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Review Article Paper Mutations and Variants of SARS- coV-2 SARS-coV-2: Mutation and Variants

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Abstract

The word virus is from a Latin word meaning "slimy liquid" or "poison". The virus is a collection of genetic codes. It can be DNA or RNA, and around it, there is a protein coat. Viruses can not be replicated alone. When a virus replicates to get several copies of itself, sometimes changes a bit. These changes are called "mutations". A virus with one or more new mutations is called a "variant" The most crucial property of viruses is mutation. Change is their DNA Sequence. Mutation can be natural or artificial. Due to mutation, a new variant appears with new challenges. This is a challenge for humans to survive the situation. Over time there were several variants found all over the world. Some of them were not that harmful and some did shake the world. The reason why new challenges arise was due to the changing behavior of the virus which is potent to escape from different tests and was able to open out more in the human population. There are many such cases in which vaccines seem to be ineffective and hence vaccines also have their own challenges. Mutation can also take place in humans and common mutation examples in humans are Angelman syndrome, Canavan disease, color blindness, cri-du-chat syndrome, cystic fibrosis, Down syndrome, Duchenne muscular dystrophy, haemochromatosis, haemophilia, Klinefelter syndrome, phenylketonuria, Prader–Willi syndrome, Tay–Sachs disease, and Turner syndrome.

Keywords: COVID-19, SARS-CoV-2, Variants, Vaccines, Mutations, Double mutant variant, Triple mutant variant, Vaccine breakthrough cases

1. Introduction

All viruses, including SARS-CoV-2, the virus that causes COVID-19, change over time. Most changes have little to no impact on the virus' properties. However, some changes may affect the virus's properties, such as how easily it spreads, the associated disease severity, or the performance of vaccines, therapeutic medicines, diagnostic tools, or other public health and social measures. The mutation is a property of viruses that keep their changing nature as time goes. These changes take place at the genetic level, hence a new variant appears. we will see different classes under which SARS coV2 virus variants are placed and there are different mutation sides in the review article.

