COVID-19 - वार्ता

YEAR 2020

Maharashtra Education Society’s
ABASAHEB GARWARE COLLEGE OF ARTS AND SCIENCE
KARVE ROAD, PUNE 411 004
Forward

As whole world is facing the pandemic COVID-19 since December, it is very much necessary to know, understand and analyze their causes, symptoms and theories. As academicians, it is our duty to make the students aware, think and analyze. We are very happy to present special edition of AGC Student Research News letter as COVID-19 वार्षिक Year 2020.

Students of Biotechnology, Biodiversity, Statistics, Hindi and Microbiology presented research articles under the able guidance of their respective teachers.

All articles are checked for plagiarism and are accepted for publication by research committee of college.

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MES Abasaheb Garware College, Pune
THE SARS-COV-2 PANDEMIC: A SYSTEMATIC REVIEW

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ABSTRACT

The recent outbreak of a novel strain of Corona virus in Wuhan turned into a public health emergency of international concern. Due to non-availability of immunization and medications, conventional healthcare systems and methods are less effective. The virus is now known as the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the resulting disease is called coronavirus disease 2019 (COVID-19). Early identification of infected patients and diagnosis is critical to stop the spread of the disease. The novel SARS-CoV-2 might have experienced adaptive evolution in intermediate hosts before becoming zoonotic and infecting humans. SARS-CoV-2 is not much different from SARS regarding its clinical features. The fatality rate of SARS-CoV-2 is 2.3% which is lower than that of SARS (9.5%). It is much less than that of MERS (34.4%). This review article was written to evaluate the existing evidence and experience related to research conducted for SARS-CoV-2.

Keywords: SARS-CoV-2; Replication cycle; Pathogenesis; Treatments; structure of Covid-19; Antiviral therapy.

INTRODUCTION

The novel coronavirus 2019 emerged in Wuhan, China, in December 2019 [1] and spread across different nations in a short amount of time [2–8]. The World Health Organization (WHO) announced a name for the epidemic disease caused by 2019-nCoV on February 11, 2020, as coronavirus disease (COVID-19). The International Committee on Taxonomy of Viruses renamed the 2019-nCoV strain temporarily as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2). On 30 January 2020, the WHO declared COVID-19 as the sixth international public health emergency. Genetically, SARS-CoV-2 is more closely related to bat-SL-CoVZC45 and bat-SL-CoVZXC21 than MERS or SARS

Coronaviruses (CoVs) belong to the subfamily Orthocoronavirinae in the family Coronaviridae, Order Nidovirales. The Subfamily consists of four genera called Alpha-coronavirus (α-CoV), Betacoronavirus (β-CoV), Gammacoronavirus (γ-CoV) and Deltacoronavirus (δ-CoV) [9,10,11]. The CoV genome is an encased, positive-sense, single-stranded RNA with a size ranging between 26 kb and 32 kb. It is the largest genome of
known RNA viruses. α- and β-CoV’s infect mammals, and δ- and γ-CoVs infect birds. The SARS-CoV-2 virus has a genomic structure similar to other betacoronaviruses. Its genome contains 14 open reading frames (ORFs) encoding 27 proteins. The ORF1 and ORF2 present at 5’ terminal encodes 15 non-structural proteins crucial for virus replication. The 3’ terminal encodes structural proteins like spike protein (S), an envelope protein (E), membrane protein (M), and nucleocapsid (N). It also transcribes eight accessory proteins [12,13]. Phylogenetic tree analysis of SARS-CoV-2 shows that it is different from MERS coronavirus and it is more phylogenetically related to Bat SARS-like coronaviruses (isolated in China from horseshoe bats between 2015 and 2018) than to SARS-CoV (Table 1).[23]. This suggests an alternate viral evolutionary path from SARS and MERS CoV strain with bats as a wild reservoir [14]. Genomic comparison between SARS and SARS-CoV-2 shows that there are only 380 amino acid substitutions between the novel strain and the known SARS-like CoVs. These substitutions are largely concentrated in the non-structural protein genes. Along with these, 27 mutations have been found in genes encoding the viral spike protein S which is responsible for receptor binding and cell entry [15].

For the replication of the CoV RNA, there should be a complete transcription of the negative-strand RNA that is present at low concentrations. This is a template for genomic RNA synthesis. The conventional model for the CoV replication cycle suggests the production of sg minus-strand RNAs through a discontinuous 3’-extension step. Transcription Regulatory Sequences (TRSs) that are present upstream of (most) ORFs mediate this discontinuous step. The minus-strand RNAs serve as templates for the synthesis of complementary sg mRNAs. Generally, only the 5’ end of this sg RNA is translated. Currently, no treatment or vaccine exists for SARS-CoV-2. However, health care providers generally treat the symptoms by using oxygen therapy for patients with severe infection. For other patients such as those with acute disorders, experimental drugs and research therapeutics are being used [16,17].

**STRUCTURE OF SARS-COV-2**

The 30 kb SARS-CoV-2 genome encodes for a non-structural polyprotein known as ORF1a/b. This protein is further proteolytically cleaved to synthesize ORF3a, ORF6, ORF7, ORF8, and ORF9 [18,19,20]. The structural proteins consist of the spike (S) surface glycoprotein, the membrane (M) protein, the envelope (E) protein, and the nucleocapsid (N) protein. These are crucial for assembly and infection. The spike protein is responsible for cell tropism and interspecies transmission of CoVs. It facilitates the binding of the virus to a cell receptor and catalyzes virus entry due to membrane fusion. S is a type I trimeric
transmembrane protein that has a cleavable signal peptide at the N terminal [21]. The S domain is divided into an N terminal domain (NTD) and a C terminal domain (CTD). A structural fold similar to human galectins which are galactose-binding lectins is present at the NTD. Due to which most coronaviruses have a sugar present at the cell surface that ultimately serves as an attachment factor. The CTD binds to the host receptor angiotensin-converting enzyme 2 (ACE2). It contains two subdomains consisting of a core structure comprised of a five-stranded antiparallel β-sheet and the actual RBM. RBM determines the receptor binding specificity [22]. Identifying the contact residues between the RBD of S protein from SARS-CoV-2 and human ACE2 is useful as it tells whether this novel strain could infect other species (Table 2) [23]. To facilitate that study, Jiumeng S. et al., aligned all available ACE2 amino acid sequences with human ACE2. They emphasized the N-glycosylation motifs present near the binding site. This was possible because the attachment site of S. Human ACE2 is glycosylated at N53, N90, and N322. The site N53 is conserved in all species. “N90 is not a glycosylation site in ACE2 of a mouse, pig, N. procyonoides, raccoon, civet, ferret, fox, E. telfairi, and chicken. N322 is not a glycosylation site in ACE2 of mouse, rat, cattle, sheep, E. telfairi, and pangolin. However, ACE2 of some species contain an additional glycosylation motif in this region. Residue L79 is a potential N-glycosylation site in chicken and M82 is a potential glycosylation site in Rhinolophus sinicus, pangolin, and rat. Notably, glycosylation of residue 82 has been shown to prevent binding of S from SARS-CoV to rat ACE2.” (Jiumeng S. et al 2020.) [23, 24]. [Table 2] [23]

**PATHOGENESIS AND TRANSMISSION:**

SARS-CoV-2 rapidly invokes an immune response after it enters and replicates inside cells. It causes a cytokine storm syndrome and pulmonary tissue damage. Cytokine storm syndromes (hypercytokinaemia), are a group of disorders with symptoms ranging from uncontrolled production of pro-inflammatory cytokines to acute respiratory distress syndrome (ARDS). It may cause multiple organ failure in severe cases [26,27,28]. Among 99 SARS-CoV-2 severe cases; 17 patients (17%) had ARDS, among whom 11 (11%) deteriorated rapidly and died of multiple organ failure [29]. CD4 + T-cells and CD8 + T-cells are decreased in infected patients, and the surviving T-cells are functionally exhausted [30], which leads to a significantly lowered immune response. ARDS decreases immunity and secondary infection further worsens the condition of respiratory failure [31].

For an animal to human transmission of SARS and MERS, the major route was reported to be direct contact with intermediate hosts. Consuming milk, uncooked meat was also considered.
a major transmission route [32]. The intermediate hosts of SARS-CoV-2 are most likely wild animals like pangolins. This is because only they are a probable intermediate reservoir and are sold in Wuhan, China for consumption [33]. One of the leading factors for the human to human transmission of SARS-CoV-2 is a close contact of people (within 1–2m). It also spreads through respiratory droplets produced when an infected person coughs or sneezes in close proximity to a non-infected person, within a range of about 2m [34,35,36]. The infection can also spread by touching inanimate objects on which the aforementioned droplets fall, followed by contact with eyes or mouth. It was reported that the virus can remain viable and infectious for hours in the air and for days on surfaces [37]. Van Doremalen et al. (2020) studied the viability of SARS-CoV-1 and SARS-CoV-2 in aerosols and tests were also conducted on various surfaces, such as plastic, stainless steel, copper, and cardboard. The viability of the coronaviruses in aerosols, plastic, stainless steel, copper, and cardboard was found to be 3, 72, 72, 4, and 24 h respectively.

**INCUBATION PERIOD**

The incubation period is the period between exposure and appearance of the symptoms to a pathogenic organism. During this period, the organism multiplies in the host, reaches a specific threshold number. After this limit is reached the symptoms start to present themselves. The incubation period of SARS-CoV-2 is considered to be between two to fourteen days, with an average of five days. It was observed that 97% of people exposed to SARS-CoV-2 showed symptoms within 11.5 days of exposure [38,39]. It has been reported that asymptomatic COVID-19 patients during their incubation period can effectively transmit SARS-CoV-2 [40, 41]. This is in contrast to SARS-CoV because most SARS-CoV cases cannot infect susceptible persons during the incubation period.

**LABORATORY DIAGNOSIS:**

**Hematology diagnosis:** In the early stage, the WBC count is normal or decreased, accompanied by a decrease in lymphocyte count. It is of significant concern if the absolute lymphocyte count is < 0.8 ×10^9/L or the CD4 + and CD8 + T-cell counts are extremely low. It is advised to re-check the CBC report every 3 days [42].

**Molecular diagnosis:** Real-time PCR (RT-PCR) can be used to analyze the samples from suspected SARS-CoV-2 patients. The samples are collected from the upper respiratory tract (nasopharyngeal and oropharyngeal), lower respiratory tract (expectorated sputum, endotracheal aspirate or bronchoalveolar lavage), Blood and feces can also be diagnosed by
RT-PCR [43]. The CRISPR-based SHERLOCK (Specific High-sensitivity Enzymatic Reporter UnLOCKing) technique allows the detection of RNA or DNA from clinically relevant samples. It is a convenient, portable, and ultrasensitive detection method. Recombinase-mediated polymerase assays are used to set up the SHERLOCK technique. It is a time-efficient method as the time required for the setup is around 15 minutes and the turnaround time is approximately an hour. Based on the RNA sequence of the novel coronavirus, two guide RNAs have been developed. One recognizes the S gene of the new coronavirus and the other recognizes the Orf1ab gene [44, 45].

**General treatment:** Patients with a mild infection may have no positive signs, and severe patients may exhibit shortness of breath, weak breath, and dull percussion [46]. Suspected or confirmed patients must immediately undergo chest radiography and a chest CT scan. In the early phase of the disease, the peripheral region of the lung in a chest radiography image shows interstitial changes and multiple small plaques. As the disease progresses, the plaques deteriorate and are prominently distributed in the middle and outer zones of the lung. This is accompanied by multiple infiltrating shadows and/or ground-glass opacities. A fibrous stripe may also appear when the condition improves [47, 48].

**TREATMENTS:**
Antiviral therapy Lopinavir/ritonavir was discovered as a protease inhibitor that interferes with the replication and synthesis of the human immunodeficiency virus (HIV). It caused the production of immature and non-infectious virus particles [47,48,49]. It has been observed that ritonavir and lopinavir bind to the endopeptidase C30 of SARS-CoV-2 protease [50]. There is much evidence to support the studies that treatment with lopinavir/ritonavir alone or in combination with other antiviral drugs improve the health of patients with severe infection with SARS or MERS [47, 51,52,53]. Lopinavir/ritonavir may have a beneficial effect against SARS-CoV-2 as phylogenetically, it is similar to these two viruses.

Chloroquine is a commonly used antimalarial drug and has been reported as a potential broad-spectrum antiviral drug [54, 55]. Wang et al. found that chloroquine effectively suppresses the recently emerged novel CoV (SARS-CoV-2) *in vitro* [56].

The nucleoside analog of Remdesivir (GS-5734) was reported to inhibit SARS-CoV and MERS-CoV *in vivo* [57]. An *in vitro* study says that remdesivir was effective in blocking SARS-CoV-2 infection at low-micromolar concentrations [58].

Arbidol (umifenovir) is an antiviral drug used against influenza infection. It is widely used in Russia and China. Arbidol and arbidol mesylate was reported to cause an inhibitory effect on
reproducing SARS-CoV \textit{in vitro} [60]. A retrospective cohort study, case reports, and case series reported that arbidol alone or combined with antiviral drugs produced satisfactory results against the symptoms of SARS-CoV-2 [59,60,61]. Currently, many randomized clinical controlled trials are being carried out studying the efficacy of Arbidol on COVID-19 pneumonia in China.

Interferon-alpha (IFN \(\alpha\)) is a member of the family of type I IFNs. It is an important factor in host resistance to viral infection. It directly interferes with viral replication thereby suppressing it. It also stimulates innate and adaptive immune responses. \textit{In vitro} experiments reported that it effectively inhibits the replication of SARS-CoV [61,62].

**CONCLUSION**

SARS-CoV-2 emerged as a pandemic and wreaked havoc across the globe. The conventional healthcare system was not sufficiently effective in combating its symptoms. Drug discovery against SARS-CoV-2 is a challenging process but is vital for human life. It is very important to follow the WHO guidelines to prevent the spread of COVID-19 until acceptable drugs and vaccines have been developed. As, many strains of coronaviruses are infecting mammals, it is evident that there exists a high degree of plasticity and mutation among the genoe of CoVs. The probabilities for adaptive mutations increase due to the large size of the CoV genome. This occurs because it is relatively easy for the spike protein find various cellular receptors for viral attachment. These features are likely the cause of this alarming propensity of CoVs for host-species expansion. Phylogenic trees show the similarities and dissimilarities of SARS-CoV-2 from known coronaviruses. No clinical treatment yet exists for combating SARS-CoV-2. However, researchers are working to find new therapeutics to effectively treat the global pandemic. Necessity is the mother of all inventions. And now the world is in the dire need of global efforts and scientific exchange of knowledge. Now more than ever, the future is dependent on the strategies of countries and world leaders.

**ACKNOWLEDGEMENTS**

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<th>Intermediate host</th>
<th>Receptor</th>
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<td>Unknown</td>
<td>Angiotensin-converting enzyme 2 (ACE2)</td>
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<td>Dipeptidyl peptidase 4 (DPP4)</td>
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Table 2. Some amino acids in ACE2 affect binding to S of 2019-nCoV are depicted for various species in table 2. The S binding site of ACE2 from macaque and chimpanzees is identical to human ACE2. ACE2 from other species revealed eleven (chicken), nine and ten (rodents), or only three (cat) amino acid differences compared with human ACE2. Of special interest are ACE2 proteins from farm animals and a pet cat, since they might become another possible reservoir for 2019-nCoV. ACE2 from pig contains six exchanges, but they are mostly located at the periphery of the binding site (Figure 4B). N90T causes the loss of the glycosylation site. E329 forms a salt bridge with R426 in S of SARS-CoV, but S of 2019-nCoV forms a salt bridge with another residue (D30) in ACE2. Thus, the exchange of E329 by N in porcine ACE2 might affect binding to S of SARS-CoV, but not to S from 2019-nCoV. A similar pattern emerges for amino acid differences between human and cattle ACE2 (Figure 4C) and cat ACE2 (Figure 4D). The few exchanges are also located peripheral to the core of the binding region and thus their exchange might not represent a large obstacle for infection of cells from these species with 2019-nCoV. [23]
COVID-19: AWARENESS AND SCIENTIFIC ASPECT

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ABSTRACT:
In early 2020, after a December 2019 outbreak in the Hubei province of China, the World Health Organization identified SARS-CoV-2 as a new type of coronavirus. On March 11, 2020 COVID-19 was considered as Pandemic by the World Health Organization (WHO). More than 187 countries and territories, including the USA, France, Italy, and many other countries are affected due to Coronavirus. On 7th January 2020, the origin of the novel Coronavirus was confirmed. It was reported that China’s ‘Wet-Market’ is where the virus affected the workers. The virus shows its effect in 2-14 days. Coronaviruses are zoonotic (transmitted between animals and humans). The respiratory tract is affected the most with other symptoms as fever, cold, cough, and fatigue. rRT-PCR and chest CT-Scan were reported to be the first diagnostic tools for novel Coronavirus (nCoV). The therapeutic drugs, such as Remdesivir, Lopinavir, and Ritonavir (with/without combination) were given to treat the patients, which showed effective results to some extent. Plasma Therapy is under experimental trials, which can be an effective treatment. Israel’s Institute for Biological Research Institute (IIBRI) claims to have developed an antibody that can neutralize the viral proteins. The scientists and the researchers are working together to make the antibody patent and commercially available to the whole world. Several vaccines have been suggested but some are ineffective against viruses. WHO has provided some illustrations to aware of people against SARS-CoV-2. It shows how to protect ourselves and prevent the spreading of SARS-CoV-2 through these images.

INTRODUCTION:
Coronavirus disease 2019 (COVID-19) is an infectious disease, caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). SARS-CoV-2 is one of seven types of coronavirus, including the ones that cause severe diseases like Middle East Respiratory Syndrome (MERS) and Severe Acute Respiratory Syndrome (SARS). It is observed that the genome sequence of SARS-CoV-2 is similar, but distinct from, those of two other coronaviruses which were responsible for the large-scale outbreaks in the past (2003-4), SARS-CoV; about 79% sequence identity and MERS-CoV; about 50% [3].

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And all are Betacoronavirus. The outbreak quickly spread around the world and now it is an ongoing pandemic. A 55-year-old from Hubei province could have been the first person to have contracted the viral infection on November 17 of 2019 and it was reported to emerge from the ‘wet-market’ in Wuhan, China [12]. Cases rapidly began to spread to more than 187 countries and territories, including community transmission in countries like the United States, Germany, France, Spain, Japan, Singapore, South Korea, Iran, Italy, and India.

As of May 8, more than 3.9 million active cases of SARS-CoV-2 and 271,415 (17%) deaths and 1,355,788 people recovered or discharged (83%). In India, more than 56,000 cases are confirmed (with the highest cases in Maharashtra – more than 14,500) and 1,895 deaths, whereas 16,867 cases are recovered or discharged [13]. SARS-CoV-2 likely to be originated in bats but it might have been amplified in an intermediate host. Earlier work showed that it can use angiotensin-converting enzyme 2 (ACE2) from bats, civet cats, swine, cats, ferrets, non-human primates (NHPs), and humans as a receptor [4]. Another study shows that Pangolins can be a potential amplifying host [3].

**Symptoms of COVID-19:**

The disease causes a respiratory tract infection and it affects sinuses, nose, and throat or lower respiratory tract organ windpipe and lungs. It spreads in the same way as other coronaviruses do, i.e., mainly through person-to-person contact. Infection ranges from mild to serious (81%- Mild symptoms, 14%- severe symptoms, 5%-critically ill). The other symptoms observed in patients are Fever, Coughing, Shortness of breath, Fatigue, Chills, Body aches, Headache, Sore throat, Loss of smell or taste, Nausea, and Diarrhea. And now most of the cases are asymptomatic.

Scientists have observed that this virus can lead to pneumonia, respiratory failure, septic shock, and death. Many COVID-19 complications thought to be caused by a condition known as Cytokine Release Syndrome or Cytokine Storm [5]. If this happens then, the infection will trigger the immune system to flood through the bloodstream with the inflammatory proteins called cytokines. They can kill tissue and damage the organs. The incubation period for COVID-19 is 2-14 days (typically 5th day) for infection.

The virus spreads between people during close contact, often via small viral droplets produced by coughing, sneezing, and talking. The viral droplets usually fall to the ground or onto surfaces rather than remaining in the air for over long distances. People may also become infected by touching a contaminated surface and then touching their face [5].
surfaces, the amount of virus declines over time until it is insufficient to remain infectious, but it may be detected for hours or days. It is observed that it is most contagious during the first three days after the onset of symptoms, although it may before symptoms appear or in later stages of the disease.

**Coronavirus Risk Factors:**

The scientists say that anyone can get COVID-19, most infections are usually mild, specifically in children and young adults, older people are at high risk. But if we are not in an area where COVID-19 is spreading, have not traveled from an area where it is spreading, and have not been in contact with the person who has it, our risk of infection is low.

**Method for Diagnosis:**

The standard method of diagnosis is by Real-Time Reverse Transcription Polymerase Chain Reaction (rRt-PCR) from a nasopharyngeal swab.

Chest CT imaging may also be helpful for diagnosis in individuals where there is a high suspicion of infection based on symptoms and risk factors but these guidelines do not recommend using it for routine screening.

**RT-PCR and CT-Scan:**

The CT-scan images showed temporal changes of COVID-19 pneumonia with reference to the time of onset of symptoms. The study also showed that the asymptomatic group of patients showed early CT changes, and it was a familial cluster with COVID-19 pneumonia [1].

