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Review Article

GENETIC VARIANTS OF SARS (COVID-19)**Kalpna B. Janrao, Yutika B. Mahale, Samadhan N. Kokate, Bhavana Kokane,
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Article Received: July 2021**Accepted: July 2021****Published: August 2021****Abstract:**

Severe acute respiratory syndrome Corona viruse-2(SARS-COV-2) infection caused more than 83 million cases known at the end of 2020 of pandemic Corona virus disease- 2019(covid-19). According to World Health Organisation announced clinical effort to advance a new vaccine booster which provides increased protection against variants of Corona virus 2019. According to database of literature review we describe the ongoing race between immunization and the natural selection of potential viral escape mutants. Also summarise serial testing of asymptomatic persons and analysis of vaccination.

Keywords- Severe acute respiratory Syndrome, Corona virus, immunization, Variants, mutants, vaccination.

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INTRODUCTION:

Corona viruses are diverse group of viruses infecting many different animals and they can cause mild to severe respiratory infection in humans. In 2002 and 2012 respectively, two highly pathogenic corona viruses with somatic origin, severe acute respiratory syndrome corona viruses (MERS cov) emerged in human and caused fatal respiratory illness, making emerging corona viruses a new public health concern in the twenty first century. At the end of 2019 a novel corona virus designated as SARS-COV 2 emerged in the city of Wuhan china and cause an outbreak of unusual viral pneumonia.

Being highly transmissible, this novel corona virus diseases 2019 (covid-19) has spread fast all over the world. It has overwhelmingly surpassed SARS and MERS in terms of both number of infected people and the spatial range of epidemic cruces. The ongoing outbreak of covid-19 has passed on extraordinary threat to global public health

History of corona virus:

The earliest reports of a corona virus infection in animals occurred in the late 1920s, when an acute respiratory infection of domesticated chickens emerged in North America. Arthur Schalk and M.C. Hawn in 1931 made the first detailed report which described a new respiratory infection of chickens in North Dakota. The infection of new-born chicks was characterized by gasping and listlessness with high mortality rates of 40–90%.] Leland David Bushnell and Carl Alfred Brandly isolated the virus that caused the infection in 1933. The virus was then known as infectious bronchitis virus (IBV). Charles D. Hudson and Fred Robert Beaudette cultivated the virus for the first time in 1937. The specimen came to be known as the Beaudette strain. In the late 1940s, two more animal corona viruses, JHM that causes brain disease (murine encephalitis) and mouse hepatitis virus (MHV) that causes hepatitis in mice were discovered] It was not realized at the time that these three different viruses were related. Human corona viruses were discovered in the 1960s using two different methods in the United Kingdom and the United States. E.C. Kendall, Malcolm Bynoe, and David Tyrrell working at the Common Cold Unit of the British Medical Research Council collected a unique common cold virus designated B814 in 1961.] The virus could not be cultivated using standard techniques which had successfully cultivated rhinoviruses, adenoviruses and other known common cold viruses. In 1965, Tyrrell and Bynoe successfully cultivated the novel virus by serially passing it through organ culture of human embryonic trachea. The new cultivating method was introduced to the

lab by Bertil Hoorn. The isolated virus when intranasally inoculated into volunteers caused a cold and was inactivated by ether which indicated it had a lipid envelope. Dorothy Hamre and John Procknow at the University of Chicago isolated a novel cold from medical students in 1962. They isolated and grew the virus in kidney tissue culture, designating it 229E. The novel virus caused a cold in volunteers and, like B814, was inactivated by ether.

Scottish virologist June Almeida at St. Thomas Hospital in London, collaborating with Tyrrell, compared the structures of IBV, B814 and 229E in 1967. Using electron microscopy the three viruses were shown to be morphologically related by their general shape and distinctive club-like spikes. A research group at the National Institute of Health the same year was able to isolate another member of this new group of viruses using organ culture and named one of the samples OC43 (OC for organ culture). Like B814, 229E, and IBV, the novel cold virus OC43 had distinctive club-like spikes when observed with the electron microscope.

The IBV-like novel cold viruses were soon shown to be also morphologically related to the mouse hepatitis virus. This new group of viruses were named corona viruses after their distinctive morphological appearance. Human coronavirus 229E and human coronavirus OC43 continued to be studied in subsequent decades. The corona virus strain B814 was lost. It is not known which present human corona virus it was. Other human coronaviruses have since been identified, including SARS-CoV in 2003, HCoV NL63 in 2003, HCoV HKU1 in 2004, MERS-CoV in 2013, and SARS-CoV-2 in 2019. There have also been a large number of animal corona viruses identified since the 1960s.

