

An Overview On Covid-19 and Invention Of Its Treatment By Drugs

By
Name: Anika Nawer
ID: 16146018

A thesis submitted to the Department of Pharmacy in partial fulfillment of the requirements for the degree of
Bachelors of Pharmacy

Department of Pharmacy
Brac University
February 2021

© 2021. Brac University

All rights reserved.

Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at Brac University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

Student's Full Name & Signature:

Anika Nawer

16146018

Approval

The thesis titled “An Overview on Covid-19 and Invention of Its Treatment by Drugs” submitted by Anika Nawer (16146018) of Spring 2016 has been accepted as satisfactory in partial fulfillment of the requirement for the degree of Bachelors of Pharmacy on February, 2021.

Examining Committee:

Supervisor:

Dr. Shahana Sharmin
Senior Lecturer, Department of Pharmacy
Brac University

Academic Coordinator:

Dr. Hasina Yasmin
Professor, Department of Pharmacy
Brac University

Departmental Head:

Dr. Eva Rahman Kabir
Professor, Department of Pharmacy
Brac University

Ethics Statement

The study does not involve any kind of animal or human trial.

Abstract:

The life threatening global pandemic Corona Virus disease (Covid-19) is spreading all over the world within a very short period of time. Therefore, different countries are facing the situation and handling it in their own ways. Based on the previous experiences and the structure of the virus, the disease is being treated by some drugs or various combinations of drugs. Along with this, research on the effects of the drugs used in previous corona viruses are going on to get the effect on Covid-19 as well. Moreover, with the drug treatment, different vitamins are also being used. Besides, so many clinical trials are still going on and practical results are about to come. On the other hand, various other complications such as diabetes, heart diseases etc have negative effects on Covid-19 patients. Here, we are going to discuss about the history and possible treatment options of Covid-19 by drugs with their positive effects and side effects as well to eliminate the difficulties caused by Covid-19 to the nation.

Keywords: Corona virus; Covid-19; pandemic; disease; treatment.

Dedication

I want to dedicate this project to my respectable supervisor Dr. Shahana Sharmin, senior lecturer in Department of Pharmacy, Brac University for her continuous guidance throughout my project.

Acknowledgments

I would like to proceed by thanking the Almighty who is the source of our strength and knowledge which have enabled me to complete this project with full diligence.

I would like to express my deepest gratitude and appreciation to my project supervisor, **Dr. Shahana Sharmin** (Senior Lecturer, Department of Pharmacy, Brac University), whose expertise, ample time spent and consistent guidance in every step have helped me to accomplish this project efficiently. I would like to thank him for his great advice and patient behavior throughout this phase whenever I encountered difficulty.

I would also like to express my sincere gratitude to **Dr. Eva Rahman Kabir** (Professor and Chairperson, Department of Pharmacy, Brac University) who has been a constant source of inspiration for me. I would also like to show my gratitude towards **Dr. Hasina Yasmin** (Professor and Academic Coordinator, Department of Pharmacy, Brac University) for her support while conducting my work.

Subsequently, I would also like to thank my parents for their support and words of encouragement which motivated me to work harder to overcome the difficulties.

Table of Content

Chapter 1.....	1
1.Introduction:.....	1
1.1.Corona virus:.....	1
1.2.Composition of Corona virus:.....	2
1.3.Origin:.....	3
1.4.Spreading:.....	4
1.5.Covid-19:.....	6
1.5.1.Signs and Symptoms:.....	8
1.6.Complications and clinical outcomes:.....	10
1.8.Key Factors:.....	10
1.9.Treatment:.....	11
Chapter 2:.....	12
Literature review:.....	12
2.1.Status of different countries:.....	12
2.1.1. .Status of USA:.....	13
2.1.2..Status of UK and British :.....	13
2.1.3. .Status of India:.....	14
2.1.4..Status of China:.....	14
2.1.5.Status of Bangladesh:.....	15
2.2.Age and Covid-19:.....	16
2.3.Survival of Covid-19 patients with other complications:.....	17
2.3.1:Patients having CVD:.....	18
2.3.2.patients with myocardial injury:.....	19

2.3.3. Patients with diabetes:.....	19
Chapter 3:.....	20
Result:.....	20
3.1. Research and data obtained about the combination of drugs:.....	20
3.1.1. Therapeutic use of some drug combinations:.....	20
3.1.2. Toxic effects of some drug combinations:.....	22
3.1.3. Side effects of some drug combinations:.....	23
3.2. Individual drug treatments:.....	24
3.2.1. Effectiveness of individual drugs in different concentrations:....	24
3.3. standard doses of drugs for the treatment :.....	27
3.4. Trials in different countries:.....	28
3.5. Outcomes of using antivirals:.....	31
3.5.1: Dosing of antivirals:.....	31
3.6. Drugs in the pipeline for the treatment:.....	33
3.7. Different studies on Chloroquine and Hydroxychloroquine in Covid-19, their result and proposed doses :.....	37
3.9. Clinical trials and outcome on some drugs:.....	41
Chapter 4.....	45
Discussion:.....	45
4.1. Drug combinations:.....	45
4.2. individual drug treatments:.....	46
4.3. Effectiveness of antiviral treatment on covid-19 disease:.....	46
4.3.1. Outcomes from Clinical trials on antiviral drugs:.....	47
4.4. Effectiveness of vitamins:.....	49
Chapter 5:.....	499
Conclusion:.....	49

5.1.Outcome:.....	49
5.2.Limitation:.....	50
5.3.Future direction:.....	51
Reference:.....	52

List of Tables:

Table 1 :Therapeutic use of some drug combinations that are being used in Covid-19 treatment.....	21
Table 2 :Toxic effects of some drug combinations.....	23
Table 3 :Side effects of some drug that are being used in the treatment.....	24
Table 4 :Effectiveness of individual drugs in different concentrations.....	25
Table 5 :Prescribed standard doses of drugs.....	28
Table 6 :Trials done on different countries.....	29
Table 7 :Doses of different antivirals and their mechanisms.....	32
Table 8 :Drugs in the pipeline for treatment.....	34
Table 9 :Guidelines for treating Covid-19 with Chloroquine and Hydroxychloroquine.....	39
Table 10 :Outcome of some drugs after clinical trials.....	43

List of Figures

Figure 1 :Corona Virus.....	1
Figure 2 :Structure of Corona Virus.....	2
Figure 3 :Transmission of Corona Virus.....	5
Figure 4 :Detailed structure of Covid-19.....	7
Figure 5 :General symptoms of Covid-19.....	8
Figure 6 :Common complications of people of Bangladesh.....	15
Figure 7 :Mortality rate depending on age.....	16
Figure 8 :Major complications observed in patients having Covid-19 symptoms.....	18

List of Acronym

RNA	Ribonucleic Acid
WHO	World Health Organization
SARS-CoV	Severe Acute Respiratory Syndrome Coronavirus 2
MERS-CoV	Middle East Respiratory Syndrome Coronavirus
ICTV	International Committee on Taxonomy of Viruses
CGS	Coronavirus Research group
ACE2	Angiotensin-Converting Enzyme 2
TNF	Tumor Necrosis Factor
NCBI	National Center for Biotechnology Information
NSAID	Non-steroidal Anti-inflammatory Drugs
FDA	Food and Drug Administration
ARDS	Acute Respiratory Distress Syndrome
CVD	Cardiovascular Disease
ICU	Intensive Care Unit
SGLT-2	Sodium-Glucose Cotransporter-2 Inhibitor

An Overview on Covid-19 and Invention of Its Treatment by Drugs

Chapter 1

1.Introduction:

1.1.Corona virus:

Corona virus is a RNA virus which is positive,single stranded and screened.Basically,the size of the virus is extremely small,its diameter is only 65-125 nm and the thoroughness of its RNA strands are about 26 to 32kbs.There are four different strains of corona virus which are alpha(a) and beta(b) along with gamma(c) and delta(d).There are some acute diseases that can cause of the presence of covid-19 such as disorder of acute inflammation because of which the lungs can be disrupted along with respiratory failure and at the end these can cause transiency (Shereen et al.,2020).

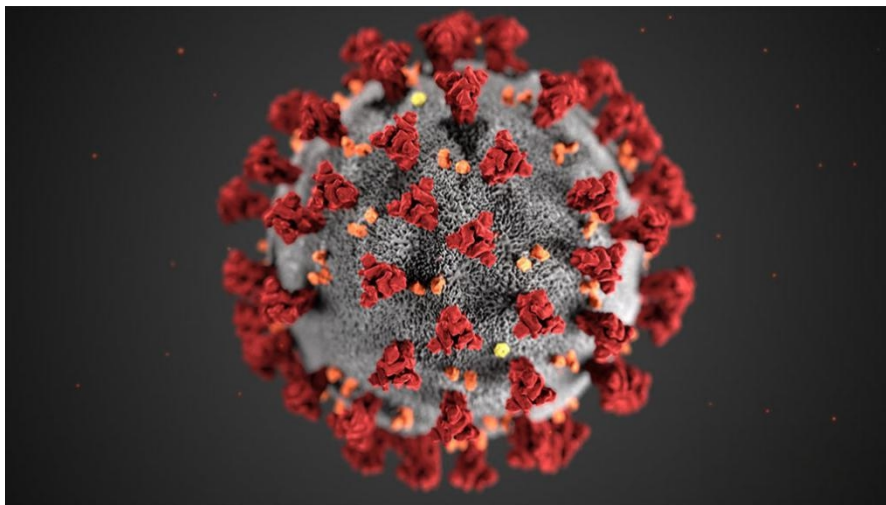


Figure 1:Corona Virus

Basically the outer surface of the structure of corona virus is pointing out wards.Corona virus is the property of orthocoronavirine.Above all,this deadly disease is belong to a group named beta which is a group of five members.For the sake of taint named 2019-n-Cov.Moreover, this is in the class number 5 among the infectious disorders which was noticed in the middle

of January of 2015 in Taiwan (Wua et al., n. d). Nationwide Corona virus is expressed by WHO (Singh et al.,2020).