Some studies state that positive RT-PCR results for SARS-CoV-2 in the absence of CT changes, or if the CT findings are abnormal with initial false-negative RT-PCR results. As the epidemic evolves, various presentations of COVID-19 pneumonia are observed, with symptomatic patients showing concordant CT and RT-PCR findings. These finding suggests that CT is sensitive to detect COVID-19 pneumonia, even in asymptomatic individuals, and could be considered as a screening tool together with RT-PCR. CT might be a particularly important screening tool in the small proportion of patients who have false-negative RT-PCR results.

**Testing for COVID-19:**

Two kinds of tests are available for COVID-19: viral tests and antibody tests.
1. Firstly, the viral test tells us if we have an infection currently.
2. Then the antibody test tells us if we had a previous infection.
3. Only the antibody test may not be able to show if we have a current infection, because it can take 1-3 weeks after infection to make antibodies.

The results shows that, if tested positive for COVID-19 by a viral test, then protective steps should be taken if sick or caring for someone.

If tested negative, then the person is probably not infected at the time of sample collection. This does not mean the person will not get sick and the test only means that the person did not have COVID-19 at the time of testing [11].

**Therapeutics for SARS-CoV-2 infections:**

Clinical trials with the nucleotide analog Remdesivir and protease inhibitors as well as other treatment options are ongoing in China and the United States, and in many other countries. Remdesivir drug works against coronaviruses, as they are closely related to SARS-CoV-2 in animal models; this also works against the related MERS-CoV.

Remdesivir was also used for the treatment of Ebola infections in humans (less successful than other treatments). The mechanism of Remdesivir, as a nucleotide analog is not clear, but it is likely to terminate the RNA synthesis, which leads to the incorporation of mutagenesis. A combination of the two licensed HIV inhibitors, Lopinavir, and Ritonavir, is also being tested in clinical trials [8]. In 2003-2004, this combination was used for the treatment of SARS-CoV-1. Lopinavir drug’s mechanism of action is not clear, but it is likely to inhibit one or more coronavirus proteases.

Other treatment options with ongoing or planned clinical trials include doing recombinant human ACE2 to neutralize the virus and prevent lung damage and using the antiviral Arbidol, a fusion inhibitor. The results will be out within months for these trials and if Remdesivir and/or Lopinavir plus Ritonavir show effectiveness against coronavirus, potentially they could be used to treat the corona patients [9].

**Plasma Therapy:**

The ICMR has initiated a multi-centre clinical trial, and they named it as “A Phase II, Open-Label, Randomized Controlled Trial to Assess the Safety and Efficacy of Convalescent Plasma to Limit COVID-19 Associated Complications in Moderate Disease (PLACID Trial)”. According to the Scientists, the plasma therapy is at its experimental stage and this
procedure may take time to fully implement for the COVID-19 patients. It is based on the concept of passive immunity, where antibodies of some disease developed in a person are used for treating others patients. As of May 4, the ICMR has approved 21 institutions in the PLACID trial [7].

As COVID-19 is a novel strain of virus so, there is no artificial antibody available to treat this disease. The people who have recovered from coronavirus might have developed antibodies in their body, which can be a benefit for others. Vaccination may take time to develop, but this therapy can treat the patients, by using these antibodies by plasma therapy.

**Monoclonal antibodies:**

Israel's Institute for Biological Research Institute (IIBRI) is no more in the race for developing a potential treatment for the coronavirus disease. The scientists have identified an antibody that can neutralize the SARS-CoV-2 in vitro or from the outside of a living organism. The team of scientists had already completed the developmental phase and now they are preparing for the mass-production of this potential treatment, after procuring a patent for their discovery.

They showed how the antibody attacked the virus in a monoclonal way and how the antibody neutralizes it. The Monoclonal antibodies (MAbs) are produced in the lab and these molecules are engineered to serve as a substitute for antibodies that can restore, enhance, or mimic the immune system's attack on cancerous cells. These are designed to bind to the antigens that are numerous present on the surface of the cancerous cells than the healthy cells.

*Statement from the Israel Ministry of Defense:*

1. The antibody produced is monoclonal, new and refined and it contains exceptionally low levels of harmful proteins.
2. The antibody produced is able to successfully neutralize the coronavirus.
3. This antibody was specifically tested on the antagonistic coronavirus [6].
Overview of Potential SARS-CoV-2 Vaccine Platforms:

Fig. 1  The structure of a coronavirus particle is depicted on the left, with the different viral proteins indicated. For developing a vaccine, S protein is the major target. In SARS-CoV-1 and SARS-CoV-2, this protein interacts with the receptor ACE2, and antibodies targeting the spike can interfere with this binding, thereby neutralizing the virus [2].

Vaccine Production Platforms and Technologies for SARS-CoV-2:

Fig.2 shows several vaccines for SARS-CoV-1 which were developed and these were tested in animal models, also including the recombinant S-protein-based vaccines, whole inactivated vaccines, attenuated vaccines and vector- based vaccines. Most of these vaccines protect animals from challenge with SARS-CoV-1, but not necessarily induce sterilizing immunity. This also shows advantages and disadvantages of vaccines [2].
The following illustrations are developed by WHO, to advise people how to protect ourselves as well as others from the spreading of COVID-19:

### Table 1

Overview of Vaccine Production Platforms and Technologies for SARS-CoV-2

<table>
<thead>
<tr>
<th>Platform</th>
<th>Target</th>
<th>Existing, Licensed Human Vaccines Using the Same Platform</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>RNA vaccines</td>
<td>S</td>
<td>No protein</td>
<td>No infectious virus needs to be handled, vaccines are typically immunogenic, rapid production possible.</td>
<td>Safety issues with reactogenicity have been reported.</td>
</tr>
<tr>
<td>DNA vaccines</td>
<td>S</td>
<td>No protein</td>
<td>No infectious virus needs to be handled, easy scale up, low production costs, high heat stability, tested in humans for SARS-CoV-1, rapid production possible.</td>
<td>Vaccine needs specific delivery devices to reach good immunogenicity.</td>
</tr>
<tr>
<td>Recombinant protein vaccines</td>
<td>S</td>
<td>Yes for baculovirus (influenza, HPV)</td>
<td>No infectious virus needs to be handled, adjuvants can be used to increase immunogenicity.</td>
<td>Global production capacity might be limited. Antigen and/or epitope integrity needs to be confirmed. Yields need to be high enough.</td>
</tr>
<tr>
<td>Viral vector-based vaccines</td>
<td>S</td>
<td>Yes for VSV (Ebola), but not for other viral vectored vaccines</td>
<td>No infectious virus needs to be handled, excellent preclinical and clinical data for many emerging viruses, including MERS-CoV.</td>
<td>Vector immunity might negatively affect vaccine effectiveness (depending on the vector chosen).</td>
</tr>
<tr>
<td>Live attenuated vaccines</td>
<td>Whole</td>
<td>Yes</td>
<td>Straightforward process used for several licensed human vaccines, existing infrastructure can be used.</td>
<td>Creating infectious clones for attenuated coronavirus vaccine seeds takes time because of large genome size. Safety testing will need to be extensive.</td>
</tr>
<tr>
<td>Inactivated vaccines</td>
<td>Whole</td>
<td>Yes</td>
<td>Straightforward process used for several licensed human vaccines, existing infrastructure can be used, has been tested in humans for SARS-CoV-1, adjuvants can be used to increase immunogenicity.</td>
<td>Large amounts of infectious virus need to be handled (could be mitigated by using an attenuated seed virus). Antigen and/or epitope integrity needs to be confirmed.</td>
</tr>
</tbody>
</table>
**COVID-19 वार्ता**  

*YEAR 2020*

*(Image courtesy by World Health Organization)*

---

**Wash your hands**

Wash your hands with soap and running water when hands are visibly dirty.

If your hands are not visibly dirty, frequently clean them by using alcohol-based hand rub or soap and water.

---

**Protect yourself and others from getting sick**

Wash your hands:
- after coughing or sneezing
- when caring for the sick
- before, during and after you prepare food
- before eating
- after toilet use
- when hands are visibly dirty
- after handling animals or animal waste

---

**Protect others from getting sick**

Avoid close contact when you are experiencing cough and fever.

Avoid spitting in public.

If you have fever, cough and difficulty breathing seek medical care early and share previous travel history with your health care provider.

---

**Protect others from getting sick**

When coughing and sneezing:
- cover mouth and nose with flexed elbow or tissue
- throw tissue into closed bin immediately after use
- clean hands with alcohol-based hand rub or soap and water after coughing or sneezing and when caring for the sick

---

**Should I avoid shaking hands because of the new coronavirus?**

Yes. Respiratory viruses can be passed by shaking hands and touching your eyes, nose and mouth.

Greet people with a wave, a nod or a bow instead.

---

**How should I greet another person to avoid catching the new coronavirus?**

To prevent COVID-19 it is safest to avoid physical contact when greeting.

Safe greetings include a wave, a nod, or a bow.
These illustrations show how to protect ourselves during the lockdown period while staying at home:

Is wearing rubber gloves while out in public effective in preventing the new coronavirus infection?

No. Regularly washing your bare hands offers more protection against catching COVID-19 than wearing rubber gloves. You can still pick up COVID-19 contamination on rubber gloves. If you then touch your face, the contamination goes from your glove to your face and can infect you.

How should I wash fruit and vegetables in the time of COVID-19?

Wash them the same way you would in any other circumstance. Before handling them, wash your hands with soap and water.

Then, wash fruit and vegetables thoroughly with clean water, especially if you eat them raw.

These illustrations show how to handle things in the time of COVID-19:

How can I grocery shop safely in the time of COVID-19?

When grocery shopping, keep at least 1-metre distance from others and avoid touching your eyes, mouth and nose. If possible, sanitize the handles of shopping trolleys or baskets before shopping.

Once home, wash your hands thoroughly and also after handling and storing your purchased products.

There is currently no confirmed case of COVID-19 transmitted through food or food packaging.

Can COVID-19 be spread through coins and banknotes?

There is currently no evidence to confirm or disprove that COVID-19 virus can be transmitted through coins or banknotes. However, respiratory droplets expelled from an infected person can contaminate and persist on surfaces. Wash your hands regularly and thoroughly after touching any frequently-touched surface or object, including coins or banknotes. Avoid touching your eyes, mouth and nose, if your hands are not cleaned.

How should I wash and dry clothes, towels and bed linen, if someone in my household is a suspected or confirmed COVID-19 patient?

- Wash the patient's clothes, towels and bed linen separately.
- If possible, wear heavy-duty gloves before handling them.
- Never carry soiled linen against your body; place soiled linen in a clearly labelled, leak-proof container (e.g., bag, bucket).
- Scrape off solid excrement (e.g., faeces or vomit) with a flat, firm object and dispose of in the patient’s toilet before putting linen in the designated container. Place the excrement in a covered bucket to dispose of in the toilet, if this is not in the patient’s room.
- Wash and disinfect linen: Machine wash at 60-90°C with laundry detergent. Alternatively, soak linen in hot water and soap in a large drum, using a stick to stir, avoiding splashing. If hot water is not available, soak linen in 0.05% chlorine for approximately 30 minutes. Rinse with clean water and let linen dry in the sunlight.
- Do not forget to wash your hands at the end of the process.
This illustration shows tips of Home care for people with suspected or confirmed COVID-19; to take care of ill people.

MES ABASAHEB GARWARE COLLEGE, PUNE
This illustration shows tips of Home care for people with suspected or confirmed COVID-19; to take care for all the members of the household.

Wash hands with soap and water regularly, especially:
- after coughing or sneezing
- before, during and after you prepare food
- before eating
- after using the toilet
- before and after caring for the ill person
- when hands are visibly dirty

Avoid unnecessary exposure to the ill person and avoid sharing items, such as eating utensils, dishes, drinks and towels.

When coughing or sneezing, cover mouth and nose with flexed elbow or use a disposable tissue and discard immediately after use.

Monitor everyone’s health for symptoms such as fever, cough and if difficult breathing appear, call your health care facility immediately.
This illustration shows tips of Home care for people with suspected or confirmed COVID-19; to take care of the caregivers.

RESULT AND CONCLUSION:
The pandemic has severely caused lives as well as the economy also. To prevent the spreading of Coronavirus Italy, Spain and France were the 1st countries to initiate lockdown. USA is the most affected country with more than 1.9 million cases worldwide. In India, the lockdown was started from 25th March 2020 for 21 days. But it extended for another 19 days till 14 April. Then due to an increase in COVID-19 cases, the lockdown was further extended till 3rd May. The Honourable PM Modi extended the lockdown till 17th of May. The highest numbers of cases are in Maharashtra, following Gujarat. There is no vaccine available for COVID-19 till now but some effective treatments are given to the patients. Researchers and Scientists are working 20 hours a day to make it possible. Some treatments are experimentally proved effective against COVID-19, to some extent only such as Monoclonal Antibodies, as claimed by scientists of IIBRI.

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COVID – 19: ORIGIN OF VIRUS, VIRUS HOST INTERACTION, SYMPTOMS, PRECAUTIONS AND CURRENT TREATMENT SCENARIO.

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ABSTRACT:

Coronavirus is a single stranded positive sense RNA genome. The length of the genome is largest among all virus ~ 32kb. All CoVs share a common genome organization where the gene consists of 5'-two thirds of the genome and is comprised of two overlapping open reading frames. The structural gene region, which covers the 3’ third of the genome which encodes set of viral structural proteins Spike (S), Envelope (E), Membrane (M) and Nucleocapsid. [2] (Hulda R. Jonsdottir and Ronald Dijkman: Coronavirus and the human airway: a universal system for virus - host interaction studies. Virology Journal 24 2016).

Origin of the virus: The coronavirus disease 19 (COVID - 19) from coronaviridae family is highly transmittable and pathogenic viral infection. It is related to severe acute respiratory syndrome (SARS) like bat viruses therefore bats could be the possible primary reservoir which emerged in Wuham, China and spread around the world.[1](Muhammad Adnan Shereen, Suliman Khan, Abeer Kazmi, Nadia Bashir, Rabeea Siddique: COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses Journal of Advanced Research 24 2020 91–98).
The virus host interaction proceeds in the following steps:

1. Attachment of Spike (S) protein of the virion to the host cell.

2. Uncoating results in the formation of corona RNA (+)

3. Corona RNA (+) undergoes translation; the replication gene encodes rep1a and rep1b which express two coterminous polyproteins pp1a and pp1ab.

4. In replication and transcription steps, the viral RNA synthesis follows the translation and assembly of the viral replication complex.

5. In assembly and release steps the viral structural protein Spike (S), Envelope (E) and Membrane (M) translated and inserted into the ER these proteins move along the secretory pathway into the ER-Golgi intermediate compartment.

**Symptoms:**

1. The most common symptoms of COVID-19 are fever, tiredness and dry cough.

2. Some people become infected but don't develop any symptoms and don't feel unwell.

   People generally develop signs and symptoms, including mild respiratory symptoms and fever on an average of 5-6 days after infection (incubation period 5-6 days, range 1-14 days).
3. Older people and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease are more likely to develop serious illness. [3](www.who.int)

Precautions:

1. Wash hands frequently with alcohol based hand rub or soap and water.
2. Wear mask and dispose of it properly.

Current treatment scenario:

1. Using available preliminary data, the median time from onset to clinical recovery for mild cases is approximately 2 weeks and in 3-6 weeks for patients with severe or critical disease.
2. Vaccine developed by CanSino Biological Inc and Beijing Institute of biotechnology entered in human trial stage.
3. India's Zydus Cadila, Serum Institute and Bharat Biotech are among the global firms working on COVID - 19 vaccine. [5](www.businesstoday.in)
4. Plasma therapy trials have already started in some states like Maharashtra, Uttar Pradesh and Madhya Pradesh on a very small scale involving only one or a couple of patients.
5. The use of hydroxychloroquine (HCQ) tablets as a preventive measure for frontline healthcare workers and on patients and their contacts also has started in some states. [6](timesofindia.indiatimes.com)

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AN OVERVIEW OF COVID PANDEMIC AND ITS RELATION WITH ANIMAL EXPLOITATION

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The worldwide pandemic of COVID-19 is spreading at an unprecedented rate and this is causing serious concerns to mankind. According to WHO, as of 14th May 2020, 42,58,866 cases are confirmed around the world, spreading across 216 countries. First case of the infection was reported in Wuhan city of Hubei province in China in December 2019, with pneumonia like symptoms. On 11th March, 2020, WHO characterized COVID-19 as a global pandemic.

Though rapid research is being carried out to trace the origin, causes and cure for the disease; researchers have not found any conclusion yet. Various social media posts are spreading rumours & misinformation, especially about Bats and Pangolins. In this difficult situation, it becomes our responsibility to believe in science. In this article we tried to focus on the scientific facts related to COVID-19.

Corona Virus Disease or COVID-19 has emerged through infection of novel corona virus SARS-CoV-2. This virus is considered to be similar with SARS-CoV. This virus was responsible for SARS (Severe Acute Respiratory Syndrome) outbreak in the year 2002. Coronaviruses belong to a large family of viruses called coronaviridae, named so after the crown like spikes on their surface. There are thousands of coronaviruses circulating in animals but they can mutate and infect humans in a phenomenon called "spill over event". Out of 7 known human coronaviruses, 3 may cause severe illness and fatalities including SARS-CoV, SARS-COV-2 and MERS-CoV. Scientists are assessing the previous coronavirus outbreaks to understand mechanism of infection and to develop a vaccine for the SARS-COV-2. (1, 2)
The zoonotic origin of SARS-CoV-2 is verified but exact origin is not confirmed yet. Scientists anticipate that SARS-CoV-2 might have originated in bats but they strongly suggest that the transmission is not direct.

Receptor Binding Domain (RBD) in the spike proteins of SARS-CoV-2 binds with the cell receptor ACE2 with high affinity. Genomes of corona virus found in horseshoe bat (RaTG13) and SARS-CoV-2 show about 96% similarity, but the structure of RBDs are different in both. Hence it is not possible for the Bat coronavirus to directly start infecting human cells. Corona viruses in Pangolins resemble nearly 85.5-92.4% with SARS-CoV-2 in DNA and their RBDs show similarity. But In case of pangolins, the resemblance in DNAs is not sufficient enough to conclude that Pangolins are host animals. (3-7)

As of now, researchers assume that bats were the original host of the coronavirus which underwent recombination with the pangolin coronaviruses, resulting in the novel SARS-COV-2 virus which was capable of infecting humans. This virus transmitted into the body of humans through the consumption of pangolin meat or other associated animals kept in the crowded markets on Wuhan.

Pangolins have been one of the most trafficked mammal in the world. Their scales and blood are believed to have medicinal properties and their flesh is considered a delicacy in some parts of Southeast Asia. Back in 2016, the international trade in pangolins was entirely banned by the 183 nations that signed up to the Convention on the International Trade in Endangered Species (Cites). However, so far this does not seem to have had any effect on the pangolin trade. (8)

After all the fingers pointed towards the wildlife trade in china, the Chinese government lurched into action. On 24 February, a ban was announced by China on the trading and consumption of wild animals, including the pangolin which came into action immediately. (9) Bats and pangolins play a crucial role in balancing the ecosystem. Bats and Pangolins provide enormous benefits like pollination, seed dispersal and pest control which benefits agro economics thereby contributing to region’s food security and our health. Unfortunately these benefits have not been given enough recognition and this is leading to extinction of these animals, especially Pangolins. Widespread trafficking of Pangolins for their scales and meat, and hunting of bats for their perceived medical properties has led to drastic decline in their numbers. This in turn is disrupting the ecosystem functioning and causing alterations in the life sustaining ecosystem good and services. Researchers have for a long time utilised the natural world and its resources for obtaining drugs, antibiotics, vaccines and other
components of medical importance. Yet there is plethora of undiscovered uses of these natural resources. Anthropogenic activities and human interventions have already resulted in the decline of many species animals and plants. If this continues, humans will not only lose out on biodiversity, but will also lose out on potential new drug sources.

Wildlife trade has turned its roots from local barter to major international routes and much of it is conducted illegally. Some global estimates indicate about 40,000 primates, 4 million live birds, 640,000 live reptiles, and 350 million live tropical fish are a victim of this trade. Live wildlife markets in China trade in exotic wild animals such as masked palm civets, ferret badgers, barking deer, hedgehogs, different species of reptiles etc.as well as domestic animals like dogs, cats, and rabbits. Religious myths and customs about medicinal and superstitious use of wildlife keeps the flow of trade illegally under the blinders even after the ban government’s exercise. In Amazon basins, the wildlife meat consumption ranges from 67 to 164 million kilograms annually of which mammals form a significant part. This trade and consumption of wild animals has led to increase in emergence of novel zoonotic infections in humans. Even the origin of HIV and Ebola diseases is likely linked to human consumption of nonhuman primates. (10)

These increased rate of zoonotic infections in the recent years serves as a much needed warning to humans. Human greed and rampant exploitation of animals and natural resources has led to disturbances in the existing natural environments of the animals and has expedited the rate of mutations in the microbial fauna. Strong measures should be taken to ensure such pandemics will not wreak havoc in the future. Cooperation between countries to curb illegal trading, strengthening laws to protect wildlife and respecting nature is the only way ahead for us.

References:-


BATS AND VIR‘US’

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ABSTRACT
Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is the pathogen that causes COVID 19. SARS-CoV-2 is classified under coronavirus. Multiple species of coronaviruses infect poultry, livestock and humans. It is seen that these viruses can jump from animal to animal and when virus jumps from other animals to human, however bats rarely get sick from viruses, they carry viruses which may cause serious disease in human beings. It is due to their immune system which has conducts an Interferon Pathway.

