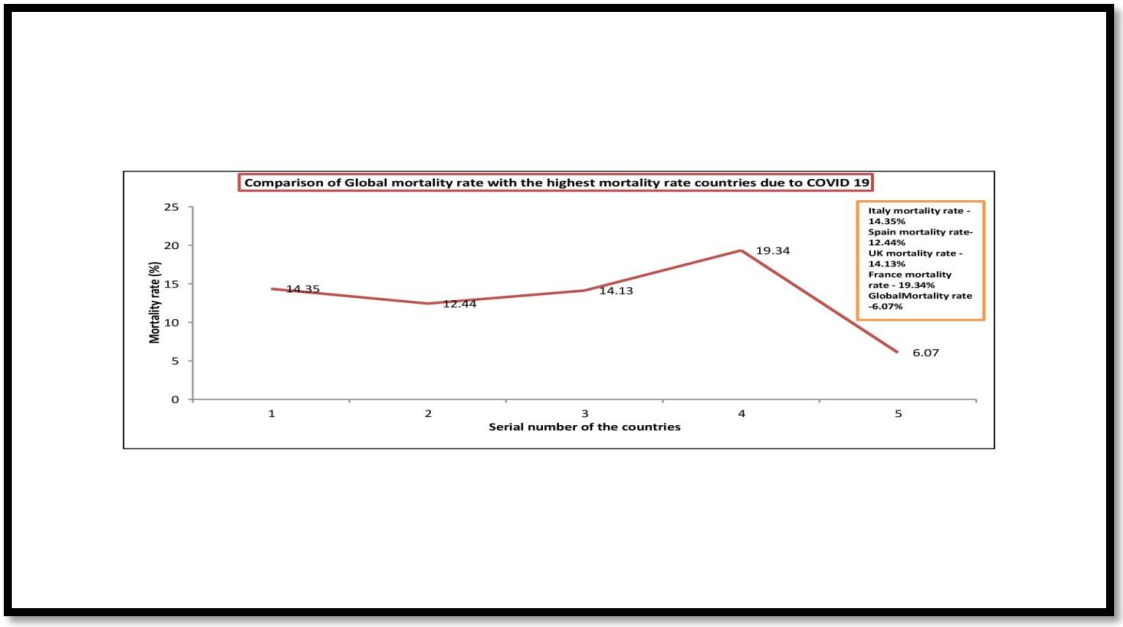

Fig 2: Comparison between global mortality rate with the highest mortality rate countries.

Treatment of the disease (Corona Virus SARS-CoV-2):

At present, no drug has been proven to be safe, effective and potential for treating SARS-CoV-2 (COVID-19). There are no Food and Drug Administration (FDA)-approved drugs available to treat patients with COVID-19. National Institute of Health (NIH) has developed treatment guidelines to inform clinicians how to care and manage the patients with COVID-19. According to NIH treatment guidelines, the main investigated therapeutic options for COVID-19 are antivirals drugs (Ramdesivir, Lopinavir, Ritonavir, etc.) and Host Modifiers/Immune-Based Therapy (convalescent plasma, Interferons, Interleukin-6 Inhibitors, etc.)[31].

At first, Suspected and confirmed cases should be isolated and treated in designated hospitals with supportive care. Chinese Center for Disease Control and Prevention(China CDC) has developed treatment protocol for COVID-19, which includes General Treatment (water and electrolyte balance ,Effective oxygen therapy, etc.), Anti-virus treatment (Use of Interferon-α, Lopinavir/ Ritonavir, Ribavirin, Chloroquine phosphate, Arbidol) and Anti-bacterial treatment (avoid use of combination with broad-spectrum antibiotics)[32].

In clinical practice, the treatment of COVID-19 in worldwide mainly includes oxygen therapy, antiviral therapy, and traditional ayurvedic medicine treatment. For patients with past disease history (like-Hypertension, Diabetes Mellitus, etc.) are managed with supportive care with different therapies and it depends with the patient health status and their health care provider.

As of May 10, 2020, we have compiled information of promising therapeutic drugs for COVID-19 from US National Institutes of Health (NIH), and other clinical and scientific research article around the world. Here, we have discussed some therapies under evaluation for the treatment of COVID-19:

Anti-viral agents:

Lopinavir/ Ritonavir:
Lopinavir is a highly potent antiretroviral protease inhibitor used in the treatment of human immunodeficiency virus (HIV) infection[33].