1.2.Composition of Corona virus:

The action of the virus is governed by some proteins that are present in their structure.Among them,one that covers the surface is called the enveloped protein which is denoted by E.Another one is the one with the pointing shape which called the spike protein and this one is denoted by S.The other two are membrane protein which is denoted by M and the nucleocapsid protein which is denoted by N.Basically,there are two major things in the structure of this virus,on is the 5'cap and the another one is a poly A chain with 3'(Vellingiri et al.,2020).

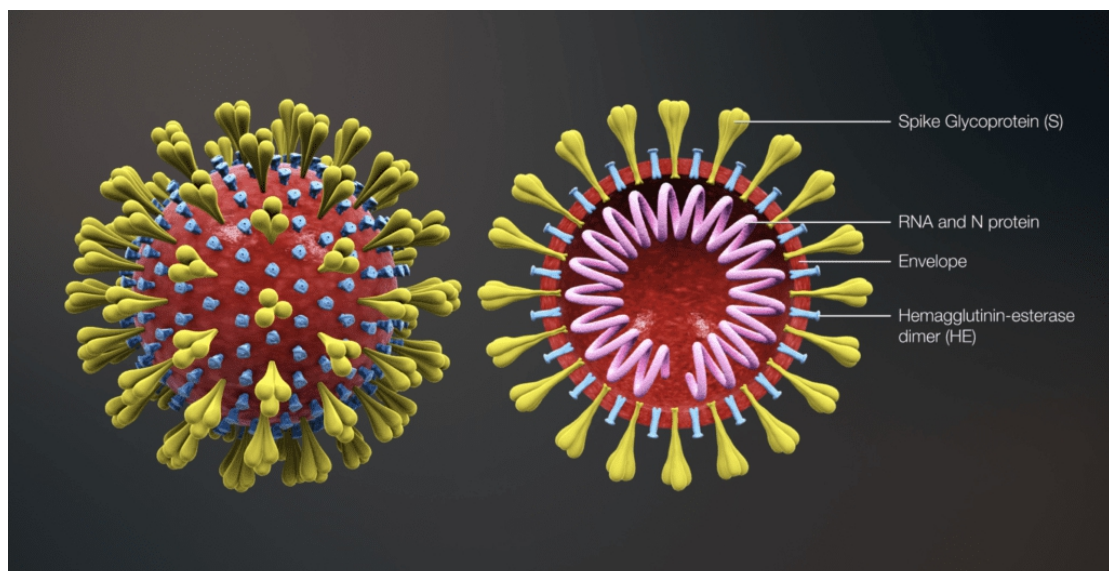


Figure 2:Structure of Corona Virus

This is the basic structure of corona virus. Many of the viruses like SARS-CoV, MERS-CoV have similarities on their structure even they work in the similar way. Even the new Covid-19 also looks similar with this structure.

1.3. Origin:

Long ago people used to think that corona virus can harm creatures rather than human but the idea has changed at 2002 after the appearance of SARS because of SARS-CoV. After a decennary in central eastern countries a local disease called MARS-CoV has taken place. In addition almost at the end of 2019 a pestilence called novel corona virus has also taken place in which within a very few days so many people has been lost their life and more than that has been invaded in Wuhan. Besides, the researchists of china designated the epidemic as 2019 novel corona virus or Wuhan corona virus. According to the naming committee ICTV the virus is named as SARS-CoV-2 which is actually causing the disorder named Covid-19. Moreover, the spreading of SARS-CoV-2 takes less time then SARS-Cov. which is maybe because of the protein S which has put on the extra transmission power by genetic modification (**Shereen et al.,2020**) .A group of pneumonia growth driven by a previously unrecognized emerged at the last of 2019 in Wuhan, China. In January 12 of the year 2020, this flu virus is recognized as the name 2019-novel corona virus by an organization called WHO. Just like WHO, the International Committee's Coronavirus Research group (CGS), in February, 11 of 2020 recommended to call the recent corona virus as a new name which is SARS-CoV-2.

On 7 January 2020 A number of experts quickly removed the virus SARS CoV-2 from a patient within a brief period of time and unveiled genome sequencing for SARS-CoV-

2.Experiments have reported the high baseline replication number and the family waves of outbreaks of pneumonia contribute to the evidence that the covid-19 crisis is gradually rising via human-to-human propagation **(Guo et al., 2020)**.

1.4.Spreading:

Corona Virus is a viral disease that spreads from one to another by fluids such as sneezing,coughing,shaking hands etc.

In 2003,In Guangdong province, the China population has been afflicted with an Extreme Respiratory Syndrome virus SARS. As a part of the Betacoronavirus sub-type,the virus was identified and called Sars-CoV.Moreover,infected individuals had indications of pneumonia with a diffuse alveolar injury that ended in Acute respiratory distress syndrome.In Guangdong,China, SARS is originated from and then start to spread quickly across the globe with higher number of infected individual and deaths.A few Saudi Arabian Nationals were treated with just another corona virus a century later in 2012 which is then named as MERS-CoV.

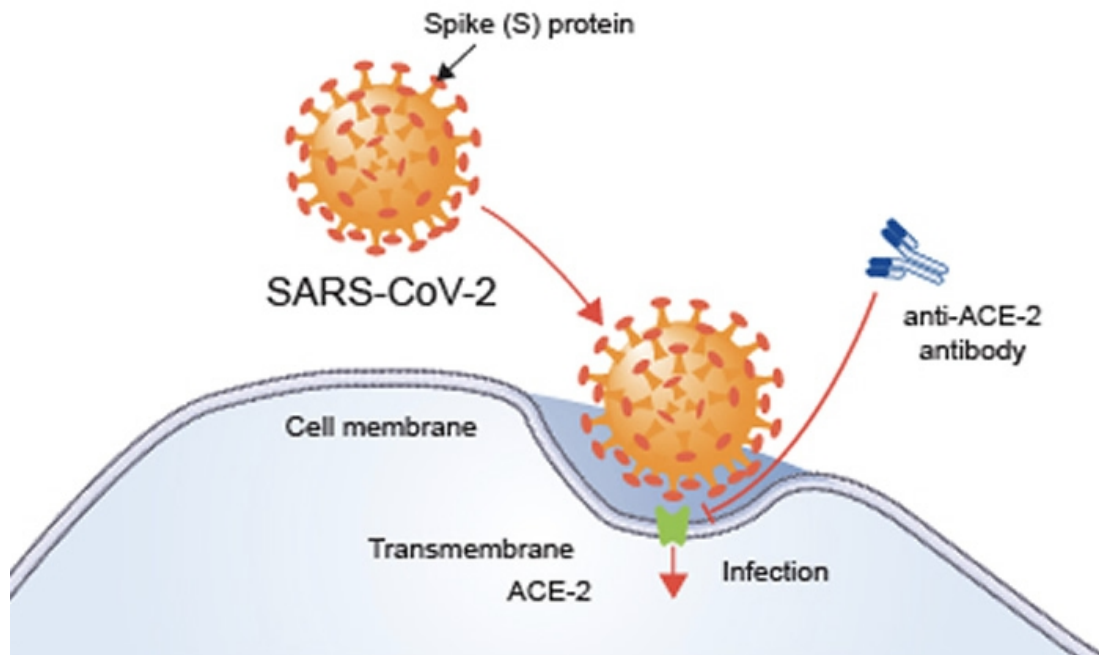


Figure 3:Transmission of Corona Virus

Thereafter,WHO confirmed the number of death and infected people.Besides,

MERS-CoV is a descriptive subgroup of beta coronavirus and is phylogenetically distinguished from other clinical infections for example other corona viruses.MERS-CoV starts with minor upper respiratory damage, while development progresses to severe respiratory disease.Alongside,individuals diagnosed with this virus,suffer from some other complications such as pneumonia, as well as problems in kidney and many more which are very identical to SARS-CoV.Recently,government of China at the end of 2019 informed WHO about some of the pneumonia cases whose cause are not certain at all.Initially the spreading has started at Hunan seafood market which is in Wuhan in China.Basically, many animals like bat,snakes along with different kind of birds are offered there.Originally,It was proposed that Wuhan corona virus-induced pneumonia suffering patients in China may have attended the market of sea food where animals that are alive were being sold .Alongside,they

may have eaten contaminated food which can be a bird or any animal which is already contaminated with the virus. Also, the outbreak was described as a novel coronavirus from the study depended on sequence of isolated from patients. Moreover for the treatment of viral infection, the genetic sequence was also given. Further studies, therefore, showed that some people acquired the infection even without the history of attending the market which was selling or offering seafood. As a result this finding revealed the human-to-human capacity to this virus to disperse which was eventually documented in more than 100 different countries. Moreover, the reason can be going close to the individual who is already infected or exposure to either cough or sneeze of a infected person. Even it can be respiratory droplets and aerosols people to other people the virus can be transmitted. Through inhalation via the mouth or nose, aerosols may reach the human lungs (**Shereen et al., 2020**). Therefore, this has been identified that if the virus called SARS-CoV-2 is present in the sample of swab or blood that suggests the possibility of various route options for transmission. Based on some research results about the genome sequencing of viruses, it can be observed that bat has indeed been accused of being a common virus host and SARS-CoV maybe conveyed from bats to human to cause disease by an enzyme called angiotensin-converting enzyme 2 (ACE2) (**Guo et al., 2020**). Alongside, nosocomial infections have occurred in healthcare facilities which emphasize the value of effective control of infections (**Wua et al., n. d**)

1.5. Covid-19:

A disease caused by corona virus which is basically originated from China and transmitted to many other countries like Vietnam, India, Bangladesh and many others has been diagnosed and treated based on the clinical conditions is named as Covid-19 (**Rothan et al., 2020**).