Keywords: Bats, interferon pathway, SARS-CoV-2

INTRODUCTION:
COVID-19 outbreak was identified in Wuhan, China in December 2019. It began in Seafood Market of Wuhan and was further transmitted through respiratory droplets and contact. Since then it has infected more than 3,807,852 people worldwide. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is the pathogen that causes COVID 19. SARS-CoV-2 is classified under coronavirus. Multiple species of corona viruses infect poultry, livestock and humans. It is seen that these viruses can jump from animal to animal and when virus jumps from other animals to human it is said to be zoonotic transmission. As bats rarely get sick from viruses, they carry which may cause serious disease in human beings, such as insect eating bats may have been source of Ebola outbreak in 2014-16 in West Africa and Egyptian fruit bats (Rosettus aegyptiacus) harbour Marburg virus. Similarly, coronaviruses may have jumped from bats via other animals to humans (SARS outbreak, 2003) and it is likely that novel coronavirus may have originated in bats.

Source: Google: Structure of Coronavirus
CLASSIFICATION OF CORONA VIRUSES

Coronaviruses are divided into three groups, alpha coronavirus (group 1), beta coronavirus (group 2), gamma coronavirus (group 3). They are enveloped, single stranded, positive sense RNA viruses. Their genome is of 25 to 32 kb. There are total 7 coronaviruses that infect human beings out of which SARS-CoV, MERS-CoV and SARS-CoV-2 have caused major outbreaks. They cause acute and chronic respiratory diseases in humans. Common symptoms include fever, dry cough and tiredness. Due to first line of defence in mammals common symptoms are observed. First line of defence are physical barriers and chemical barriers, such as skin, mucus, fever, stomach acid and tears. Second line of defense is based on action of phagocytic cells such as macrophages, neutrophils. Third line of defense is where antibodies come into play and it is an antigen specific response. Based on a study by Meng-Yuan Li and colleagues, coronavirus also has the ability to infect enteric, hepatic and central nervous systems. The coronavirus shows spikey glycoproteins on the surface which resembles the structure of crown, ‘corona’ means crown in Latin, which gives it the name coronavirus. Entry of the virus into host cell is mediated by these spikes and it is able to cross lines of defence causing illness in mammals. SARS-CoV-2 uses angiotension – converting enzyme (ACE-2) as a cell receptor to invade human cells. There is significant correlation between ACE-2 expression levels and CD 8+ T cell enrichment levels, B cells and Natural Killer cells. It further triggers cytokines and chemokines which alert the immune system. However, cytokines cause inflammation as well in respiratory tract and production of mucus. When the infection worsens, the air sacs (alveoli) infected there is difficulty in breathing causing shortness of breath. Therefore, response of the immune system to entry of virus results in severe acute respiratory syndrome in human beings.

HOSTS OF CORONA VIRUS: BATS

Among the animals which are hosts of coronaviruses, diverse population is seen in bats and birds. Coronavirus belonging to group 1 and group 2 are present in bats. A sample taken from patient infected by coronavirus in Wuhan city, on genetic sequencing, showed 96% match with coronavirus found in Horseshoe Bats (Rhinolophus spp) in southwest China. Bats make great natural incubators of these viruses due to their species diversity, ability to fly, environmental pressure, habits of roosting and flocking.
Bats roost in crowded colonies. Members of different species tend to share caves. Under these circumstances they can easily pass viruses interspecies. They have lifespan of approximately 30 years. It is a long duration to be infected and shed the virus through saliva, faeces and urine. Linfa Wang, studies bat viruses at Duke NUS Medical School, Singapore, says it seems bat have developed special immune system to deal with stress of flying. During flight, temperature of the body of a bat rises over 37 degree Celsius and the heart rate surges to more than 1000 beats per minute. As in most mammals such heightened response would trigger death; bats seem to have adapted to the stress, where system doesn’t overreact in terms of inflammation and which keeps bats from falling ill. The response given by immune system of bat to the coronavirus isn’t the same as response given by immune system of humans.

When bats are infected by virus, in most of the bats, interferon pathway is activated. The molecular mechanism in bats immune system starts fast production of signalling molecule. This signalling molecule is Interferon alpha. It is a protein. It binds to specific receptors on target cells which leads activation of certain proteins to prevent of virus from producing and replicating its RNA. When interferon alpha is secreted by the infected cell, nearby cells are signalled to enter antiviral state. Even though humans have interferon alpha, the mechanism of action is different. In most mammals such vigilant response may cause harmful inflammation. But bats have adapted to anti-inflammatory traits. It includes loss of certain gene that normally promote inflammation. However, interferon alpha seems to be beneficial for virus even though it alerts nearby cells, as bats carry the infection. Bats don’t show any symptoms but the virus starts adapting to defensive regime. Here bat immune system may be stimulus for evolution of faster transmitting virus. When virus leaps from bat to other animals to us, our immune system isn’t equipped to counter these highly transmissible pathogens.
SCIENTIFIC STUDY ON BAT VIRUSES

A new study on bat viruses by Cara Book, an ecologist at University of California, Berkley, says, “Pathogens can spread fast internally before killing the host. But if host has an immune system that can defend against rapidly spreading viruses, a virus might evolve to infect new cells even faster than it would in a different environment and if a quick spreading virus from bats were to infect another species that lacked bat like defences? It would probably cause extreme virulence.”

Bats do carry species of coronavirus without getting sick, but they are susceptible to other viruses. These viruses include rabies virus, nipah virus, hantavirus, etc. They aren’t asymptomatic carriers of these. Rabies is a disease seen in bats caused by lyssavirus. For example, Australian Bat Lyssavirus is a species found in bats that causes rabies. Symptoms of a rabid bat include behavioural changes where bats become more aggressive, they have difficulty flying and disorientation. It is a zoonotic disease which can be transmitted via saliva, urine, faeces or bite of the infected bat.

CONCLUSION

Although the bats provide environment to virus where it can adapt and may further cause serious infection in human beings, they aren’t only the source of virus, but major pollinators, ingest plenty unwanted insects. They have a vital role in the ecosystem. As they have adapted to carrying viruses and not falling sick, there’s a possibility of new therapies if we study their immune system.

ACKNOWLEDGEMENT:

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CONVALESCENT PLASMA THERAPY AGAINST COVID-19

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ABSTRACT

The worldwide pandemic of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-COV-2), which originated in Wuhan, China, has become a major concern all over the world. An infection induced by the SARS-COV-2 is named Coronavirus disease 2019 (COVID-19). There is no specific treatment has been proven to be effective for COVID-19 till date. Specific drugs for this disease are still being researched. Now-a-days to manage large number of SARS-COV-2 infected patients the symptomatic treatment is given to the patients. Some anti-viral drugs, anti-malarial drugs like chloroquine phosphate and hydroxychloroquine and herbal treatment is provided along with supportive care systems like oxygenation and ventilation. These measures are not that effective in treating the disease. The pandemic is becoming severe day by day. Hence there is a need to investigate for such treatment option which will reduce the number of patients in shorter time. In this review, we reviewed one such effective therapy; Convalescent Plasma Therapy, which might be an immediate strategy for SARS-COV-2 treatment. In this therapy, blood from the person who have recovered from the infection is collected. Then the plasma is separated. This plasma is then injected into a newly infected patient. The plasma contains antibodies raised because of SARS-COV-2 infection which will help the patient to recover from the disease. Convalescent plasma therapy can reduce the time of recovery for the patient from 15 days to 3-4 days. It is a passive immunization therapy. In China, five patients are successfully recovered from COVID-19 by using convalescent plasma therapy. Also, in many other countries like USA, Spain, India this treatment is in the phase of clinical trials.

Keywords: Convalescent Plasma Therapy, SARS-COV-2, coronavirus, COVID-19

INTRODUCTION

Coronavirus Disease (COVID-19), which emerged in December 2019 in China, presents a global challenge. The coronavirus is a family of viruses that can cause a range of illnesses in human. The illnesses due to this family of virus can range up to severe forms like Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS). The recent outbreak of severe illness caused by the novel SARS-COV-2 coronavirus (COVID-19)
COVID-19 varna

YEAR 2020

is pandemic and spread almost throughout the world. More than half a million people worldwide have been infected by the novel SARS-COV-2 coronavirus. Also, there is increase in the number of cases and number of deaths worldwide almost every hour (Kumar et al. 2020). Hence it is a necessary to find an effective therapy against this virus.

Presently there is no specific anti-viral drug or vaccine used to treat affected and critically ill patients. Now a days, the management of patients focuses on the provision of supportive care like oxygenation and ventilation. Some anti-viral drugs like oseltamivir, ganciclovir, lopinavir; anti-malarial (Chloroquine phosphate) and herbal treatment are the reported therapeutic agents used to treat patients symptomatically. These therapies are not sufficient in treating COVID-19. There are some issues of toxicity with chloroquine phosphate and hydroxychloroquine (Cunningham et al. 2020).

Novel Coronavirus is a spherical virion with a diameter of approximately 125 nm. The viral genome codes for four structural proteins – Surface spike glycoprotein (S), Membrane protein (M), Envelop glycoprotein (E), and Nucleocapsid protein (N). The protein which is ~180KD glycoprotein and present on the surface of the virus is called spike protein. This protein is important for the entry of coronavirus into the host cell. There are two subunits of spike protein namely S1 and S2. Binding of the protein to the receptor of the host cell is carried out by S1 subunit whereas S2 subunit mediates the cell membrane fusion. Hence focus of the research is identifying antibody molecules targeting spike proteins as they mediate viral entry and as they can induce host immune responses (Kumar et al. 2020).

CONVALESCENT PLASMA THERAPY

Convalescent means a person who is recovering after an illness or medical treatment. We can consider convalescent plasma therapy as an effective way to control SARS-COV-2 pandemic. In this treatment method, the blood is collected from a person who has recovered from the infection of COVID-19 and the plasma is separated. The plasma contains antibodies raised because of specific antigen. The plasma is then injected into a newly infected patient to combat the virus antigen. Convalescent plasma therapy is a passive immunization therapy.

Hence, we can use this technique to achieve immediate short-term immunization against infectious agents by administering pathogen specific antibodies (Marano et al. 2016).

In the wake of such a large epidemic, Convalescent plasma has been the subject of increasing attention. This therapy is applied to the prevention and treatment of many infectious diseases from last century (Duan et al. 2020). In 20th century, this therapy was identified as a potential

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therapy for number of viral infections like measles, Argentine hemorrhagic fever, influenza, chickenpox, infections by cytomegalovirus, parvovirus B19, MERS-COV, Ebola virus and Severe Acute Respiratory Infections (SARI) viruses (Marano et al. 2016). Convalescent plasma therapy was effectively used in the treatment of SARS by providing hyper-immunoglobulins (Zhang et al. 2005). The convalescent plasma therapy was proved better than high-dose methylprednisolone treatment in treatment of SARS, (Soo et al. 2004). This therapy was used successfully in the treatment of infection spread because of Influenza A (H1N1) virus. This treatment also reduced mortality in patients with severe H1N1 virus infection (Hung et al. 2011). In the year 2006 there was an epidemic of avian flu (H5N1) virus; that time the convalescent plasma therapy was effectively used to treat H5N1 infection (Zhou et al. 2007).

For the recent pandemic of COVID-19, the convalescent plasma therapy is in clinical trial phase in many countries.

**METHOD**

Donor is the patient recovered from COVID-19. Plasma part of blood is removed from body of donor which contains antibodies against the disease (Refer figure 1). It is transfused into patient suffering through COVID-19.

![Figure 1: Convalescent Plasma Therapy](image)

Convalescent plasma is obtained from each donor by apheresis & the plasma is immediately transfused to the recipients (Shen et al. 2020). The transfusion needs to be performed on the same day blood is drawn. From blood, plasma part is separated using the technique called apheresis which uses an instrument called cell separator. Ideally, one day prior to transfusion, serum of recipient should be tested for neutralizing antibody titre (Shen et al. 2020). Each patient receives 2 consecutive transfusions of 200-250 mL of ABO compatible convalescent
plasma on the same day it is donated by donor. Patients also should also receive simultaneous antiviral treatment continuously (Shen et al. 2020).

MECHANISM OF PLASMA THERAPY

One possible mechanism for working convalescent plasma therapy is that the antibodies from convalescent plasma might suppress viremia (Chen, 2020). Virus specific neutralizing antibodies serve as main mechanism for virus clearance by host. These antibodies are specific for antigenic structures present on surface.

A key feature in the patho-mechanism of the disease is that the virus can induce an immunological over-reaction which is termed as 'cytokine storm' (Mehta et al. 2020). Since cytokines play role in signalling, this hyper-inflammation itself is a significant burden for susceptible person. It may even inhibit the body to generate antibodies against the virus in adequate quantities. Some fraction of COVID patients go through this. Therefore, supplementing such patients with convalescent plasma from recovered donors may be a life-saving treatment option.

Specifying the medical conditions for who can be the donor & who can be the recipient is necessary. Specifications reviewed here have not been still standardized. Hence, they can represent serious shortcomings.

CRITERIA FOR DONORS

Convalescent plasma can be collected from patients who had recovered from COVID-19. Recovery was defined as: “an afebrile status for at least 3 days, alleviation of respiratory symptoms, negative for SARS-CoV-2 nucleic acid for consecutive two RT-PCR tests, & at least 3 weeks following disease onset” (Mingziang, 2020). Some investigations suggest that donor should have a serum SARS-CoV-2– specific ELISA antibody titer higher than 1:1000 & a neutralizing antibody titer greater than 40 (Shen et al. 2020).

“The donor should be sero-negative for anti-HBV, HCV and HIV, & sero-positive for anti-SARS-CoV-2. As a routine check with plasma donation, the convalescent plasma should be confirmed free of residual SARS-CoV-2 by real time PCR” (Mingziang, 2020). Some investigations suggest use of quantitative reverse transcriptase–polymerase chain reaction (qRT-PCR) (Shen et al. 2020).

CRITERIA FOR RECIPIENT
Patients are said to be eligible to receive convalescent plasma treatment if they fulfilled the following criteria: (1) had severe pneumonia with rapid progression & continuously high viral load despite antiviral treatment (2) PAO2/FIO2 of <300 (PAO2 measured in Mm Hg & FIO2 measured as fraction of inspired oxygen) (3) were currently or had been supported with mechanical ventilation (Shen et al. 2020).

CONCLUSION
All reviewed studies indicate that Convalescent plasma treatment showed improvement in COVID patients. Without occurrence of any severe adverse events, it can be used successfully to treat critical patients along with other treatments. Still several shortcomings have been reported in the studies. The limited sample size & study design are some of the limitations of studies reviewed here. Hence, these observations need to be studied in clinical trials. Seriousness of disease & previous successfully treated diseases, taking into account, such treatment should be implemented effectively.

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COVID-19: CHALLENGES, PREVENTION
AND FUTURE PROSPECTIVE

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ABSTRACT

The COVID-19 which originated from Wuhan and has now spread throughout the China and received whole worldwide attention. COVID-19, the disease caused by SARS-CoV-2, is a highly contagious disease. Globally, this novel coronavirus is a major public health problem causing respiratory infections. The most common symptoms associated with infection caused by SARS-CoV-2 are fever, cough, shortness of breath, etc. Recently U.S. health protection agency centers for Disease Control and Prevention added six new symptoms to its official list of COVID-19 symptoms. The symptoms are chills, repeated shaking with chills, muscle pain, headache, sore throat and loss of taste and smell.

Rapid isolation and diagnosis, prevention of infection, clinical management will matter not only to patient with COVID-19 but also to health care worker and other patients who are at the risk. Involvement of bilateral lung with ground glass opacity was common finding from Computerized Tomography (CT) images of the chest.

Currently, the research on SARS-CoV-2 is in its primary stages whereas controlling infection to prevent the spread of SARS-CoV-2 is crucial intervention being used. This review summarizes the challenges of SARS-CoV-2 (COVID-19) and prevention of COVID-19.

Keywords: COVID-19, Challenges, Prevention

INTRODUCTION:

A novel infectious disease, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first detected in Wuhan, China in December 2019 and poses new public health challenges worldwide. Its clinical characteristics were similar to those of viral pneumonia. After the analysis of respiratory samples, the experts at People's Republic of China (PRC) Centers for Disease Control declared, that the pneumonia was caused by novel

Then the International Committee on Taxonomy of Viruses named the virus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This virus belongs to beta coronavirus family and similar to other viruses like SARS-CoV, MERS-CoV. SARS-CoV-2 has many potential natural hosts. This poses major Challenges for the prevention and treatment of viral infection (Lisheng Wang et al., 2020).

GENETIC STRUCTURE AND PATHOGENESIS OF SARS-COV-2:

Coronaviruses are spherical or pleomorphic, large family of single stranded enveloped RNA viruses that can infect animals and humans, causing various disease conditions involving respiratory, gastrointestinal, neurological and hepatic systems. There are only two sero-groups of human coronavirus (HCoV) that have been characterized in detail: these are HCoV-229E and HCoV-OC43 as the representative strains (Di Wu, et al., 2020). Coronavirus are divided into four genera: alpha, beta, gamma and delta-coronavirus. To date, there have been six human coronaviruses (HCoVs) identified, including the alpha-CoVs HCoVs-NL63, HCoVs-229E, the beta-CoVs HCoVs-OC43, HCoVs-HKU1, severe acute respiratory syndrome-CoV (SARS-CoV) and Middle East respiratory syndrome-CoV (MERS-CoV) (Di Wu et al., 2020).

The genome sequence homology of SARS-CoV-2 and SARS virus is approximately 79% (Kevin J. Clerkin et al., 2020). Several analyses have shown that SARS-CoV-2 uses angiotension-converting enzyme 2 (ACE2) as its receptor. The SARS-CoV-2 recognize host cell surface ACE 2 receptor through spike protein (S protein) and facilitating virus entry and replication (Haibo Zhang et al., 2020). A structure model analysis shows that SARS-CoV-2 binds to ACE2 with more efficiently than SARS-CoV and therefore increasing the ability of transmission of SARS-CoV-2 (Haibo Zhang et al., 2020). The detailed mechanism by which SARS-CoV-2 infects humans via binding of S-protein to ACE2, the strength of the interaction for risk of human transmission, and how SARS-CoV-2 causes organ damage remain unknown, and more studies are needed. Considering the higher affinity of SARS-CoV-2 binding to ACE2, soluble ACE2 may be a potential candidate for the treatment of COVID-19 ( Lisheng Wang et al., 2020).
CHALLENGES OF SARS-COV-2 INFECTION CONTROL:

The challenges for the effective controlling of COVID-19 outbreak include absence of validated vaccine and treatment, ability of the viral antigen to stay longer in the air (Brhane Berhe, et al., April 2020), socio-cultural behavior of people, lack of awareness about spread of disease in society, viral capacity of staying on animate object for longer time, overcrowding environment, having asymptomatic carriers, unavailability of diagnostic test kits or limited kits, unknown infective dose, unknown degree of infectivity, etc. As there is no specific, effective antiviral medication available for COVID-19 treatment so far, and also no vaccine is available till now, so, currently, these are challenge for the WHO and many countries to defeat the virus to prevent them from being infected (Brhane Berhe, et al., 2020).

Studies to date indicate that 2019-nCoV is transmitted primarily through airborne droplets rather than through the air. Coronavirus can spread among people through feces, so it is must to maintain good hygiene all the time after using the toilet (Tarek Mohamed Abd El-Aziz and James D. Stockand; 2020).

Another problem is that, at this time, very little is known regarding the effect of 2019-nCoV on pregnant women and infants and there are no special recommendations for pregnant women regarding the disease. The Centers for Disease Control and Prevention (CDC) does not have any evidence indicating the possibility of negative pregnancy outcomes for pregnant women with COVID-19, although two of the other coronaviruses SARS-CoV and MERS-CoV have been associated with more severe diseases and greater mortality in pregnant women (Huijun, et al., 2020).

It appears that children, in general, well tolerate the virus presenting few complications (Brhane Berhe, et al., April 2020). Adults are more susceptible to disease than children, because they may be suffering with other diseases such as diabetes, high blood pressure or heart disease, which weakens their ability to ward off infection (Ping-Ing Lee. et al., 2020). It is found that the angiotension-converting enzyme 2(ACE2) receptor in lungs and heart, is involved in regulating blood pressure but it is also the entry point for the coronavirus which causes COVID-19 (Ping-Ing Lee. et al., 2020).

The virus first infects the lining cells of the throat, trachea and lung, transforming these cells into virus factories that produce huge amounts of viruses that infect more cells. The high temperature and feeling of general malaise are caused by the response of the immune system
to the virus and sending signals to the body to release cytokines (CaibinFan, et al., February 2020). However, the virus disrupts the immune response and the body gets more inflammation than needed. The problem may not be limited to the lungs, as COVID-19 attacks other important organs in the body include the kidneys, which may lead to organ failure. Virus might affect renal tubular cells and testicular cells and cells in seminiferous ducts of the testis (CaibinFan, et al., 2020).