It is formulated with a small amount of ritonavir to increase and maintain adequate lopinavir concentrations in blood. These formulations are known as Kaletra and may have therapeutic effects in SARS and MERS by reducing the ability of the replicated virus to infect cells.

Lopinavir/ritonavir is an inhibitor of SARS-CoV 3CLpro *in vitro*, and this protease may also function as inhibitors for other coronaviruses (SARS-CoV-2) with similar Mpro binding sites and pocket structures[34][35]. Due to unfavorable pharmacodynamics and negative clinical trial data, the National Institutes of Health (NIH) COVID-19 treatment guidelines recommend against the use of lopinavir; ritonavir outside of clinical trials[36].

Remdesivir:

Remdesivir is a Adenosine nucleotide analogue used to treat Ebola virus, Marburg virus, MERS and SARS infections[37]. It's mainly binds with viral RNA-dependent RNA polymerase enzyme and inhibits viral replication process through premature termination of RNA transcription. It's acts as a prodrug and it transfer to its active form by hydrolysis.

Remdesivir showed *in-vitro* activity against SARS-CoV-2 infected Vero E6 cells[38], and *in vitro* and *in-vivo* activity against SARS-CoV and MERS-CoV replication in human airway epithelial cell (HAE) and effective against a diverse array of human and zoonotic CoV in HAE [39][40][41]. Due to a lack of clinical data, the National Institutes of Health (NIH) coronavirus disease 2019 (COVID-19) treatment guidelines do not give recommendations for or against the use of remdesivir

Ribavirin:

Ribavirin is a guanosine analogue, used as broad-acting antiviral drug[42]. It interferes with the replication of RNA and DNA viruses and inhibits natural guanosine generation by directly inhibiting inosine monophosphate dehydrogenase in a pathway that is vital for the production of the guanine precursor to guanosine[43].

Recently, *in silico* model, Ribavirin shows potent drug against the newly emerged HCoV disease and tightly bind to RdRp enzyme which may high potential to fight with SARS-CoV-2 strain [44][45].

Clinical trials of Potential Antiviral Agents for COVID-19:

As 11 May, 2020, according to National Institute of Health, U.S. National Library of Medicine, there are 1358 Clinical Trials registered for treatment of COVID-19 by searching keyword as COVID-19[46]. Table 3 further describes some of the drugs which are in clinical trial.

Different biotechnological companies, Research institutes have applied for clinical trials to repurpose existing drugs as well as to develop vaccines and drugs to fight against the fast spreading COVID–19.

According to National Institutes of Health (NIH), COVID-19 treatment guidelines, the major drugs undergoes clinical trials that might have the potential to treat this viral infection are Azithromycin, Chloroquine, Hydroxychloroquine, Lopinavir/Ritonavir, and Remdesivir [47]. Here we have showed some potential candidate drugs under clinical trials (**Table 2**) evaluation for treatment of COVID-19.

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Table 2: Status of clinical trial of the choice of drugs against COVID-19 infection:

Sl. No.	Candidate Drugs	Number of Clinical Trials Registered (As 11 May, 2020)	Number of Clinical Trials in Recruiting Status (As 11 May, 2020)	Recommendations Status by National Institutes of Health (NIH), COVID-19 Treatment Guidelines.
1	Azithromycin (When Used with Hydroxychloroquine in Reported Cases)	75	35	Recommends against the use of Hydroxychloroquine plus azithromycin except in a clinical trial setting
2	Chloroquine	54	29	There are insufficient data for the Panel to recommend for or against the use of chloroquine
3	Hydroxychloroquine	173	83	There are insufficient data for the Panel to recommend for or against the use of Hydroxychloroquine
4	Lopinavir/Ritonavir	55	32	The Panel recommends against the use of lopinavir/ritonavir and other HIV PIs except in a clinical trial setting
5	Remdesivir	21	10	Insufficient data for the Panel to recommend for or against RDV use.