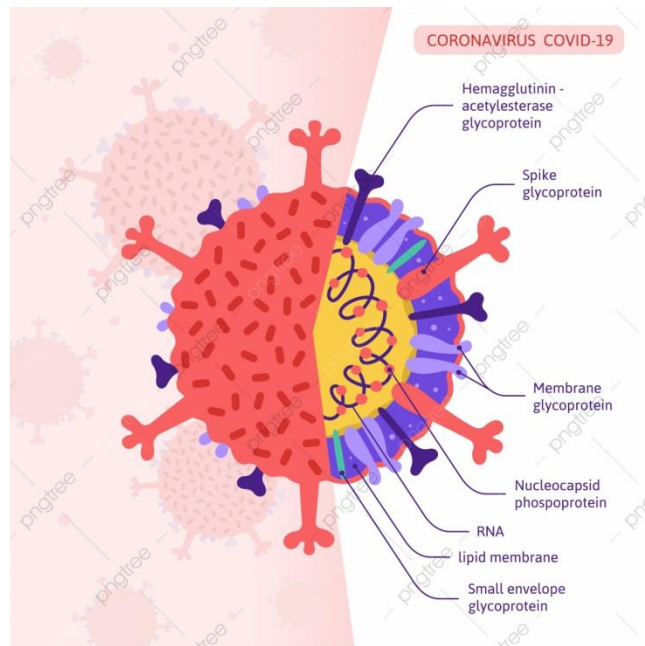


Figure 4:Detailed structure of Covid-19

This disease is originated from the Wuhan seafood market,China.Basically it is a beta corona virus in by nature which is single stranded and the structure is very similar to other Corona viruses such as SARS-CoV.Its genetic code was compared to something like the previously described coronavirus strain that triggered the epidemic of SARS in 2003.Because of having structural similarities with SARS-CoV,many unknown mechanisms are being assumed about Covid-19 which is still not trialed in laboratories (**Lancet,2020**).Pneumonia was the early diagnostic indication for COVID-19 which is basically related toSARS-CoV-2 that allowed that helped in the identification process (**Velavan et al.,2020**).By observing some signs and symptoms such as high temperature of the body,cough,sour throat etc

individuals are being diagnosed and treated. In the early time Covid-19 detected, the death rate was high. Among the infected individuals, 45.7% is female and the other half is male where the average age of the male is around 56 (Lancet, 2020).

1.5.1. Signs and Symptoms:

The symptoms of Covid-19 can be seen after a time period which is approximately 5.2 days. Moreover, death caused by Covid-19 can happen between 6 days to 41 days (in average 14 days) which is basically depended on the age of the patient. According to a report of WHO on the Covid-19 disease which is done on 55924 patients in February of 2020, symptoms of Covid-19 can be clearly seen.

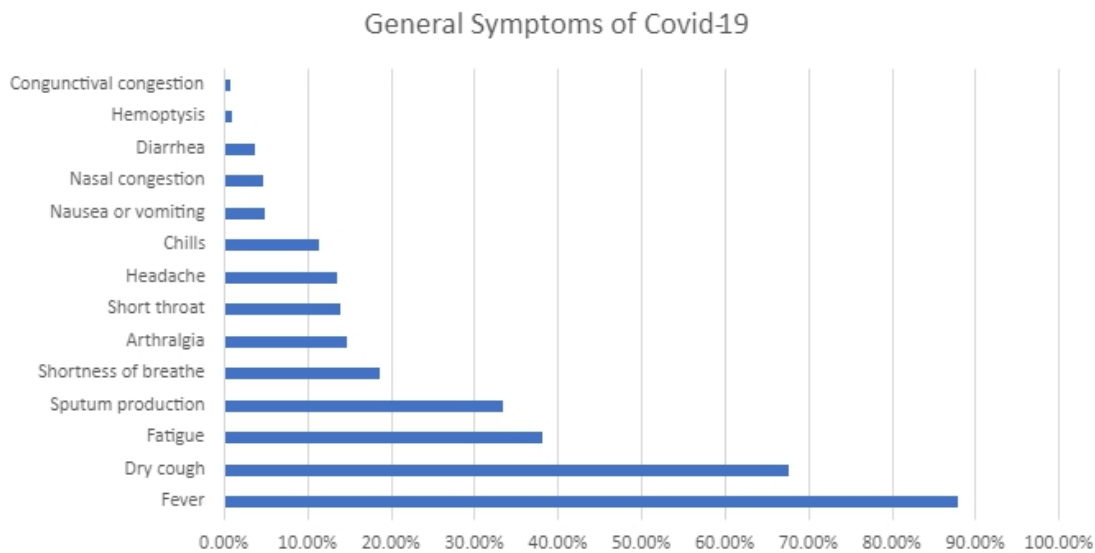


Figure 5: General symptoms of Covid-19

Moreover, Covid-19 has some similar symptoms as other betacoronaviruses such as fever along with dry cough and dyspnea as well as some unique symptom such as rhinorrhoea. COVID-19 infected patients has reported elevated numbers of leukocytes, irregular respiratory findings, and raised levels of pro-inflammatory cytokines in plasma. along with this, high ESR rate is also observed. Based on the symptoms, patients are treated in various ways. Unfortunately, the treatment in certain patients with interferon inhalation did not have a therapeutic benefit and only tended to intensify the disease by increasing pulmonary opacities **(Rothan et al.,2020)**.

Prominent symptoms can be observed in a patient of pneumonia such as the saturation level of oxygen and the amount of gas of blood can be lowered, the results of the X-ray done on the chest and other similar tests can have uncommon results, and irregularities in ground glass , awkward convergence, exudates in alveolai and activity of interlobule, gradually suggesting worsening. Lymphopenia tends to be a widespread. **(Velavan et al.,2020)**. A new analysis conducted by a team which is lead by professor Nan-Shan Zhong, testing so many cases (1099) laboratory confirmed instances, found the symptoms mostly high temperature, cough and also exhaustion as well as septum development. Along with this some other symptoms are observed in minor case4s such as shortness of breath, headache also the sore throat which are the typical clinical manifestation. Furthermore, some patients have digestive problems with diarrhea and vomiting. However, the predominant indications were high temperature along with cough while some unusual symptoms like upper respiratory symptoms as well as gastrointestinal symptoms were reflecting variations in viral tropism relive to SARS-CoV and also with MERS-CoV and influenza. Additionally, older people and those who mare suffering from hypertension, chronic pulmonary obstructive disease as well as diabetes or cardiovascular disease, evolved rapidly into ADRS along with septic shock as well as

metabolic acidosis and an abnormal blood clotting. Moreover, these can also cause mortality. Most of the patients had regular or reduced number of white blood cell and in the test results they are affected with lymphocytopenia. Additionally, the number of neutrophil, D-dimer, creatinine level as well as blood urea were considerably higher in extreme cases. On the other hand the number of lymphocyte continued to decline. In addition, inflammatory variables and tumor necrosis factor (TNF-alpha) are growing, suggesting patients immunity status (Guo et al., 2020)

1.6. Complications and clinical outcomes:

Many sufferers had a high success rate, based on current knowledge, whereas a few sufferers were in serious state, particularly the elderly and those with progressing medical condition. Moreover, the poor clinical result was linked to the seriousness of the illness. In elderly people, the disease appears to develop quicker, with a reduced median amount of days from the very first signs to death in people with the age of 65 and above. Furthermore, the number of children were more than hundred who were also contaminated within only 30 hours of taking birth. Owing to their impaired or poor immune response, neonates and people with older ages require more treatment and care (Guo et al., 2020)

1.8. Key Factors:

1. A combination of chloroquine and hydroxychloroquine which is playing a key role to treat covid-19, can have some negative effects too, such as the eyesight can be changed, lethargy as well as nausea etc.

2. According to NCBI, persons already having pulmonary disorders have high risk of having Covid-19. Therefore, they should be closely monitored and handled for pulmonary

disorders. Besides, vasodilator drugs have been used in some patients with hypoxemia refractory to conventional treatments. However, extensive study has not been performed in patients with COVID-19.

3. People having disease like stomach ulcer, can not take ibuprofen which is basically a NSAID as a treatment of covid-19

4. In experimental trials, using NSAIDs for such long period, drugs like Ibuprofen, has been linked with Greater percentage of cardiovascular risk, such as myocardial Infarction, heart disease, and stroke. More drugs such as naproxen, and diclofenac have the same effect.