Local center for disease control and prevention, China collected samples of respiratory, blood and faces specimens to detect the pathogen. 41 patients were confirmed to be infected with COVID-19. The presence of pathogen was detected by real time RT-PCR methods (Chaolin Huang et al., 2020). In 98% cases of COVID-19, CT scan showed bilateral pulmonary involvement with the typical findings being multiple areas of consolidation and bilateral ground-glass opacity (Matteo Bassetti et al., 2020). NHC Key Laboratory of Systems Biology of Pathogens and Christophe Merieux Laboratory, Beijing, China declared that 25% patients showed leukopenia where as 63% of patients showed lymphopenia with procalcitonin being normal (<0.1 ng/mL) in 69% of them (Chaolin Huang et al., 2020). On the other hand, an increased release of anti-inflammatory markers such as IL4 and IL10 was also measured in COVID-19 patients. The overall case fatality rate was 15%. This clinical report is useful for highlighting some key issues surrounding both the emergence and the management of the COVID-19 that are currently being investigated by experts worldwide (Matteo Bassetti et al., 2020). There are other challenges in clinical management, in infection prevention, ICU infrastructure capacity, staffing, triage and research. They are as follows (Jason Phua, et al., 2020):

<table>
<thead>
<tr>
<th>Challenges</th>
<th>Recommendations</th>
</tr>
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<tbody>
<tr>
<td>A Global Stock Of Masks</td>
<td>Consider Disinfect And Reuse Of Medical Masks</td>
</tr>
<tr>
<td>Prediction Of Disease Trajectory From The Time Of Symptom Onset Is</td>
<td>Support Research To Develop And Validate Prognostic Tools And</td>
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<tr>
<td>Difficult</td>
<td>Biomarkers</td>
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<tr>
<td>Sensitivity Of RT-PCR Assays For Critically Ill Patients Is Unknown</td>
<td>Repeat The Sampling If Necessary</td>
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<tr>
<td>Increasing ICU Capacity Requires More Equipment Like Ventilators, Pharmaceuticals, Which Might Be In Short Supply</td>
<td>Consider Transport, Operation Theaters And Ventilators Only In Urgency</td>
</tr>
</tbody>
</table>
PREVENTIVE MEASURES FOR COVID-19:

To overcome the problems associated with COVID-19, there is no specific vaccine or effective antiviral therapies known and therefore there is urgent need to develop a safe COVID-19 vaccine. But we have to take proper precautions and must follow the guidelines given by the authorities for avoiding or decrease the chances of infection. As we know, SARS-CoV-2 is mainly spread through airborne droplets, so after sneezing or coughing the virus can be transmitted to other person via airborne droplets. Hence, we can use masks to overcome the spread of this virus, but wearing mask alone will not prevent us from infection, other than that hand washing and social distancing must also be followed. To decrease the spread of coronavirus, on 23 January 2020, chinese government isolated and locked down millions of people of Hubei province. Because of the locked down, incidence of new cases slow down and finally on March 2020, no new cases were reported in Hubei province (Maurizio Cecconi, Guido Forni and Alberto Mantovani., 2020). Some studies have been shown that, Vitamin C prevent the lower respiratory tract infection and therefore supplementation of moderate amount of Vitamin C may be a way to prevent COVID-19 infection. Another way to overcome the fast spreading COVID-19 infection is that, researchers should develop specific and validated vaccine and antiviral treatment (Lisheng Wang et al., 2020). There should be community awareness among the people on the transmission and early prevention, active case detection, using hand washing jars, use of hand sanitizers and respirators, avoiding over-crowding, avoiding intimate contact with animals and applying hand glove to protect touching different contaminates should be practiced (Brhane Berhe, et al., 2020).

FUTURE PROSPECTIVE AND RECOMMENDATIONS:

For creating the awareness among the people, some recommendations be followed, some of that are: At government level, international, national, religion bodies should participate by allocating budget for training, isolation of suspects, testing and supportive cares and awareness creation.

At health institutions, they should also screen and early detection of cases, giving supportive care and treatment, distributing medical protective equipment, give health education and introducing hand washing practices to customers and preparing isolation rooms.
At religion/social levels and University levels, we can minimize conferences and Sunday schools, avoiding movement along different places, avoid lecturing in classes and replace with alternative lecture methods, posting posters that thought about the outbreak, preparing and distributing hand washing jars for the university community at the entry and exit and empowering the community on the usefulness of social distancing and on hand washing practices.

For the fast spreading outbreak of COVID-19 infection researchers should develop validated vaccine and treatment. If in case delay unenviable, substances that boost the immune response is recommended (Brhane Berhe, et al., 2020).

CONCLUSION:

The novel virus (COVID-19) was responsible for severe acute illness and because of this virus various challenges have emerged. We have limited knowledge about this novel coronavirus and drug discovery against the SARS-CoV-2 is challenging job for the mankind. For the development of new drugs/vaccines, we need to understand more details about the structure, biology or mode of action, mechanisms, pathways involved in the infection of the COVID-19. Studies of antiviral therapies and vaccinations are currently under the evaluation. Again, according to preventive measures criteria, strict vigilance of viral changes in different hosts for prediction of an event is important aspect. Serological assays for emerging coronavirus is another problem. During the serological assay, there may be reactivity with more conserved antigen and will often manifest false positive results. In order to implement a standardized protocol for validating new assays, we need to improve and co-ordinate the development of serological assay with well characterized subset of sera. This is another very important aspect for development of new serological assays. Other than that we have to think about preventive measures and future prospective and further research should be directed towards the study of SARS-CoV-2 in suitable animal models for analyzing replication, transmission and pathogenesis.

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CURRENT SCENARIO OF COVID-19 IN INDIA

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ABSTRACT

Corona virus disease (COVID-19) caused by infectious severe acute respiratory syndrome corona virus -2 (SARS-CoV-2). Corona virus is newly discovered virus causes disease in animals (civet cats, tiger, and bat) as well in humans. The initial outbreak of COVID-19 was identified in Wuhan, China in December 2019. After outbreak in China the virus has spread rapidly throughout the globe creating pandemic situation along with European countries who are affected more. India is also one of the affected countries and the first COVID-19 positive case was reported on January 30, 2020 in Kerala state. The Government of India and Ministry of Health and Family Welfare applied first protective measures in January 30, 2020 like the thermal screening of passengers returning from China and other countries. In India as of May 1, 2020 the number of cases reported by the Government of India and Ministry of Health and Family Welfare are 35000+, 1100+ died and 8000+ recovered. The Government of India on March 24, 2020 announced the nationwide lockdown to prevent the transmission of COVID-19 and has implemented several precautionary measures to avoid further spread.

In this review we briefly describe the current scenario of COVID-19 outbreak in India considering factors like mode of transmission, diagnosis, treatment, effects of lockdown and vaccine development. This review will also give strategy of Government of India and guidelines provided by World Health organization (WHO) for effective handling of the current situation.

Keywords: COVID-19; India; WHO; Current Scenario

INTRODUCTION

The newly emerged corona virus (SARS-CoV-2) is thought to cause infectious disease in many types of animals- civet cat, tiger, bats etc. as well as transmitted from human to human. COVID-19 infection has become pandemic, now spreading rapidly in the entire world, originated in Wuhan, China (December 2019) [1]. In India the first case of COVID-19 reported on January 30, 2020 in Kerala and on February 3, 2020 cases rose to three- all were
students who had returned from China. The virus has thought to have zoonotic origin [2] [3]. The nCoV, a newly emerged virus closely related to bat corona virus but the current scientific review is that the nCoV has natural origin [3]. In 2002 the similar kind of outbreak had happened in China known as SARS-CoV, it was transmitted to human through civet cat. In 2012 the MERS-CoV outbreak had happened in Saudi Arabia and it was transmitted to humans from infected camels [1].

The COVID-19 pandemic has worsen the situation in other countries like Spain, Italy, Japan, Iran, France, USA and other countries. As on 1 May 2020 more than 3.25 million of cases of COVID-19 reported in 187 countries and territories. More than 23,300 death and 1.01 million people have recovered [4]. The virus spreads through close contact often via small air droplets produced while coughing and sneezing [6]. People may also become infected by touching a contaminated surface and touching mouth and nose, because the viral droplets fall to the ground or on objects rather than remaining in air [7] [8]. COVID-19 is contagious disease mostly affecting the people with old age, immune-compromised conditions and person having medical history of respiratory and any lung related problems [9].

The person infected with COVID-19 shows symptoms similar to flu that are fever, cough, cold, fatigue, shortness of breath etc. The severity of disease may include pneumonia and acute respiratory distress syndrome [10]. The incubation period of COVID-19 from exposure to onset of symptoms is 7 to 14 days. [11] Currently there is no vaccine or effective treatment available for COVID-19 disease [11]. World Health Organization (WHO) recommend the preventive measures for COVID-19 are frequently washing hands with soap and water, alcohol (70%) based hand rub, covering mouth while coughing and sneezing, maintain social distancing and wearing mask in public [1]. India is developing and highly populated country, so possibly rate of transmission of COVID-19 from human to human is high as compared to other countries. The Government of India and Ministry of Health and Family Welfare implementing travel restrictions, self-isolation, curfew, lockdown and stay at home orders to control the virus transmission in beginning stage. Currently the most affected/ epicentres of the disease in India includes Maharashtra, Gujarat, Rajasthan, Delhi, Madhya Pradesh and Uttar Pradesh.

Currently whole world is fighting the great battle of COVID-19. In India situation is not different. In India first positive case of COVID-19 was reported on January 30, 2020 in Kerala state [25]. The patient Considering the worldwide scenario of COVID-19 it was necessary to be prepared for the upcoming danger. Regarding that the Prime Minister's Office
(PMO) and Ministry of Health and Family Welfare (MoHFW) started monitoring the "preparedness and response efforts" needed for management of COVID-19. Additionally, the surveillance at entry points, follow up and contact tracing of positive cases were strengthened [12]. MoHFW and Ministry of Civil Aviation also announced the checking of passengers coming from China for symptoms like cold, cough and fever. This checking was initially being carried out at 21 airports [12].

Three confirmed cases of COVID-19 were reported in Kerala state between January 30, 2020 and February 3, 2020 [25]. The conditions of patients were stable and they were monitored closely. Also 91 contacts of these three patients were successfully traced and they were being followed up too [13]. As a part of COVID-19 management Government of India (GoI) issued travel advisory asking people to avoid the unnecessary travel to China and the people with travel history from China since January 15, 2020 were quarantined [13].

As of February 28, 2020 no new case had been reported after the three cases reported in the period between January 30 and February 3, 2020 [15]. Already reported three cases were showing good progress. On February 20, 2020 they got a discharge from hospitals [15]. In that period, GoI evacuated 757 people from Wuhan, 124 people from Japan. Along with the Indian nationals the people included citizens of other countries like Peru, USA, South Africa, Nepal etc. They all were quarantined [14, 15, 16].

As of March 9, 2020 total 44 cases were confirmed [25]. States/UTs like Delhi, Haryana, Telangana, Jammu, TamilNadu, Uttar Pradesh, Punjab, Rajasthan, Kerala and Ladakh reported the positive cases. The increasing number of cases worldwide and sudden increase in number of cases in India, was high alert for all other states. To cope up with the situation, Indian Council for Medical Research (ICMR) gave permission to 52 laboratories for testing of COVID-19 while 57 laboratories were allowed to collect samples [17].

As of March 14, 2020 total 84 cases of COVID-19 were confirmed and 2 deaths were reported [25]. Kerala state reported the highest, 19 cases. As a part of COVID-19 management with few exceptions all the visas were suspended until April 15, 2020. Also Indian nationals coming from countries like Spain, Italy, Republic of Korea etc. were quarantined for the 14 days [18].

As of March 22, 2020 the number of COVID-19 cases increased to 360 with 7 deaths [25]. On March 22, 2020 Prime Minister of India called for 'Janata Curfew' asking people to stay indoors except people in emergency services. Also all flight, train services were suspended until March 31, 2020 [19].
On March 24, 2020 Prime Minister of India issued an order of 21-day lockdown under the section 6(2)(i) of the Disaster Management Act of 2005 [20]. The lockdown period was from March 25, 2020 to April 14, 2020. In this lockdown only essential services like medical facilities, grocery shops were open to avoid the inconvenience of citizens. As of March 28, 2020 total 909 positive cases were reported with death of 19 patients [25].

On April 2, 2020 GoI launched the "ArogyaSetu" app for citizens where all the relevant information of COVID-19 was there [21]. As of April 5, 2020 total 3577 positive cases and 83 deaths were confirmed [25].

Considering the constantly increasing numbers of COVID-19 positive cases WHO is supporting India in assessments of COVID-19 dedicated hospitals. As of April 12, 2020 GoI had set up more than 550 dedicated facilities with more than 1 lakh isolation beds and more than 11,000 ICU beds [22]. Till April 12, 2020 total 8447 positive cases and 273 deaths were confirmed [25].

Ahead of end of 21-day lockdown Prime Minister of India announced the extension of lockdown till May 3, 2020 [23]. As of April 19, 2020 the number of confirmed COVID-19 cases reached up to 16,116 with 519 deaths [25].

As of April 26, 2020 total number of positive COVID-19 cases was 26,917. Until the date total 826 deaths had been occurred [24]. (The recovered cases were also included in total number of cases.)

On May 1, 2020 (8.00 pm) total number of active cases (did not include recovered cases) of COVID-19 was 25,148 and the number of cured patients was 9064. Total 1152 deaths had been occurred in the country [25].

With respect to the situation of this pandemic in rest of the world, the situation in India seemed to be well handled. The quick decisions from government of lockdowns, response of public towards these decisions, implementation of the decisions and also maintenance of law and order by police force, public-police co-operation, respect and support towards the health care workers, participation of media and celebrities in spreading awareness were some key points in the fight against COVID-19.

CONCLUSION:
India's response against COVID-19 was definitely pro-active. Lockdown and its extension really helped to break the chain of transmission to some extent. Though India is developing country, the nation was a helping hand to many other countries. Despite of overpopulation
(nearly 1.33 billion), sufficiently high illiteracy rate, poverty and all other odds, India did manage well as compared to the developed countries and became an example to the entire world in handling the situation.

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EFFECT OF TEMPERATURE AND HUMIDITY ON THE TRANSMISSION OF CORONAVIRUS.
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ABSTRACT
A severe acute respiratory disease caused by coronavirus (SARS-CoV-2) has spread throughout the world. On 30th January 2020 World Health Organization (WHO) officially declared this acute respiratory disease, COVID-19 as a Pandemic. Stability of the coronavirus can be demonstrated by studying the seasonality of the virus. SARS-CoV-2, which is responsible for COVID-19, shows temperature and humidity preferences to some extent, like various strains of Coronaviridae family, SARS-CoV-1 and MERS-CoV. The virus is transmitted through the direct contact with the infected person, aerosols and fomite. Different studies on virus suggests, due to its strong adherence to the surfaces different temperature and humidity conditions affects the stability of the virus and it also shows that low temperatures and 30-50% humidity conditions favors the increase in the half-life of virus.

Key words: Temperature, humidity, transmission rate, COVID-19

INTRODUCTION
In December 2019, a cluster of pneumonia cases caused by corona virus were detected in Wuhan, China. It was initially named as novel coronavirus (2019-nCoV) on 12th January 2020 by WHO [2]. The coronavirus was named as SARS-CoV-2 and the disease caused by it was named as COVID-19 [2]. It was soon isolated from patients in China and used for genome sequencing. The -coronavirus causing COVID-19 is enveloped non-segmented positive-sense RNA virus [2]. It causes severe acute respiratory disease. Due to high transmission rate it was soon declared as global pandemic. The features of COVID-19 are somewhat similar to common influenza causing cold [8]. The influenza virus shows seasonality, which implies that increase in infection is expected in colder temperatures and it subsides with warming air temperature [6][8]. Even though this assumption is not supported by any scientific analysis and investigation, the relation is commonly observed. Implying
same to COVID-19, studies are carried out about non-physiological causes augmenting the survival and spread of disease. This study can provide valuable information for policy maker dealing with management and effective control measure. After originating in Wuhan, China, it led the massive loss of life in various countries such as Italy, France, Spain, US [5]. The lack of vaccine and inaccuracy of the exact treatment has led the focus to control the transmission of virus. Meteorological factors such as temperature and relative humidity influence the stability of virus which further affects the transmission [5].

A meteorological factor varies with the change in geographical areas. According to generalized additive model study of Xie, J., & Zhu, Y. the relationship between mean temperature and COVID-19 confirmed cases were approximately linear in the range of $<30^\circ C$ and became flat $>30^\circ C$ [8]. Random effect meta-analysis including 28 provisions in mainland China found statistically significant association between temperature and relative risk during study period by use of meta regression. The result confirms negative relationship between the temperature and relative risk in 28 provisions [6]. The study carried out in Hubei province suggested that, association between COVID-19 and temperature and relative humidity was not consistent but shows positive relation with transmission rate. Studies carried out which claims relative decrease in temperature and humidity is prone to enhance the suspended particles in atmosphere facilitating ideal condition for virus attachment and transmission. This certainly favors the drying out of nasal mucosa followed by rupturing of cilia creating opportunity for virus invasion [5]. 600,000 positive COVID-19 cases were found in US amongst which 26,000 were reported dead by US government till 14th April 2020. The increase in daily basis was reported to be 30000/day, which shows high rate of transmission [3]. India, which is second most populated country showed 11490 cases and 398 deaths till 14th April, 2020 and daily increase of 1000 cases/day[3]. Transmission of COVID-19 in India is comparatively slow. This might be, because of high temperature and relative humidity. Recent studies have suggested that rate of emergence of COVID-19 was more in cold and temperate climate as compared to warm and tropical one. It was also studied that daily temperature and relative humidity influence an occurrence and transmission of COVID-19. The risk of increase in daily incident cases of COVID-19 was 95% times greater at lower temperature during outbreak than warmer region [3]. A laboratory study suggests that coronavirus was stable over 5 days at 22 – 250 C on smooth surfaces, while loses its stability at temperature above 380C [1].
CONCLUSION
The relation between temperature, relative humidity and COVID-19 positive cases shows that COVID-19 may not perish itself without any public health interventions when weather becomes warmer but the increasing temperature and humidity has some effect on rate of transmission [1]. Though some theories state the positive relation between the change in temperatures and humidity with the transmission of COVID-19, there is no scientific evidence for same. Other than meteorological factor population size also plays a measure role in rate of transmission of virus [4]. The studies so far have revealed that the temperature of US and Iran is colder but the rate of transmission of COVID-19 in US is greater than that of Iran because of higher population size. Whereas, highly populated countries like India having relatively warmer temperature and humidity shows the slower rate of transmission [3]. Estimating impact of temperature and relative humidity on transmission rate of COVID-19, these factors should be taken into consideration while planning controlling measures.

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OVERVIEW OF PATHOPHYSIOLOGY AND IMMUNOLOGY OF COVID 19 INFECTION

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ABSTRACT:
Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the causative agent of the coronavirus disease 2019 (COVID-19) pandemic. Parallel investigations into the virology of SARS-CoV-2, understanding the foundational pathophysiological and immunological processes underlying the clinical manifestations of COVID-19 is requisite for the identification and rational design of effective therapies. The pathophysiological and the immune response is essential to control and eliminate CoV infections, however, maladjusted immune responses may result in immunopathology and impaired pulmonary gas exchange. Literature survey for understanding the interaction between Coronaviruses and the innate immune systems of the hosts may shed light on the development and persistence of inflammation in the lungs and hopefully can reduce the risk of lung inflammation caused by CoVs. In this review, we provide an update on CoV infections; particularly the host defence against CoV induced inflammation of lung tissue, as well as the role of the innate immune system in pathogenesis. We also provide an overview of the pathophysiology of SARS-CoV-2 infection. We describe the interaction of SARS-CoV-2 with the immune system and the subsequent contribution of dysfunctional immune responses to disease progression. We highlight the overall impact of these approaches for potential therapeutic interventions that target viral infection and/or immunoregulation.

Keywords: Pathogenesis, pyroptosis, interferons, lymphopenia.

INTRODUCTION:
Human coronaviruses have been studied for more than 20 years as they have been the causative agents of major respiratory diseases like SARS and MERS [1]. At the end of 2019, in the month of December the world witnessed the emergence of yet another novel coronavirus strain [1]. The new novel coronavirus strain caused respiratory illness and various associated symptoms in the infected individuals [1]. Initially the infection was
constricted to Wuhan city in China [1]. Gradually it spread across the mainland of China from where it further travelled to other parts of the globe [1, 2]. It caught global attention due to its high transmission rate, intense morbidity and mortality rates [2]. The lack of specific antiviral treatments and increased pressure of primary clinical treatments has been a major cause of increased mortality rate throughout the world [4]. What started as an epidemic took a shift when WHO declared it as ‘Public Health Emergency of International Concern’, on 30th of January, 2020 implying that it poses a potential risk to many countries and requires a coordinated global response [4]. The International Committee on Taxonomy of Viruses (ICTV) named this newly identified novel coronavirus as SARS-CoV-2 on 11th February, 2020 [3, 4]. It was declared a pandemic by WHO on 11th March, 2020, as it had established its roots in many countries across the world [4]. This review article tries to put light pathophysiology and immunology of COVID 19 infection

**SARS COV2 STRUCTURE AND ITS PATHOGENESIS**

Coronaviruses are enveloped; nonsegmented, positive sense single stranded RNA viruses with genomes in the size ranging from 26 to 32 kilo-bases (the largest known viral RNA genome). The virion has a nucleocapsid composed of genomic RNA and phosphorylated nucleocapsid (N) protein, and two different types of spike proteins: the spike glycoprotein trimer (S) and the hemagglutinin esterase (HE). The membrane (M) protein (a type III transmembrane glycoprotein) and the envelope (E) protein are located in the middle of the S proteins in the virus envelope. CoVs were given their name based on the characteristic crown like surface appearance [5]. Spike glycoproteins are composed of two subunits (S1 and S2). Homo-trimers of S proteins constitute the spikes on the viral surface, guiding the link to host receptors [6]. SARS-CoV-2, the S2 subunit composed of a fusion peptide, a transmembrane domain, and cytoplasmic domain is highly conserved. Therefore, it could be a target for antiviral (anti-S2) compounds [13].

