Review Article

Covid-19 infection and Prevention: A brief review

Abstract-

Corona viruses, a broad group of viruses that have an ability to infect a wide range of animals, or people. It can lead to mild to severe respiratory illnesses. In humans it caused fatal respiratory illness in 2002 and 2012, making it a new concern for public health in the 21st century. Its origin was in Wuhan from where it is rapidly spreading to the rest of the world. In terms of both the number of sick people and the geographic span of epidemic locations, it has crossed the counts of SARS and MERS. The ongoing COVID-19 outbreak has caused a significant threat to worldwide public life.

Keywords: Coronavirus disease, respiratory illnesses, health emergency, clinical symptoms

Introduction

Covid-19 was first emerged in 2019 in Wuhan, China. It is a virus which has changed the mental and physical state of a person after 2019. It was declared as a pandemic by WHO in 2020.

Emergence and spread

Many facilities for health care in Wuhan, China, reported wide number of patients with pneumonia of unclear reason in late December 2019. The majority of the first twenty seven confirmed hospitalised diseased people were related to Huanan Seafood Wholesale Market, a wet market in downtown Wuhan that sells not just seafood but also live animals including as poultry and wildlife4,8. According to a retrospective analysis, the first known case occurred on December 8, 2019. (ref.9). On December 31, the Wuhan Municipal Health Commission warned the public of an undetermined pneumonia outbreak and notified the World Health Organization (WHO)9.

Independent teams of Chinese scientists identified the causative agent of this emergent disease as a betacoronavirus that had never been observed before. The outcome of this etiological diagnosis was made public on January 9, 2020. On 10 January, the first genome sequence of the novel coronavirus was published on the Virological website, and on 12 January, the GISAID database released more nearly full genome sequences determined by several research institutes. All of these cases showed that the novel virus was transmitted from person to person4,12–14. 14. in the lunar new year the outbreak lead to virus transmission in China was aided by travel between cities prior to the festival. This new coronavirus pneumonia quickly spread throughout Hubei Province and the rest of China. Within a month, it had spread throughout China's 34 provinces. Thousands of fresh cases were detected everyday in late January15, bringing the total number of confirmed cases to thousands. The new coronavirus outbreak was declared a public health emergency of worldwide concern by the WHO on January 30th16. The novel coronavirus was called 'SARS-CoV-2' by the International Committee on Virus Taxonomy on Feb 11th, and it was called 'COVID-19' by the WHO [72]. By Feb the COVID-19 outbreak in China reached a proportion to be called as a pandemic. According to National Health Commission of China, in early February the total number of cases increased rapidly, with new confirmed 3,000

cases every day on average. China implemented significant public health steps to combat COVID-19.

On January 23, the total shut down of city of Wuhan took place, halting all the movement and transit within the city. In the following weeks, all events and gatherings taking place outside were prohibited, and in some towns and rural areas were shut down. As a result of these steps, the number of new cases in China has consistently decreased. Because some of the earliest cases in Wuhan had no epidemiological link to the fish market22, it's been hypothesised that the market wasn't the first source of SARS-CoV-2 infection in humans. However, this single early report is unable to provide a definitive response as to the source of SARS-CoV-2 infection and contamination, and so a false positive result cannot be ruled out. Further research which included a larger number of samples from people, animals, and surroundings, as well as well-validated tests, are needed to answer this extremely contentious subject.

Epidemiology and Pathogenesis

People of all ages are at risk. Spread of the disease was through large droplets which was produced by people who were having symptoms, when they cough and sneeze, although it can also be spread by asymptomatic people and before the development of symptoms [9]. According to studies, the throat has larger viral loads than the nasal cavity, with no change in viral burden between symptomatic and asymptomatic persons [12].