1.9. Treatment:

Where covid-19 is a pandemic but there is still a very few FDA approved drug and the treatment of this pandemic is being done based on the the signs and symptoms of the patients. Moreover, the number of affected people is increasing day by day and the need for drugs is also increasing. Therefore, time and effort should be given to research about the drugs as much as possible because it will need few months to discover new, effective and unique medication for covid-19. (Vellingiri et al., 2020). For treating covid-19, so many substances are already being tested to see their effects and appropriateness such as western drugs, organic ingredients etc. During the clinical trials which are conducted on the different different substances, some of them showed very quick and tentative results and effectiveness towards covid-19 which is helping a lot to diagnose and fight this global pandemic. (Dong et al., 2020). Until definitive and precise medications for covid-19 is found, people have to maintain some safety measures and personal hygiene such as washing hands repetitively, masking face, maintaining distance from people, taking proper rest etc. Along with these, the persons who are already having symptoms should be separated from others so that

other people do not get affected and also be monitored and supportive therapies should be given to them to get well. .Some classes of drugs such as antibiotics,antiviral therapy,systemic corticosteroids along with anti-inflammatory medications are frequently used to diagnose regimens for ADRS accompanied by secondary infections.Additionally,some inhibitors such as neuraminidase inhibitors, inhibitors that inhibits the RNA synthesis etc with antiviral and antibiotics.The effectiveness of these medication regimen,however remains to be validated by adequately designed clinical studies.(Wu, R et al.,2020)

Chapter 2:

Literature review:

Depending on the information and findings of various articles,an overview can be showed on Covid-19.

2.1.Status of different countries:

Covid-19,the biggest pandemic, has affected so many countries in the world.Different countries are facing the situations in different ways.Though there are similarities in some of the treatment methods,various countries have their own ways to fight against Covid-19.As the economical condition of all the countries are not same and also the population number is identical,the ways of handling the situation also varies.

2.1.1. .Status of USA:

In USA,patients submitted themselves to the ED for examination in the initial stages of the epidemic.As the epidemic has developed,recommendations have changed such that patients are very well recommended not to visit the ED for examination without any advance notice.Furthermore,it is recommended that the patients have to dial 111,the non emergency public health-care line of UK and after that the patients is screened and identified whether they are unwell or not and based on what they arrange ambulance if the patients require swabbing.Supporting this program,the government has offered all EDs with evaluation pods which are detached and enclosed frameworks with a mobile from which patients themselves can both dial 111 and be evaluated by safety equipment from medical personnel.In the EDs disinfection area,patients who are hired for swab samples are being swabbed but the pods are being used as a “overflow” area.Drive through swabbing is popular way to screen well for patients who are being suspected of having SARS-CoV-2.Patients inspected via 111 get the option of going to the hospital and being examined and swabbed via the windshield of the car and driving home again.this reduces the need for patients to be brought into the pod (Avery& Bloom,2020).

2.1.2..Status of UK and British :

Till the date of 14th February,2020,there are only nine suspects reported.After that,the government has taken various steps like the many other countries such as strict check up in airports,taking information from the travelers about their last journey,safety measures like personal protective equipment etc.Therefore,people who have visited many countries during that time,they have isolated themselves to inhibit the spreading the disease (Lancet, 2020).

2.1.3. .Status of India:

India has a very high number of cases reported between January 30 to April 22 with a very high mortality rate. Therefore, they have given lockdown and closed the borders within a very short period of time (**The Lancet, 2020**). However, the spreading of the virus was from the students traveled from China and the first case of mortality was also because of a person who had traveled Saudi Arabia who was 76 years old. There are many infected people in different part of India and also number of death reported from there too. Among them Maharashtra has reported the maximum number of infected and dead. However, India is a developing country which does not has the proper medical facility but they are trying to overcome by the help of the limited sources and personal safety (**Kaushik, 2020**).

2.1.4. Status of China:

The broader implications of COVID-19 China are integral to virtually every area of the global economy. As one of the most populated country in the world, China has also experienced infectious pandemics, including the outbreak of SARS in 2003. At 6 o'clock. Furthermore, Nominal gross domestic revenue was 4 per cent of the global estimate now 17 per cent. The latest epidemic of COVID-19 already has threatened an infrastructure weakened by currency wars with the US; national growth reached a 30-year low in 2019. Provinces accounting for more than 90% of Export markets have since directed their industries to remain closed or operate at low speed. Besides this, China's status as the nation's biggest producer and distributor of crude oil has prompted economists to cut their estimates of full-year global growth. However, the main distinction between COVID-19 and SARS is the difficulty of the supply chains that China is actually embodied in. There is no historical proof to direct the fragmentation of supply chains, since worldwide dependency on them would be a relatively recent phenomenon (**Clerkin et al., 2020**).

2.1.5. Status of Bangladesh:

Just like the other Asian countries, Bangladesh has also followed various steps which are not therapeutic but helpful to fight the pandemic situation. On the other hand there has been confusion of maintaining all the measures properly or not. 7th of March, the first case of covid-19 is reported in Bangladesh. It is hypothesized that there has been patients of covid-19 even before 7th March. Notwithstanding, because of lack of evidence it is not proven.

Bangladesh also has followed the trend of lockdown and blocked the airports but because of many other problems after few days lockdown has been withdrawn. Moreover, it is difficult for Bangladesh as the people here have so many physical complications that can cause to worsen the situation of covid-19.

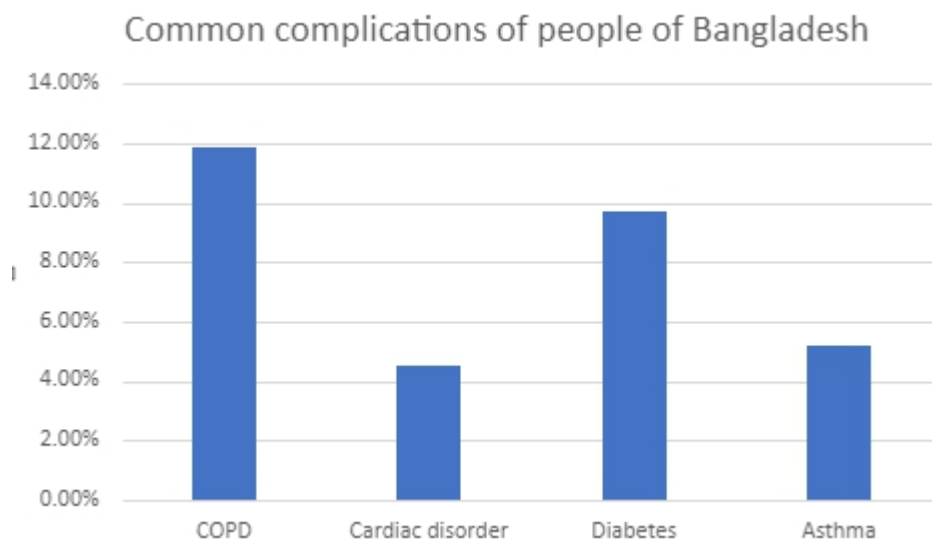


Figure 6: Common complications of people of Bangladesh

Along with this complications, fighting covid-19 is much more difficult. Alongside the number of smoker is too high here which can also increase the chance of the infection. Moreover, must needed medical equipment to fight the pandemic is not enough here. Therefore, with the limited resources and too many complications, it is difficult to hope to fight with this situation and back to the normal life (Anwar et al.,2020).

2.2. Age and Covid-19:

In case of Covid-19, age is a very big factor. The harm of the disease may vary depending on the age. In case of younger children, covid-19 is not that much harmful as much as for the people. older age (Avery et al.,2020).

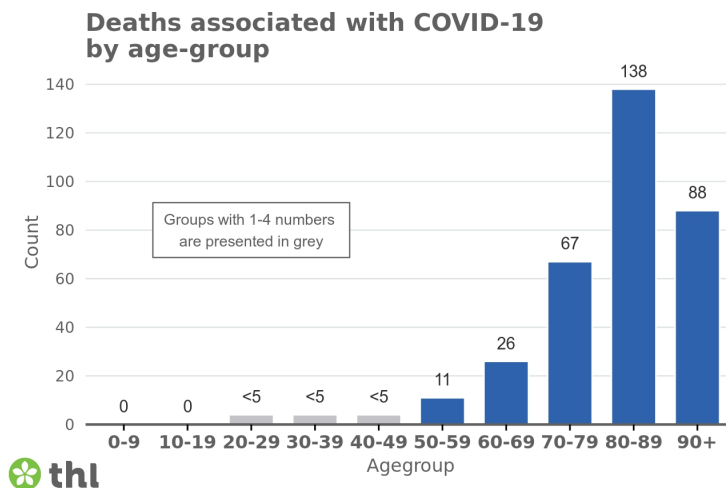


Figure 7: Mortality rate depending on age

Information from China have shown that around 20 per cent of people with extreme illness, o

Older people, especially those with significant underlying health problems, are at greater risk of mortality than pediatric people. A minority of patients had respiratory arrest, septic shock, and multi-organ dysfunction resulting in 4 per cent fatality. In extreme COVID-19, while lymphocytes have been triggered in patients with lymphocytopenia. One analysis examined lymphocyte subsets and cytokines in 123 patients, all patients had lymphocytopenia, the CD8 + T cell reduction percentage was 28.43 percent and 61.9 percent respectively in the moderate and extreme category, and the NK cell reduction was 34.31 percent and 47.62 percent respectively. Simple anti-virus therapy TCZ was given once intravenously to 20 patients with 400 mg. Within several days, the temperature went back to normal and other conditions changed significantly. 75.0 percent of the country had increased oxygenation. The visibility lung lesion on CT scans was absorbed by 90.5 percent of patients. In comparison, the number of peripheral lymphocytes started to improve in 52.6 per cent of patients. Their results indicate that TCZ could be useful in the treatment of serious COVID-19 cases (**Zhang et al.,2019**).

2.3.Survival of Covid-19 patients with other complications:

Surviving Covid-19 with some other health complications is very troublesome. Besides, other complications can decrease the chance of fighting with corona virus in many times. Because of having those, even some drugs can not be used to treat covid-19 as it can worsen the condition.

