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Review Article

COVID-19: New Challenge in 21st Century

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Abstract

COVID-19 pandemic turned into the proven existence-threatening virus in-line with World Health Organization (WHO) has declared a public health emergency of International Concerned and our healthcare system found a challenge to save human civilization. This evaluation gives a brief idea of COVID-19 epidemiology, pathophysiology, treatment, and prevention of COVID-19. Exclusive drugs like Dexamethasone and Remdesivir were found effective to treat the virus was covered in this review article. Pathophysiology of virus in the body of diabetes and cancer patients, there mechanism of action and risk involved in that patients were studied. This review turned to conduct on data found in science direct, various information sources on the internet and different review articles were studied. The major objective is to provide a brief overview of this disease, study infectious virus effect on human beings proves to be an existence-threat to the world population and brief overview of COVID-19 was covered in this review article.

Keywords: SARS-CoV-2, MERS, Vaccine, Dexamethasone, Remdesivir.

INTRODUCTION:

Coronavirus is an imperilment and existence-threatening virus. Severe acute respiratory syndrome coronavirus is a unique sickness that particularly affect the top breathing tract and greater infections within inside the lungs.[1] Its family is an epidemic-virus that may motive ailments along with not unusual places bloodless Severe Acute Respiratory Syndrome(SARS), and Middle East Respiratory Syndrome (MERS).[2]In march 2020 World Health Organization (WHO) declared the COVID-19 outbreak a pandemic. The call of such a virus is due to its outer form of crown-like spikes so they called the virus relative as Corona. Corona has the equal etiology as pneumonia its an infectious sickness as a result of the SARS CoV-2 virus.[3] Most of the humans inflamed via way of means of the virus will revel in slight to mild breathing contamination. Each person can get ill with COVID-19 and get end up severely unwell or die at any age. Both SARS-CoV-2 and MERS-CoV can cause Acute Respiratory Distress Syndrome (ARDS).[4]

The virus can unfold from an inflamed individual to a wholesome individual through the mouth and nostril in small liquid debris whilst they're cough, sneeze, speak, breathe. The particle length from large breathing droplet to smaller aerosol can seem at the human frame 2 to 14th day. After contamination then after check additionally for screening for COVID-19 along with opposite transcription-polymerase chain response and rapid antigen check.[5] Rise in body temperature is one of the common symptoms in COVID-19.[1]

The first case of Corona virus was found in December 2019, in Wuhan where sufferers began to confess to nearby hospitals. However, daily the range of patients increased the surveillance system was activated and collected respiratory samples of patients and sent to reference labs for investigation.[6] On 7th January 2020 the virus was identified as corona virus that had >95% homology with bat corona virus. All investigations conclude that corona originated from bat meats but day by day number of cases increases finally China government announces a lockdown in Wuhan and other cities in Hubei on 23rd January 2020 but the COVID-19 spread to more than 228 countries in the world.[8]

COVID SPREAD IN THE WORLD:

Around 228 countries around in the world have reported a total of 532,022,559 confirmed cases of the COVID-19 and 6,311,923 deaths.

All numerical data are studied in the following table:[9]

Table 1: Countries where COVID-19 Spread [9]

Sr no	Country	Cases	Deaths
1	United states	85,730,597	1,031,286
2	India	43,158,582	524,630
3	Brazil	30,977,661	666,568
4	Russia	18,327,837	379,029
5	Australia	4,250,457	18,651
6	Belgium	4,147,568	13,727
7	Thailand	4,450,457	30,022
8	South Africa	3,954,971	101,162
9	Portugal	4,066,674	22,583
10	Canada	3,867,057	40,281
11	Iraq	2,328,019	25,219
12	Bangladesh	1,953,481	29,131
13	North Korea	3,549,590	70
14	Serbia	2,017,189	16,080
15	Romania	2,908,704	65,678

EPIDEMIOLOGY:

(1) Most recently determined (2019-2020) virus belongs to the arbovirus genus of the coronaviridae family and its 7th coronavirus known to canker humans.