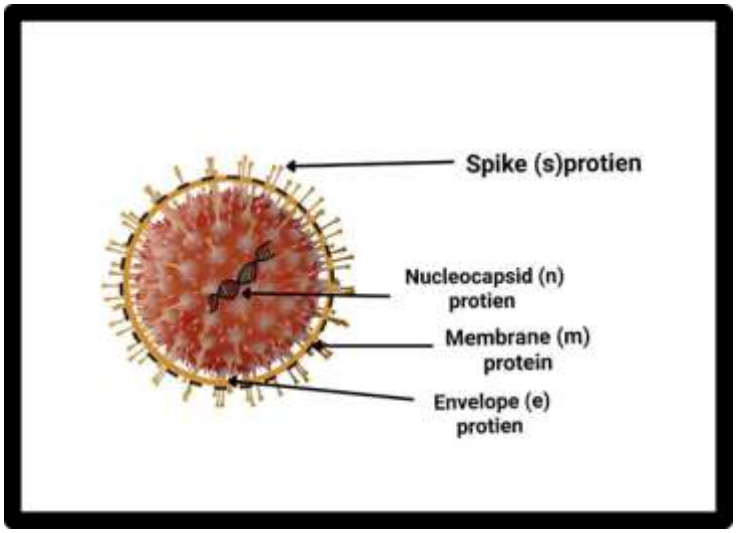

Fig.1 SARS Cov 2 virus structure

2. Nature of viruses

We all have listened, learn, and studied about it. They are dead until they find out a host and infect the cells and soon the whole body of the host. The most renowned property of virus is that tends to get change, get mutated, and form a completely new version of themself. this ability to mutate constantly Leads to variants. On December 31, 2019, World Health Organisation (WHO) made aware of Cases of pneumonia of a strange etiology occurring in the City of Wuhan in the Hubei Province of China.[1] The virus isolated from the airway epithelial cells of the infected patients was named 2019-nCoV but only for a short time.[2] When it was determined that the virus is related to SARS-CoV, it was again named SARS-CoV-2 by the Coronavirus Research Group (CSG) of the International Committee for the classification of viruses on February 11, 2020.[3] An acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a beta coronavirus that belongs to the CoroNaviridae family. This family has single-stranded Positive ribonucleic acid (RNA) viruses.[4] It is found that Coronaviruses has four genera, and in that alpha and beta genera, viruses are known to cause disease in humans. Viruses that can get transferred from animals to humans are called Zoonotic viruses. Two coronaviRuses found in bat they are RaTG13 and RmYN02 were Found to be 96.2% and 93.3% sequence homology, respectively with SARS-CoV-2. [5, 6] As we know that it is a virus so it was estimated that it may get changed into a different variant. viruses have a strong shell of protein that is hard to break or invade and the same is here in the case of SARS-CoV-2, it is an enveloped spherical-shaped virus.[1] It has four structural proteins and 16 nonstructural proteins. The structural proteins are the nucleocapsid (N) protein, the Membrane (M), the S protein, and the envelope (E) protein. If we take a look of its RNA orientation it is 5'-3'direction which makes it a positive Sense RNA virus, and the RNA can be read directly as a messenger RNA, it replicates and encoded At the 5' terminal end. The S protein causes the virus to attach to the host cell at the angiotensin-converting enzyme 2 receptor (ACE2), The ACE2 receptors are found in abundance on alveolar cells. which is located on the host cell membrane. Of the host cell. The nonstructural protein 14 (nsp14) has proofreading activity which allows the rate of mutations to remain low. The attachment causes fusion of the viral lipid membrane with the cell membrane of the host thus internalizing the virus. The Host cell translates the viral RNA and leads to the production of the replicate and structural proteins of the virus. Replicase is cleaved into non-structural proteins of which RNA-dependent RNA polymerase (RdRp) is one of them. Viral replication and amplification are carried out, and virion assembly is carried out in the endoplasmic reticulum and Golgi apparatus of the host cell. During the replication process, errors can occur in the genome, resulting in mutations that give rise to variants. The virions are finally released from the cell by exocytosis.[7, 8]

3. COVID-19 Mutations and Variants:-

A change that takes place in the genetic sequence is called a mutation. the Genomes is differing from each other in gene strain hence are called variants. Variants can differ from each other by having one or more than one mutation. When a phenotypic difference is found among the variants, they are known as strains.it's important to take note that many such mutations are minor, and don't have an overall impact on a virus that spreads or potentially and how severe a viral infection might be.it is also possible that some mutations could make the virus less infectious and weak than past variants.[9]

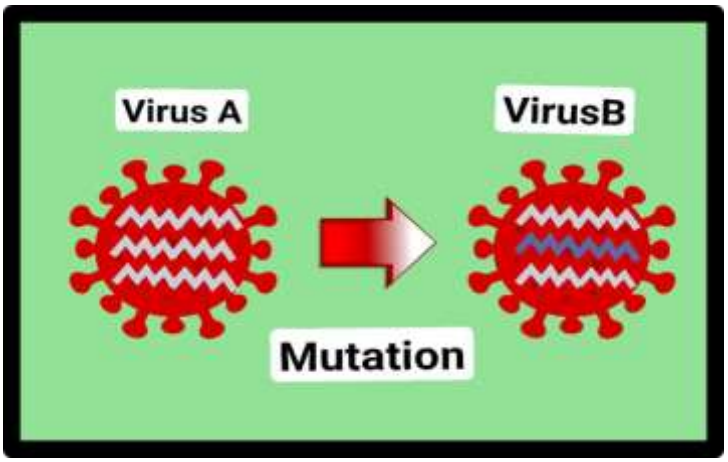

Fig 2. mutation in virus

The USA government has divided the SARS-CoV-2 variants into three classes. supported the scientific evidence, the variant status can sometimes be escalated or de-escalated, and hence, the Centers for Disease Control and Prevention (CDC) will update the variant strains within the different classes.[10] consistent with the report of April 21, 2021, the classes are variant of interest, a variant of concern, and a variant of high consequence. Characterization of specific Variants of Interest (VOIs) and Variants of Concern (VOCs)