2.3.1:Patients having CVD:

From the previous cases of corona virus such as MERS-CoV we can see that patients who are having underlying CVD are more prone to death. Besides, in case of Covid-19 it can also have the negative effect on the patients as they are already showing acute signs. Moreover, people with the symptoms of covid-19 are having some common diseases.

Other complications in patients with Covid-19 symptoms

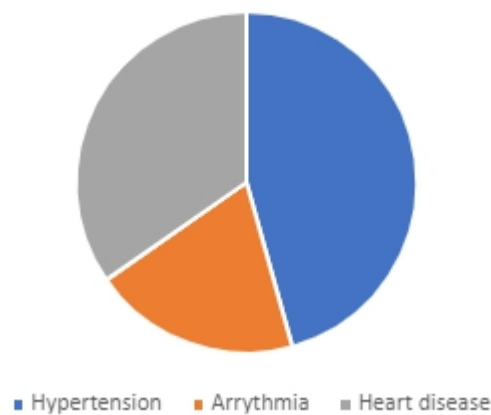


Figure 8:Major complications observed in patients having Covid-19 symptoms

In case of SARS-Cov-2, if the patient has diseases in heart, it will worsen the condition of pneumonia and ultimately the patient will lead to death. Most importantly, patients with SARS-Cov-2 are supposed to take antivirals which is very normal. On the other hand, patients with underlying heart diseases or CVD are more carefully monitored if taken any type of antivirals as it can be harmful for them by increasing the toxic level. Therefore patients who have SARS-CoV-2 and CVD all together, should be careful during taking any antivirals (Zheng et al.,2020).

2.3.2.patients with myocardial injury:

Myocardial injury is basically increased concentration of cardiac troponin more than 99th percentile. In China,a research has been done on 138 hospitalized patients where it is observed that,7.2% patients are having cardiac damage and almost 22% patients are in need of ICU treatment.Another study of China from NHC shows that among the CVD patients,12% have increased troponin level which is above 99th percentile (**Clerkin et al.,2020**).

2.3.3.Patients with diabetes:

Patients having Covid-19 are very likely to have CVD,hypertension and diabetes.Trials on diabetic mice shows the increased level of ACE-2.Moreover,glycemic regulation is essential for any individual who has COVID-19.As direct data on the connection of diabetes with Covid-19 is not available,other data on the connection of elevated blood glucose level with the previous strains of corona viruses are studied to know the risks that chance of mortality can have.Many patients with moderate disease and regular oral intake may proceed with the regular antihyperglycemic drugs. Even then, it is advised that inhibition of SGLT-2 should be eliminated otherwise dehydration as well as euglycemiketosis may occur. Metformin would still need to be stopped if vomiting or inadequate dietary treatment is present.In the present situation,exercising and maintaining physical and mental health is mostly impossible because of the lockdown as everyone is suppose to be at home.Therefore,the patients have to take care of their daily food and have to take care of the other physical complications such as feet complications etc and have to contact the doctor over phone to be safe in this situation (**Singh et al.,2020**).

Chapter 3:

Result:

After doing so many researches on the mechanism of action and the signs and symptoms that Covid-19 has, in the purpose of getting rid of this pandemic, various trials are done. Moreover, many drugs that have already shown their results on previous corona virus strains, also showed effective results on Covid-19.

3.1. Research and data obtained about the combination of drugs:

Many drugs are being used in different combinations and giving different therapeutic effects in various ratio. Moreover, drug combinations are used to get more efficient results than the single use of the drugs.

3.1.1. Therapeutic use of some drug combinations:

Here are the therapeutic use of some special drug combinations that have used to treat so many diseases before and playing key roles to treat the outbreak of Covid-19 in recent days.

Drug Combinations	Therapeutic use	Reference

1.Cloroquine with hydroxychloroquine	Approved medication(India 2014) for diabetes	(Singh et al.,2020).
	front-line treatment of malaria for the prophylaxis , rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE)	(Zhang, et al., 2019)
2..Nitric Oxide with Epoprostenol	pulmonary vasodilator, Decrease the average pressure of the pulmonary artery with enhancing the oxygenation power.	(Wu et al.,2020)
3.Nitazoxanide and Tizoxanide	MERS-C0V resisting effect as well as groups of other Corona Virus Such as Murine.	(Wu et al.,2020)

Table 1:Therapeutic use of some drug combinations that are being used in CoV-19 treatment.

3.1.2.Toxic effects of some drug combinations:

Not all the drug combinations are safe. There can always have some risk if the information is not properly known. Therefore, the drug combination which will be used to treat Covid-19, can also have negative effects if wrong combination is used or used in an incorrect ratio. Most importantly the dose and time period should be correct. There are some drug combinations having toxic effect on the table below.

Drug combination	Overdose	Reaction	Reference
1. Chloroquine with hydroxychloroquine	Over 20mg/kg, Between 1-3 hours	Shows toxicity	(Singh et al.,2020).
	Over 30mg/kg	Fetal in case of chloroquine but in case of hydroxychloroquine toxicity is observed rarely	(Sinha & Balayla, 2020).
	2 doses of 600mg for 10 consecutive days or total 12g	Cardiac arrest	

2.Nitric Oxide and Epoprostenol:	Over 30mg/kg/minute(In adult) Over 30mg/kg/minute(in children)	May decrease the pressure of the pulmonary artery.	(Wu et al.,2020)
3.Ribavirin with IFN- α	Over 500mg , More then times a day(for adults)	If taken in a much higher dose,worse condition of cardiac disease and fatal or no fatal myocardial infraction can occur.	(Dong et al.,2020).

Table 2:Toxic effects of some drug combinations

3.1.3.Side effects of some drug combinations:

Several drug combinations can have such side effects but the harm from that may be pardoned if the benefit is more than that.Notwithstanding,the side effects must be known while using the combinations.There are some side effects in the table below.

Drugs	Side Effects	percentage	Reference
1.Cloroquine with hydroxychloroquine	Gestrintestinal symptom,changes in skin	(10%people)	(Singh et al.,2020).
2.lopinavir-ritonavir	Some common side effects such as nausea,diarrhea and Asthma are observed.		(Wu et al.,2020)

Table 3:Side effects of some drug that are being used in the treatment

3.2.Individual drug treatments:

There are some effective drugs that severally give effects on Covid-19 and do not need to use in combinations.Basically,individual drugs used in various concentrations and in different doses.

3.2.1.Effectiveness of individual drugs in different concentrations:

Some drugs that are being used in various concentrations in many similar diseases as Covid-19 are showed in the table below.

Name of Drug	Effectiveness	Concentration	Reference

Niclosamide	Anthelmintic drug, Effects on SARS-CoV	1.56 μ M	(Wu et al.,2020)
ivermectin	Effects towards SARS-CoV-2	500 fold	(Wu et al.,2020)
Chloroquine	Antimalarial and antiviral effect(broad spectrum) resist SARS-CoV-2 efficacy in Avian influenza A	1.13 μ M	(Hu&Gao,2020).
	Activate immunity		(Yan et al., 2013)
		1.13 μ M	(Wang et al., 2020a, 2020b, 2020c; Vincent et al., 2005)

	Broad spectrum antiviral effect		(Dong et al.,2020)
Ribavirin	Effects on hepatitis C.	109.5 μ M	(Elfiky, 2020).
<u>Arbidol</u>	Medicate influenza virus and effects on SARS-CoV-2.	10-30 μ M	(Dong et al.,2020).
.Favipiravir:	Medicate influenza(february20,2020 in China)		(Dong et al.,2020).
	Recovery rate 71.43%against covid-	61.88 μ M	(Dong et al.,2020).

	19(China,Japan)		
--	-----------------	--	--

Table 4:Effectiveness of individual drugs in different concentrations

3.3. standard doses of drugs for the treatment :

Both the combination and individual drug treatments have specific doses for a specific period of time. Moreover, the route of administration can be different and the dose is also different. There are some drugs with their dose, time period and route of administration in the table beneath.

Drug	Dose	Method of Administration	Duration of treatment
Chloroquine	500mg/2times/day		
Vitamin C	1.5mg/kg	oral	
IFN- α	5 million U,twice a day	Inhaled	Maximum 10 days
Lopinavir/ritonavir	100 mg 2 times a day(50 mg)	oral	About 10 days
Ribavirin with	500 mg daily in	Infused	About 10 days.

IFN- α / lopinavir/ritonavir	total,2-3 times a day.		
Chloroquine phosphate	500mg,daily in two doses	oral	About 10 days
Arbidol	200mg,daily two times	oral	About 10 days

Table 5: Prescribed standard doses of drugs

3.4. Trials in different countries:

A huge number of research and clinical trials are done on different group of people in different countries. These are essential to know the actual effect of drugs on human and also to know about the mechanism of covid-19 along with its response. Among all of the trials some of them are mentioned in the table below.

Drugs	Number of trial/study	Type of trial	Country	outcome	Reference

	conducted				
1. Chloroquine and hydroxychloroquine	15	Research on safety profile	China	Safety profile and effectiveness is observed	(Zhanget et al., 2019)
2. lopinavir/ritonavir with ribavirin	1	Treatment of ribavirin monotherapy on SARS (111 people included), Combined therapy of lopinavir/ritonavir and ribavirin (41 people included)		The combination therapy has reduced risk of ARDS and mortality.	(Dong et al.,2020).

3.favipiravir, umifenovir	1	Prospective study		Decreased fever and cough	(Wu et al.,2020)
4. Umifenovir	2	Randomized test	China	Effectiveness and safety profile is compared.	(Wu et al.,2020)
5.Vitamin C	1	Phase II clinical trial	China	Effects of vitamin-C in high does on the patients with pneumonia is observed.	(Wu et al.,2020)

Table 6:Trials done on different countries

3.5.Outcomes of using antivirals:

Antivirals has very vital effects on Covid-19.Many clinical trials are done on them and the effects are recorded.