First covid case according to author Robert adds

Using methods from conservation science, a new analysis suggests that the first case of COVID-19 arose between early October and mid-November, 2019 in China, with the most likely date of origin being November 17. David Roberts of the University of Kent, U.K., and colleagues present these findings in the open-access journal PLOS Pathogens.

The origins of the ongoing COVID-19 pandemic remain unclear. The first officially identified case occurred in early December 2019. However, mounting evidence suggests that the original case may have emerged even earlier.

To help clarify the timing of the onset of the

pandemic, Roberts and colleagues repurposed a mathematical model originally developed by conservation scientists to determine the date of extinction of a species, based on recorded sightings of the species. For this analysis, they reversed the method to determine the date when COVID-19 most likely originated, according to when some of the earliest known cases occurred in 203 countries.

The analysis suggests that the first case occurred in China between early October and mid-November of 2019. The first case most likely arose on November 17, and the disease spread globally by January 2020. These findings support growing evidence that the pandemic arose sooner and grew more rapidly than officially accepted.

The analysis also identified when COVID-19 is likely to have spread to the first five countries outside of China, as well as other continents. For instance, it estimates that the first case outside of China occurred in Japan on January 3, 2020, the first case in Europe occurred in Spain on January 12, 2020, and the first case in North America occurred in the United States on January 16, 2020.

The researchers note that their novel method could be applied to better understand the spread of other infectious diseases in the future. Meanwhile, better knowledge of the origins of COVID-19 could improve understanding of its continued spread.

Roberts adds, “The method we used was originally developed by me and a colleague to date extinctions, however, here we use it to date the origination and spread of COVID-19. This novel application within the field of epidemiology offers a new opportunity to understand the emergence and spread of diseases as it only requires a small amount of data.”

Symptoms of covid 19

COVID-19 affects different people in different ways. Most infected people will develop mild to moderate illness and recover without hospitalization.

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 discoloration of fingers or toes

Serious symptoms:

Difficulty breathing or shortness of breath Chest pain or pressure

Loss of speech or movement

Seek immediate medical attention if you have serious symptoms. Always call before visiting your doctor or health facility.

People with mild symptoms who are otherwise healthy should manage their symptoms at home.

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.

VIROLOGY

Corona virus virology --- Positive-stranded RNA viruses are enveloped by corona viruses. COVID-19 is a betacoronavirus in the same subgenus as the severe acute respiratory syndrome (SARS) virus which are indicated by full genome sequencing and phylogenetic analysis, but this are in different clade. This virus be designated The Coronavirus Study Group of the International Committee on Taxonomy of Virus the Coronavirus Study Group of the International Committee on Taxonomy of Viruses. Betacoronaviruse and another Middle East Respiratory Syndrome (MERS) virus appears more distantly related. The closest RNA sequence similarity is to two bat coronaviruses, and it appears likely that bats are the primary source; whether COVID-19 virus is transmitted directly from bats or through some other mechanism is unknown.

For SARS- CoV the host receptor for SARS-CoV -2 cell entry is the same, the angiotensin-converting enzymes 2 (ACE2) . Through the receptor – binding domain spike Protein of SARS-CoV-2 binds to ACE2. The cellular protease TMPRSS2 also appears important for SARS-CoV-2 cell entry.

Alpha (B.1.1.7 Lineage) – This variant was first identified in the United Kingdom in late 2020 also known as 20I/501Y.V1 and was temporally associated with an increase in regional infection. As compared with circulating strains this variant contains more than dozen mutations, with several within the spike protein. Including United States, it has subsequently been identified in other countries.

Alpha is approximately 50 to 75 percent more transmissible than previously circulating strains indicated by the several studies and was associated with higher secondary attacks rates. For increased transmissibility the underlying mechanisms is uncertain. In respiratory secretion some studies have suggested that Alpha is associated with a higher median in viral level and compared with wild-type strains, some have also suggested that viral RNA may be detectable in respiratory specimens for longer. Whether these findings are associated with increased transmission and which mutations

contribute are under investigation. In Alpha variant one of the mutations is N501Y, is in the receptor binding domain of spike protein and infectivity of SARS-CoV-2 increased in a mouse model. The Variant P618H is another spike Protein mutations, abuts the furin-cleavage site, which is thought to have a role in SARS-CoV-2 cell entry.