(2) Coronavirus is single-stranded ribonucleate acid having 9 - 12 nm lengthy spikes surface.

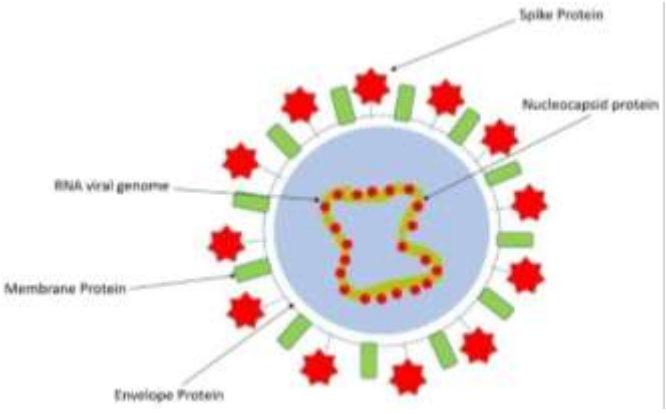

Figure 1: Coronavirus structure [36]

(3) One of the spikes protein binds to Angiotensin-Converting Enzyme 2 (ACE 2) receptor which results in a subsequent fusion between envelope and host cell membrane to aid viral entry in host cells.

(4) Over 1.5 million cases in US only and over 5 million globally.[10]

Case study as follows:

- First case identified in Wuhan, China
- 31st December 2019-WHO China office (cases of pneumonia of unknown etiology were reported).
- 01 January 2020-Wuhan seafood market closed
- 07 January 2020- China government identifies "novel coronavirus".
- 09 January 2020-First death in Wuhan, China.
- 13 January 2020- Thailand report first case beyond China.
- 30 January 2020- two important crucial instances happened:

1. India reports the first case in January 2020.
2. Public Health Emergency of International Concerned was announced by World Health Organization (WHO).

On 11th February 2020 - the Corona virus Study Group (CSG) of the International Committee of the taxonomy of Virus Finally categorized it as Severe Acute Respiratory Syndrome (SARS) based on taxonomy and then World Health Organization named the disease caused by a coronavirus. The host will inhale droplets or touch a contaminated surface and get infected.[11]

Its spread by the infected person by:

- Talking
- Singing
- Sneezing
- Coughing

Symptoms include:

- Coughing (59-82% common in all patients)
- Fever (83-99% common symptom in all patients)
- Shortness of breathing (31-40% common symptoms)
- Sore throat (5% common symptoms in all patients)
- Muscle pain (20% common in all patients)
- Loss of taste or smell (15% Common in all Patients)

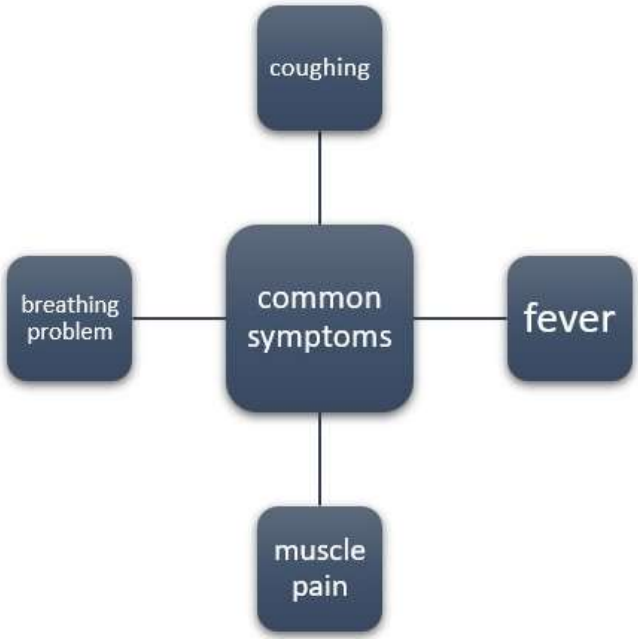

Figure 2: Most Common symptoms in COVID-19 effected patients [11]