3.5.1:Dosing of antivirals:

Outcome of research on antivirals and on their mechanism of actions and differences in dosing are showed in the table below.

Groups	Name of the drugs	Function	Dosing
Inhibit the viral RNA polymerase /RNA synthesis	Remdesivir (GS-5734)	Adenosine nucleotide analogue, prodrug, RdRp inhibitor	On the first day: 200mg, IV Day 2–5 (or 10): 100 mg/day, IV
	Favipiravir	Guanosinenucleotid analogue, prodrug, RdRp inhibitor	On the first day:2X1600 mg 2 nd to 7 th day (or 10): 2 × 600 mg/ day

Inhibit the viral protein synthesis	Lopinavir/ritonavir	Inhibitor of Protease	First to 10 th day(or14): 400mg/100mg × 2/day, orally
Inhibits Viral entry	Hydroxychloroquine Chloroquine	Increasing endosomal pH required for virus/cell fusion, as well as interfering with the glycosylation of cellular receptors of SARS-CoV (ACE-2)	1rst day to 5 th day: 2 × 200 mg/day, orally 1rst day to 5 th day(or 10): 2 × 500 mg/day, orally
Imunomodulators	Nitazoxanide	Intervention with host-regulated signaling pathways in viral replication, cytoplasmic RNA sensory amplification and IFN processes Inhibitors of the	

	Ivermectin	nuclear production of cellular and viral proteins by inhibition of importin 1 heterodimer	
--	------------	---	--

Table 7: Doses of different antivirals and their mechanisms

3.6. Drugs in the pipeline for the treatment:

Effects of some drugs maybe unknown or unsure but there are some drugs who can be used to treat Covid-19. This assumption is done based on their previous reports. Based on the past history and mechanism on other diseases or epidemics, some drugs are proposed on table below that can have the expected effects.

Drugs	Types of drugs	Mechanisms of action	Prior history
Chloroquine	4-aminoquinoline	Not clear, changes the pH of endosomes and believed to prevent viral entry, transport and post	Inhibits cell penetration SARS-CoV-2 in vitro, authorized for malaria prophylaxis and treatment

		entry events	
Hydroxychloroquine	4-aminoquinoline	Not clearly understood, the pH of the endosome varies and is thought to inhibit virus replication, transport and post-entry.	Regulates cell infection SARS-CoV-2 in vitro, authorized for malaria prophylaxis including autoimmune disease (e.g. rheumatic diseases). Licensed diagnosis of T2DM in India
Remdesivir	Adenosine nucleotide analogues	Stops the replication of viruses.	Shows result against SARS and MERS
Ribavirin	Nucleoside analogue	Regulates viral RNA proliferation and mRNA capsizing	No proof of effectiveness on SARS and MERS
Ribavirin plus Interferon		Stops the replication of virus.	Combined effect on MERS
Camostat Mesilate	Protease inhibitors	Prevents viral development and blocks the cell	Effectively blocked SARSCoV-2 in lung cells in vitro

		entrance	
Lopinavir/Ritonavir	Protease inhibitors	Do not let the viruses to enter into the cell.	Shows result on SARS-CoV,also has in vivo and in vitro effects.
Darunavir/Cobicistat	Protease inhibitors	Do not let the viruses to enter into the cell.	Developed anti-HIV medications. No action towards coronavirus or any other respiratory diseases. No clinical or in vitro results.
Favipiravir	Inhibits RNA polymerase	Inhibits the polymerase dependent viral RNA	Broad-spectrum anti-influenza virus, arenavirus, bunyavirus and filovirus

Umifenovir	Inhibits the fusion	Stops the fusion between the membranes of virus and cell wall	Antiviral effects on some other corona viruses.
Interferon-β1	Cytokines	Increases resistance of endogenous antiviral.	MERS-CoV tends to become more responsive than the SARS-CoV in vitro sample.experiments..Anti-MERS-CoV activity recorded in clinical trials.
Interferon beta plus Lopinavir/Ritonavir	Interferon beta inhibits viral replication		Continuing research for the SARSCov-2 and MIRACLE MERS trials
Aerosolized interferon α	Cytokines	Accelerate innate antiviral immunity.	Benefits reported on MERS
Oseltamivir	Inhibitor of Neuraminidase	Stops the replication of virus.	No impact on in vitro SARS experiments. There is no proof in SARS and MERS
Baloxivir marboxil	Viral endonuclease inhibitor	Prevents the replication of influenza virus	Licensed only for uncomplicated influenza in Oral route:

Tocilizumab, Sarilumab Eculizumab	Monoclonal antibody	IL-6 inhibitor, inhibits the storm of cytokine .	No formation about SARS or MERS Tocilizumab decreased temperature and oxygen demand in COVID-19, authorized for rheumatoid arthritis.
SARS-Cov-2 specific protease drug candidate	Protease inhibitors	Blocks the viral pathway	Unavailable information.
SARS-Cov-2 specific antibodies	Antibody	It links the virus and prevents infection, attaches to the infected cells and changes the immune response.	In in-vitro studies,blocks the entry of SARS-CoV- 2.

Table 8:Drugs in the pipeline for treatment

3.7.Different studies on Chloroquine and Hydroxychloroquine in Covid-19,their result and proposed doses :

Different studies	Proposed dose
-------------------	---------------

<p>Specialist agreement of the Department of Science and Technology and Health Commission of Guangdong Province, China</p>	<p>Chloroquine phosphate BID 500 mg about 10 days.</p>
<p>A research by Central Clinical Task Force of Korea</p>	<p>Medium to extreme effect on COVID-19. Some drugs such as Lopinavirs in 400 mg. Ritonavir 100 mg BID or Chloroquine 500 mg in oral route daily or Hydroxychloroquine 400 mg oral daily for about mostly 10 days.</p>
<p>A research done in Centre for Disease Control and Prevention in Atlanta in 12 of March in 2020 which is the MICC Version 1.</p>	<p>Positive PCR and URTI :</p> <p>Treatment with chloroquine phosphate (500 mg) and oseltamivir (150 mg) for 5 days BID.</p> <p>Pneumonia during COVID-19 :</p> <p>Treatment plan with chloroquine phosphate(500 mg) of BID which will be continued for consecutive 5 days and at the same time Darunavir(800 mg) or Cobicistat(150mg)</p> <p>Which will be continued for 14 days.</p> <p>Another combination therapy can be Atazanavir (400mg) which will be continued for 14 days of OD with 5 days treatment of Oseltamivir(150 mg) of BID.</p>

<p>Research done on The Dutch Center of Disease Control</p>	<p>Treatment with Chloroquine base</p> <p>First day(first half):600 mg</p> <p>First day(last half):300 mg</p> <p>Second to fifth day:300 mg twice</p>
<p>Study done in Italian Society of Infectious and Tropical Diseases</p>	<p>Treatment in moderate Covid-19:</p> <p>Treatment for 10 days with the combination of Lopinavir or Ritonavir with chloroquine (500 mg in total) twice a day or Hydroxychloroquine (200 mg) once a day.</p> <p>Treatment in severe Covid-19:</p> <p>Combined therapy of Remdesivir and Chloroquine total 500mg twice a day. Another option is treating with Hydroxychloroquine 200 mg about 10 to 20 days.</p>
<p>Study done in Mount Sinai Health System, Canada</p>	<p>Treatment of medium to extreme COVID-19:</p> <p>Treatment with Hydroxychloroquine</p> <p>First 12 hours 400mg of BID twice a day</p> <p>After 12 hours to 5 to 10 days: 400 mg OD</p>
<p>Studies and researches done in Surviving Sepsis Campaign, The Society of Critical Care Medicine and</p>	<p>Inadequate research to include guidelines for the use of chloroquine or hydroxychloroquine in chronically sick individuals with COVID-19 at this stage.</p>

<p>the European Society of Intensive Care Medicine</p>	
<p>Treatment trials for patients believed or reported to have COVID-19 in Belgium</p>	<p>Treatment option for low,medium or extreme level of Covid-19:</p> <p>Treatment with Hydroxychloroquine :</p> <p>At the time of diagnosis:400 mg</p> <p>12 hour later:400 mg</p> <p>Later 5 days:200 mg BID.</p> <p>Treatment with Chloroquine :</p> <p>At the time of diagnosis:600 mg</p> <p>12 hour later:300 mg</p> <p>Later 5 days:300mg BID</p> <p>If the above ones show complications,another option can be lopinavir 400 mg or ritonavir 100 mg for 2 weeks.</p> <p>Treatment for high COVID-19: Treating with Remdesivir :</p> <p>Loading dose:200 mg IV (within half an hour)</p> <p>Till 2nd to 10th day:100 mg OD</p> <p>If contraindicated,Hydroxychloroquine can be an second</p>

	option.
Medical advice for patients believed or reported to have COVID-19 in Netherland	<p>Treatment option for low,medium and high COVID-19:</p> <p>First day:Chloroquine(600 mg)</p> <p>Letter 5 days:300 mg</p> <p>Lopinavir or ritonavir can be chosen as second option.</p>

Table 9:Guidelines for treating Covid-19 with Chloroquine and Hydroxychloroquine

3.9.Clinical trials and outcome on some drugs:

Name	Identifier	Location	1. Type of study 2. What to measure	Treatment arm	Active comparator	Placebo arm