Some, but not all, studies suggest that the greater disease severity associated with the Alpha variant. Thus far, there is no proof that the Alpha variant is associated with clinically significant immune escape. Serum from COVID-19 vaccine recipient maintain neutralizing activity against the Alpha variant, several studies indicates and efficacy against the variant maintained by some vaccines. These data are discussed elsewhere

However, another sequence in spike protein, E48K, in some sequences has identified by ongoing genomic analysis of the Alpha variants circulating in the United Kingdom. This mutation is present in the Beta (B.1351) and Gamma (P.1) variants, and some studies have suggested that it is associated with immune escape, as discussed below.

A deletion in the spike protein at amino acids 69-70 is the another mutation of this variant (alpha Variant). When this deletion is present some SARS -CoV-2 molecular test is unable to detect the S gene target (which encodes the spike protein).

These tests would still be able to detect viral RNA since they employ more than one gene target and thus would not result in false – negative results. Nevertheless, to detect the Alpha variant S gene target failure has been used as a marker, with the caveat that del 69-70 has also been reported in other variants

Delta (B.1.617.2 Lineage) --- This Lineage was first identified in India in December 2020, also known as 20A/S:478k and has become more prevalent variant which also called variant of concern and in several countries, including the United States and United Kingdom variant.

Some studies or data suggest that the Delta variant is highly transmissible, more than Alpha or other variants, so it also called as variant of concern. The proportion of SARS-CoV-2 infection caused by Delta rose as that caused by alpha declined; in the reports of United Kingdom, and the secondary household infection rate associated with Delta infection was 13.6 percent compared with 9.0 percent for Alpha.

The household attack rate associated with the Delta variant was 53 percent which is in another report of a small outbreak in the United States. Initial respiratory tract viral RNA levels are about 1000 times higher with Delta than were observed with ancestral virus circulating during the first phase of the pandemic, suggested by an unpublished study of an outbreak in China

Infection with Delta is associated with a higher risk of hospitalization than Alpha; suggested by the several reports.

Vaccine effectiveness is slightly attenuated against symptomatic infection with Delta but remains high against severe disease and hospitalization suggested by several studies

Beta (B.1.351 lineage) – This variant was identified in South Africa in late 2020 which also known as 20H/501Y.V2. Beta variant Beta variant (b.1.351) is phylogenetically distinct from Alpha (B.1.1.7) but shares several mutations, including the spike protein mutations N501Y. Beta variant rapidly became the dominant strain which is indicated by surveillance data in South Africa, also suggesting that it has the potential to increased transmissibility. In other countries it has been subsequently identified, including United States.

Gamma (P.1 lineage) – This variant was first identified in Japan which is known as 20J/501Y.V3 It is identified in Japan in four travelers from Brazil and was later reported to account for 42 percent of 31 sequenced specimens in the Amazonas state of Brazil in December 2020. In other countries it has been subsequently confirmed, and also in United State. P.1 Lineage has several mutations, including three in spike Protein receptors binding domain, N501Y, E484K, and K417T, which raise concern about the potential for increased transmissibility and an impact on immunity.

Epsilon (B.1.427 and B.1.429 lineages) – This variant also known as 20C/S452R or CAL.20C. fact about that variant is that in October 2020 only four case's globally identified, and in South California; and had been identified in other countries. Several spike protein mutations of epsilon variant includes L452R, which is associated with increased cell entry and reduced susceptibility to neutralization by convalescent and vaccine recipient plasma in vitro. Nevertheless, many proof suggest that the reduced susceptibility to neutralization of B.1.429 is modest compared with that of Beta. As compared with wild

type the variants also associated with a twofold higher viral RNA level on nasal swabs.

EPIDEMIOLOGY

Globally, cases of covid-19 have been reported over 200 million. On the World Health Organization and European Centre for Disease Prevention and Control website updated case in English can be found.

Throughout the world an interactive map highlighting confirmed cases can be found here.

A City in the Hubei Province of China, the first reports of cases from Wuhan, at the end of 2019, in all continents have been reported.

The overall burden of covid-19 the reported case counts underestimates, as only a fraction of acute infection is diagnosed and reported. The rate of prior exposure to SARS-CoV-2 as reflected by seropositivity, when seroprevalence surveys in the United States and Europe have suggested that after accounting for potential false positive or negative, which exceeds the incidence cases by approximately 10- fold or more.