Favipiravir

The antiviral drug Favipiravir (6-fluoro-3-hydroxy-2-pyrazinecarboxamide) is the selective and potent inhibitor of the RNA-dependent RNA polymerase (RdRp) of RNA viruses[48]. In 2014, Japan approved Favipiravir (FPV) to treat pandemic influenza virus infections[49]. China tested FPV for the management of the COVID-19 in February 2020[50]. Japan has also made the idea for trials of the drug in this pandemic situation[51][52]. In March 2020, the drug was also used in mostly affected three regions of Italy for experimental treatment to prevent COVID-19. Drug Controller General of India has approved to organize clinical trials of favipiravir or Avigan as a potential agent for COVID-19[53]. Well therapeutic effects have been found by using FPV to treat COVID-19 in terms of disease progression and viral clearance[54].

Tocilizumab

The immunosuppressive drug Tocilizumab (TCZ) is used in the treatment of rheumatoid arthritis [55]. The use of tocilizumab has been included by China's National Health Commission to treat COVID-19[56]. Tocilizumab has also been recommended by The Australasian Society for Clinical Immunology and Allergy for COVID-19 patient with acute respiratory distress syndrome[57]. Separate trials are being launched by Roche and the WHO for severe COVID-19 diseases[58]. A randomized study was started to compare favipiravir versus tocilizumab at eleven places in China in March 2020[59][60].

Chloroquine and Hydroxychloroquine

Chloroquine and hydroxychloroquine are 4-aminoquinoline antimalarials drugs. Chloroquine has been used for malaria prophylaxis. It has been shown that chloroquine has an effect against several viruses, including severe acute respiratory syndrome coronavirus (SARS-CoV). Multiple mechanisms of action of chloroquine have been found, which includes disruption of the early stage of coronavirus replication. Additionally, chloroquine mediates the anti-inflammatory activity by influencing immune system[61]. Chloroquine and Hydroxychloroquine have been recommended for the treatment of the infection due to SARS-CoV-2. These drugs have been given alone or combination with azithromycin which have both immunomodulatory and antiviral response for the management of the pandemic diseases without any experimental proof[62][63].

Corticosteroids

It has been reported that corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs) may intensify the symptoms of COVID-19. Caution should be taken for the use of corticosteroids and NSAIDs in COVID-19 disease according to current literatures[64]. It has been found that there has been no relation between corticosteroids treatment and outcome in COVID-19 patients without acute respiratory distress syndrome[65]. Two recent publications between February and March 2020 have reported that corticosteroids are not suitable for the COVID-19 patients[66][67].

Antibodies

Eli Lily has introduced first potential antibody LY-CoV555 which attacks SARS-CoV-2 virus. The antibody can be administered safely in phase I clinical trial. So, it can be moved in phase II study in non-hospitalized COVID-19 patients[68]. In the meantime, the research is going on for the development of monoclonal antibody treatment for this infectious disease. A set of neutralising antibodies, collected from blood sample of a person who had overcome from severe acute respiratory syndrome (SARS) in 2003, were tested. A monoclonal antibody TY027 which specifically attacks SARS CoV-2, will be tested on healthy volunteers in phase I clinical trial by Singapore biotech firm Tychan. The National Medical Products Administration has approved human monoclonal antibody of the Institute of Microbiology at the Chinese Academy of Sciences for clinical trials for COVID-19 [69].