Measurement of risk:

To calculate the rate (%) it's crucial to decide the frequency of the disease which includes,

- Population at hazard

- Period of calculating the rate
- Number of the case of COVID-19.[11-12]

$$\text{Rate (\%)} = \frac{No.of\ Cases}{Population\ at\ Risk} \times 100$$

(1) From the beginning of the pandemic, the percentage of children having a virus is very low according to data from the Chinese center for disease control and prevention from Feb 2020 children within ages 11 to 19 years occupied 1% of total cases while the pediatric population affected 205 of patients.

(2) In a report of up to 2134 pediatric patients with COVID-19 from China's center for disease control and prevention (CDC), 4.4%, 50.9%, 38.8%, 5.9% of patients where were diagnosed with sub-clinical, mild moderate severe respectively While 18.5% of adult patient have severe diseases Infants were most vulnerable to some infections.

(3) The proportion of severe and critical cases was 10.6%,7.3%,4.2%,4.1% and 3.0 % of age group 1,1-5,6-10,11-15,16 years .[13]

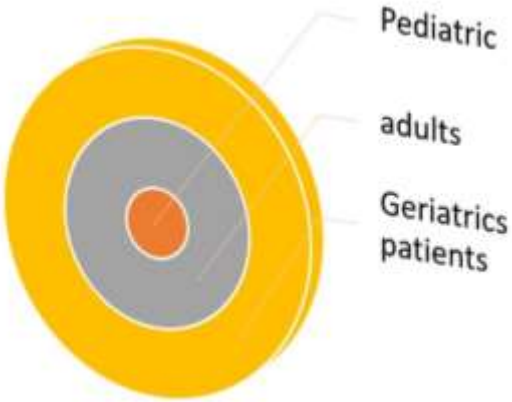

Figure 3: Risk of COVID-19 towards varoius age groups [13]

Total Ten countries with the highest number of New Cases Over the past: [9]

- Chile- 36,179
- Brazil-34,918
- USA-27,921
- India- 12,881
- Russia Federation-7,790
- Pakistan-5,358
- Mexico-4,599
- Peru-4,164
- South Africa-4078
- Saudi Arabia- 4919

ROUTE OF TRANSMISSION:

Person-to-persons transfer through the respiratory tract is basic means of transmission of severe acute respiratory syndrome. It is thought to develop especially through straight-contact with any person approximately (6 feet or two meters) via respiratory particles it also occurs if a person's hand is contaminated by touching the contaminated surface and then they touch their eyes, nasal area, or mouth although the contaminated surface is not thought to be in the major route of transmission.

PATHOPHYSIOLOGY:

1) Mechanism of SARS – CoV-2 penetration into host cells. Coronavirus is single-strand, envelop, RNA viruses. They infect a range of host species. They are sectioned into four genera: alpha, beta, delta, and gamma.

2) Alpha and beta infect mammals.

3) Most common coronaviruses in clinical practice are 229E, OC43, NL63, and HKUI, which typically causes cold symptoms while SARS-CoV-2 is the third coronavirus that has caused severe diseases in human to spread globally.

(a) The first coronavirus caused severe diseases in acute respiratory syndrome (SARS) which originated in China and resulted in SARS-CoV-2 (2002-2003) pandemic.