SARS-CoV-2 is mainly transmitted by airborne respiratory droplets, direct contact with the infected individuals [7]. Although the fecal-oral route might serve as an additional mode of transmission, much study has not been carried out in this respect [7]. The average incubation period of COVID-19 disease is 5.2 days [8]. Upon ingestion into the host system through any of the above-mentioned modes, the Virions enter the cells through ACE2 receptors [8, 9]. Mucosal epithelial cells lining the upper respiratory tract serve as the primary target of the virus [3]. The virus, upon invasion, initiates viral replication in the host cell by integrating its
genetic material into host DNA [8, 9]. After completion of replication the virions are released by lysis of mucosal epithelial cells leading to dryness and irritation in the throat [9]. The disease further progresses down the lower respiratory tract where Alveolar type I cells are targeted followed by Alveolar type II cells. [9]. Alveolar type II cells undergo apoptosis and fill up the lung cavity causing breathing problems [8, 9]. Loss of Alveolar Type II cells triggers the secondary pathway for Alveolar epithelial cell I regeneration leading to aberrant wound healing, severe scarring and fibrosis [3]. The respiratory damage caused due to SARS-CoV-2 infection is irreparable [2, 3, 8, 9]. In severe cases, bilateral ground glass symmetries can be observed in the radiographs due to inflammation [8]. Few other symptoms exhibited by the infected individuals include leucopenia, increased levels of plasma pro-inflammatory cytokines, high blood leukocyte numbers [9, 10]. Severe infection of SARS-CoV-2 causes Acute Respiratory Distress (ARD) syndrome, which ultimately results in death due to respiratory failure [9]. Elderly individuals are at a higher risk of contracting the disease as they have decreased mucociliary clearance [9]. Also the ability of epithelial regeneration is diminished in such individuals [9]. Certain cases of COVID-19 disease have presented unique clinical symptoms such as diarrhoea [8, 10]. The mucosal epithelial cells of gastrointestinal track express the ACE2 receptor which facilitates viral entry into the cells [11, 12]. Figure 1 summarises the pathogenesis of SARS-CoV-2.
Figure 1: Flowchart connecting pathogenesis with the affiliated immune responses.
ROLE OF IMMUNE CELLS AND CYTOKINES

SARS-CoV targets airway epithelial cells, alveolar epithelial cells, vascular endothelial cells and macrophages in the lung. All these cells express the angiotensin-converting enzyme 2 (ACE2) host target receptor [14-16]. Infection with SARS-CoV and the destruction of lung cells initiates a local immune response. The response involves recruiting macrophages and monocytes that respond to the infection, and release of cytokines. This process is effective most of times but this in some cases, a dysfunctional immune response occurs, which can cause severe lung and even systemic pathology [17]. In the incubation period and non-severe stages, a specific adaptive immune response is required to eliminate the virus and to prevent disease progression to severe stages. In case of dysfunctional, virus will propagate and massive destruction of the organs that have high ACE2 expression, such as lungs, intestine and kidney will take place. The damaged cells induce innate inflammation in the lungs that is largely mediated by pro-inflammatory macrophages and granulocytes [2]. In case of SARS-CoV patients it was seen that viral infection and replication in airway epithelial cells causes high levels of virus-linked pyroptosis with associated vascular leakage [18]. Pyroptosis is a highly inflammatory form of programmed cell death that is commonly seen with cytopathic viruses [19]. During SARS-CoV-2 infection levels of IL-1β, one of the important cytokines released during pyroptosis, is elevated [20]. Using a variety of pattern recognition receptors (PRRs), alveolar epithelial cells and alveolar macrophages detect the released pathogen-associated molecular patterns (PAMPs), such as viral RNA, and damage-associated molecular pat- terns (DAMPs), including ATP, DNA and ASC oligomers. A wave of local inflammation ensues, involving increased secretion of the pro-inflammatory cytokines and chemokines IL-6, IFNγ, MCP1 and IP-10 into the blood of afflicted patients [20]. These cytokines are indicators of a T helper 1 (Th1) cell-polarized response, which parallels observations made for SARS-CoV and MERS-CoV [21]. Secretion of such cytokines and chemokines attracts immune cells, monocytes and T lymphocytes, but not neutrophils, from the blood into the infected site [2].

In some patients, a dysfunctional immune response takes place, which triggers a cytokine storm that mediates widespread lung inflammation. It was observed that patients with severe COVID-19, requiring intensive care in hospitals, exhibited higher blood plasma levels of the cytokines IL-2, IL-7, IL-10, granulocyte colony-stimulating factor (G-CSF), IP-10, MCP1, macrophage inflammatory protein 1α (MIP1α) and tumour necrosis factor (TNF)[20]. Higher levels of IL-6 are seen in non-survivors than survivors [22]. In case of COVID-19
infection patients a highly inflammatory monocyte-derived FCN1+macrophage population is seen in the broncho-alveolar fluid. A significantly higher percentage of CD14+ CD16+ inflammatory monocytes is seen in peripheral blood of these patients. [23]. These immune cells secrete inflammatory cytokines that contribute to the cytokine storm, including MCP1, IP-10 and MIP1a. (Figure 3) The mechanisms by which SARS-CoV-2 topples the body’s innate antiviral cytokine responses are yet to be studied, but research on SARS-CoV shows that multiple viral structural and non-structural proteins antagonize interferon responses. Antagonism occurs at various stages of the interferon (IFN) signalling pathway, including by preventing PRR recognition of viral RNA [24-26], PRR signalling through TBK1/inhibitor of nuclear factor-κB kinase subunit-ε (IKKε), TRAF3 and IRF3, downstream interferon signalling through STAT1 and by promoting host mRNA degradation and inhibiting host protein translation [27]. It is very likely that at least few of these pathways are conserved in SARS-CoV-2. Antagonism of the interferon (IFN) response aids in viral replication, resulting in increased release of pyroptosis products that can further induce anomalous inflammatory responses. Unconstrained inflammatory cell infiltration can itself mediate damage in the lung through excessive secretion of proteases and reactive oxygen species, additionally to the direct damage resulting from the virus. This results in diffuse alveolar damage, desquamation of alveolar cells, hyaline membrane formation and pulmonary oedema. This restricts the efficiency of gas exchange in the lung, causing difficulty in breathing and low blood oxygen levels. The lung also becomes more prone to secondary infections [2, 28]. Uplifted levels of cytokines such as TNF (tumour necrosis factor) can cause septic shock and multi-organ failure. These may result in myocardial damage and circulatory failure observed in few patients [29]. Literature evidence suggests that SARS-CoV may infect other targets besides lung cells. In particular, virus was found in T lymphocytes [31], macrophages [32-34] and monocyte-derived dendritic cells [35]. Direct infection of lymphocytes could contribute to the observed lymphopenia in some patients [31].

CONCLUSION:
The COVID-19 pandemic has proven to be worse than previous SARS and MERS outbreaks caused by viruses of the same family. SARS-CoV-2 is more infectious and has exhibited high transmission rates as compared to SARS and MERS. Currently transmission rates can be reduced only by following strict isolation protocols. Although there is no specific medication that has been developed against the disease, current treatment aims at symptomatic care.
Immunocompromised and old aged people are at higher risk of the disease. Researchers are working towards development of a prophylactic vaccine which may aid in preventing COVID-19 disease in the upcoming days.

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PATHOGENESIS OF SARS-COV-2-THE CAUSATIVE AGENT OF COVID-19

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is a kind of viral pneumonia which is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). This is the third corona virus outbreak 21st century has seen. It was declared as pandemic by WHO on 11th February 2020. Though, detailed knowledge about pathogenesis of nCoV (Novel Corona Virus) is not known, comparing it with other known corona viruses gives us a brief view about it. Pathogenesis at cellular level has been discussed in this review as it may lead to a possible understanding of its treatment or prevention as we are still fighting for finding vaccination and we have to rely on symptomatic treatments.

Key words: - pathogenesis, nCoV, SARS – CoV 2.

INTRODUCTION:

Corona virus belongs to a family of viruses known for their crown like proteins. They compose largest number of positive sensed, single stranded and enveloped viruses. Their size ranges from 26-32 kb, this is the largest known viral genome. Virion has a nucleocapsid composed of genomic RNA, Nucleocapsid protein (N) which is buried inside phospholipid layer and surrounded by Glycoprotein trimmer(S). CoV (Corona Virus) are genotypically and serologically classified into 4 subgroups - α, β, γ, and δ coronaviruses. α and β CoV’s are responsible for human infections [7]. CoV responsible for COVID 19 is a β CoV [6]. SARS-CoV-2 (Severe Respiratory Syndrome-Corona Virus-2) is the virus responsible for COVID 19. It is also referred to as nCoV (Novel Corona Virus). SARS- CoV-2 is not the first corona virus that caused a severe respiratory disease outbreak. Earlier epidemics include SARS (Severe Acute Respiratory Syndrome) in 2002-03 and MERS (Middle East Respiratory Syndrome) in 2012 [3].
Pathogenesis of nCoV was found to be similar with SARS-CoV and research was done considering those similarities. In order to find a cure, treatment or vaccine for this pandemic, it is important to understand its epidemiology and pathogenesis. Pathogenesis of SARS-CoV-2 the causative agent of COVID-19 in short is as below:

**PATHOGENESIS:**

Coronaviridae family has an extraordinary host range and this range is attributable to the Spike (S) protein. This was confirmed by nucleotide sequences which revealed that virulence of different CoV is due to different S genes. Some strains of Coronaviridae family like HCoV-229E, HCoV-OC43, HCoV-NL63 etc. are responsible for upper and lower respiratory tract infections, it was also observed that some CoVs can potentially infect various animals including bats, birds, whales etc.[1] The nCov showed similar clinical manifestation as SARS-CoV and MERS-CoV can cause severe or mild pneumonia in humans. Targeting this spike protein can be a possible treatment strategy. If we are able to target this S protein with the help of vaccines, we can stop the virus from adhering to the cell and thus avoid infection itself. Infected people with COVID-19 may show symptoms like fever, cough, fatigue, decreased leukocyte levels which are indicative of the disease. These symptoms are similar to MERS and SARS infections. Pathogenesis of SARS-CoV 2 is still not fully known, but its similarity with MERS and SARS gives us a lot of information. Understanding pathogenesis will help us with better diagnostics. Various structural and non-structural proteins play an important role in virion assembly, infection and replications of corona viruses.
Considering which cells are infected at what stage, pathogenesis can be divided into 3 stages [10]:

Stage 1: (Asymptomatic state) Initial 1-2 day’s prior infection The virus is transmitted via droplets formed by the infected person, SARS-CoV-2 once inhaled, binds to the epithelial cells and starts replicating using cell machinery of host. The spike glycoprotein (S) helps viral entry into the host cell. The S proteins attach to host receptor, ACE2 - Angiotensin Converting Enzyme (specific for SARS COV-2) [16]. Structural proteins such as S are responsible for production of spikes on virus which plays role in attachment to host receptors [1]. The S subunit is essentially made of S1 and S2 domains for receptor binding and membrane fusion, the interaction of S1 causes change in conformation of S2 domain which leads to fusion of viral envelope and cellular membrane leading to release of nucleocapsid [4]. It was found that the genome transcription and replication is mainly coordinated by enzyme 'viral repliase'. N proteins along with nsp3 (non-structural protein3) helps in packaging of encapsulated genome into virions and also plays beneficial role in viral replication [4]. There is local development of virus but the innate immune response is very low. At this stage, presence of virus can be detected using nasal swab. But the viral load may be very low hence RT-PCR can be used for precise detection.

Stage 2: Entry in respiratory tract (Next few days)
The virus starts migrating to upper respiratory tract and induces vigorous immune response. Such person is highly infectious but can be easily monitored at home because in 80% of infected people, SARS-CoV-2 remains put in the respiratory tract itself. From patients with early stage of outbreak, It was found that the virus induces a cytoplasmic storm which is a deadly uncontrolled inflammatory response resulting from release of large amount of pro inflammatory cytokines and chemokines. This cytoplasmic storm leads to multiple organ failure in body which leads to death of patient in severe cases [8].

Stage 3: Hypoxia and progression to ARDS (Acute Respiratory Distress Syndrome)
This is the most crucial stage and must be monitored thoroughly. Only 20% of the infected population will reach this severe stage and 2% from them may die. But this may differ according to age and other physiological factors. The virus in the stage reaches for the Gas exchange units in the lungs and targets Alveolar type 2 cells. Virus keeps on replicating in these cells which leads to apoptosis.
Fig 2: Life cycle of SARS-CoV-2:
Virus enters the host cell by binding to ACE2 (host receptor). After binding, conformation changes occur in domain 2 of spike protein(S) which helps in fusion of virus envelope with host cell membrane. In this manner viral RNA is released inside the host cell. This RNA is translated firstly into polyproteins and then final viral proteins. Finally, newly formed viral proteins and genomic RNA together are assembled into virions, which takes place in the ER. These assembled virions are then transported and released out of the cells via vesicles. Released Viruses are now able to infect other cells [13].

CONCLUSION:
There are significant knowledge gaps in the pathogenesis of COVID-19 that is and will be filled in over the next few months. Considering the similarities in SARS-CoV-2 and SARS-CoV, pathogenesis has been hypothesized and treatment strategies can be planned in same manner. Based on structure of SARS-COV-2, blocking the binding of S protein to ACE2 receptor is important in treatment of virus infection. Antibody and plasma therapy also seem promising in preliminary tests. Induced mutation in viral replicase enzyme can inhibit synthesis of viral proteins in host cell which can probably be used as treatment strategy in
patients affected with COVID19. Vaccine development is the best shot to curb this infection but it may take months before commercial production starts. Since there is no effective therapy or vaccine which is confirmed, best steps to be taken now are early diagnosis, isolation, and social distancing.

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REFERENCES:


POTENTIAL TREATMENTS FOR NOVEL SARS COV-2.
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ABSTRACT:
The pandemic of novel Coronavirus disease 2019 (COVID-19) belongs to the family Coronaviridae. The SARS CoV-2 is known as a novel virus due to its unique feature of possessing a Furin cleavage site, in the spike protein that is absent in the previous COVID clad. It is responsible to cause respiratory, enteric, hepatic and neurological infections. A large number of people are rapidly infected by SARS CoV-2, worldwide. No effective therapies are scientifically proven yet. But a few potential drugs are assumed to help combat the wide spread of Coronavirus. Remdesivir has a potential antiviral activity against the novel SARS CoV-2. But it is not yet approved by the US FDA and still under phases of clinical trials. Chloroquine, an antimalarial drug, has proved its efficacy in inhibiting the spread of viral infection in COVID-19 patients. On the other hand, use of Monoclonal antibodies could be a promising strategy to treat CoV-2 infection as it helps to block the interaction between human cells and spike protein of the SARS CoV-2 which will eventually not allow the viral replication cycle to occur. Tocilizumab, a humanized anti-IL-6 receptor antibody is an effective strategy to increase the levels of Interleukin 6 by continual synthesis. In this way there are many possible therapeutic approaches to deal with COVID-19. In the history of vaccine and drug production, Vaccine for COVID-19 will be of early occurrence due to its speedy research studies. Here in this review we discussed about various targets or strategies to develop treatment against the novel Coronavirus.

Keywords: Coronavirus, SARS CoV-2, SARS CoV, MERS CoV, Remdesivir, Chloroquine, Monoclonal antibodies, Tocilizumab.

INTRODUCTION:
History and Origin:
The SARS-CoV-2 is Severe Acute Respiratory Syndrome Coronavirus 2, which was first discovered in China’s Hubei province, Wuhan city in December 2019. It was officially
named as COVID-19 that is Coronavirus disease 2019. The emergence of SARS-CoV-2 is the third introduction of a highly pathogenic coronavirus into the human population after the Severe acute respiratory syndrome coronavirus (SARS-CoV-2) and the Middle East respiratory syndrome (MERS-CoV). (Cascella M, et al,2020) Coronavirus is a positive sense, single stranded RNA (ribonucleic acid) virus. It is name so due to its Crown-like appearance. Coronaviruses are of four types namely 1) Alpha, 2) Beta, 3) Gamma and 4) Delta. They are originated from Bats, Rodents (1.2) and Avian species (3,4) respectively. SARS-CoV belongs to Beta-Coronavirus. It is elliptical, pleomorphic, and a size of 60-140nm. Whereas it is sensitive to UV (ultraviolet) rays and heat. It can be inactivated by Ether, Ethanol, Chlorine containing disinfectant. (Cascella M, et al,2020)

![Figure 1: Graphical representation of SARS-CoV, MERS-CoV, SARS-CoV-2 an its cellular receptor.](Balamurugan Shanmugaraj,et al,2020)

**CURRENT THERAPEUTIC STRATEGIES:**

**Anti-viral drugs:**

**Remdesivir**, prodrug, is a nucleoside analogue, it resembles the structure of adenosine, a broad spectrum antiviral drug. When experiments were carried out *in vitro*, the drug is capable of inhibiting human as well as animal viruses, including SARS-CoV-2. It is an RNA-dependent RNA polymerase (RdRp) inhibitor that does not allow replication of viral accessory proteins and inhibits viral RNA synthesis. As of the current date, top US infectious
disease official Anthony Fauci said that the Gilead, US based research pharmaceutical company has obtained positive effect of Remdesivir drug on COVID-19 patients. The *New England Journal of Medicine* study showed that 36 of 53 hospitalized patients, or 68%, with severe complications got better after they took it. (Wang.Y, et al, 2020)

According to the in vitro studies carried out earlier **Chloroquine** blocked COVID 19 infection at low micromolar concentration EC 50 of 1.3 μm and half a cytotoxic concentration (CC 50) greater than 100μl (Gao.J, et al, 2020). The mechanism of chloroquine was studied which effectively shows antiviral activity against SARS-CoV -2. The drug prevents the endocytosis by increasing the endosomal pH which avoids the virus – endosome fusion. It also inhibits the glycosylation of cellular receptors, Angiotensin converting enzyme 2 (ACE 2) on the viral cells. (Devaux.C.A, et al, 2020)

The C-reactive protein level (CRP) was far above the normal range in a patient before start of **Tocilizumab** treatment and improved after the treatment. Also the CRP level was decreased after the treatment. Increased Interleukin 6 indicates use of Tocilizumab in COVID-19 treatment. An inflammatory **cytokine** or **proinflammatory cytokine** is a type of signaling molecule (a cytokine) that is secreted from immune cells like helper T cells (Th) and macrophages, and certain other cell types that promote inflammation. (Luo.P, et al. 2020)

Using these drugs in longer doses may affect human health. Longer doses of Chloroquine can cause macular retinopathy, depending upon the cumulative dose and might lead to cardiomyopathy (Devaux.C. A, et al. 2020). Risk of adverse event with tocilizumab is that the dose of TCZ if greater than that of specified dose causes immunosuppressive effects, which causes significant risk of infection in patient with COVID-19 (Saiz.L, et al.2020). Including sepsis, gastrointestinal hepatotoxicity; perforation, bacterial pneumonia. Also causes alteration in blood parameter. (Saiz L, et al.2020)
ANTIBODY THERAPY:

From different proteins of SARS-CoV-2, Spike (S) protein is of considerable importance because it allows the adherence of viral particle to the host surface (ACE2, Angiotensin Converting Enzyme (Balamurugan Shanmugaraj, et al. 2020)). S1 subunit of spike protein interacts with the host cell receptor, therefore using monoclonal antibodies (mAbs) which binds S1 subunit can inhibit the interaction of SARS-CoV-2 with receptor. (Balamurugan Shanmugaraj, et al. 2020) (Figure 3) Schematic representation of SARS-CoV-2 neutralization mechanism.

For production of Monoclonal antibodies, against the SARS-CoV-2 spike protein, single intrasplenic immunization of plasmid DNA coding for antigen can be done (Yu X.F, et al. 2005). To construct the plasmid, there is need to identify the antigenic determinants in ACE2 binding domain of SARS-CoV-2 spike protein. This can be done by using various platforms, e.g., PROTEIN (DNASTAR Lasergene program package) (Yu X. F, et al. 2005). When mice are immunized with plasmid DNA, it develops antibody producing cells which can be then fused with myeloma cells to produce mAbs on large scale (Hybridoma technology). (Yu X. F, et al. 2005)
The large scale production of mAbs is labour intensive, time consuming and cost effective. Therefore, more work should be done to increase the large scale production of mAbs. (Yu. X. F., et al. 2005)

Figure 3: Schematic representation of SARS-CoV-2 neutralization mechanism. (Balamurugan Shanmugaraj, et al. 2020)

PLASMA THERAPY:
One of the hopeful treatments that has emerged is convalescent plasma (CP), or immune plasma, which is plasma that is collected from an infected individual, such as by COVID-19 (i.e., human anti–SARS-CoV-2 plasma), is then transfused into infected patients as a post-exposure prophylaxis.3 Unlike immunoglobulin (IgG)-derived antibodies such as plasma-derived monoclonal antibodies, CP is a passive antibody therapy that showed some success as a neutralizing antibody against other coronavirus epidemics, SARS-1 and Middle East respiratory syndrome (MERS), in the first two decades of the 2000s. CP-derived antibodies can neutralize a virus by preventing replication (e.g., by complement activation or phagocytosis) or by binding without interfering with replication. (Marano, G. et al. 2015)

Conclusion:
The COVID-19 pandemic is the greatest global public health crisis of this generation. The speed of clinical trials launched to investigate potential therapies for COVID-19 is increasing on a large scale. The individual’s immune system factors include genetics, age, gender, nutritional status, neuroendocrine-immune regulation, and physical status. These factors all
contribute to whether an individual is infected with the virus, the duration and severity of the disease, and the reinfection.