3.1 Variants of interest (VOI):-

Genetic changes that are able to be estimated or known to affect virus characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape; and can be Identified to cause multiple COVID-19 infection rates, in all different countries with increasing relative prevalence

alongside the increasing number of cases over time, or other apparent epidemiological impacts to suggest an emerging risk to global public health. No SARS-CoV-2 variants are designated as VOI.[11]

WHO label	Pango lineage	GISAID clade	Nextstrain clade	Earliest documented samples	Date of designation
Lambda	C.37	GR/452Q.V1	21G	Peru, Dec-2020	14-Jun-2021
Mu	B.1.621	GH	21H	Colombia, Jan2021	30-Aug-2021

Table 1. Currently interested variants in VOI

3.2 Variants of concern (VOC):-

SARS-CoV-2 variant matches the definition of a VOI, with one or more of the following changes at a degree of global public health significance, and that is an Increase in transmissibility or detrimental change in COVID-19 epidemiology. Increase in virulence or change in clinical disease presentation. Decrease ineffectiveness of public health and social measures or available diagnostics, vaccines, and therapeutics.

The variant of Concern (VOC)

- Delta (B.1.617.2 and AY lineages)
- Omicron (B.1.1.529 and BA lineages).[11]

WHO label	Pango lineage	GISAID clade	Nextstrain clade	Additional amino acid changes monitored	Earliest documented	Date of designation
Alpha	B.1.1.7	GRY	201 (VI)	+S:484K +S:452R	United Kingdom, sep-2020	18-Dec-2020
Beta	B.1.351	GH/501Y.V2	20H (V2)	+S:L18F	South Africa, May-2020	18-Dec-2020
Gamma	P.1	GR/501Y.V3	20J (V3)	+S:681H	Brazil, Nov-2020	1 1-Jan-2021
Delta	B.1.617.2	GK	21A, 21l,21J	+S:484K,+S:417 N	India, Oct-2020	VOC: 11-May-2021 VOI: 4-Apr-2021
Omicron*	B.1.1.529	GRA	21K, 21L,21M	+S:R346K	Multiple countries,Nov-2021	VUM: 24-Nov-2021 VOC: 26-Nov 2021

Table 2 currently designed variants of concern

3.3 Variant Being Monitored

The SIG Variant classification scheme defines four classes of SARS-CoV-2 variants including the above three classes(1)

Variants as VBM include those where data shows there is a potential impact on authorized medical countermeasures or that has been associated with more severe disease or increased transmission but are no longer detected, or are circulating at very low levels, in the United States. These variants do not pose a significant and imminent risk to public health in the United States.[11]

1. Variant Being Monitored (VBM)
2. Alpha (B.1.1.7 and Q lineages)
3. Beta (B.1.351 and descendent lineages)
4. Gamma (P.1 and descendent lineages)
5. Epsilon (B.1.427 and B.1.429)
6. Eta (B.1.525)
7. Iota (B.1.526)
8. Kappa (B.1.617.1)
9. Mu (B.1.621, B.1.621.1)
10. Zeta (P.2)

3.4 Variant of High Consequence (VOHC)

This class combines the variants which give clear evidence that the medical measurements and preventive measures have a major decrease and effect compared to previous variants.[12] have significantly reduced effectiveness relative to previously circulating variants. Significantly reduced susceptibility to multiple EUA or approved therapeutics. this required notification under the international health regulations reporting to an announcement of a strategy to vent or content transmission and recommend it to update treatment and vaccines. Currently, no SARS-CoV-2 variants are designated as VOHC[11, 12]

Pango lineage	GISAID clade	Nextstrain clade	Earliest documented	Date of designation
B.1.1 .318	**G R**	**-**	**Multiple countries, Jan-2021**	**02-Jun-2021**
C.1.2	**GR**	**-**	**South Africa, May 2021**	**01-sep-2021**
B.1.640	**GH/490R**	**-**	**multiple countries, sep2021**	**22-Nov-2021**

Table 3. Currently designated variants under monitoring

4. The COVID-19 Variants:-

Over the course of time, many variants were found in different places of the world . The following are the different variants identified in different Countries. There are many variants but few of them were spread wildly all over. these, the three variants which have Rapidly become dominant are B.1.1.7(Alpha variant), B.1.351(beta variant), and P.1(gamma variant).