(b) Bats are considered a natural true reservoir for SARS-CoV-2, but it has been suggested humans get affected by SARS-CoV-2 via an intermediate host. [13-14]

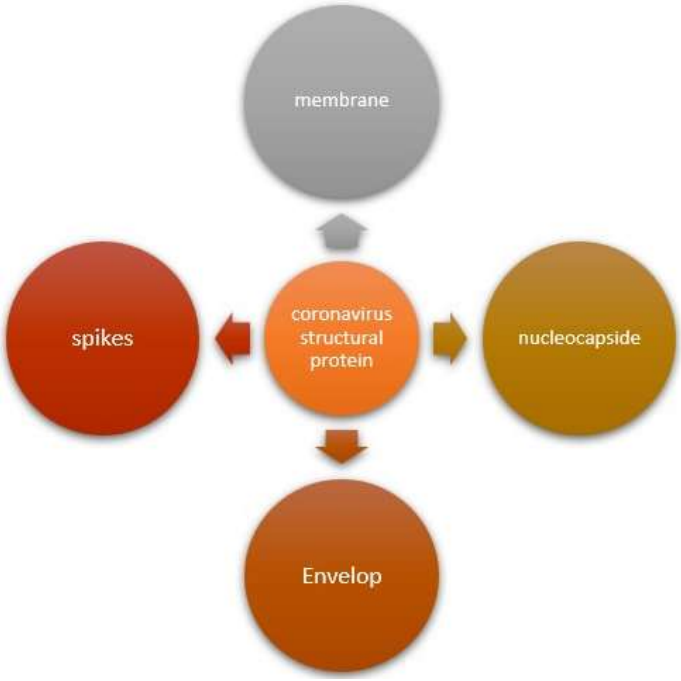

Figure 4: Structural proteins in coronavirus[14]

Spike has two functional units

- S1 is responsible for binding the host receptors.
- S2 is responsible for Binding with the cellular membrane.[14]

COVID –19 DIAGNOSIS:

Corona virus diagnosis helps you to get seek medical care tested. If you have been exposed to the virus or show mild symptoms of COVID-19, call the doctor for advice about how and when to get tested. COVID-19 symptoms are similar to other respiratory disease, therefore the lab tests are necessary for the diagnosis. COVID-19 symptoms start anytime from 2 to 14 days after exposure to SARS – CoV-2.[15]

Common symptoms:

- Fever
- Cough
- Fatigue
- Shortness of breath

Other symptoms:

- Headache
- Chills
- Sore Throat

- Muscle aches and pains
- Loss of smell or taste
- Diarrhoea

Few people show no signs of illness during the early phases of infection but can transmit the virus to others.[15-16]

CORONAVIRUS TREATMENT:

Scientists seeking to make new drug substances and test some existing drugs effect they can deal with COVID–19 or not. In the meantime, several things can relieve symptoms, both at the Home & Hospital.

1. At-home coronavirus remedy: If the symptoms are mild you can recover at home.

2. Stay home; don't go to job, school, or public places

3. Rest, it could make you feel great and spread your betterment.

4. Monitor, if your symptoms get adverse, call your doctor right away don't go to their office without calling first. They might tell you to stay home, or they may need to take redundant steps to defend staff and other patients

5. Drink fluids, you lose more water when you seek, dehydration can make symptoms worse and causes other health problem

6. Ask your doctor about over-the-counter medicine that may help, like acetaminophen to decrease your fever .[16-17]

HOSPITALIZED TREATMENT

[a] Patients who don't not required supplement oxygen: If your oxygen saturation is fine and you have no signs or symptoms other than fever all you need is paracetamol.

(1) Dexamethasone: Patients with COVID-19 who are receiving Dexamethasone or another corticosteroid for an implicit condition should continue this therapy as directed by their healthcare provider. Dexamethasone-Other corticosteroids for the treatment of COVID-19 in hospitalized patients. do no longer require supplemental now any longer require supplement oxygen until the affected person has any other indication for corticosteroid remedy. Dexamethasone – Take in 6mg by Intravenous route once daily for up to 10 days or until the hospital discharge. If dexamethasone isn't to be had an equal dose of any other corticosteroid can be used.