Transmission -. The main mode of SARS-CoV-2 transmission is person to person

The chief or primary means of transmission of severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2] is the direct person-to-person. When Contact range between two persons, it is thought to occur. (i.e distance between two agent is less than two feet or six meters) via respiratory particles ; in the respiratory secretion virus released when person to person with infection cough , sneezing , or talks can infect another person if it is inhaled or makes direct contact with the mucous membrane. The infection also caused by if a person's hands are contaminated by these secretions or by touching these contaminated surfaces and then they touch their nose or mouth as well as eyes although Major routes of transmission contaminated surfaces are not including.

Through the airborne route SARS-CoV-2 can also be transmitted longer distances (through inhalation of particles that remains the air over time and distance), but the extent to which this mode of transmission has contributed to the pandemic is uncertain . For longer distance airborne transmission is in enclosed, poorly ventilated spaces have highlighted the potential by the scattered reports of SARS-CoV-2 outbreaks. (e.g in a restaurant, on bus) . The feasibility of airborne transmission have been also supported by

experimental studies. . As examples, studies using specialized imaging to visualize respiratory exhalations have suggested that respiratory droplets may get aerosolized or carried in a gas cloud and have horizontal trajectories beyond six feet (two meters) with speaking, coughing, or sneezing .Doing other study viral RNA in ventilation system and in air samples of hospital rooms of patients with Covid-19 have been identified , including patients of mild infection attempts to find viable virus in air and surface specimens in health care settings have only rarely been successful . However long-range airborne transmission is not a primary mode which suggested by overall transmission and secondary attacks of SARS-CoV-2 . Besides ,In a few reports of health care workers exposed to patients with undiagnosed infection while using only contact and droplet precautions, no secondary infections were identified despite the absence of airborne precautions Reflecting the current uncertainty regarding the relative contribution of different transmission mechanisms, recommendations on airborne precautions in the health care setting vary by location; when aerosol – generating procedure are performed the airborne precautions are universally recommend.

In the non-respiratory specimens, like stool, ocular secretions, blood , and semen SARS -CoV-2 has been detected , but in the sites of transmission the role is uncertain. A specific, detection of SARS-CoV-2 RNA from stool specimens have described in several reports, even after viral RNA could no longer be detected, and in rare cases replicative viruses has been cultured from stool. The possibility of transmission through aerosolization of virus from sewage drainage has been suggested by the scattered reports of clusters in a residential building and in a dense urban community with poor sanitation. However, transmission through the fecal-oral route did not appear to be a significant factor in the spread of infection –according to a joint WHO-China report,

Noticing of SARS- CoV- 2 RNA in blood has also been reported in some but not all other studies that have tested for it . Although, the probability of transmission of bloodborne (e.g , through blood products or needlesticks) appears low ; through the bloodborne route respiratory viruses are generally not transmitted., and for SARS-CoV-2 or for the related Middle East respiratory syndrome coronavirus (MERS-CoV) or SARS-CoV transfusion -transmitted infections has not been reported yet .

There is also no evidence of transmission of SARS-CoV-2 through the contact with non-mucous

membrane site (eg. Abraded skin) .

Diagnosis test for COVID-19:

Detection of the virus is usually done either by looking for the virus' inner RNA , or pieces of protein on the outside of the virus. Tests that look for the viral antigen (parts of the virus) are called antigen tests. There are multiple types of tests that look for the virus by detecting the presence of the virus's RNA. These are called molecular tests, after molecular biology. As of 2021, the most common form of molecular test is the reverse transcription polymerase chain reaction (RT-PCR) test. Other methods used in molecular tests include CRISPR, isothermal nucleic acid amplification, digital polymerase chain reaction, microarray analysis, and next-generation sequencing. Reverse transcription polymerase chain reaction test.

Polymerase chain reaction (PCR) is a process that amplifies (replicates) a small, well-defined segment of DNA many hundreds of thousands of times, creating enough of it for analysis. Test samples are treated with certain chemicals that allow DNA to be extracted. Reverse transcription converts RNA into DNA.

Reverse transcription polymerase chain reaction (RT-PCR) first uses reverse transcription to obtain DNA, followed by PCR to amplify that DNA, creating enough to be analyzed. RT-PCR can thereby detect SARS- CoV-2, which contains only RNA. The RT-PCR process generally requires a few hours. These tests are also referred to as molecular or genetic assays.