4.1 Naming of variants

There is a typical question once we read or listen about these variants which is how the naming of those variants comes from. there's a longtime nomenclature system for naming and tracking SARS-CoV-2 genetic lineages by GISAID, Nextstrain and Pango are currently they're employed by scientists and in research, WHO convened a bunch of scientists from the Technical Advisory Group on Virus Evolution, the reference laboratory network, representatives from GISAID, Nextstrain, Pango and extra experts in virological, microbial nomenclature and communication from several countries and agencies to think about an easy-to-pronounce and non-stigmatizing labels for VOI and VOC., this expert group assembled by WHO has recommended using letters of the alphabet, i.e., Alpha, Beta, Gamma, Delta which can be easier and more practical to be discussed by non-scientific audiences.

A study made by Korber [30] in 2020 presented data showcasing that amino acid changes the virus's spike protein, D614, this variant got introduced early during the pandemic, but this virus variant did not spread early and fast but viruses containing G614 are now dominating the world. Korber found that the rapid spread of G614 was more as compared to the D614 because it is more infectious than D614. In support of their hypothesis, the authors provided evidence that clinical samples. It is seen that G614 infections have higher levels of viral RNA and produce higher titers in pseudoviruses from in vitro experiments. This study did not say that D614 is not dangerous to humans.[13]

4.2 Double and triple variant mutation.

4.2.1 Double mutant variant (B.1.617):-

This variant was first found in India. As two mutations are Seen in the same virus, this variant is called a "double mutant" Variant. The notable mutations are seen in E484Q and L452R. These variants were found to be increased the risk of transmission and also resistance to vaccination. According to the Indian Council of Medical Research Virology Lab, Bharat Biotech's COVAXIN vaccine has effectively neutralized the infection and was found to be 78% effective against the double mutant variant. It was also found that significant increase in covid-19 cases in India due to this variant the first case in the USA was identified in San Francisco on April 5th, 2021.[14-16]

4.2.2 Triple mutant variant (B.1.618)

A new triple variant discovered on April 20, 2021, was characterIzed by deleting two amino acids, H146del and Y145del In the S protein. a total of 1,189 samples Were tested positive in Maharashtra, Delhi, West Bengal, and Chhattisgarh, India. I have higher transmissibility. Three mutations in this variant are resistant to antibodies and Also possess the ability to escape the body's natural acquired Immunity to COVID-19.[17, 18]

4.2.3 South African variant (B.1.351or 20H/501Y.V2):-

In October 2020 Nelson Mandela Bay in South Africa there was a new variant found known as 501Y.V2 is also known as The B.1.351 variant, it was also detected in Zambia. There were 323 reported cases By April 1, 2021, in 31 jurisdictions in the USA. There were found in 23 patients with 17 acid changes but only a few notable mutations in this variant are K417N, E484K, and N501Y on the S protein. It is suggested to have Increased transmissibility and is most commonly seen in young People without underlying diseases.[19]

4.2.4 US Midwest variant (20C-US or COH.20G/501Y):-

This virus was found in Ohio by other Midwest on December 2021 January 2021. This variant mutation was placed on S protein (Q677H), M protein (A85S), and the N protein (D377Y). Another variant with the mutation S N501Y, a markEr of the B.1.1.7, with no other associated mutations with that Strain has been identified.[20] But currently, there is no evidence of increased transmissibility or virulence for this variant.

4.2.5 N440K:-

One more new variant N440K was found. This variant was found to be get mutated in s protein. It was seen in a sudden increase in the cases in Andhra Pradesh India. This variant has enhanced The Center for Cellular and Molecular Biology found that this variAnt has enhanced binding to ACE2 receptors.[21]

4.2.6 US San Francisco Bay Area variant (B.1.427 and B.1.429):-

This variant was seen in California in February 2021 in this the notable mutations in B.1.427 are L452R and D614G; while mutations in B.1.429 are S131, W152C, L452R, And D614G. Both variants have a 20% increased risk of transMissibility and reduction in therapeutic efficacy.[10, 22]

4.2.7 20A/S:439K:-

The experience was found in Ireland. This Variant has S: N439K mutation with the deletions of amino acids at positions 69 and 70 of S proteins that results in an increase in ACE2 binding, resistance to antibodies, and convaLescent plasma.[23]