Rational effect of Dexamethasone: Few patients in the Dexamethasone arm than in the standard of care arm died within 28 days of enrolment (23.3 % Vs 26.2% rate ratio 0.82:95% Cl, 0.72 – 0.94). Some specialists prefer not to use Dexamethasone Monotherapy in sufferers who require supplemental oxygen because of the theoretical challenge that corticosteroids might slow viral clearance when administered without an antiviral drug.[18]

Dose effect of Dexamethasone: 1) A totalof 2104 patients were assigned to receive dexamethasone and 4321 to receive usual care. 2) 482 patients (22.9%) in the Dexamethasone group and 1110 patients (25.7%) in the usual care group pass awaywithin 28 days after randomization.

[b] Patients who required supplement oxygen:

A patient who needsupplemental oxygen, but not high-flow oxygen, noninvasive ventilation, or mechanical ventilation are a heterogeneous group.[18-19]

ANTIVIRAL DRUGS USED IN COVID-19:

(1) Molnupiravir: Molnupiravir it is a newest antiviral API that has recently used in COVID-19. Molnupiravir was developed by drug innovation ventures at Emory university. Molnupirvir and Remdesivir targets RdRp (RNA – dependent RNA- polymerase) enzyme is used to inhibition of transcription and replication of coronavirus RNA genome. Molnupiravir has identical mechanism of action pretty similar to favipiravir.[32]

Molecular formula: C13H19N3

Molecular weight:-329.31

(2) Remdesivir-For patients who need minimal supplemental oxygen Remdesivir. Does not work in all patients, patientsrequire oxygen but are not sick enough that they require ventilation.it doesn't reduce mortality, but probably helps early recovery. [20]

Rational use of Remdesivir–Remdesivir was associated with improved time to recovery in the 435 patients who require oxygen supplementation but not high flow oxygen or mechanical ventilation.

The rate of in-hospital deaths among patients those receives deliver and who receive a standard of care by the solid trial report. Over all study of population for ratio death in 0.95; 95% cl, 0.67-1.11; rate ratio for death in patients who did not require mechanical ventilation at entry 0.86, 99 % ,0.67-1.11.

In hospitalized patients: Intravenous-200mg as a single dose on day first, followed by 100mg once daily. Duration is generally 5 days or until hospital discharge, initiate possible after the diagnosis of symptomatic COVID-19 Within 72 hours of a positive SARS-CoV-2 Test

In non-hospitalized patients: 200mg in one single dose on day 1 st, followed by 100 mg daily on days 2 and 3. Initiate possible within 7 days of sign and symptoms onset. Administration condition in adult patients: Intravenous – administered in intravenous infusion over 30- 120 Minutes.

ADVERSE EFFECTS:

(1) Hypersensitivity and infusion related reactions: Slower infusion rates may be considered in patients to potentially prevent hypersensitivity or infusion-related reactions. Patients may experience tachycardia & Wheezing hypoxia, nausea, hypotension, hypertension, and fever. may be considered in patients to potentially prevent hypersensitivity or infusion-related reactions.

(2) Hepatic effect: Most amino transferase elevation during treatment for COVID – 19 was reversible & not associated with jaundice, cases with jaundice rarely occurred, and increased serum alanine amino transferase & increased serum aspartate aminotransferase.

(3) Cardiac acid effect: Postmarketing reports of bradycardia, including sinus bradycardia and severe bradycardia, have been reported in patients receiving remdesivir for COVID-19. It has been suggested that the active metabolite of remdesivir, a nucleotide triphosphate derivative, may slow sinoatrial node automaticity due to its similarity with adenosine triphosphate. [18-21]

Risk of a diabetic person coming in contact with COVID-19: If a patient suffers from diabetes mellitus and indirectly came in touch with COVID-19 infection then a significant rise in blood glucose level is observed it is well known as a factor with the diabetic patients when they come in contact with coronavirus it Is due to the increasing release of cytokinin and other inflammatory mediators which result in rising in insulin

resistance and hyperglycemia various report suggest COVID-19 can be involved in growing acute diabetic Mellitus in some patient by directly targeting ACE2 receptor located in pancreatic islet.[25-26]