Convalescent plasma transfusion: Till date there is no established clue to get rid of COVID-19. There are lots of proposed drugs which may help to treat SARS-CoV-2. But different drugs show different result in COVID-19 positive patients. Hydroxychloroquine, Remdesivir shows some collective positive result all over the world. But it also reflected some negative result also in some countries. U.S.A is one of them. Since 1890 there was an established treatment called passive immunization which has a tremendous potency against infectious disease. According to this treatment one who has infected with the disease his or her blood can be withdrawn and this blood sample may use as antibody for the specific microorganism[70]. In case of the SARS-CoV-2 a group of scientists claimed that convalescent plasma transfusion is a potent treatment against it. Covalent plasma therapy contains the neutralizes antibody which can be administered to a SARS-CoV-2 patient. It has that capacity to reduce the mortality rate specially in antiviral disease[71][72]. In past decades also it was used in the dangerous Spanish influenza 1915-1917, Ebola, SARS, H1N1, etc.[73][74]. A good number of patients got cure after using it. So, it takes the attention of the researchers for treatment in SARS-CoV-2 also. This disease is already pandemic and killed huge number of people. Food and Drug Administration suggested that convalescent plasma transfusion can be given to the COVID-19 affected patients for clinical observation and also it can be used for the research in this health emergency situation [75]. As per the research and peer reviewed review article it has observed that with the treatment or application of the convalescent plasma therapy the viral reproduction can be minimize and also the viral load remarkably decreases so the patients may be out of danger[76]. It has stated that the CPT(Convalescent plasma transfusion) can be administered to the critically affected COVID-19 patient[77]. As per the report C.P.T was administered to 27 patients and they got a good result and most of them are now out of danger. So, it has a good potency for treating the deadly SARS-CoV-2. For the dose of the C.P.T there is no clear image, it is actually varies with the age sex and also with the body weight. A group of Chinese researchers reported that 200 ml of the CPT can neutralize antibody >1:640. In some another study it has stated that maximum 2400 ml of CPT was administered to an old man of 73-year age. So, there is no fixed dose of the CPT till now. After the administration of CPT from day one to day thirty it has observed that the viral load became decreased and became zero also after thirty days treatment of CPT. Patients IgG and IgM also remarkably increased. After the treatment with CPT almost all the patients have no fever the body temperature became normal there was no shortness of the breath and no such of cough and sneeze[78][79][80]. The research is continuing with the CPT treatment and some of the CPT treatment is in clinical state (Table 3). The survival rate of the patients was excellent. Mortality was become nearly zero percent. In India Indian Council of Medical Research also permitted the Convalescent plasma transfusion therapy to the patients for treatment. So, this therapy is in clinical state now but surely it will take a big role for treating the SARS-CoV-2 within a short time. Clinical trial of the convalescent plasma transfusion therapy is shown in **[Table 3].**

Table 3: A list of Clinical trial of convalescent plasma transfusion therapy [81]

Sl. No.	Register number	Title	Sponsor's name	Key indicator
1	ChiCTR2000029850	Study on convalescent plasma treatment for severe patients with novel coronavirus pneumonia (COVID-19)	Zhejiang University School of Medicine	Mortality rate
2	NCT04292340	Anti-SARS-CoV-2 inactivated convalescent plasma in the treatment of COVID-19	Shanghai Public HealthClinicalCenter	Throat swab, sputum for the virological clearance rate
3	ChiCTR2000030039	Clinical study for infusing convalescent plasma to treat patients with new coronavirus pneumonia (COVID-19)	Affiliated Hospital of Xuzhou Medical University	COVID-19 Infection levels, Viral load

Vaccine: Corona virus or SARS- CoV2 was first noted on 31st December 2019. But still date there is no established treatment regarding the COVID-19. Scientists reveal the structure of the SARS-CoV-2[82]. It is basically the S glycoprotein which is responsible for the rapid replication of this virus. Till now there is no molecule or vaccine developed to denature the protein structure. So, it is a challenge for the world to develop a vaccine regarding this pandemic situation. Most of the scientists are trying to strike the S-glycoprotein or spike glycoprotein[83]. But vaccine development or the processing of vaccine is not an overnight task. It needs a long time to develop it. Ebola epidemic was notified in 2013. This was more deadly than SARS-CoV-2. But for the development of the rVSV Ebola vaccine also took three year to prove itself safe and it is in clinical trial phase one[84]. In 2019 the Ebola vaccine was come to market through the giant pharmaceutical company Merck Sharp and Dohme B.V. Moderna announced that they have already develop a mRNA vaccine against COVID-19 virus named mRNA-1273 which is now under clinical human trial[2]. Tianjin university developed an oral SARS-CoV-2 vaccine where used a food grade Saccharomyces cerevisiae it is absolutely safe and it is also targeting the S-glycoprotein. There are several institutions and several companies trying to develop the SARS-CoV-2 vaccine and there are also some positive results till found. Hope fully within this year it will come to the market. The present status of the vaccines is in **[Table 4 and Table 5].**

Table 4: Some selected clinical trial status of global vaccine development against COVID-19