4.2.8 20C/S:80Y:-

This variant was found in at least 10 countries all over Europe. Has 3 nucleotide mutations, it is related to apolipoprotein B editing complex (APOBEC)-like editing within the host which are found in at least 10 countries in Europe.[23]

4.2.9 20A.EU2:-

This variant was found in France in June 2020 and it became the second dominant variant in whole Europe. Beautiful mutations were seen in S477N, E484K, and N501Y, this demonstrated a somewhat increase in ACE2 binding, resistance to multiple Antibodies, and convalescent sera. They confer a modest increase In infectivity as measured by soluble mACE2.[24]

4.2.10 20A.EU1/ S:A222V:-

This variant was found on 20 June 2020 in Spain but it spread across Europe and many other countries very fast. This variant has non-terminal domain (NTD) mutations, which have no important t role in receptor binding or Membrane fusion.[25]

4.2.11 US Southern California variant (CAL.20C):-

It was found in July 2020 in Southern California. Its notable mutations are ORF1a: I4205V, ORF1b: D1183Y, S: S13I; W152C, and L452R. The binding of the S Protein could be made easier by the latter three mutations.[26]

4.2.12 UK variant (B.1.1.7 or 20I/501Y.V1):-

VOC202012/01 was detected in September 2020 in the UK. This is also known as B.1.1.7 . It has been found that this variant has 23 mutations when compared to the Original strain found in Wuhan, China. And Eight of these mutations took place in the S protein.[27, 28]

4.2.13 Brazilian variant (P.1 or 20J/501Y.V3):-

P.1 variant also known as B.1.1.28.1 was first detected in North Brazil in the city of Manaus in the Amazonas state in December 2020. Also found among 4 travelers from Brazil outside Tokyo at Haneda airport at the National Institute of Infectious Diseases (NIID) in Japan.[28, 29]

4.2.14 B.1.526 (20C/S:484K) and B.1.525 (20A/S:484K):-

These variants were first found in New York, USA. The Notable mutations were E484K and S477N. And it was found E484K decreases antibody response, and on other hand, S477N increases the attachment Process.[20]

4.2.15 20A/S:98F:-

This variant was mainly found in Belgium and the Netherlands. It has S:98F mutation.[23]

4.2.16 20B/S:626S:-

This variant was identified in 15 countries of Europe mainly in Norway Denmark and UK. The 20B/S:626S variant has S:626S mutation.[23]

4.2.17 20B/S:1122L :-

The 20B/S:1122L variant has S:V1122L mutation and is found predominantly in countries like Sweden, Norway, and Denmark.[23]

4.2.18 Omicron Variant: Background (As of 12/22/2021)

On November 30, 2021, The omicron variant, B.1.1.529, of SARS-CoV-2, was designated by the United States as a Variant of Concern. Omicron has some deletions and more than 30 mutations, for example, 69–70del, T95I, G142D/143–145del, K417N, T478K, N501Y, N655Y, N679K, and P681H. This division and mutation are known to increase transmissibility, have a higher viral binding affinity, and have higher antibody escape. The first Confirmed case of omicron in the United States was identified on December 1, 2021. The omicron variant has significantly more mutations than previous SARS-CoV-2 Variants, particularly in its S-gene, the gene that encodes the virus's spike protein. This variant was also successfully able to escape from the detection test.[30]

These are the tests that have been modified or have addressed the issue of being unable to detect the omicron variant.

1. Tide Laboratories DTPM COVID-19 RT-PCR Test
2. Test Name (Link to EUA): DTPM COVID-19 RT-PCR test (/media/138815/download) Manufacturer: Tide Laboratories, LLC

The FDA's Analysis:-

'This test is now expected to detect the SARS-CoV-2 omicron Variant (B.1.1.529). The original test was a single target test that was expected to fail to detect the SARS-CoV-2 omicron variant (B.1.1.529) due to a nine- nucleotide deletion in the N-gene, spanning positions 28370-28362, which is Tests with N-Gene Drop Out – SARS-CoV-2 Detection Should Not Be Significantly Impacted For each of the tests listed in the below table, one genetic target is expected to haveSignificantly reduced sensitivity due to a mutation in the SARS-CoV-2 omicron Variant (B.1.1.529). A nine-nucleotide deletion in the N-gene, spanning positions 28370-28362, results in an N-gene dropout, also referred to as an N-gene target'.[31]