Randomized Controlled Clinical Trials of Lopinavir/Ritonavir or Hydroxychloroquine in Patients With Mild Coronavirus Disease (COVID-19)	NC T04 307 693	Sung-Han Kim, Asan Medical Center, Seoul, South Korea	1. Multicentre, open-labelled, randomized clinical trial 2. Viral load	Lopinavir/ritonavir 200mg/100 mg two tablets by mouth, every 12 hours for 7–10 days	Hydroxychloroquine 200mg two tablets by mouth, every 12 hours for 7–10 day	No lopinavir/ritonavir and hydroxychloroquine
Hydroxychloroquine Post Exposure Prophylaxis for Coronavirus Disease (COVID-19)	NC T04 318 444	Elizabeth Oelsner, Columbia University, NY, USA	Parallel assignment (randomized)	Hydroxychloroquine two tablets (400mg) twice daily on day 1; for days 2–5, they will be instructed to take one tablet		Two tablets (400mg) twice daily on day 1; for days 2–5, they will be instructed to take one tablet (200mg) twice daily

				(200mg) twice daily		
Hydroxychloroquine Chemoprophylaxis in Healthcare Personnel in Contact With COVID-19 Patients (PHYDRA Trial) (PHYDRA	NC T04 318 015	National Institute of Respiratory Diseases, Mexico City, Mexico	1. Triple blinded, randomized controlled trial 2. Symptomatic covid-19 infection rate	1. High risk: hydroxychloroquine 200mg per day for 60 days 2. Low risk: hydroxychloroquine 200mg per day for 60 days		1. High risk: placebo tablet per day for 60 days 2. Low risk: placebo tablet per day for 60 days
Chloroquine Prevention of Coronavirus Disease (COVID-19) in the Healthcare Setting (COPCOV	NC T04 303 507	Oxford University, Oxford, UK	1. Parallel assignment 2. Number of symptomatic covid-	Chloroquine A loading dose of 10mg base/kg followed by 150mg daily (250mg		Placebo

			19 infectio ns	chloroquine phosphate salt) will be taken for 3 month		
Safety and Efficacy of Hydroxychloroq uine Associated With Azithromycin in SARS CoV-2 Virus (Alliance COVID-19 Brazil II)	NC T04 321 278	Hospit al Israeli ta Albert Einste in, Sao Paulo, Brazil	Parallel assignm ent 2. Evaluati on of clinical status	Hydroxychl oroquine (400mg 2 times per day, 12/12 hours)+azit hromycin (500mg once a day	ydroxychl oroquine (400mg 2 times per day, 12/12 hours)	
Post-exposure Prophylaxis for SARS- Coronavirus-2	NC T04 308 668	Unive rsity of Minne sota, Minne sota, USA	1. Parallel assignm ent 2. Inciden ce of disease	Hydroxychl oroquine 200mg tablet; 800mg orally once, followed in 6–8 hours by 600mg,		Placebo four placebo tablets once, followed in 6–8 hours by three tablets,

				then 600mg once a day for four consecutive days		then three tablets once a day for four consecutive days
--	--	--	--	---	--	--

Table 10: Outcome of some drugs after clinical trials.

Chapter 4

Discussion:

Treating a pandemic is not for a moment easy. Scientists are trying several drugs as well as variant drug combinations to treat the patients in this pandemic. Nevertheless, some combinations are working, some of them are giving negative result as well as side effects. Moreover, umpteen clinical trials on human with different doses of drugs are going on. However, not all of them are effective enough to reach the goal. On the other hand, there are some promising treatments which are already showing effects and saving lives of so many people.

4.1. Drug combinations:

From table 1, we can see that there are some medications that are already being used to treat some other diseases such as cloroquine with its derivative hydroxycloquine in the treatment of diabetes, systemic lupus, prophylaxis of malaria etc. Additionally, combination of nitric oxide and epoprostenol is treating the pulmonary pressure and working as a vasodialator. By researching on their effectiveness on human and previous history, they can be used in covid-19 treatment. In addition, there are some other combinations which have already used in

treatments of some previous corona viruses that have similar structure of covid-19. For example, in the nitazoxanide and tizoxanide combination is used to deal with the previous corona virus strain MERS-CoV and group of some other corona virus such as murin. As they work on this kind of viruses, hopefully they will give effects on covid-19 too and will help to reach the goal in this pandemic. However, there are some other drug combinations such as lopinavir along with ritonavir that are already working and being used in covid-19 directly as they are showing results on covid-19 infected people in different countries like China and Korea. But not all of these combinations are 100% safe, rather also have some side effects such as nausea, diarrhea, gastrointestinal effects and asthma as well. Therefore, before using any of the combinations, one should know the side effects so that they can estimate the benefit over the side effects.

4.2. individual drug treatments:

Not only the drug combination are showing effective results to treat covid-19 but also some individual drugs of different classes such as anti-malarial drugs, anthelmintic drugs, antiviral drugs (even broad spectrum antivirals) are playing key roles on human body affected with covid-19. Among them, drugs like Niclosamide, Ivermectin, Chloroquine and Arbidol have effects on some of the corona viruses such as SARS-CoV-2 as well as covid-19. Therefore, these drugs can also have remarkable effect on covid-19 too. Along with them, some drugs like ribavirin, favipiravir are also being used in the treatment of covid-19 who are actually the treatment of some other diseases like hepatitis C and influenza. All of these drugs are being used in different concentrations according to their effectiveness.

4.3. Effectiveness of antiviral treatment on covid-19 disease:

Effectiveness of antivirals is already observed in patients with SARS-CoV as well as MERS-CoV. Likewise, tremendous effectiveness of some antiviral drugs are noticed on covid-19 in variant routes of administration like oral administration, intravenous administration as well as

vapor inhalation. Among the antivirals, lopinavir, ritonavir, arbidol and chloroquine phosphate are administered orally in different different doses (200mg-500mg) for 2 or 3 times daily about 10 days. Besides, ribavirin is infused with ritonavir and lopinavir or IFN- α for twice or thrice a day for maximum 10 days. Also IFN- α is inhaled alone in a dose of 500 million U twice or thrice a day for 10 days maximum.

Lopinavir has a very little bio-availability and the stature is transformed very fast while taken alone orally. Therefore, this antiviral drug is used with a combination with ritonavir which increases the bio-availability and inhibit the manifestation of lopinavir and incenses the antiviral effect towards covid-19. This efficient combination of the two antivirals are called Kaletra.

4.3.1. Outcomes from Clinical trials on antiviral drugs:

There are different groups of drugs based on their inhibitory activity with antiviral effects. Basically, their mechanism of action and dosing vary from each other.

One of these groups, the drugs blocks the viral synthesis. Remdesivir and Favipiravir are of that group. Remdesivir, an adenosine nucleotide analogue, is basically a pro-drug, is infused with a dose of 200 mg in the first day and with a dose of 100mg for maximum 10 days. Furthermore, this drug is also used for variant RNA viruses because of having broad-spectrum antiviral activity. Moreover, the first cure of covid-19 in USA is the effect of Remdesivir. Another drug of this group, having similar mechanism of action, Favipiravir which is a guanosine nucleotide analogue, is also a pro-drug. o many clinical trials are done on

this drug for getting the benefits from it in case of covid-19 as it has already shown effective response in SARS-CoV-2. Comparing this drug with other antiviral drugs such as arbidol, percentage of recovery rate is much more higher in it (71.43%). However, Favipiravir may have some negative issues such as it can cause increase in the concentration of uric acid in the serum, can recompose digestive tract and the function of the liver can also be altered.

After that, comes another group of drugs that stops the production of protein in virus. Lopinavir and Ritonavir are the members of this group. They are basically protease inhibitor. Among them, lopinavir is a drug which is already a FDA approved antiviral drug and also has the record of recovering pneumonia caused by covid-19 by combining with another drug named Oseltamivir. Along with this, lopinavir also has record of working on HIV virus and both of the drugs of this group have in vitro effect on corona virus. Several studies on these drugs shows that they reduce the mortality rate when used to treat different strains of corona virus such MERS-CoV.

Another group resist the viruses from into the cell. The members are Chloroquine and Hydroxychloroquine. They have shown the antiviral activity with effectiveness on covid-19 and are being used to treat the patients in this pandemic a lot. The medication is continued for 1-5 days and 500mg in total is given orally per day.

The immunomodulator group includes Nitazoxanide and Ivermectin. Ivermectin has shown inhibitory activity towards the virus SARS-CoV-2 and in other clinical trials, antiviral effects are observed. Ivermectin is basically an inhibitor of HIV-1 virus. On the other

hand,Ivermectin,in clinical trials,does not show any efficacy towards some other viruses such as dengue and zika virus.

4.4.Effectiveness of vitamins:

Vitamins have some vital effects to fight against Corona viruses.Besides,some of the vitamins boost up the immune system such as vitamin E,it increases the immunity and sometimes act like killer cells.Along with this Vitamin C and D also play key roles in case of corona virus.Among them,vitamin D reduces the chance of infections that can be caused by microbes and viruses.Furthermore,like the activity of vitamin E,vitamin D also boosts up the immune system.In case of Covid-19,there is chance of having sepsis which can be reduced by taking vitamin C as it is a good anti-inflammatory.Besides,taking vitamin C can also reduce chance of organ failure.On the other hand any vitamins in concentration more than the recommendation can be harmful for the patient suffering from Covid-19.

Chapter 5:

Conclusion:

Covid-19 is such a disease for which so many other viral infections are not getting importance nowadays and which is ultimately scaring people a lot.Therefore,treating this disease and eliminating the panic among the people of the whole world is important.