Sl. No.	Developer	Vaccine type	Current state	Target Virus
1	University of Oxford and Astrazeneca	ChAdOx1-S	Phase 2b/3	SARS-CoV-2
2	Moderna/NIAID	LNP-cncapsulated m RNA	Phase 2	SARS-CoV-2
3	Wuhan institute of biological products	Inactivated	Phase1/2	SARS-CoV-2
4	Sinovac	Inactivated+ alum	Phase 1/2	SARS-CoV-2
5	BioNTech/Fosunpharma/Pfizer	3 LNP- mRNAs	Phase 1/2	SARS-CoV-2
6	Beijing institute of biological products	inactivated	Phase 1/2	SARS-CoV-2

Table 5: Some selected pre-clinical trial status of global vaccine development against COVID-19

Sl. No.	Developer	Vaccine type	Current State	Target Virus
1	Osaka University/AnGes/ Takara Bio	DNA Plasmid type	Pre - clinical	SARS-CoV-2
2	Zydus Cadila	DNA Plasmid type	Pre - clinical	SARS-CoV-2
3	BioNet Asia	DNA Vaccine	Pre- Clinical	SARS-CoV-2
4	Symvivo	bacTRL- Spike	Pre- Clinical	SARS-CoV-2

5	Janssen Pharmaceutical Companies	Ad26	Pre- Clinical	SARS-CoV-2
6	University of Waterloo	DNA Vaccine	Pre- Clinical	SARS-CoV-2
7	Entos Pharmaceuticals	DNA Vaccine	Pre- Clinical	SARS-CoV-2
8	Osaka University/BIKEN	TBD	Pre- Clinical	SARS-CoV-2
9	Valneva/Dynavax	Inactivated+CpG1018	Pre- Clinical	SARS-CoV-2

CONCLUSION

It was stated previously that this virus was originated in China Wuhan in December 2019. It has a tremendous capability of spread through human droplet formation. It can infect human mild to moderate. For both mild to moderate the human causalities are still very nominal whereas for the severe it already touched more than 6 % mortality rate. As per the recent scenario the number of infected people is more than 70lakhs. To be honestly there is no treatment still. W.H.O has given some guideline already to all over the world. All the countries are following these. All the countries are restricted the travel to minimize the contamination. Using of mask gloves is also protecting people from the contamination. W.H.O also prescribed for washing hands with soap at least for 20 sec. Hand sanitizers should contain 70% iso propyl alcohol. But all these are basically for protective manner. Still there is a gap in proper treatment. As per report there are some potential molecules may be useful for the treatment of COVID-19. Scientists are working on it. There are some promising molecules is under trial. Some of the molecules are also working fine to the infected people. But all are in the trial stage. None of them are conformed till. But still there need an identified molecule which can treat COVID-19 infected patients. In case of the diagnosis RT- PCR is one of the best ways to detect the RNA virus from the respiratory secretion. But till now in the whole world there is a huge lacking in testing. Mostly it affects the third world countries like China, India, Pakistan, and Bangladesh. The rate of test is really poor as per W. H. O also. As a result, the infection rate is also high and a huge number of people are found COVID-19 positive but asymptomatic. As per the pattern this virus infects the older people more, so that the older people in every country should take the extra care. However, it also affects the neonates in the time of vaginal delivery or in the time of breast feeding if the mother was infected previously with COVID-19. Symptom of this disease is very common fever, headache, sneeze, cough and shortness of breath. It also increases some time and often severe. However, 60-75% cases are mild to moderate. Which can be manageable with some potent molecules discussed earlier. But around 15 % case is really serious. But the cases turn to death if there are some other complication like diabetes, kidney issue, hypertension etc. Some pharmaceutical giants claim regarding Remdesivir, Hydroxycholoroquine, Favipiravir etc. are working good against mild and moderate infection. But all are under clinical trial. Some of the universities are working for the vaccines, some biotech companies tagged with some reputed universities to invent a new vaccine to fight against Corona virus. But all the things we need very urgently because all ready more than 70,00000 people infected and a huge number of people have died due to COVID-19. W.H.O published some valuable guideline to make sure people are taking precaution. but in this pandemic situation only guideline is not enough. Health system should be improved and need specialized doctors, nurses and pharmacist. So, a huge investment requires to change the system. World needs lots and lots of ventilators, antiviral drugs. Without medicine with the prescribed isolation and quarantine we got positive result but somehow, we have to fight against it. Lock down or restriction is not the only way. So that vaccine and some anti-viral agents should be developed as urgent basis to fight against the deadly COVID-19.

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