A recent study made by Philippe Colson of IHU shows that Mediterranee Infection in Marseille, France, and his team found the first solid evidence for the recombinant virus. So far, 17 confirmed cases of the recombinant virus have been detected so far in the US and Europe. Three patients in France were infected with a version of SARS-CoV-2 that combines the spike protein from an Omicron variant with the "body" of a Delta variant. Another two unrelated Deltacron infections have been identified in the United States, according to an unpublished report by genetics research company Helix that has been submitted to medRxiv and seen by Reuters. Colson said adding, "genetic recombinations of coronaviruses have been known to happen when two variants infect the same host cells."[32]

4.2.19 Florona

Israel was the first country to announce the first case of Florona disease, on December 31, 2021, which is a double-infection of COVID-19 and influenza. COVID-19 and influenza (flu) are both different infectious respiratory diseases and they share some similar symptoms. Florona is a condition when a patient suffers from both Covid-19 and Influenza. Covid-19 and influenza both are known to affect the respiratory system, both have different treatments and different vaccines. Double infection with both viruses can cause complications in the body and stress out the immune system. According to a tweet by Arab News, Israel reported its first "Florona" case, Florona occurs after "double infection" or "co-infection" with both SARS-CoV-2 and the flu virus. The case was detected in an unvaccinated pregnant woman who had been admitted to a medical center. Now the question arises, is florona a new variant because The last Covid-19 variant that was detected was Omicron and no further variants have been identified by the World Health Organisation. But WHO does confirm that co-infection with any variant of Covid-19 and the flu virus is possible. Symptoms of Florona are high fever, consistent chest pain or constriction, shortness of breath and loss of appetite, states of confusion, and anxiety in some cases it can also be pneumonia, myocarditis, and inflammation in heart muscles. Mild symptoms of a double Covid-19 and flu infection can be treated at home itself without requiring any hospitalization says WHO Florona is not a new variant, the occurrence might be indicative of a weakened immune system under attack from two virus infections, Dr.

Nahla Abdel Wahab, Cairo University Hospital doctor, was quoted by Israeli media following the emergence of the disease. COVID-19 has a long-term damaging effect on our bodies, and in this case, if our body catches both Coronavirus and flu at the same time, then it would be very difficult for our bodies to fight both viruses. To protect ourselves from florona Following social distancing protocols, wearing masks, and getting vaccinated against both Covid-19 and influenza is the only way to prevent Florona.[33]

4.2.20 Delmicron

Just like Florona, Delmicron is also not a new variant of Coronavirus, it is the term used for the infections spreading together due to twin spikes of Delta and Omicron variants as per experts. Delmicron name itself states the combination of the names of the previous two variants of COVID-19. symptoms of the Delmicron are similar to Delta and Omicron variants of COVID-19 as it is a combo of both variants. These are the symptoms of delmicron. High fever, Persistent cough, Loss of smell, Loss of sense of taste, Severe headache, Sore throat, and Runny nose. UK government scientists, however, have claimed that people who contract the Delta variant are more likely to fall sick with serious symptoms than those who get infected with the Omicron variant[34].

4.2.21 NeoCov

The NeoCov virus is one of the closest known genetic relative to the MERS that is the Middle East Respiratory Syndrome virus, there is no risk to humans from NeoCov yet. NeoCov virus is discovered in a bat population in South Africa. It is seen currently spreading only in animals, but the scientists said that NeoCoV and PDF-2180-CoV use some types of angiotensin-converting enzymes, including bat ACE2 and human ACE2 for entry. “Just one mutation is enough for the virus to be able to infiltrate human cells." The MERS-CoV virus is similar to SARS-CoV-2 in terms of symptoms like fever, cough, and shortness of breath and was prevalent in the middle-eastern countries in 2012 and 2015. Many people died due to the infection. According to Chinese researchers, NeoCoV carries the potential combination of MERS-high COV mortality rate (one in every three infected persons dies) and the current SARS-CoV-2 coronavirus’s high transmission rate. The research said MERS-CoV belongs to the lineage C of Beta-CoV (Merbecoviruses), which poses a great threat considering its high case-fatality rate of approximately 35%.[35]