5.1.Outcome:

After discussing the condition of Covid-19 pandemic and the available treatment options till date,it can be said that the permanent solution can be invention of a vaccine which is very

time consuming and practical trial based. Vaccination treatment is more beneficial for such pandemics and more effective than drugs as they prevent the disease, but for saving the lives treatments by drugs are being used till now. Besides, the drugs that are being used in the treatment, they are showing results in case of reducing the symptoms and also some of the patients are being out of the danger. All drugs that are being suggested for the treatment are not FDA approved. Therefore, for getting more efficient and effective results, more clinical trials should be done on human which will need a lot of time but after that there is a possibility of getting more FDA approved drugs. Above all, every patient may not have the similar physical condition. Consequently, they will be needing different treatments. Hence, more clinical trials is needed on different group of people with different physical condition.

5.2.Limitation:

- The drugs that are being used to treat or reduce the symptoms of Covid-19, their feasibility of therapeutic use is not tested completely.
- As the process of testing the drugs on human is ongoing, the results are continuously coming and the data are constantly changing.
- Moreover, dose of some drugs are still not induced properly, therefore toxicity can be showed in some doses.
- Additionally, the data are based on theoretical values from journals, not based on proper human trials. Therefore, practical effects on human is not properly known.

- Alongside,there is no proper record of the safety profile and the effectiveness of these drugs which can be sometimes harmful for the patients.
- Use of some medications such as vitamin-C in patients who are in critical condition is controversial because of lack of authentic data.

5.3.Future direction:

From the analysis of the present and the previous history it can be said that,pandemics are very likely to occur any time.Therefore, preparation is very essential and to be prepared more research is needed.Moreover,to fight the present state of Covid-19,developing new drugs and doing research on the existing one is also very emergent.Besides,many works is going on such as monoclonal antibodies are being developed which can be a treatment option for the global pandemic.Alongside,some drugs such as lopinavir and ritonavir should have more trials.Alternative options should be searched to have more efficient treatment option.Finally,safety measures should be followed more strictly to stop the spread.

References

Avery, J., & Bloom, B. (2020). COVID-19, a UK perspective. *European Journal of Emergency Medicine*, 27(3), 156–157. doi:10.1097/mej.0000000000000700

Dong, L., Hu, S., & Gao, J. (2020). Discovering drugs to treat coronavirus disease 2019 (COVID-19). *Drug Discoveries & Therapeutics*, 14(1), 58–60. doi:10.5582/ddt.2020.01012

Guo, Y.R., Cao, Q.D., Hong, Z.S., Tan, Y.Y., Chen, S.D., Jin, H.J., ... Yan, Y. (2020). The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status. *Military Medical Research*, 7(1), doi:10.1186/s40779-020-00240-0

Lancet, T. (2020). India under COVID-19 lockdown. *The Lancet*, 395(10233).

doi:10.1016/S0140-6736(20)30938-7

MacKenzie, D. (2020). The hunt for covid-19 drugs. *New Scientist*, 245(3273), 10.

doi:10.1016/s0262-4079(20)30525-x

Muhammad,A.S., Khan, S., Kazmi, A., Bashir, N., Siddique, R.(2020). COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. *Journal of Advanced Research,S2090123220300540*–. doi:10.1016/j.jare.2020.03.005

Rothan, H. A.,Byrareddy, S.N. (2020). The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *Journal of Autoimmunity*. doi:10.1016/j.jaut.2020.102433

Saeed,A., Mohammad,N., Jakir,H.M. (2020). COVID-19 and Bangladesh: Challenges and how to address them. *Frontiers in Public Health,(8)*, 154.
doi:10.3389/fpubh.2020.00154

Samander,K., Sulochana,K., Yashika,S., Ramesh,K., Parkash,Y.J. (2020). The Indian perspective of COVID-19 outbreak. *Virus Disease*. doi:10.1007/s13337-020-00587-x

Serap,A.Y.,Serhat,A.N. (2020). Antiviral treatment of COVID-19. *TURKISH JOURNAL OF MEDICAL SCIENCES, 50(SI-1)*, 611–619.
doi:10.3906/sag-2004-145

.Singh, A. K., Singh, A.,Shaikh, A.,Singh, R.,Misra, A.(2020). Chloroquine and hydroxychloroquine in the treatment of COVID-19 with or without diabetes: A

systematic search and a narrative review with a special reference to India and other developing countries. *Diabetes & Metabolic Syndrome: Clinical Research & Reviews*, doi:10.1016/j.dsx.2020.03.011

Sinha, N., Balayla, G. (2020). Hydroxychloroquine and covid-19. *Postgraduate Medical Journal*.doi:10.1136/postgradmedj-2020-137785

Velavan, T. P., Meyer, C. G. (2020). The COVID 19 epidemic. *Tropical Medicine & International Health*, 25(3), 278–280. doi:10.1111/tmi.13383

Vellingiri, B., Jayaramayya, K., Iyer, M., Narayanasamy, A., Govindasamy, V., Giridharan, B., ... Subramaniam, M. D. (2020). COVID-19: A promising cure for the global panic. *Science of The Total Environment*, 138277. doi:10.1016/j.scitotenv.2020.138277

Wu, R., Wang, L., Kuo, H.-C. D., Shannar, A., Peter, R., Chou, P. J., ... Kong, A.-N. (2020). An Update on Current Therapeutic Drugs Treating COVID-19. *Current Pharmacology Reports*.doi:10.1007/s40495-020-00216-7

Wu, Y.C., Chen, C.S., Chan, Yu,J., (2020). The outbreak of COVID-19. *Journal of the Chinese Medical Association*,83(3),217-220.

doi:10.1097/JCMA.0000000000000270

Zhang, W., Zhao, Y.,Zhang, F.,Wang, Q.,Li, T.,Liu, Z.,Wang, J.,Qin, Y., Zhang, X., Yan, X., Zeng, X.,Zhang, Shuyang (2020). The use of anti-inflammatory drugs in the treatment of people with severe coronavirus disease 2019 (COVID-19): The experience of clinical immunologists from China. *Clinical Immunology*, 214, . doi:10.1016/j.clim.2020.108393

Zheng, Y.Y.,Ma, Y.T.,Zhang, J.Y., Xie, X. (2020). COVID-19 and the cardiovascular system. *Nature Reviews Cardiology*. doi:10.1038/s41569-020-0360-5

Covid 19 treatment

ORIGINALITY REPORT

9%

SIMILARITY INDEX

7%

INTERNET SOURCES

8%

PUBLICATIONS

4%

STUDENT PAPERS

PRIMARY SOURCES

1

rssdi.in

Internet Source

2%

2

Ankit Kumar Dubey, Aakansha Singh, Shardendu Prakash, Manoj Kumar, Ashok K Singh. "Race to arsenal COVID-19 therapeutics: Current alarming status and future directions", Chemico-Biological Interactions, 2020

Publication

2%

3

www.ijpdll.com

Internet Source

1%

4

Submitted to University of Stirling

Student Paper

1%

5

journal-center.litpam.com

Internet Source

<1%

6

link.springer.com

Internet Source

<1%

7

raiith.iith.ac.in

Internet Source

<1%

covid19biblio.com

8	Internet Source	<1%
9	Submitted to Kookmin University Student Paper	<1%
10	Awadhesh Kumar Singh, Akriti Singh, Altamash Shaikh, Ritu Singh, Anoop Misra. "Chloroquine and hydroxychloroquine in the treatment of COVID-19 with or without diabetes: A systematic search and a narrative review with a special reference to India and other developing countries", <i>Diabetes & Metabolic Syndrome: Clinical Research & Reviews</i> , 2020 Publication	<1%
11	www.hindawi.com Internet Source	<1%
12	Submitted to University of Huddersfield Student Paper	<1%
13	Hussin A. Rothan, Siddappa N. Byrareddy. "The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak", <i>Journal of Autoimmunity</i> , 2020 Publication	<1%
14	Gaurav Chauhan, Marc J. Madou, Sourav Kalra, Vianni Chopra, Deepa Ghosh, Sergio O. Martinez-Chapa. "Nanotechnology for COVID-19: Therapeutics and Vaccine Research", ACS	<1%

Nano, 2020

Publication

15	Neeraj Sinha, Galit Balayla. "Hydroxychloroquine and covid-19", Postgraduate Medical Journal, 2020 Publication	<1%
16	Maryam Rameshrad, Majid Ghafoori, Amir Hooshang Mohammadpour, Mohammad Javad Dehghan Nayeri, Hossein Hosseinzadeh. "A comprehensive review on drug repositioning against coronavirus disease 2019 (COVID19)", Naunyn-Schmiedeberg's Archives of Pharmacology, 2020 Publication	<1%
17	id.wikipedia.org Internet Source	<1%
18	Balachandar Vellingiri, Kaavya Jayaramayya, Mahalaxmi Iyer, Arul Narayanasamy et al. "COVID-19: A promising cure for the global panic", Science of The Total Environment, 2020 Publication	<1%
19	explora.unex.es Internet Source	<1%
20	Yan-Rong Guo, Qing-Dong Cao, Zhong-Si Hong, Yuan-Yang Tan, Shou-Deng Chen, Hong-Jun Jin, Kai-Sen Tan, De-Yun Wang, Yan Yan. "The origin, transmission and clinical	<1%

therapies on coronavirus disease 2019 (COVID-19) outbreak – an update on the status", Military Medical Research, 2020

Publication

21

www.frontiersin.org

Internet Source

<1%

22

Jatin Machhi, Jonathan Herskovitz, Ahmed M. Senan, Debashis Dutta et al. "The Natural History, Pathobiology, and Clinical Manifestations of SARS-CoV-2 Infections", Journal of Neuroimmune Pharmacology, 2020

Publication

<1%

Exclude quotes On

Exclude matches < 4 words

Exclude bibliography Off