People can either infectious for the time they have symptoms or even after recovering clinically. A resident of United Kingdom who attended a conference in Singapore was responsible for infecting 11 people while his vacation in a resort in the French Alps and his return to the UK [6]. The droplets from infectious people have ability to travel up to 12 metres and deposit on surfaces. In favourable climatic circumstances, it can survive for days on surfaces, but standard disinfectants such as sodium hypochlorite, hydrogen peroxide, and others kill it in less than a minute [13]. Infection is contracted by inhaling these droplets or by contacting infected surfaces and then it spreads by touching the nose, mouth, and eyes.

The virus was also been found in stool, water supply with subsequent transmission via aerosolization/fecooral pathway has been proposed [6]. Transplacental transfer was also described the foetus was not getting infected from the pregnant women as far as we know [14]. Neonatal illness caused by postnatal transmission, on the other hand, has been documented [14]. 2 to 14 days is the known incubation period. Angiotensin receptor 2 (ACE2) has been identified as the receptor via which the virus enters the respiratory mucosa [11]. Various modelling studies [11] estimate the basic case reproduction rate (BCR) to be between 2 and 6.47. SARS had a BCR of 2 and pandemic flu H1N1 2009 had a BCR of 1.3.

Clinical Features

The symptoms of COVID-19 are of wide range, asymptomatic, acute respiratory distress syndrome or multi-organ failure. Often fever (not always), cough, sore throat, headache, weariness, headache, myalgia, and dyspnea are all common clinical symptoms. There has also been mention of conjunctivitis. As a result, they are difficult to distinguish from other respiratory infections. In a small percentage of patients, the condition can develop to pneumonia, respiratory failure, and mortality by the end of the first week. Inflammatory cytokines such as IL2, IL7, IL10, GCSF, IP10, MCP1, MIP1A, and TNF are all related with

this progression [15]. The time for the onset of symptoms to dyspnea was 5 days, hospitalisation was 7 days, and ARDS was 8 days.

In published series, 25–30 percent of affected patients required intensive care admission. Complications like acute lung injury, ARDS, shock, and acute kidney injury were seen. Beginning of recovery takes place in the second or third week. The average length of people who were getting recovered to stay in the hospital was 10 days. The elderly and those with underlying co-morbidities are more likely to have negative outcomes and die. The mortality rate was 4 percent to 11 percent in adults who were hospitalised. The overall case mortality rate [2] is between 2 and 3 percent.

This could be owing to selection bias, with only the most severe cases reported from Wuhan, or a propensity of the Asian population to the virus due to greater ACE2 receptor expression on the respiratory mucosa [11]. Disease in neonates, babies, and children has also been found to be much less severe than in adults. There were 14 males and 20 females among 34 youngsters hospitalised to a hospital in Shenzhen, China, between January 19th and February 7th. The average age of children having this problem was 8 years and 11 months, and 28 of them had a family member infected, and 26 of them had visited or lived in China's Hubei region. All of the patients were asymptomatic (9%) or had a minor form of the condition.

There were no cases that were severe or critical. Fever (50 percent) and cough (25 percent) were the most frequent symptoms (38 percent).

Diagnosis

Someone who has a fever is called a suspect case, sore throat, or cough can also be a symptom and has travelled to China or somewhere else where COVID-19 is persistently transmitted locally, or who has had contact with patients who have travelled to China or other areas where COVID-19 is persistently transmitted locally, or who is confirmed to be COVID-19 infected. Cases can, be asymptomatic. Someone who is suspected and gets a positive molecular test is called a confirmed case. Specific molecular tests on samples taken from respiratory tract (throat swab, nasopharyngeal swab, sputum, endotracheal aspirates, and bronchoalveolar lavage) can used for diagnosis. Viruses are also be found in the stool and, in the blood too. It's worth noting that the COVID-19 isn't included in any of the existing multiplex PCR panels. There are currently no commercial tests available.

In the event of a case in India, the sample should be forwarded to one of the designated labs of the country or the National Institute of Virology in Pune. Commercial tests will become accessible as the epidemic progresses. Other types of laboratory tests are frequently non-specific.

In most cases, the count of white cell is normal or low. In most cases, the platelet count is near to normal or slightly lower. The values of CRP and ESR are usually high, whereas the levels of procalcitonin are normal. A level of high procalcitonin could be indicated for bacterial co-infection.