5. What is XE, XD, XF recombinant virus?

While the number of covid patients is declining in India, the number is increasing in some countries including China and France. The growing number of cases in the country is a matter of concern to the people.Experts say the new strain is spreading 10 times faster.[36] According to the World Health Organization, another new strain of the corona virus has been discovered. Which has been named as XE. This new variant has raised concerns. The virus is said to be more contagious than Omicron.Worryingly, the Omaicron variant caused a third wave worldwide.Deltacron was the first recombinant, and in recent times there have been several other recombinants of the corona virus, one of which is fluorona. A total of 637 cases of XE have been confirmed in the UK so far, the WHO said in its latest report.[37] XE is a recombinant virus notified by the WHO. It is said to be a combination of Omicron BA.1 and Omicron BA.2. not only XE but two other viruses are found and they are XD and XF. XD is known to be new name for the French Delta x BA.1 lineage, this variant contains the Spike protein of BA.1 and the rest of the genome is of Delta. It found to be comprises several 10s of sequences currently , talking bout XF variant , it is a UK Delta x BA.1 lineage. It has the Spike and structural proteins from BA.1 but the 5' part of its genome from Delta.[38]

BQ.1 and BQ.1.1-

now regard for half of COVID- 19 cases in theU.S. the, according to the Centers for Disease Control andPrevention.Lab studies suggest the viral descendants ofBA.5 andBA.2, which include all the new dominant variants, might beget slightly more severe complaints thanBA.1 or the original omicron. Pfizer and its vaccine mate BioNTech say that the rearmost supporter increases the position of negativing antibodies against both BQ.1 andBQ.1.1, which cover against infection. The symptoms of BQ.1 and BQ.1.1 appear to be the same as for other COVID- 19 variants. The most common symptoms include prostration, fever, a cough, traffic, briefness of breath, sore throat, nausea, diarrhea, and muscle pangs or headache. Loss of smell, which first characterised COVID- 19 infections, is no longer as common.[39]

BF.7 variant-

The COVID VariantBF.7 is a new mutation of the Omicron Variant which is spreading fleetly in China. TheBF.7 variant is more contagious than all the other available variants though it has not been linked with severe mortality in cases. This variant is anticipated to infect further than 60 of the population of China. It has indeed appeared in India too. high R0 or introductory. The reduplication Rate of the BF.7 variant, it can indeed transfer from asymptomatic cases to other people.(40)

XBB.1.5

- The OmicronXBB.1.5 variant is a sublineage of XBB, which is a recombinant of two BA.2 sublineages. From 22 October 2022 to 11 January 2023, 5 288 sequences of the Omicron XBB.1.5 variants have been reported from 38 countries. ultimate of these sequences are from the United States of America(82.2%), the United Kingdom(8.1), and Denmark (2.2%). WHO and the Marker-VE recommend Member States prioritize the following studies

to further address misgivings relating to the growth advantage, antibody escape, and strictness ofXBB.1.5. Along with BQ.1 * variants, XBB * variants are the most antibody- resistant variants to date. 2 – 4 Using pseudotyped contagion neutralization assays,XBB.1.5 is shown to be equally vulnerable fugitive asXBB.1. predicated on its heritable characteristics and early growth rate estimates,XBB.1.5 may contribute to increases in case frequence encyclopedically. To date, the overall confidence in the assessment is low as growth advantage estimates are only from one country, the United States of America.

6. New symptoms associated with XE variants

Loss of appetite

Sore throat

There is a headache

Limb pain

Feeling tired

Diarrhea

Feeling sick

Shortness of breath

Runny nose

7. COVID-19 Vaccines against the COVID-19 Variants:-

There are many other platforms that have been utilized in the development of vaccines, Which include protein subunit, viral vector with replicating and Non-replicating, deoxyribonucleic acid (DNA), inactivated Virus, RNA, virus-like particle, and live attenuated. Novavax, Janssen, and Astra-Zeneca Conducted trials in South Africa. This country has dominant with B.1.351 Mutated strains. The studies demonstrated the lower vaccine efficacy compared to that of the other variants where this strain was not dominant.[42]

Here we will see three countries with vaccine efficiency, the Indian Council of Medical Research Virology Lab, Bharat Biotech's COVAXIN vaccine has been found to be78% effective against the double mutant variant.[16-18] It is effective to counteract the infection.