Type 2 diabetes mellitus has a risk: Type 2 diabetes mellitus is a risk factor in COVID-19 many mechanisms were been defined to explain the worse outcome of COVID-19 in diabetics. Some mechanism explain it has impaired neutrophil degranulation and complementary activation resulting in rising in glucose concentration in airway secretion. Due to this a significant rise in viral replication was observed. Anti-diabetic drugs like metformin, pioglitazone, Sulfonylureas, DPP-4 inhibitors, SLGT-2 inhibitors, and GLP-1 Receptors agonists can be used in treatment.[25-26]

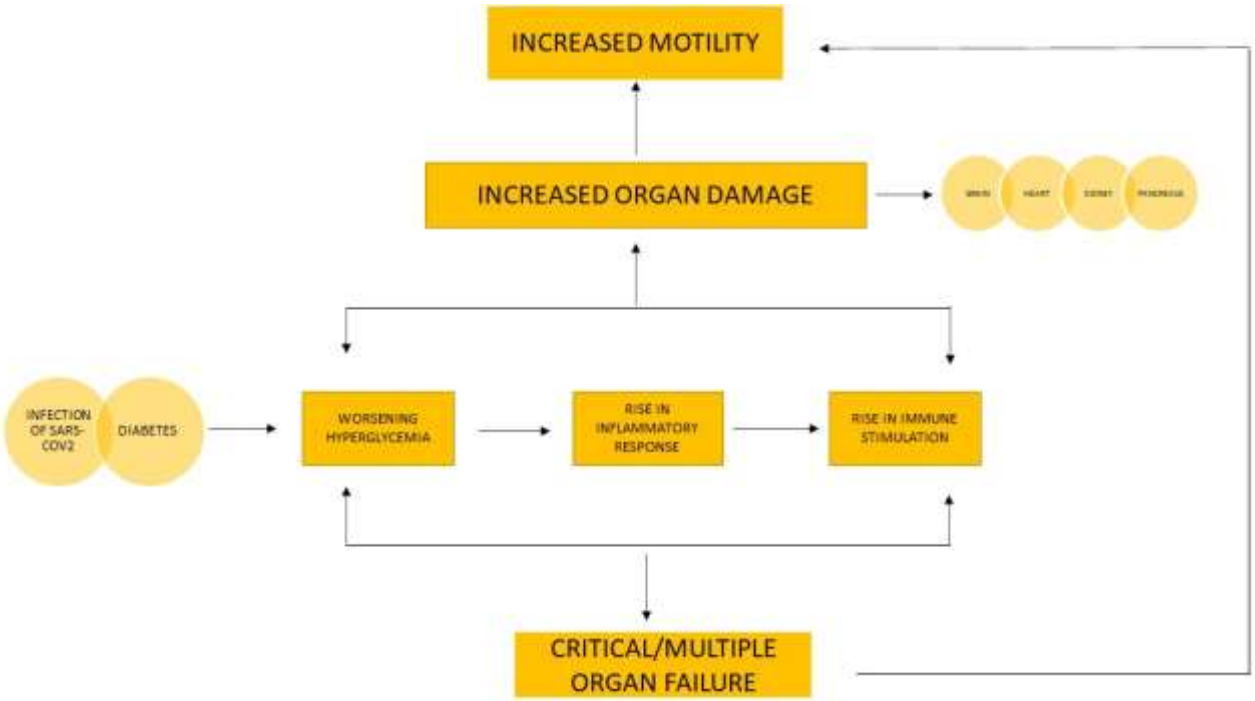

Figure 5: Pathophysiology of diabetes patients in contact with COVID-19

Effect of Cancer therapy on SARS - CoV-2 patients: Cancer is a disease which is the increasing the abnormal growth of cells which often leads to death. The SARS - CoV-2 virus are entering the human body in part of the lungs which is the present in the respiratory tract with the help of air droplets virus enters the body and binds with specific cells such as type 2 pneumocytes having angiotensin-converting enzyme 2 (ACE2) and transmembrane protease serine 2 (TMPRSS2) virus binds with ACE2 with the help of spike proteins & spread out the multiplication of the viral DNA takes place. Cancer patients occur the following molecular events. Such a cytokine storm is basically observed in cancer, and ACE 2 & TMPRSS2 expression is found higher in cancer patients.