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ROLE OF IMMUNE SYSTEM IN COVID-19 INFECTION

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ABSTRACT:
COVID-19 (Coronavirus Disease 2019) is an infectious disease characterized by fever, dry cough, dyspnea, myalgia, and fatigue. It is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS CoV-2) named so due to its relatedness to the coronavirus that caused SARS outbreak of 2003. SARS CoV-2 is a single stranded RNA virus that enters via nose, mouth or eyes and travels to alveoli of lungs. ACE2 (Angiotensin converting enzyme 2) receptors on lung, kidney, gastrointestinal tract and cardiac epithelia serve as binding sites for the spike glycoprotein of the SARS CoV-2. The severity of the infection depends on the immunity of infected person, age, sex and previously presents health issues such as cardiac diseases, diabetes, blood pressure, kidney disorders etc. Multiple studies have shown that cytokine storm during infection lead to acute respiratory distress syndrome (ARDS) leading to respiratory failure. In case of severe inflammation ARDS leads to systemic inflammatory response syndrome (SIRS) leading to septic shock and multi organ failure. Current fatality rate of COVID-19 is 1-7%. Patients that have succumbed to COVID-19 have shown terminal respiratory failure; septic-shock, multiple organ failure and cardiogenic shock. In depth study of immune response in a symptomatic patients, non-critical patients and critical patients will be useful in understanding the cause of cytokine storms and other elevated immune reactions. In this review we have presented an overview of immune response seen during the illness.
Keywords: SARS CoV-2, cytokine storm, ARDS, multiple organ failure

INTRODUCTION
Respiratory syndrome COVID 19 which is caused by SARS-CoV-2 was declared as a pandemic by WHO on 11 February 2020 due to its rapid spread in 210 countries. As of 30th of April 2020, more than 32 lakh infections and more than 2 lakh deaths have been reported across the world (X. Li et al., 2020, Worldometer). SARS-CoV-2 is transmitted via cough or
sneeze of infected person. Even though clinical manifestations of COVID-19 are dominated by respiratory symptoms, newer studies have documented effect of infection on nervous and cardiovascular systems as well. Mortality rate is approximately 2% with large variation across population. Higher mortality rate of infected patients has been associated with impaired immunity. Common symptoms of COVID-19 include fever, dry cough, breathing issues, diarrhoea, and general body ache. (X. Li et al., 2020, Ye et al., 2020). However; in critical conditions the patient shows high fever, pneumonia which can further lead to kidney failure or multiple organ failure and death. The ongoing research investigations are directed towards the study of pathogenesis of the virus and cytokine storm that manifests during the infection. Cytokine storm is excessive or uncontrolled release of cytokines leading to hyper inflammation and at times, death.(Barnes et al., 2020) Cytokines are signalling molecules involved in immune system response. In order to device a treatment for this viral infection it is important to understand its interaction with the immune system.

**Virus structure and Pathogenesis**

Coronaviruses belong to the family *Coronaviridae* and order *Nidovirales*. They are classified in four genera, *Alphacoronavirus, Betacoronavirus, Gammacoronavirus* and *Deltacoronavirus* of which *Betacoronavirus* members infect humans. Coronaviruses are enveloped viruses having positive stranded RNA as genetic material. They have corona like projections or spikes on the outer surface. These spikes play an important role in infecting host cells. These viruses have largest genome among all the viruses ranging from 27-32 kb (F. Li, 2016). The genetic material is packed inside helix shaped capsid which consists of nucleocapsid protein (N) surrounded by an envelope. Three structural proteins viz. membrane protein (M), envelope protein (E) and spike protein (S) are associated with viral envelope (F. Li, 2016). Coronaviruses gain entry into host cells using spike proteins which bind to ACE2 receptors present on apical surface of polarized epithelia (Jia et al., 2005). The viral RNA undergoes translation in the host cytoplasm to produce an RNA dependent RNA polymerase which helps in the synthesis of the negative strand. The negative strand undergoes discontinuous transcription to produce multiple RNA species which in turn translate to various viral proteins essential for replication. Progeny virions come out of the cell by membrane budding without lysing the host cell.

**Humoral and Cellular Response**

In the starting phase of infection, host’s body produces virus specific B and T lymphocytes (Li et.al 2020). Predominantly IgM & IgG antibodies are produced of which IgM antibody
disappears in 12th week while IgG antibody can be found for relatively longer (2-4 years) period of time (Prompetchara et al., 2020). In cases, CD4+ and CD8+ T-cells reduce considerably in proportion. In severe cases polyfunctional CD4+ cells (IFNγ, TNFα and IL2) and CD8+ T-cells (IFNγ, TNFα and degranulated stage) are present in higher proportion as memory cells (Prompetchara et al., 2020)

**Cytokine storm**

Cytokine storm is uncontrolled, massive immune response against the viral infection. It is marked by increased concentrations of IL1β, IL6, IL7, IL8, IL10, IFNγ, IFNγ inducible protein 10 (Barnes et al., 2020). In COVID-19 infection there is delayed immune response consisting of release of cytokines and chemokines (figure 1). These inflammatory mediators regulate neutrophil activity and induce the expression of chemo-attractants. Rapid replication of SARS CoV-2 induces delayed release of interferons which induce inflammatory monocytes, and macrophages. These macrophages produce a large number of pro-inflammatory cytokines such as IL6, IL1β etc. These pro-inflammatory cytokines induce apoptosis of T-cells. (Barnes et al., 2020) IFN-αβ and IFNγ induce accumulation of inflammatory cells through the mechanisms involving Fas-Fas ligand (FasL) or TRAIL death receptor 5(DR5) and cause apoptosis of alveolar epithelial cells. (Ye et al 2020) Cytokine storms can lead to acute lung injury, Acute Respiratory Distress Syndrome (ARDS), and death. Cytokine storm also leads to neutrophilia. Neutrophils have three mechanisms to kill pathogens viz. oxidative burst, phagocytosis and formation of Neutrophil Extracellular Traps (NETs). NETs are web like DNA or protein structures (Barnes et al., 2020). They are released into extracellular space by neutrophils to trap or kill pathogen. The three enzymes involved in formation of NETs are Neutrophil Elastase (NE) (responsible for degradation of intracellular proteins and nuclear disintegration), Peptidyl Arginine Deiminase 4 (PADI4) (responsible for decondensation and release of DNA) and Gasdermin D (responsible for formation of pores in the membrane of neutrophil) (Barnes et al., 2020).
Figure 1: Immune response during SARS-CoV-2 infection comprises of two steps namely release of primary cytokines and release of secondary cytokines. Secondary cytokines in excess can cause cytokine storms.

Immunotherapy
Considering the role of immune system in controlling viral infection and in worsening of the situation by cytokine storms, therapies are being explored to modulate immune system (Tufan et al. 2020). Until now the approaches which are taken into consideration are polyclonal antibody by plasma therapy, Polypeptide hormone for maturation of T-cells, SARS-CoV2 Receptor Binding Domain(RBD)-specific antibodies, ACE2 immuno-adhesion, and monoclonal antibody against IL6 (Tocilizumab) (Cao, 2020, Phua et al., 2020, Mehta et al., 2020, K. Yuki, 2020). Viral vectors, nanoparticles are also being studied for their potential therapeutic application. DNA vaccine and inactivated whole virus vaccine can be the potential target for vaccine production. Another therapeutic approach is the use of mesenchymal stem cells (MSC) due to their anti-inflammatory and anti-apoptotic effects. MSCs can thus be used for the repair of respiratory epithelial cells damage (Cao, 2020, Shi et al., 2020).
CONCLUSION

COVID-19 is similar to influenza SARS and MERS in pathogenesis. In case of SARS also cytokine storms are reported. There seem to be two clear situations. Situation one- SARS-COV2 infects the lung epithelial cells gaining entry in the system. Inflammation is initiated and virus particles are destructed by immune cells. Inflammation is in control and hence patient recovers after destruction of virus particles. Situation two - SARS-COV2 infects the lung cells and inflammation is initiated. Virus particles are destructed by lymphocytes. During interaction viral cells lymphocytes are damages. It results in reduction of CD4 and CD8 T-cells. As a result of destruction of lymphocytes more cytokines are released. These secondary cytokines cause cytokine storm. This results into the complication such as lung damage and sometimes in multiple organ failures. Immune compromised patients have more chances of facing cytokines storms i.e. excessive inflammation and hence there is more possibility of fatal reaction. The severity of disease depends on also factors such as genetic makeup, age, gender, nutritional status and physical status. Immunoglobulins such as IgM and IgG play very important role in avoiding disease progression. Various immunotherapeutic agents including vaccines, monoclonal antibodies and stem cells are under clinical trials which may be useful in avoiding spread of COVID-19. Understanding the role and reaction of individual immune system will play important role in defining the strategies to evade SARS-COV2 infection.

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INFORMATION ABOUT COVID-19 (Coronavirus)

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ABSTRACT:

The word corona means “crown,” and when examined closely, the round virus has a “crown” of proteins called peplomers jutting out from its center in every direction. These proteins help the virus identify whether it can infect its host. Coronavirus disease (COVID-19) is an infectious disease caused by a newly discovered coronavirus. COVID-19 virus spreads primarily through droplets of saliva or discharge from the nose when an infected person coughs or sneezes. Older people, and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious COVID-19 which affects different people in different ways.

INTRODUCTION:

Some common symptoms that have been specifically linked to COVID-19 include:

- shortness of breath.
- having a cough that gets more severe over time.
- a low-grade fever that gradually increases in temperature.
- fatigue.

Less common symptoms:

- aches and pains.
- sore throat.
- diarrhoea.
- conjunctivitis.
- headache.
- loss of taste or smell.
- a rash on skin, or discolouration of fingers or toes.
SERIOUS SYMPTOMS:

- difficulty breathing or shortness of breath.
- chest pain or pressure.

Seek immediate medical attention if you have serious symptoms. Always call before visiting your doctor or health facility. On average it takes 5–6 days from when someone is infected with the virus for symptoms to show, however it can take up to 14 days.

WHAT CAUSES CORONAVIRUSES?

Coronaviruses are zoonotic. This means they first develop in animals before developing in humans. For the virus to pass from animal to humans, a person has to come into close contact with an animal that carries the infection. Once the virus develops in people, coronaviruses can be spread from person to person through respiratory droplets. This is a technical name for the wet stuff that moves through the air when you cough or sneeze. The viral material hangs out in these droplets and can be breathed into the respiratory tract (your windpipe and lungs), where the virus can then lead to an infection. Researchers believe that the virus may have been passed from bats to another animal — and then transmitted to humans. This transmission likely occurred in the open food market in Wuhan, China.

WHO’S AT INCREASED RISK?

Without taking proper prevention measures, you’re also at high risk if you:

- live with someone who has contracted the virus. Also, have an intimate partner who has contracted the virus.

Older people and people with certain health conditions have a higher risk for severe complications if they contract the virus. These health conditions include:

- lung conditions, such as COPD and asthma.
- certain heart conditions.
- immune system conditions, such as HIV.
- cancer.
- severe obesity.
- other health conditions, if not well-controlled, such as diabetes, kidney disease, or liver disease.
Pregnant women can have a higher risk of complications. Like, transmitting the virus from mother to child during pregnancy isn’t likely, but the newborn is capable of contracting the virus after birth.

**WHAT TREATMENTS ARE AVAILABLE?**

There’s currently no treatment specifically approved for COVID-19, and no cure for an infection, although treatments and vaccines are currently under study.

Seek medical help if you think you have COVID-19. Your doctor will recommend treatment for any symptoms or complications that develop, and let you know if you need to seek emergency treatment.

**HOW CAN YOU PREVENT CORONAVIRUSES?**

The best way to prevent the spread of infection is to avoid or limit contact with people who are showing symptoms of COVID-19 or any respiratory infection.

The next best thing you can do is practice good hygiene and physical distancing to prevent bacteria and viruses from spreading.

**PREVENTION TIPS**

- Wash your hands frequently for at least 20 seconds at a time with warm water and soap. Don’t touch your face, eyes, nose, or mouth when your hands are dirty.
- Don’t go out if you’re feeling sick or have any cold or flu symptoms.
- Stay at least (2 meters) away from people.
- Cover your mouth with a tissue or the inside of your elbow whenever you sneeze or cough. Throw away any tissues you use right away.
- Clean any objects you touch a lot. Use disinfectants on objects like phones, computers, utensils, dishware, and doorknobs.

**SHOULD YOU WEAR A MASK?**

If you’re out in a public setting where it’s difficult to follow physical distancing guidelines, it is important that that you wear a cloth face mask that covers your mouth and nose. You can make your own mask using basic materials such as a bandana, a T-shirt, or cotton fabric. It’s critical to keep the mask clean. Wash it each time you use it. Avoid touching the front of it with your hands. Also, try to avoid touching your mouth, nose, and eyes when you remove it. This prevents you from possibly transferring the virus from a mask to your hands and from your hands to your face.
COVID-19 : A PANDEMIC LIKE NEVER BEFORE.

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ABSTRACT

The 2019 Novel Corona virus infection [COVID-19] is an ongoing health emergency of international significance. In this article we focus on what is exactly the pandemic of covid-19, the mode of transmission of the virus, symptoms of the disease, prevention measures taken by the government to control the pandemic. The information on various methods through which individuals can protect themselves from getting infected are discussed along with various organizations which are working and responding to this pandemic. Also various laws that are implemented in the countries due to pandemic of covid-19 are mentioned. Last but very important about our role and responsibilities in major steps against the spread of virus among the public by following the orders of the respected authorities in government.

INTRODUCTION:

On February 11, 2020 the World Health Organization [WHO] announced an official name for the disease that is causing the 2019 novel corona virus outbreak, first identified in Wuhan, China. The new name of this disease is corona virus disease 2019 abbreviated as CoViD-19. In covid-19 ‘Co’ stands for ‘corona’, ‘Vi’ stands for ‘virus’, and ‘D’ for ‘disease’. Formerly, this disease was referred to as ‘2019 novel corona virus’ or ‘2019-nCoV’. There are many types of human corona viruses including some that commonly cause mild upper respiratory tract illness. Covid-19 is a new disease, caused by novel (or new) corona virus that has not previously been seen in humans. Covid-19 is an emerging threat to the globe and it is very important that we make common people aware about its spread. This article is written to spread awareness among the people about the virus. Many people don’t know about how this disease? And how deadly it is? In order to keep ourselves and our society protected from this virus we must know more and more about this. We should know about the law implemented to control the spread of the virus and our responsibilities towards the law. Every must know about the social distancing and its importance. People should know why it is necessary to put a mask while going out in public place.
1. What are pandemics?

The occurrence in a community or region of cases of an illness, specific health related behavior or other health related events clearly in excess of normal expectancy.

An epidemic is an outbreak that occurs over a wide geographic area and affects an exceptionally high proportion of the population whereas a pandemic is related to geographic spread and is used to describe a disease that affects a whole country or the entire world.

Till date the entire world is suffering from the pandemic of corona virus disease which is also known as COVID-19.

2. What is COVID-19 Pandemic?

Corona virus disease [Covid-19] is an infectious viral disease. The disease was first discovered in Wuhan, China in late 2019 and has set off a global pandemic. Expert says SARS-CO-2 originated in bats and that’s how similarly the corona virus behind the Middle East Respiratory Syndrome [MERS] and Sever Acute Respiratory Syndrome [SARS] also originated. SARS-CoV-2 made the jump to human at one of Wuhan’s open air ‘wet-markets’. They’re where customers buy fresh meat and fish, including animals that are killed on the spot. This has caused the spread of this new corona virus which is known as covid-19. Covid-19 is emerging as a great pandemic all over the world. Until now the new corona virus [covid-19] has affected 212 countries and territories around the world and 2 international conveyances infecting more than 3,586,271 people with 248,789 confirmed deaths.

India has reached to the number of 50,000-mark cases of covid-19. The figure includes 33,514 active cases, 14182 patients who have been cured and 1,694 fatalities. According to the data reported it took nearly 5 days to reach the no of 40000 from the number of 30000, when it took nearly a week to reach 30000 from 20000. While India recorded its first 10000 cases in 43 days but the contagiousness of corona virus is increasing everyday and now it only three days to add another 10000. Only in Maharashtra’s Pune 2000 cases of covid-19 has been reported.

3. Why pandemic of COVID-19 has happened?

The pandemic of covid-19 is frightening and genuinely threatening to humans being. A virus is another organism or another being trying to thrive Covid-19 infects one person to another
and harm them, it’s very quick and deadly in doing so. In order for a disease to infect people and then spread to the extent that it becomes a pandemic, it needs certain combinations of conditions. In essence pandemic occurs because of an intersection of their biological, social and other environmental factors. Bats are the reservoir for SARS-CO-2 but the new corona virus disease i.e. covid-19 jumped the species barrier to human from another intermediate animal host. This intermediate animal host could be a domesticated wild animal. The agent that causes this disease is responsible for the pandemic is the corona virus itself. And when the environmental features are such that infected people are regularly exposing others to the agents; then we have the conditions that are ripe for this pandemic.

4. How COVID-19 spreads?

Covid-19 is an infectious disease which is spreading from one person to another very quickly and deadly frightening the entire world. The virus that causes covid-19 is mainly transmitted through droplets generated when an infected person cough, sneezes or exhales. These droplets are too heavy to hang in the air and quickly falls on floors or surfaces. One can be infected by breathing in the virus if comes in close proximity of someone who is infected with covid-19 or by touching contaminated surface/s and then touching own eyes, nose or mouth.

Symptoms for covid-19:

Common symptoms

- Fever
- Tiredness
- Dry cough

Some people may experience

- Aches and pains
- Nasal congestion
- Runny nose
- Sore throat
- Diarrhoea
On average it takes 5-6 days from when someone is infected with the virus for symptoms to show, however it can take up to 14 days. People with mild symptoms who are otherwise healthy should self isolate and seek medical attentions. If somebody have a fever, cough and difficulty in breathing should immediately seek for medical attentions.

5. Who gets affected?

Most people infected with the covid-19 virus will experience mild to moderate respiratory illness and recover without requiring special treatment. Older people and those with underlying medical problems like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more susceptible to develop serious, deadly illness.

6. Prevention:

To prevent the spread of covid-19 -

- Clean your hands often use soap and water or an alcohol based hand rub
- Maintain safe distance from anyone who is coughing or sneezing.
- Don’t touch your eyes nose or mouth when you are in a public place.
- Cover your nose and mouth with your bent elbow or a tissue when you cough or sneeze.
- Stay home if you feel unwell.
- If you have a fever, cough or difficulty in breathing, seek medical attention, call in advance
- Follow the directions of your local health authority.
- Avoiding unneeded visits to medical facilities, allow health care system to operate more effectively.

7. How to control?

This is very important that we take some initiative to control the spread of covid-19. It can be achieved by public education, legal regulations and direct actions.

- Public education
  - Providing people with the information about how to protect themselves.
  - Promoting best hand washing and hygiene practices and providing hygiene supplies.
- Cleaning and disinfecting school, buildings, public places, hospitals, especially water and sanitation facilities.
- Increasing airflow and ventilation

Educating people about the spread of pandemic can encourage them to become advocates for disease prevention and control at home, work place and in the community by taking about how to prevent the spread of virus.

❖ Legal regulations

As covid-19 spread around the globe, government has imposed quarantines and travel bans on an unprecedented scale. Thousands of people have been subjected to legally enforceable quarantines or are in “self quarantine “. Quarantine and travel bans are often the first response against new infectious disease. However, these old tools are usually of limited utility for highly transmissible disease and if imposed with too heavy a hand or in too haphazard a manner, they can be counter-productive. With a virus such as covid-19 they cannot provide a sufficient response.

❖ Direct actions:

In India, Joint Secretary Ministry of health classified all the districts in the country into three categories. Hotspot districts are those where the number of cases is high, while non hotspots are those region that have reported case of covid-19 but the figure is limited. The green zone refers to regions where there are no cases of Novel corona virus. Also the home ministry announces of lockdown that is all public services such as inter-state, inter-district movement of people, bus, metro services to be barred. Domestic international air travel, train services educational institutions and coaching centers are been shut. All the public places such as cinema halls, malls, bars, shopping complexes, swimming pools, gyms, sports complexes are also closed in order to maintain social distancing among the people. even all the social, religious places and places of worship are shut.

8. Who is responding?

There are many organizations, governments, non- governmental organizations and private entities responding to it at various levels. At international level WORLD HEALTH ORGANISATION [WHO] is responding to pandemic of covid-19 by:
● Funding research

● Creating policy framework

● Implementing various awareness programs including vaccinations trainings and emergency responses

● WHO also oversees International Health Regulations.

When it comes to the regulations and response at national level it is undertaken by the health ministries and similar agencies

Public health officers are there to respond to the pandemic at local and state level. All these agencies are interconnected with each other in a form of network at various levels.

Individuals also have a constructive role to play in both shaping and influencing the strategies applied to get a control over the pandemics.

CONCLUSION:

This pandemic of covid-19 has created threat all over the world. Many people are dying due to this contagious disease. We must need to take care of us and our community by just following the orders of the government, following social distancing and not going out of our houses. By doing this we can stop the spread of this virus at some level and ensure that we do not get infected with the same. Government and other organizations are doing their level best but we as responsible youth should spread awareness about the virus. During such time we must encourage our society to follow best hygiene practices and preventing the spread of virus to some extent. This can help us to at least keep ourselves, our family and also our society safe from this contagious disease. And even if someone got infected with the virus they must get themselves quarantine. Even the person who is not infected should follow social distancing. In this time of great pandemic we must be kind towards others and help the one who is in need.

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ABSTRACT
The occurrence of severe acute respiratory syndrome or novel coronavirus or COVID-19 in Wuhan during month of December 2019, has resulted in a huge global outbreak and is one of the serious public health issues nowadays. Corona viruses can cause symptoms such as the fever, cough, sore throat, severe headache and SARS etc. In 2019, a new corona virus was identified as the cause of a disease outbreak that originated in China. In this paper I have studied the spread of corona virus depending on age & gender using statistical reference. Till date it is observed that number of cases are increasing in India, so to predict the number of cases exponential model has been made. The proportion of deaths to number of cases and total population of respective states in India has been examined.