The Food and Drug Administration (FDA) has acquiesced in three different Vaccinations for emergency use in the USA, and it says that the mRNA vaccines provide protection against B.1.1.7 COVID-19 variant.

The Vaccine efficacy for the Brazilian variant (B.1.1.28) has not yet been reported yet, but B.1.351 and P.1 is of the same receptor-binding mutations. Hence, the vaccine efficacy against P.1 strain is assumed to be equally effective to B.1.351.[17,42]

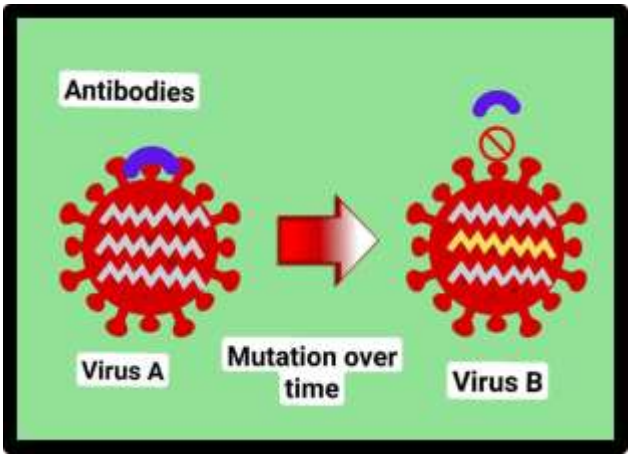

Fig 3 rejection of binding antibodies

8. COVID-19 Vaccine Challenges:-

More than 75 million people have been fully vaccinated as of April 13, 2021, Since December 14, 2020. During the same duration, there have Been 5,814 vaccine breakthrough cases reported across the world. A breakthrough case is a case in which victims have successfully gotten vaccinated but still get

infected. In a case study, it has been seen that 45 percent of the total cases were female, 29% Were asymptomatic, 45% were over 60 years of age, 7% of the Total cases were hospitalized, and 1% died.[40] 5,814 vaccine breakthrough cases were reported across the USA.and such scenario was also seen in different countries all over the world. and due to such incidents, Vaccine refusal has been an issue. Doctors and nurses have to had to deal with this mindset of people even in pre-pandemic times.[41] There is growing COVID-19 vaccine hesitancy.[43] Not only that but there are also other management problems that have put a significant impact across different areas of the world such as Equitable Vaccine distribution, storage requirements, and cost are factors. Due to the mutation of variants, none of them is 100% effective in the prevention of COVID-19 Illness. On another hand, there were many cases to work on in general like Pregnant and breastfeeding women, immunocompromised, and diverse Races and ethnicities have been underrepresented populations in Vaccines studies.

9. Conclusions:-

The virus changes itself according to time and it makes itself more or less harmful and so it also changes its effect on living beings. Viruses affect the individual on how strong one immunity is. Different variants not only result in increasing transmissibility or spreadability, mobility and mortality but can also escape from detection and diagnostic test. The longer the virus propagates chances are much higher to get a mutation and hence different variants can appear. It is important to keep ourselves safe and protected from the virus by avoiding contact by wearing masks and having a hygiene isolation quarantine. Vaccination plays an important role to prevent the spread of the virus. Vaccines cannot be 100% percent cured of the virus but it is essential. There are also some vaccine breakthrough cases that take place in some conditions but that doesn't mean that one should not get vaccinated for or it will happen in each and every case change in variants can also show different symptoms and hence there is a need of different treatments and diagnosis for each of them the detection test it also needs to be upgraded. The mutation causes changes in viruses and hence it also decreases susceptibility to treatment including antiviral monoclonal antibodies and Convalescent plasma. Genome surveillance and vaccination are important for early identification, prevention of mutation, and viral replication**.**

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