Cytokinines: In the bronchi, the cytokines storm responsible for bronchoalveolar fluid accumulation, multinucleated syncytial cells, squamous metaplasia of epithelial cells, inflammatory cells infiltration & intra-alveolar haemorrhage. [27]

The anti-cancer therapy during the COVID-19 in pandemic situation it will depend on 2 Central variables:

1) A patient's risk of COVID-19 over the course of the anticancer therapy.

2) A patient's additional risk for serious complications or death, should the patient become infected.

The cumulative incidence for patients with cancer there may be independent of potential immune suppression by the anticancer therapies. In the patients which are treatments of anticancer may increases the severity of COVID-19.[28]

The large multi-center randomized controlled trial of remdesivir versus placebo for COVID-19. Therapies combining with remedesivir & another antiviral drug or an immune modulator may reduce risk of treatment failure & Improved treatment and there overcomes.[29]

Figure 6: effect of COVID-19 on cancer patients[27]

COVID-19: MONOCLONAL ANTIBODIES AGAINTS COVID-19:

(1) TOCILIZUMAB: First introduced in 2008 in Japan. This chemical molecule is a genetically engineered humanized monoclonal antibody. Its block inflammation without compromising the immune defense against bacterial infection.[30] IL-6 is of superb significance in the pathogenesis of numerous inflammatory diseases including infectious inflammation associated with tissue fibrosis. [31]

USE OF VACCINE AGAINST COVID-19:

1. SPUTNIK V:

It is also known as Gam - covid - Vac. It is created by the Gamaleya National Center of Epidemiology and Microbiology. SPUTNIK V is up to 91.8 infective in prevention of SARS-CoV - 2. It works when the COVID-19 virus entering the body. It attaches to human cells using proteins called spike proteins on its outer surface. After binding to the cell via these spike proteins, the virus can then alter its structure and enter cell. Once COVID-19 is within the cell, it starts to reproduces. [33]

2. COVAXIN:

Covaxin were developed by Indian pharmaceutical company Bharat biotech in collaboration with the Indian council of medical research. CDSCO (Central drugs and standards committee, India's top drug regulator, issued an emergency approval for Covaxin on 3 Jan 2021.[34]

3. COVISHEILD:

This Vaccine made to immunise people against SARS-CoV-2 or coronavirus or COVID-19. This is not effective treatment of COVID-19 however an emergency solution to save the transmission of the virus to bigger extents. People above 18 years of Age can take this vaccine.[35]

Covisheild vaccine ingredients:

1. L-Histidine hydrochloride monohydrate
2. L-Histidine
3. Magnesium Chloride Hexahydrate
4. Ethanol
5. Polysorbate 80
6. Disodium edetate dihydrate (EDTA)
7. Sodium Chloride
8. Sucrose
9. Water

CONCLUSION:

In conclusion, we summaries that Coronavirus (COVID-19) proved to be new challenge to the world in 21st century. Although first case was found in Wuhan, China and spread to whole world till now millions of people died due to this virus and our healthcare system try to safe life of millions of people. Virus pathophysiology, epidemiology, structure, symptom was studied. COVID-19 impact in most cancers patient and diabetic patient was studies under this review article and powerful vaccine against coronavirus (COVID-19) had been found after clinical trials like Tocilizumab, Molnupiravir, Sputnik-V, Covaxin, Covisheild was found effective to deal with COVID-19 and effectively accepted in different parts of world. The primary problem face by author was small number of clinical articles associated with this field. The use of published work makes us aware to continue research this article. This is the purpose why we study this topic COVID-19 to fillup loop hole and to make continue contribution to unfold knowledge about COVID-19.

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