Keywords: COVID-19, exponential model, chi square distribution, proportion test, death rates.

INTRODUCTION:
The COVID – 19 pandemic, caused by severe acute respiratory syndrome coronavirus. The first case of COVID-19 was identified in Wuhan, China, during the month of December 2019. The novel coronavirus SARS-CoV-2 disease has been named “COVID-19” by the World Health Organization (WHO) and on January 30, the COVID-19 outbreak was declared to constitute a Public Health Emergency of International Concern by the WHO Director-General [5]. As of 15th May there are around 4.5 million cases and 306,000 deaths worldwide. The origin of COVID-19 are of a zoonotic, possibly of bat origin [4, 11].

Similarly to SARS-CoV and MERS-CoV, the novel virus is transmitted from person to person principally by respiratory droplets, causing such symptoms as fever, cough, and shortness of breath after a period believed to range from 2 to 14 days following infection, according to the Centers for Disease Control and Prevention (CDC) [1, 3, 6]. The virus is
primarily spread between people during close contact, most often through small droplets produced by coughing, sneezing and talking. The droplets usually fall on ground or on to surfaces rather than travelling through air over long distances. Less commonly, people may become infected by touching a contaminated surface and then touching their faces. It is most contagious during the first three days after the onset of symptoms. This virus can spread before any kinds of symptoms appear and also from the people who do not show any symptom.

The pandemic has caused severe global economic disruption, including largest global recession since the great depression, leading towards cancelation of sporting, religious, political and cultural events. Though we can say decreased emission of pollutants and greenhouse gases is one of the eco friendly side effects of this pandemic. Schools colleges and universities are been closed either nationwide or local basis[2].

METHODOLOGY:

The data is secondary data which I have collected from internet. It has number of Corona cases, number of deaths, total Corona population day wise and state wise [8, 9, 10]. It also contains number of males and number of females for different states. Exploratory analysis is done for the collected data. For statistical analysis I have used statistical tools like chi square test of independence, death rate, proportionality test [7].
EXPLORATORY ANALYSIS:

- Cumulative number of cases in India:

From this graph we can conclude that number of cases is exponentially increasing.

- Number of Deaths vs number of cases:

As number of cases increases number of deaths also increases.
● Number of new cases per day:

From this graph we may say that number of new cases are increases day by day.

● Number of cases age wise:

Age group of 21-40yrs are getting highly infected to corona.

STATISTICAL ANALYSIS:
The data of number of cases in India shows exponential trend so number of cases till 15th may is clubbed into the interval of 15 days so that the fitted exponential model will predict total number of cases in next 15 days and so on. I get the model,

\[ Y = 49343.29 \times (5.2499)^X \]

Above model can predict the total number of cases in next 15 days.

Hence predicted value of \( Y = 136247 \) in next 15 days.

**Death Rate:**

Death rate is calculated for all states. Death rate of West Bengal (9.1426), Gujrat (6.1021) and Maharashtra (4.8767) is more whereas it is minimum for Odisha (0.4464).

**Proportion Test:**

\( H_0 \): Proportion of deaths to the number of cases is same for all states.

\( H_1 \): Proportion of deaths to the number of cases is not same for all states.

Chi-square calculated = 1096.9, df = 22, p-value = 2.2e\(^{-16}\)

Therefore, we may say that the proportion of death to total population of state and to that of number of cases is different for all states in India. Similarly, proportion of number of cases to population is different for all the states in India.

**Chi square test:**

It is used to check dependency of number of cases of Covid-19 on gender.

\( H_0 \): Number of cases are independent of the gender.

\( H_1 \): Number of cases are dependent of the gender.

Chi-square calculated = 129.6 and Chi-square table = 9.3926.

Therefore, we may say that number of cases increasing is dependent on the gender of patient. It is observed that number of cases in males are high as compared to female.

**CONCLUSIONS:**

- Number of cases is exponentially increasing.
- Number of cases in India are increasing day by day. Number of deaths in India due to corona are also increasing day by day.
• Age group of 21-40yrs are getting highly infected to corona. Whereas deaths of age group above 75yrs are high, this is because the immunity power of working population is more as compared to old people.

• Predicted total number of cases in India till 30th may is around 136274.

• Number of cases increasing is dependent on age group. Working population has high rate of getting infected.

• Male has more probability of death due to corona to that of female.

• Number of cases increasing is dependent on the gender of patient, number of males getting affected is high. Therefore, chances of getting infected for males is more than that of female. This is maybe due to most of the men are working outside which increase their chances of getting exposed to the virus.

• Proportions of deaths to the number of cases and to that of total population is not same for all the states in India. Also, proportion of number of cases to total population is different for all states.

LIMITATIONS:

• Data collected is from internet so there are certain limitations.

• Predicted number of cases may vary because we have proper data of only 2-3 months.

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IMPACT OF CORONA VIRUS: A STATISTICAL STUDY

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ABSTRACT:

The coronavirus disease has become a public health emergency of international concern affecting almost all countries. In the prevalence of COVID 19, everyone is stressful due to the exponential increase in number of confirmed cases of the corona virus. The main focus of this article is to study the impact of COVID-19 on various districts of Maharashtra, increase or decrease in number of confirmed, recovered, deceased, active cases on the daily basis in all states. According to the Union health ministry, almost 63% of corona virus deaths in India of people of 60+ age. According to our study the main reason behind this rate may be decreased in lung capacity of people who are above age 50 or 60.

The study of capacities of lungs were done in the month of September and October 2019 for the annual project submission at the graduation level. Here for this research we were linked this project to the study of corona virus. To study the impact of COVID-19 we have studied the data of two months from 14th march to 26th April.

This data is available on https://www.covid19india.org/deepdive In this pandemic situation, the districts like Mumbai, Pune, Thane has large outbreak of corona virus and number of confirmed cases along with the number of deceased cases increases exponentially. In this prevalence of COVID-19 almost 100 people between the ages 50 to 70 lost their lives.

As per the previous research of WHO, the corona virus affects the lungs of the patients and causes difficulty in breathing. According to our study of lung capacity, lung capacity decreases with the age. That’s why older people are at more risk of corona virus. This study suggest that lung capacity is significantly associated with the exercises. It can be increased by doing stamina increasing exercises like aerobics, gym, jogging etc and also the most important “Pranayam”.
INTRODUCTION:

a. Corona virus

At the close 2019, Wuhan in china has reported the case of pneumonia of unknown cause to the WHO [121]. Later on, the number of infected people were increased and on 30th January 2020 the WHO declared this outbreak as a Public Health of Emergency of International concern. On 11th February the WHO announce the name for new virus as COVID-19. According to WHO and other research, the corona virus typically affects the respiratory system and have 3 types of symptoms at different levels.

Most common symptoms: fever, dry cough, tiredness

Less common symptoms: aches and pains, sore throat, diarrhoea, conjunctivitis, headache, loss of taste or smell, a rash on skin, or discolouration of fingers or toes.

Serious symptoms: difficulty breathing or shortness of breath, chest pain or pressure, loss of speech or movement.

On 30th January India reported the first case [122] of corona virus in Kerala and until 3 February it was rose up to 3 cases, all students were returned home from China. Until 3rd of march there were no cases of COVID-19 but on 4th march there ware total new 22 cases [122] of corona virus came into the light. And from 15th march there is exponential growth in the number of infected people. So as a preventive major government decided to completely lockdown 82 districts in 22 states till 31st march. After that there were 3 lockdowns done until today’s date.

To study the impact of COVID 19 on different states we have plotted the time series plots and subdivided bar diagrams to illustrate the results. To study the age wise death of people due to corona we have plotted the histogram. We have given the logistics regression model for the data of deceased and recovered people along with their age. Which gives the chances of people will die due to COVID impact if age of a person will be increased. (here all remaining conditions like immunity of person, habits of a person, whether he or she comes in a contact with infected people or not, person’s health conditions etc were not taken into under consideration)
Lung Capacity

Lung capacity the aggregation of residual volume, inspiratory reserved volume and expiratory reserved volume. The average lung capacity for adult male on the basis of previous research is 6 litre and for females it is 4.2 litre [122]. Lung capacity is depending upon the various factors like age, height, weight, exercise, smoking etc.

For lung capacity study we have used the spirometer method to estimate the lung capacity of an individual. For making a spirometer we require a bottle, pipe, Water tub, measuring flask, tape, and marker. Firstly, using measuring flask fill 250 ml of water into water bottle and mark the line on water bottle using marker do that until the water bottle gets completely filled with 5litre water. So, there are total 20 lines on the water bottle in which each line is of 250 ml. Now at the time of experiment allow the performer to take a rest and settle down for a while to normalize the breath. The half of water tub should be filled with the water and water bottle should be inverted into the water tub by taking the precaution that no water should be displaced from the bottle in to the tub. Now the one side of the pipe should be given to the performer and the other side of the pipe will be inserted into that water bottle from the side which is in the water tub. The performer asked to take a deep breath and allow to blow into the water bottle through that pipe. Due to air pressure the water gets displaced in to the water tub. Remove the water bottle from the tub and measure the lines upto that extent where the surface area of remaining water meets to that particular line. Number of lines measure multiplied by 250 and divided by 1000 will give the lung capacity of an individual.

We have taken the sample of 310 people and using the spirometer method we estimated the lung capacities of them. To study the variation of lung capacities among age groups, weight groups, gender wise we use some basic statistical tests and interpreted the same.

Statistical Concepts

The statistical test includes Shapiro test which is used to check is the distribution of lung capacity is normal or not. According to that distribution of lung capacity is non normal so we decided to use non parametric tests for the interpretation purpose. We have used Mann Whitney and Kruskal Walli test for the testing of variation in lung capacities of an individuals. Kruskal Wallis test used in situations where the normality assumption is unjustified. It is the alternative procedure to the F test analysis of variance. It is used for
testing the equality of average mean of sample across the considered groups. Mann Whitney test is the another non parametric test which is used to check whether two sample have the same median or not. Under the assumptions that both samples are independent and random in nature, also both distribution of random variable should be continuous in nature. To check the association between two qualitative data Cramer’s V test can be used but before that there is need to check that both qualitative characteristics are dependent on each other with chi square test. Cramer’s V test gives the amount of association between that two characteristics. The required test statistics can be given as \[ V = \sqrt{\frac{\chi^2}{n(q-1)}} \] Where q is min (row and column).

Logistics regression model is a type of regression model in which the response variable is dichotomous or binary. These values are usually coded as \( Y=1 \) for success and \( Y=0 \) for failure. The event of interest can be treated as success. In this person will recovered will be the success and person will be died due to corona impact will considered as a failure. It is assumed that \( Y \) has binomial distribution. The regression model is given as follows:

\[
Y = \frac{e^{\beta_0 + \beta_1 X}}{1 + e^{\beta_0 + \beta_1 X}} + \varepsilon
\]

\( \beta_0 \) and \( \beta_1 \) are regression coefficients. \( \varepsilon \) is the error term of Bernoulli random variable with \( E(\varepsilon)=0 \) and \( \text{var}(\varepsilon)=\Pi(X)\left(1-\Pi(X)\right) \)

**DISCUSSION AND RESULTS:**

We focus on the daily figures of the number of confirmed cases, recovered cases and deceased cases of all states for 2 months from 14th March to 14th May. We have studied the number of confirmed, recovered, deceased and active cases of Maharashtra state particularly for Mumbai, Pune, Thane, Akola, Aurangabad, Jalgaon, Nashik, Palghar, Raigad, Solapur. Figure 1 shows the exponential increased in total number of confirmed cases and total number of recovered cases in all states of India per day. Till 14th may there were around 4500 cases were reported as confirmed and total 1500 cases were reported as recovered in overall states of India. But we have to noticed that the number of confirmed cases is the upper bound of number of tests were performed in that area. In the region of Pune, Mumbai, Thane there are many test done at a time but in the region of West Bengal or Chandigarh performed number of tests were very less as compared to Pune, Mumbai or Thane. So there may be a chance of more number of people present who are infected by the various or there are some carriers may be present.
Figure 2 shows the total number of people deceased in states per day due to corona virus. This is the exponential increase in the number of deceased people. Figure 3 and Figure 4 represents the total number of cases district wise. From these graphs it is very clear that Mumbai, Pune, Thane became the hotspots of corona virus till that date.

Figure 5 represents the frequency of people died of corresponding age groups. From this histogram it is very clear that people who have age more than 50 have high risk of corona virus.

More than 100 people between the age group 50 to 60 died due to corona virus. Around 90 to 95 people died between the age group 60 to 70 and around 40 people died between the age group 70 to 80. According to descriptive statistics of deceased people, the average age of people who died due to corona virus is 54 years for male and for females. According to kurtosis value, the distribution of deceased people is leptokurtic and it is negatively skewed for both males and females. (see Table 1 below)

Descriptive statistics for age of deceased people

Table 1

<table>
<thead>
<tr>
<th>Measures</th>
<th>Female</th>
<th>Male</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>54</td>
<td>54</td>
</tr>
<tr>
<td>Standard Error</td>
<td>0.7462</td>
<td>0.7456</td>
</tr>
<tr>
<td>Median</td>
<td>57</td>
<td>57</td>
</tr>
<tr>
<td>Mode</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>Standard Deviation</td>
<td>17.08</td>
<td>17.15</td>
</tr>
<tr>
<td>Sample Variance</td>
<td>291.81</td>
<td>294.13</td>
</tr>
<tr>
<td>Kurtosis</td>
<td>0.61</td>
<td>0.57</td>
</tr>
<tr>
<td>Skewness</td>
<td>-0.784</td>
<td>-0.765</td>
</tr>
</tbody>
</table>

Regression model:
Here using the data of people deceased and recovered along with their age has considered. The person will be recovered is taken as a success of event and the person will die is taken as a failure of event. The response variable is taken as the status of a person i.e. recovered (1) and deceased (0). Age factor is taken as the regressor.

The model summary is given as:

| Regressors      | value | Pr(>|t|) |
|-----------------|-------|---------|
| Intercept       | 1.8849| 3.97e-09|
| Age             | -0.0586| <2e-16 |
| Null deviance   | 492.34| Df =431 |
| Residual deviance| 416.72| Df =430 |

Akaike information Criterion (AIC) for model is 420.72

Let G be the test statistic for checking the significance of regressor

\[ G = \text{Null deviance} - \text{Residual deviance} = 75.62 \]

\( \chi^2_{1,0.05} = 3.841 \) here G greater than table value so we are unable to accept the null hypothesis at 5 % los. Hence regressor age is significant at 5 % los.

Thus, the model is given as:

\[ \text{Status} = \frac{e^{1.8849 - 0.0586 \times \text{age}}}{1 + e^{1.8849 - 0.0586 \times \text{age}}} + \varepsilon \]

Odds ratio is given as \( e^{-0.0586} = 0.9430 \) which interpreted as if a person’s age increases then chance of person will live becomes decreases with 6%.

Here also we can conclude that as age increases the chance of person will die who is already affected by corona virus becomes increases.

**Why old aged people or people above age 51 are at high risk:**

According to our study of lung capacity which was done in the month of September and October 2019, Lung capacity is negatively correlated with the age. For our data set of size 310 in which 158 were males and 152 were females. The average lung capacity for males was observed to be 3.36 litre for males and 2.85 litres for females. To estimate the correlation, we have used the correlation test and estimated the following result:

Correlation test table:
<table>
<thead>
<tr>
<th>Lung capacity</th>
<th>Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>r</td>
<td>-0.2498987</td>
</tr>
<tr>
<td>t statistic</td>
<td>4.5294</td>
</tr>
<tr>
<td>Df</td>
<td>308</td>
</tr>
<tr>
<td>p value</td>
<td>4.234e-06</td>
</tr>
<tr>
<td>Decision</td>
<td>negative correlation</td>
</tr>
</tbody>
</table>

The graphical representation is given in Figure 6.

**Time series plot for number of recovered and confirmed cases per day in the states**

![Graph of recovered and confirmed cases per day](image)

*Figure 1*

**Time series plot for total number of deceased people per day in states**
Figure 2

Multiple bar diagram for number of cases reported in the districts

Figure 3
Multiple bar diagram for number of cases reported in the districts

![Bar diagram showing number of cases district wise](image)

*Figure 4*

Histogram for analysing the frequency of deceased people in different age groups
Figure 5

Figure 6 also support the claim that as age increases the lung capacity decreases. The corona virus affects the lungs of a patients and resulting into difficulty in breathing. As study suggest age increases lung capacity decreases so obviously corona virus can damage the lungs as fast as possible of people above age 50 than the people age below 50.

For checking the dependencies of lung capacity with smoking and exercise we have used the chi square test of independence. p value = 0.000013 and 0.00023 respectively which are less than the level of significance alpha 0.05 supports that smoking and exercise both depends on
the lung capacities. Using Cramer’s V test we estimated that there is strong association between exercise, smoking with lung capacity respectively. People who do power yoga have 3.41 litre average lung capacity, people who do regular yoga have average lung capacity equals to 3.08 litre and people who don’t do any kind of yoga activity have 2 litre as average lung capacity.

CONCLUSIONS:

There is exponential increase in the number of active cases, deceased cases, confirmed cases and recovered cases. The distribution of age of deceased people is leptokurtic and are negatively skewed for both males and females. Number of people of age group greater than 50 have high risk as they have low lung capacity than other due to age factor that’s why they should take the at most care and stayed to be isolated also do the exercises on daily basis. As corona virus impacts on the lung functions and which creates the difficulty in breathing so minimize this impact one should increase the lung capacity. For that one should do power yoga and more specifically Pranayam. Smoking should be avoided as it affects the lung functions of an individual. Logistics regression model for the data of deceased and recovered people with their age groups is given below:

\[
\text{Status} = \frac{e^{1.8849 - 0.0586 \times \text{age}}}{1 + e^{1.8849 - 0.0586 \times \text{age}}} + \varepsilon
\]

Where, The response variable is taken as the status of a person i.e. recovered (1) and deceased (0). Age factor is taken as the regressor.

if a person’s age increases then chance of person will live becomes decreases with 6%.

Here also we can conclude that as age increases the chance of person will die who is already affected by corona virus becomes increases.

ACKNOWLEDGEMENT

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हमारे के हैं। करने सामान्य श्वसन गया। सामाजिक रोग को है। 

(Severe Acute Respiratory Syndrome- SARS) के फ़ॉर्म था। यह वाले रोजमराष एक टॉपिक है। 

में अंतराष्ट्रीय संगठनों के और COVID-19 से लिये वायरस सरकार के अध्यक्ष, स्वास््य सुनक और तरह से निर्देशक उपहारों के पान से अनुकूलित प्रदान कर सकते हैं। 

 वायरस में कोरोनावायरस के वायरस 2019-19 और अनुसार, कोरोनावायरस की अनुसार रोगविज्ञान का क्षेत्र। 

COVID-19 के वायरस के आधीशन अनुभव करने हैं। 

COVID-19 वायरस के संक्रमित अवशेष लोग के समस्या स्वास््य की का अनुभव करने और विशेष उपचार आधार के क्षेत्र में दी गई है। दृष्टिकोण की कोरोनावायरस, अनुसार बढ़ावा को करने की सहकर्मी और अनुभवी व्यक्ति में अनुकूलित प्रदान करता है। 

COVID-19 के फॉर्म के लिए विभिन्न श्वास्त्र सामाजिक दिनों दोनों और स्वास््य सुनक और तरह से निर्देशक उपहारों के पान से अनुकूलित प्रदान कर सकते हैं। उन संचार के लिए विभिन्न नियम कोरोनावायरस और तरह से निर्देशक उपहारों के पान के लिए अनुकूलित प्रदान कर सकते हैं। 

COVID-19 के वायरस कंट्रोल और अनुभव अनुभव करने हैं। 

COVID-19 के वायरस कंट्रोल और अनुभव अनुभव करने हैं।
फैलता है। अगर हांकों को धोने या अनाकहेल अधारात्मक रूप से उपयोग करके और अगर खांसी को धोने से अपने आप को और व्यायांक तक संक्रमण से बचाए।

COVID-19 कारक बुद्धि रूप से लाल की रंगी या लाल से लवकर है जब इससे संक्रमित त्वचा की दर्दनाक या ठीक आती है। इसलिए यह महत्वपूर्ण है कि आप राहने वाले क्षेत्र का स्वास्थ्य अपनाने के लिए, एक लघुस्ती कोट्टे की तरह संचालित करें।

इस समय, COVID-19 का लक्षण विश्लेषण का एक अभ्यास करने के लिए, एक लघुस्ती कोट्टे की तरह संचालित करें।

**रोकथाम:****
संक्रमण को रोकने और COVID-19 के संक्रमण को दीवार करने के लिए, निम्नलिखित कार्य करेंः
- अपने हांकों को नियमित रूप से धोने के लिए छोटे से लघुस्ती कोट्टे की तरह संचालित करें।
- अपने खांसी या रेत को धोने के लिए, एक लघुस्ती कोट्टे की तरह संचालित करें।
- अपने आप को अपनाने और हांकों को धोने के लिए, एक लघुस्ती कोट्टे की तरह संचालित करें।
- अगर आप अपना स्वास्थ्य संबंधित करते हैं तो पर रहें।

**लक्षण:**
COVID-19 असंग्रह असंग्रह लक्षणों का अन्य अभ्यास करने और अपने आप को अपनाने के लिए आम भाषा में भी है। अभिक्रिया संक्रमित त्वचा की कारणों के लिए आयोजित करने के लिए आयोजित करें।