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Treatment

Supportive and symptomatic care is the mainstay of treatment. For the prevention of transmission of the disease to others, patients, and healthcare professionals, the first step is to provide proper isolation (described below). The treatment of mild illnesses could be done at home with education on warning signs. Provision of oxygen via nasal prongs, face mask, high flow nasal cannula (HFNC), or non-invasive breathing is recommended in hypoxic patients. It's possible that there can be requirement for mechanical ventilation or possibly extra corporeal membrane oxygen assistance. In some cases, renal replacement treatment may be required. If co-infections are suspected or confirmed, antibiotics and antifungals are required.

COVID-19 has no approved treatment at this time. Patients treated with lopinavir-ritonavir with ribavirin showed better outcomes than those treated with ribavirin alone in a historical control trial in patients with SARS. In a case series of 99 hospitalised patients with COVID-19 infection from Wuhan, oxygen was given to 76%, noninvasive ventilation to 13%, mechanical ventilation to 4%, extracorporeal membrane oxygenation (ECMO) to 3%, continuous renal replacement therapy (CRRT) to 9%, antibiotics to 71 percent, antifungals to 15%, glucocorticoids to 19%, and intravenous immunoglobulin therapy to 27% [15]. 75 percent of the patients received antiviral medication that included oseltamivir, ganciclovir, and lopinavirritonavir.

Non-invasive ventilation lasted 4–22 days [median 9 days], while mechanical ventilation lasted 3–20 days [median 17 days]. All of the children in the case series reported earlier recovered with basic treatment and did not require critical care.

Anecdotal evidence suggests that remdeswir, a broad-spectrum anti-RNA medication developed for Ebola, can be used to treat COVID-19 [27]. Before these medications are advised, more evidence is needed. Arbidol (an antiviral medicine available in Russia and China), intravenous immunoglobulin, interferons, chloroquine, and plasma from COVID-19 patients are among the other treatments indicated for treatment. In addition, the Chinese rules provide instructions for using traditional Chinese herbs.

Prevention

It is suggested that confirmed or suspected cases of mild sickness be isolated at home. To enable for viral eradication, proper ventilation and sunlight should be provided at home. Cough hygiene and the use of a basic surgical mask should be required of all patients. When in patients room, a surgical mask should be worn and wash their hands frequently. The spread of COVID-19 to healthcare personnel poses the greatest danger.

In the 2002 SARS pandemic, healthcare professionals accounted for 21% of those afflicted [31]. In China, about 1500 healthcare personnel have been affected, with six deaths. To preserve continuity of care and avoid infection transfer to other patients, it is critical to protect healthcare staff. Patients should be kept in different rooms or in groups. Negative pressure chambers are rarely required. Decontamination of the rooms, surfaces, and equipment should be done on a regular basis, ideally using sodium hypochlorite. There should be provision for N95 respirators, protective suits, and goggles for healthcare personnel who have been fit tested.

During procedures for aerosol-generation which includes intubation, suction, and tracheostomies, airborne transmission precautions should be considered. The development of COVID-19 symptoms should be followed in all contacts, including healthcare staff. Patients can be released from isolation after three days of afebrile status and two consecutive negative molecular tests at one-day intervals. This differs from the pandemic flu recommendation, which said that patients should return to work/school once afebrile for 24 hours or by day 7 of illness. Negative molecular tests were not required to be released. People should avoid

crowded locations and postpone travels which are not required to areas where transmission is still active at the community level. They should be encouraged to cough into a sleeve or tissue rather than their hands, and to wash their hands every 15–20 minutes. Surgical masks should be required for patients with respiratory complaints. The use of a mask by healthy people in public settings has not been proved to protect against respiratory virus infections, and the World Health Organization does not recommend use at this time. In China, however, the public is required to wear masks in public, particularly in congested areas, and large-scale gatherings are outlawed (entertainment parks etc). China is also drafting legislation that would restrict the sale and trade of wild animals. The international outpouring of support has been overwhelming. People returning from China/evacuated from China are being assessed for clinical symptoms, isolated, and tested for COVID-19 for two weeks, even if asymptomatic.