Real-time PCR (qPCR) provides advantages including automation, higher-throughput and more reliable instrumentation. It has become the preferred method.

Other molecular tests

Isothermal nucleic acid amplification tests also amplify the virus's genome. They are faster than PCR because they don't involve repeated heating and cooling cycles. These tests typically detect DNA using fluorescent tags, which are read out with specialized machines.

CRISPR gene editing technology was modified to perform the detection: if the CRISPR enzyme attaches to the sequence, it colors a paper strip. The researchers expect the resulting test to be cheap and easy to use in point-of-care settings . The test amplifies RNA directly, without the RNA-to-DNA conversion step of RT-PCR.

Antigen test

An antigen is the part of a pathogen that elicits an immune response. Antigen tests look for antigen proteins from the viral surface. In the case of a coronavirus, these are usually proteins from the surface spikes. SARS-CoV-2 antigens can be detected before onset of COVID-19 symptoms (as soon as SARS- CoV-2 virus particles) with more rapid test results, but with less sensitivity than PCR tests for the virus.

Antigen tests may be one way to scale up testing to much greater levels.[53] Isothermal nucleic acid amplification tests can process only one sample at a time per machine. RT-PCR tests are accurate but require too much time, energy and trained personnel to run the tests. "There will never be the ability on a [PCR] test to do 300 million tests a day or to test everybody before they go to work or to school," Deborah Birx, head of the White House Coronavirus Task Force, said on 17 April 2020. "But there might be with the antigen test."

Samples may be collected via nasopharyngeal swab, a swab of the anterior nares, or from saliva (obtained by various methods including lollipop tests for children). The sample is then exposed to paper strips containing artificial antibodies designed to bind to coronavirus antigens. Antigens bind to the strips and give a visual readout. The process takes less than 30 minutes, can deliver results at point of care, and does not require expensive equipment or extensive training.

Swabs of respiratory viruses often lack enough antigen material to be detectable. This is especially true for asymptomatic patients who have little if any nasal discharge. Viral proteins are not amplified in an antigen test. According to the WHO the sensitivity of similar antigen tests for respiratory diseases like the flu ranges between 34% and 80%. "Based on this information, half or more of COVID-19 infected patients might be missed by such tests, depending on the group of patients tested," the WHO said. While some scientists doubt whether an antigen test can be useful against COVID-19, others have argued that antigen tests are highly sensitive when viral load is high and people are contagious, making them suitable for public health screening. Routine antigen tests can quickly identify when asymptomatic people are contagious, while follow-up PCR can be used if confirmatory diagnosis is needed.

Antibody test

The body responds to a viral infection by producing antibodies that help neutralize the virus. Blood tests

(also called serology tests or serology immunoassays) can detect the presence of such antibodies.

Antibody tests can be used to assess what fraction of a population has once been infected, which can then be used to calculate the disease's mortality rate. They can also be used to determine how much antibody is contained in a unit of convalescent plasma, for COVID-19 treatment, or to verify if a given vaccine generates an adequate immune response.

SARS-CoV-2 antibodies' potency and protective period have not been established.] Therefore, a positive antibody test may not imply immunity to a future infection. Further, whether mild or asymptomatic infections produce sufficient antibodies for a test to detect has not been established. Antibodies for some diseases persist in the bloodstream for many years, while others fade away.

The most notable antibodies are IgM and IgG. IgM antibodies are generally detectable several days after initial infection, although levels over the course of infection and beyond are not well characterized. IgG antibodies generally become detectable 10–14 days after infection and normally peak around 28 days after infection. This pattern of antibody development seen with other infections, often does not apply to SARS-CoV-2, however, with IgM sometimes occurring after IgG, together with IgG or not occurring at all. Generally, however, median IgM detection occurs 5 days after symptom onset, whereas IgG is detected a median 14 days after symptom onset. IgG levels significantly decline after two or three months.

Genetic tests verify infection earlier than antibody tests. Only 30% of those with a positive genetic test produced a positive antibody test on day 7 of their infection.

CONCLUSION:

It is studied that according to World Health Organisation announced clinical effort to advance a new vaccine booster which provides increased protection against variants of Corona virus 2019. According to database of literature review we describe the ongoing race between immunization and the natural selection of potential viral escape mutants.

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