**काम सामान्य लक्षण:**
- खांसी
- श्वसन
- लक्षणों का अभ्यास

**सामान्य लक्षण:**
- आत्ममृत्यु
- असंग्रह
- दराल-सराल
- असंग्रह

1. **कोरोनावायरस का सामान्य लक्षण क्या है?**
कोरोनावायरस सामान्य लक्षण का एक बड़ा परिवार है जो जानवरों से मणुन्द्रों में बीमारी का कारण हो सकता है। मणुन्द्रों में एक कोरोनावायरस को सामान्य रूप से संक्रमित किया जाता है। यह असंग्रह और बीमारी से पूर्व कोरोनावायरस (MERS) और बीमारी से दोस्त लक्षण (SARS) के कारण व्यायांक व्यायांक का कारण बनाना जाता है।

सबसे हां की है तो दोनों को बीमारी का कारण कोरोनावायरस से COVID-19 है।
2. COVID-19 क्या है?
COVID-19 संक्रमक कर्सी है जो हालांकि हमी 3 खोजे गए कोरोनावायरस के करार करता है। यह यमा लक्षण और कैम्प्सी दिसंबर 2019 में चीन के जूहु से फैलने अगला था। COVID-19 के विरोध के क्षेत्र पर कई देशों का प्रभाव करने वाली महामारी है।

3. COVID-19 संक्रमण क्या है?
COVID-19 के साथ आम लक्षण हैं घुटने, गर्मी, तंगी और लक्षण। आम लक्षण जो कम आम हैं और कुछ दृश्यों को प्रभावित कर सकते हैं उनमें दो तरह: अगला और दूसरा नाक के नाय, फिब्रिय, निस्वासाबल रोगियों में ख्यात, लाल, रक्त या गाम का संक्रमण और ठंडा में दर्ज करने या इलाज में दर्ज करने या अन्य लक्षणों का उपस्थिति को।

4. क्या मुझे COVID-19 संक्रमण हैं और मुझे चिकित्सा / देखावाम कर लेनी पड़ती है?
यदि, आपके मामले मध्य लक्षण हैं, जैसे कि हांगकांग या हांगकांग इलाज के लिए एक आमतौर पर विश्लेषण डेटाबेस की आवश्यकता नहीं होती है। पर पर हों, लक्षण का जानकारी अदालत करने और अपने लक्षणों के निर्णय करने के लिए आमतौर पर राजनीतिक मामलों का पालन करने के लिए।

5. क्या COVID-19 का ऐसे त्वचा से फक्का जा सकता है?
कभी कभी किसी दूरी से चिकित्सा का उपग्रह वहाँ जाता है। दूसरा लक्षण दो अन्य हैं। कभी कभी यह गुलाम तहत है हो जाता है। दूसरे के साथ हो कि कभी 1 मीटर रह रहा महत्वपूर्ण है। यह भी त्वचा का पारी और की चलती और संस्कृति जैसे संस्कृति को उच्च से अलग करता है। लेख इन मामलों को तकनीक संक्रमण हो सकता है। फिर उनकी अनुभव तक होते हैं। यह तब कभी होती है कि कभी होती है कि कभी होती है। यह तब कभी होती है कि कभी होती है। यह तब कभी होती है कि कभी होती है। यह तब कभी होती है कि कभी होती है।

6. क्या COVID-19 का ऐसे त्वचा से फक्का जा सकता है?
कभी कभी किसी दूरी से चिकित्सा का उपग्रह वहाँ जाता है। दूसरा लक्षण दो अन्य हैं। कभी कभी यह गुलाम तहत है हो जाता है। दूसरे के साथ हो कि कभी 1 मीटर रह रहा महत्वपूर्ण है। यह भी त्वचा का पारी और की चलती और संस्कृति जैसे संस्कृति को उच्च से अलग करता है। लेख इन मामलों को तकनीक संक्रमण हो सकता है। फिर उनकी अनुभव तक होते हैं। यह तब कभी होती है। यह तब कभी होती है। यह तब कभी होती है। यह तब कभी होती है। यह तब कभी होती है।
हालाकि, यदि आप संक्रमित या इंगु मूल्य वाले क्षेत्र में रहते हैं तो यह महसूल है कि आप बुखार के लक्षणों को नोटिफाई न करें। चिकित्सा सहायता ले। उन्होंने आपका स्वास्थ्य सुरक्षित करने के लिए लक्षित करते हैं, जिसमें आप पर्याप्त स्वास्थ्य सुरक्षा होती है। आपके साथ की जा सकती है। हालाकि, यदि आप संक्रमित या इंगु मूल्य वाले क्षेत्र में रहते हैं तो यह महसूल है कि आप बुखार के लक्षणों को नोटिफाई न करें। चिकित्सा सहायता ले। जब आप स्वास्थ्य सुरक्षा में भाग लेते हैं, तो यह संकेत होता है कि आप बुखार के लक्षणों को नोटिफाई न करें। चिकित्सा सहायता ले। यदि संकेत होता है कि आप स्वास्थ्य सुरक्षा में भाग लेते हैं, तो यह संकेत होता है कि आप स्वास्थ्य सुरक्षा में भाग लेते हैं। यदि वह एक बच्चा है जो बीमार है, तो यह संकेत होता है कि आप स्वास्थ्य सुरक्षा में भाग लेते हैं। यदि वह एक बच्चा है जो बीमार है, तो यह संकेत होता है कि आप स्वास्थ्य सुरक्षा में भाग लेते हैं।

## 9.आलोक-अलग होने का क्या मतलब है?

आलोक-अलग उन लोगों द्वारा लिखा गया एक महसूल यूनार्ड है, जिसके परिचालन के लक्षणों हस्तलक्षण हुए से दूसरों को सहभागिता करने से बचने के लिए COVID-19 स्वास्थ्य कारण है।

आलोक-अलग तब होता है जब एक व्यक्ति जो इंगु मूल्य वाले क्षेत्र में रहते हैं तो यह महसूल है कि आप बुखार के लक्षणों को नोटिफाई न करें। चिकित्सा सहायता ले। जब आप स्वास्थ्य सुरक्षा में भाग लेते हैं, तो यह संकेत होता है कि आप स्वास्थ्य सुरक्षा में भाग लेते हैं।

## 10.यदि भेज पाया कोई त्वचा नहीं है, तो मुंह क्या करना चाहिए, लेकिन मुंह क्या समझाना है कि मुंह COVID-19 से अवरोध कराया गया है स्व-संग्रह का क्या अर्थ है?

स्व-संग्रह का अर्थ है, स्वयं के दूसरों से अवरोध करणे व्यक्ति आप किसी के साथ COVID-19 के संकेत में आ गए हैं, तो गर्दन, स्वस्थ, भावना न हो।

स्व-संग्रह और आप आपके लक्षणों के साथ बचने के लिए स्वयं की निर्गमन करें। स्व-संग्रह का लक्षण संग्रह को रोकना है।

यदि आप इंगु मूल्य वाले क्षेत्र में रहते हैं तो यह महसूल है कि आप बुखार के लक्षणों को नोटिफाई न करें। चिकित्सा सहायता ले। जब आप स्वास्थ्य सुरक्षा में भाग लेते हैं, तो यह संकेत होता है कि आप स्वास्थ्य सुरक्षा में भाग लेते हैं।

## 11.आलोक-अलग, स्व-संग्रह और भेद के बीच अंतर क्या है?

संग्रह का महत्व मालिकियत को प्रभावित करने वा उन लोगों को अवरोध करने का और बीमार है जो रासायनिक रूप से छुड़ रहे हैं। यदि वह एक बच्चा है जो बीमार है, तो यह संकेत होता है कि आप स्वास्थ्य सुरक्षा में भाग लेते हैं।
13. कूद को बचाने और बीमारी से प्रसार को रोकने के लिए क्या कर सकता हूँ?

WHO जेवीसैट और अपने राष्ट्रीय और राज्यीय स्वास्थ्यप्राध्यापक में संबंधित क्रियाओं का समन्वय करते हैं और कई लोग प्रक्रिया का समन्वय कर रहे हैं। सीओवीआईडी के लिए निरीक्षण को सहभागी होने पर आप COVID-19 क्वॉन्ट्युम स्वास्थ्य अस्तित्व से संगत से सकते हैं।
- जीवनार्थी आर्थिक जीवन गार्ड जरूरी हो सकता है, तथा आपकी स्वास्थ्य अस्तित्व को पूरी तरह से बचाने का प्रयास करें।
- जीवनार्थी आर्थिक जीवन गार्ड का समन्वय करने में सहभागी होने पर आप अपने आर्थिक स्वास्थ्य स्थिति से भी सुरक्षित हो सकते हैं।
- जीवनार्थी आर्थिक जीवन गार्ड का समन्वय करने में सहभागी होने पर आप अपने आर्थिक स्वास्थ्य स्थिति से भी सुरक्षित हो सकते हैं।
- जीवनार्थी आर्थिक जीवन गार्ड का समन्वय करने में सहभागी होने पर आप अपने आर्थिक स्वास्थ्य स्थिति से भी सुरक्षित हो सकते हैं।

14. कूद का कोई दौरा, दवा या उपचार है?

हालांकि कुछ पत्रकारों ने इस समस्या के लिए कुछ नए उपचारों का समाचार दिया है, लेकिन सही दवाओं के समक्ष कहीं भी निरीक्षण होने के लिए कॉल करने के लिए कुछ नए उपचारों का समाचार दिया है। लेकिन सही दवाओं के समक्ष कहीं भी निरीक्षण होने के लिए कॉल करने के लिए कुछ नए उपचारों का समाचार दिया है।

WHO COVID-19 के के संबंध में एंटिडर्टिक दवाओं निरीक्षण किसी भी दाटा के लिए स्व-दाटा की
15. क्या WHO COVID-19 के प्रसार को रोकने के लिए मेडिकल मास्क पहनने की सलाह देता है?

दर्जन में, व्यापक समूह में स्वास्थ्य व्यक्तियों में भी (विविधता या अनुभव) के उपयोग के लिए निर्देशों का उपयोग नहीं किया गया है। हालांकि, इसीसे संबंधित रूप से मास्क पहनने के लिए सलाह दी जा सकती है। मुख्य रूप से व्यापक देखभाल सेंटरों में विविधता मास्क की स्थिरता की जाती है, लेकिन अन्य विविधताओं में विवाद किया जा सकता है (नीचे देखें).

विविधता मास्क को अन्य दवाओं संबंधित की गई और नियोजन उपभोक्ताओं जैसे अंध में नियोजन और शारीरिक गतिविधियों के साथ जोड़ा जाना चाहिए।

स्वास्थ्य देखभाल के लिए जानकारी का उपयोग करने वाले मास्क और शारीरिक जैसे N95, FFP2 या संबंधित के लिए स्वास्थ्य कर्मचारीओं के लिए आवश्यक होता है। स्वास्थ्यविभाग का उपयोग करने वाले मास्क और शारीरिक जैसे N95, FFP2 या संबंधित के लिए स्वास्थ्य कर्मचारीओं के लिए आवश्यक होता है।

स्वास्थ्यविभाग का उपयोग करने वाले मास्क और शारीरिक जैसे N95, FFP2 या संबंधित के लिए स्वास्थ्य कर्मचारीओं के लिए आवश्यक होता है।

त्याग के से सारों को COVID-19 के लिए मास्क और शारीरिक जैसे N95, FFP2 या संबंधित के लिए स्वास्थ्य कर्मचारीओं के लिए आवश्यक होता है। स्वास्थ्यविभाग का उपयोग करने वाले मास्क और शारीरिक जैसे N95, FFP2 या संबंधित के लिए स्वास्थ्य कर्मचारीओं के लिए आवश्यक होता है।

COVID-19 में स्वास्थ्य विभाग के किसी भी व्यक्ति का देखभाल करने वाले मास्क और शारीरिक जैसे N95, FFP2 या संबंधित के लिए स्वास्थ्य कर्मचारीओं के लिए आवश्यक होता है।
COVID-19 के संक्रमण के लिए एक विकल्प नहीं है। चीन में 2019 के दिनांक 17 तक सास का सीओवीआईडी के याद मीटर - करना है। जानवरों द्वारा वायरस की उपस्थिति है। इन जानवरों में COVID-19 से बीमार होने के पश्चात् सभी सीस्टेम छोड़ देता है, जिससे वायरस की रोकथाम करने में सक्षम भी है। यह जानवरों के साथ-साथ संलग्न उपायों को हमेशा लाभ कराता जानवर का जीवन परिवर्तन नहीं है। उन्हें अयोग्य जानवरों के साथ-साथ कोई प्रभाव नहीं है।

18. क्या में अपने पालतू जानवर से COVID-19 पकड़ सकता है?
संक्रमण कुत्तों के संक्रमण में सबसे बड़े विकल्प और भिडियों (पालतू बिल्लियों और एक बाचक) ने COVID-19 के लिए संक्रमण करती है। इसके अलावा, संक्रमण के लिए अफिसेबस्टेंशन ही नहीं है। वायरस के रूप में आत्मविश्वास के लिए फेफड़ों द्वारा रखा जाता है। प्रश्निक बिंदुओं में, दोनों बिंदुओं के संक्रमण के लिए एक ही प्राकृतिक प्रकार के अन्य जानवरों में संक्रमण में समय लगता है, लेकिन इस बात को सूचित करने वाला है कि कई जानवरों को जीवन तक भी पकड़ सकता है। क्या में, इसके बाद को कोई सामान्य उपाय लगा सकता है?

19. सत्यों पर वायरस कितने समय तक जीवित रहता है?
सत्यों पर कोरोनावायरस की आपसी संसार के लिए सक्षम महानालृतयों के लिए परिवर्तन होने में घटता है। उसके बाद को कोई सामान्य उपाय नहीं है। क्या में, इसके बाद को कोई सामान्य उपाय नहीं है।

20. क्या कृत्रिम जूत को उद्भव सुरक्षित कैसे बनाया?
कृत्रिम जूत की बाहरी को सुरक्षित करने के लिए उपयोग किया जाता है। जूत की सही शाब्दिक और पायर भरी में साथ-साथ का रखने के लिए सीस्टेम्स और बाहरी के लिए सुरक्षित किया जाता है।

21. कृत्रिम कोरोना ड्रिफ्ट जूत को कैसे बनाया?
कृत्रिम कोरोना ड्रिफ्ट की बाहरी को सुरक्षित करने के लिए उपयोग किया जाता है। जूत की सही शाब्दिक और पायर भरी में साथ-साथ का रखने के लिए सीस्टेम्स और बाहरी के लिए सुरक्षित किया जाता है।

22. क्या COVID-19 का परिचय या उसका इजाज़ करने में कारण है?
COVID-19 का परिचय या उसका इजाज़ करने में कारण नहीं है। इसके बाद को कोई सामान्य उपाय नहीं है।
नहीं। एंटीबायोथेस काम करते हैं नहीं। एंटीबायोथेस काम करते हैं।

COVID-19 वायरस के कारण होता है, इसलिए एंटीबायोथेस काम करते हैं।

COVID-19 की रोकथाम या उचार के लाभ के रूप में नहीं किया जा सकता है। अभावताओं में चिकित्सकों को कबीलेज एंटीबायोथेस दवाओं का उपयोग करना होगा जो समानानुपातिक जीवाणु संक्रमणों को रोकते हैं या उनका इलाज करते हैं जो गंभीर रूप से बीमार रोगियों में सीओवीआईडी - 19 की जितावश हो सकती है। नया एक जीवाणु संक्रमण के इलाज के लिए एक नए चिकित्सक द्वारा निर्देशित के रूप में इस्तेमाल किया जा सकता है।

23. क्या मैं COVID-19 को बीमारी बनाना कर सकता हूं?
हां, क्योंकि प्रायोगिक जांच से पता चलता है कि वायरस ङ�ुप मामलों में मास में दूरी हो सकता है, जो एक, COVID-19 के मास-मासिक प्रसारण की रिपोर्ट नहीं है। इसके अलावा, बच्चों या मास में COVID-19 वायरस के लेखित रूप के बारे में कोई प्रमाण नहीं है।

WHO COVID-19 के प्रसार के तरीकों पर चल रहे होंगे का आकार से रहे हैं और इस विषय पर जारी जानकारी को साझा करना जरूरी रखेगा।
आरोग्य सेतु मोबाइल ऐपः

आरोग्य सेतु (शाहिद क बूम से होने वाली मृत्यु के लिए पुल) भारतीय COVID-19 ट्रैकर मोबाइल ऐप्लाइकेशन है जो राष्ट्रीय सुरक्षा विभाग के द्वारा निर्मित किया गया है और यह सरकार के इनकडक्यक्त्रिक और सुरक्षा प्रदूषणकोशी संबंध के अर्थात आता।

अवस्थानकः
इस ऐप्लाइकेशन का विषयक उद्देश्य COVID-19 के बारे में जानकारी पैकेज और भारत के लोगों के लिए आवश्यक COVID-19 संबंधी स्वास्थ्य सेवाएं को जोड़ना है। यह ऐप कोरोनानुप्रस्तावना संबंधित स्वास्थ्य सेवाएं को जोड़ने के लिए उपलब्ध और सक्षम बनाता है।

एजेंसी: 
इस ऐप्लाइकेशन अंतरराष्ट्रीय स्वास्थ्य नीति का अनुयाय करता है। यह ऐप कोरोनानुप्रस्तावना संबंधित स्वास्थ्य सेवाएं को जोड़ने के लिए उपलब्ध और सक्षम बनाता है।

प्रविष्टियाँ के बारे में परवाह है

(PM CARES Fund)

उद्देश्य:
- सर्वजनिक स्वास्थ्य आवास का उद्देश्य को इस उद्देश्य को पूरा करने के लिए स्वास्थ्य सेवाएं को जोड़ना।

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- सर्वजनिक स्वास्थ्य आवास का उद्देश्य को इस उद्देश्य को पूरा करने के लिए स्वास्थ्य सेवाएं को जोड़ना।

उद्देश्य:
- सर्वजनिक स्वास्थ्य आवास का उद्देश्य को इस उद्देश्य को पूरा करने के लिए स्वास्थ्य सेवाएं को जोड़ना।
यह राहत या सहयोग का कार्य करता, या तो मानव निम्नलिखित या प्राकृतिक, जिनमें स्वास्थ्य कोशल या अन्य विभिन्न परिसंपत्तियों का निर्माण या उन्मुक्ति कार्यक्रम है, अथवा अन्य दुनियाभर में जिसे अन्यों, प्रायः अन्य संस्थानों या किसी अन्य गठन की सहयोग के लिए दान देना।

• किसी सहयोग कार्य करने के लिए, धन के मुद्दों का अनुमोदन न्याय के या ऐसे अन्य कदम उठाएं, जिनें अवैधता से लैंगिक नियमों के लिए न्यायी के दृष्टि के अनुसार समझा जा सकता है।
• किसी अन्य निर्देशनिक को कदम करने के लिए, जो उपरेक्षा बदलूचे के साथ अनंतर नहीं है।

रुपांतरण के माध्यम: 
• प्रधान मंत्री पीयूष के कोश के पदों अपना और राज के, गृह मंत्रालय के नंबर और निम्नलिखित भारत सरकार निम्नलिखित पदों न्यायी होते हैं।
• क्षुद्र पीयूष (प्रधान मंत्री) के अनुसार, जो न्यायी के पास तीन न्यायी बोर्ड को नामित करने की शक्तिहीन जो अनुशंसा, स्वास्थ्य, विज्ञान, सामाजिक कार्य, कानून, लोक प्रशासन और परीक्षण के क्षेत्र में प्रशिक्षित व्यक्ति होंगे।
• किसी भी व्यक्ति का एक इंटरनेट नियुक्त किया गया तो एक निश्चित शक्ति लेने के कार्य करेंगे।
अन्य आवश्यकताएँ: 
• इस कोश में व्यक्तियों / संगठनों से पूर्ण स्वीकृतिके कोशाद्ध कर देना है और इसे कई विभिन्न सहयोग नहीं मिलती है। निम्नलिखित उपयोग अंतर करने का उद्देश्य कुछ पूरे करने में किया जाएगा।

PM CARES फंड के लिए दान आयकर अध्यक्ष, 1961 के तहत 100% एक के लिए 80G ताज़ा के लिए अधिकता प्राप्त करें। PM CARES फंड के लिए दान भी कर्मी अध्यक्ष और 2013 के तहत कॉर्पोरेट सामाजिक दानियाँ (CSR) के रूप में निम्न जारी करें।

PM CARES फंड को भी FCRA के तहत पूरे मिलते हैं और विदेशी दान प्राप्त करने के लिए एक अन्य खाता खोलना चाहिए है। यह पीयूष CARES फंड को मिला, जो प्रत्येक में विज्ञान और संस्थागत से दान और योजनाओं को लेकर करने के साथ बनाता है। यह प्रामुख्य के राष्ट्रीय राहत कोष (पीएमआरएफ़आरएफ़) के संघ एंड है।

पीएमएनआरएफ़आरएफ़ को 2011 से एक सार्वजनिक दृष्टि के रूप में दिखने योजना भी मिलता है।

प्रमुख दान खाते का विवरण:
• खाते का नाम: पीएम केयर
• खाता संख्या: 2121PM20202
• IFSC कोड: SBIN0000691
• UPI: pmcares@sbi
• भारतीय रेलवे बैंक, नई दिल्ली में बंगार कोश
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इस लेख को समाप्त करने के लिए मैं सलाह देना सिंद करेगी कक हमें कोरोनावायरस से "स्टे एट होम" और "स्टे सेफ" रहना चाहिए। इससे इस महामारी की स्थिति से जबरदस्ती ही उड़ने से मदद लीजिए। -जय दहन्ि।

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