Vaccines

Vaccines are based on a living microorganism which is weakened so that disease cannot be caused by it. Particularly affective microorganisms are attenuated microorganisms in increasing the immune system power and it creates a strong and permanent immunological memory that is beneficial for prevention of infection since they retain the ability to multiply in vivo and cause a restricted disease. Using attenuated vaccines, hundreds of millions of individuals have been protected from diseases that are both crippling and lethal.

Vaccines : inactivated SARS-CoV-2 viruses

Vaccines which are on the concept of killed microorganisms are part of a long-standing technical platform that has resulted in a large number of vaccines. This method produces more stable vaccines than live attenuated vaccines.

Strategy

Various chemical approaches are used to inactivate the SARS-CoV-2 virus. All of these potential vaccinations are given intramuscularly.

Frontrunners

Clinical testing of 7 vaccine candidates based on differently inactivated SARS-CoV-2 virions are in process, with 4 of them being licenced to limit their use in Phase III trials. Phase II trials reports where available which demonstrated that the vaccination is safe and elicits a high antibody titer. The following organisations are in charge of the seven clinical trial.

Vaccines : SARS-CoV-2 proteins

Several human vaccinations are based on proteins found on bacteria' surfaces [1]. Originally, these proteins were extracted from bacteria, but today, they are synthesised in vitro using recombinant DNA technology in the vast majority of situations.

Strategy

The enormous aggregates of the Spike protein that are protruded outside the virion are said to be critical for the SARS-docking CoV-2's to human cells. As a result, all of these vaccines target the Spike protein or its components, albeit other SARS-CoV-2 proteins, most notably the nucleoprotein (N).

Frontrunners

The numerous vaccine projects which are based on SARS-CoV-2 proteins, their fragments, or their fragments combination. At least 16 candidate vaccines are already in human trials and 2 in Phase II trial

1. Spike protein - Adimmune, Taiwan; Biotechnology Vector, Russia; Clover Biopharmarm plus GSK adjuvant, China-Italy; CoVaxx, US; Medigen, Taiwan-US, plus CpG adjuvant; Sanofi plus GSK adjuvant, France - Italy; The Univ of Queensland, Australia; Vaxine, Australia, plus adjuvant; West China Hosp Sichuan Univ., China
2. Proteins carried by nanoparticles, Novavax, US, US, Australia
3. Microneedle skin patch delivering Spike proteins, Univ Queensland, Australia
4. Tobacco plant-produced proteins in virus like particles (VLP), Medicago plus GSK adjuvant, US – Italy.

Vaccines based Naked DNA

The DNA and mRNA-based platforms have a lot of versatility when it comes to manipulating the coded antigen and have a lot of speed potential. No DNA vaccines for human use is available for use in this time; nonetheless. High quantities in bacteria are mostly produced by DNA vaccines and they are the ones which are mostly used in veterinary medicines.

Strategies

After using a local electric pulse, the DNA plasmids enter human cells. They are injected into the muscle or skin. Plasmid DNA enters the cell and causes it to manufacture the target protein for a short period of time. DNA vaccination increases the generation of antibodies. They also help in activation of killer T cells in this fashion.

Frontrunners

Six DNA vaccines are entering human trials. All code the Spike protein or its fragments.

1. Naked DNA plasmids- Zydus Cadila, India;
2. Naked DNA plasmids plus electroporation- In vivo, US;

Vaccines based on m-RNA

While no vaccines based on messenger RNA (mRNA) have been approved, multiple vaccine programmes are using this technology to develop SARS-CoV-2 vaccines. RNA, unlike DNA,

must be delivered in a variety of ways in order to enter a human cell. The mRNA vaccination causes the cell to manufacture the antigen protein, which is coded by the mRNA

Strategies

Lipid microvesicles are the carriers of most mRNA in most of the vaccine projects. Mostly in case of the covid 19 vaccine, the target antigen is found to be the spike protein, and the preparations must be at -30 to -80 ^{o}C.

Frontrunners

1. Lipid vesicles (Liposomes)- Abogn, China; CureVac, Germany; Moderna, US Pfizer, US - BioNTech, Two candidate vaccines were tested in parallel, and one finished Phase III trial; University Oxford, UK An inhaled form of the vaccine is also tested but has not yet reached Phase III trial.
2. Nanoparticles- Arcturus Ther, Singapore. Vaccines based on viral vectors

Viral vectors can deliver the DNA code for the Spike protein into cells. It is feasible to take advantage of a virus's high capacity to distribute in the mRNA into the human cells and also to infect also.

Strategy

It's possible that the virus that has the incorporated DNA loses its replicating ability. Primate viruses (from chimps, gorillas, etc.) are frequently used as vectors since pre-existing immunity to the virus vector can alter efficiency of the vaccine. In other circumstances, the DNA is put into replication active virus vectors, which can cause a stronger immune response because they can disseminate to some extent.

Frontrunners

Many vaccine projects are based on viral vectors and they are already in advanced clinical trials:

1. Engineered non-replicating virus vectors

    1. Chimpanzee adenovirus:- AstraZeneca, Univ. Oxford, Sweden-UK-Italy;

    2. Gorilla adenovirus:v - ReiThera, Italy.

    3. Human adenoviruses: Acad Mil Med Sci, China Gamaleya Res Inst, Russia: this vaccine based on two human adenoviruses injected one after the other has been approved for limited use.

    4. Adenoviruses specifically modified for nasal spray: Beijing Wantai Biol Pharm Enterprise, China; Bharat Biotech-Washington Univ, India-US;

5. Other viruses- Engineered replicating virus vectors

1. Injected intramuscularly: Measles virus, Merck, US;.

2. Influenza virus administered by nasal spray: Influenza virus: Univ Hong Kong; Valavax-Abogn, China;

Vaccines which are selected for clinical evaluation.

Approximately eleven candidate vaccines had reached to the most advanced stage of clinical evaluation as this report was being written. Results from Phase II have been published in peer-reviewed publications for five of them [15,16,17,18,19,20,21]. The number of patients registered ranged from 100 to 1077, with single-arm studies being the most common.

SARS-CoV-2 production was mainly elicited by Oxford/AstraZeneca vaccine. They neutralise T cell reactivity in the humoral response of all the vaccinated patients. A Phase I trial was carried out for 195 individuals. This was done to compare the reactivity of two Pfizer vaccine, and both the vaccine candidates, showed same dose dependent antibody titters in young adults as well as old people.

Despite the excitement around this finding, which places the Oxford/AstraZeneca vaccine on par with Pfizer-BioNTech and Moderna vaccines in terms of efficacy, the meaning of the findings has yet to be determined. It's fairly uncommon for the severity of the produced immune response to be potentiated by varied doses between the first and second vaccination. A smaller first dosage of the vaccination, on the other hand, might not generate a significant response against the chimp adenovirus. The adenovirus might more successfully deliver the mRNA during the booster vaccine if there was no substantial antibody reaction.

CONCLUSION

Pandemics represent a significant threat to public health, health-care systems, and global economic stability. New zoonotic coronaviruses are anticipated to continue to spread from animals to humans as a result of modern agricultural techniques that enhance the human-animal interface, producing future epidemics. Gaining a thorough understanding of coronaviruses is essential for implementing effective control strategies to either avoid outbreaks or reduce their impact on persons and society if they do occur. Understanding their mechanism is crucial for better tailoring and developing successful pharmacological treatments and vaccines. Nonetheless, our ability to deal with future epidemics will be determined by the steps we take based on previous pandemic lessons. We are hopeful that the quickly evolving research on the present COVID-19 epidemic will contribute to the fresh information required to close these gaps.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

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