

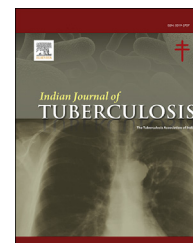


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Editorial

Covid-19 vaccines and new mutant strains impacting the pandemic

Vaccines are the key for preventing the zoonotic virus pandemic caused by SARS-Cov-2 with no specific antidote. Various countries are working to roll out the vaccines.^{1,2} There are four categories of vaccines in clinical trials namely; *WHOLE VIRUS, PROTEIN SUBUNIT, VIRAL VECTOR and NUCLEIC ACID (RNA AND DNA)*. Some of them try to induce the antigen into the body, while others use the body's own cells to make the viral antigen. Till February 2021, at least seven different vaccines across three different platforms have been rolled out in various countries. Around 100 plus vaccine candidates are in development in different phases.³

Three new clinically important mutant variants of the virus, taking the world by storm have been identified as:

- The United Kingdom: Identified a London variant called B.1.1.7 (variant VUI-202012/01) with 23 mutations, many of them associated with alterations in a protein made by the virus in the spike protein. Compared to other variants, it spreads more easily and quickly.^{4,5} Experts reported (January 2021) that it may be associated with an increased risk of death compared to other variant viruses, but more studies are needed to confirm this finding. It has been detected in many countries.
- South Africa: A variant called B.1.351 emerged independently of B.1.1.7. Detected in early October 2020, B.1.351 shares some mutations with B.1.1.7. Many cases were reported from US in January 2021.
- Brazil: A variant called P.1 emerged among travellers from Brazil, who were tested during routine screening at an airport in Japan, in early January. Variant contains an additional set of mutations that may affect its ability to be recognized by antibodies. This variant was detected in the US in January 2021.

These new variants are capable of spreading faster are emerging and leading to inevitable questions about whether they will make the newly approved vaccines less effective. PCR is the main diagnostic tool which targets 3 parts of the virus to confirm presence of an infection. As per researchers, one target showed repeated negative samples from some parts in England with rapidly rising case numbers, while other

two showed positive results. Scientists found that the virus in these samples had picked up a mutation – a deletion at the same H69 and V70 positions in the protein meaning that PCR was unable to pick the result in some cases. A new lineage of the Covid-19 virus was discovered that had picked up multiple mutations over a relatively short period of time. They designated B117 – the new British Covid-19 variant, also known as VOC 202012/01 which has spread to 50 other countries by mid-January. It is estimated to be 50–75% more transmissible than the original Covid-19 virus.

1. Other new strains

Other new strains of significance spreading in the US were 20C-US and the CAL.20C in California. There are reports of this variant infecting people who have already been infected with a different variant of the virus last year. One of the mutations carried by CAL.20C, (L452R,) found on the spike protein is being associated with a decreased sensitivity to antibodies, which suggests that it may be able to evade parts of the immune system. Another variant (B1.526) is circulating in New York in February 2021 has also worried scientists. By mid-February, it accounted for 12.3% of the viruses analysed. It contains two E484K and N501Y, which was also present in variants from Brazil and South Africa. In most cases, treatments and vaccines causes the viruses to evolve and continue spread. Those viruses that resist treatment survive for longer to replicate and spread their genetic material. Hence according to researchers, efforts to spot new variants of Covid-19 as early as possible should include testing sewage samples in cities like Belo Horizonte in Brazil. Hence genome sequencing is the need of the hour.

Another new variant has been located in Finland (Fin-796H) and is reported to have mutations similar to those seen in B.1.1.7 and B.1.351. It also has a mutation in one of the regions (N) recognized by PCR testing. But as per experts, that should not cause a major problem as PCR relies on 2/3 different assays that detect different parts of the virus. Similar issue was seen with in B.1.1.7 variant which escaped the assay that detects the S gene of the virus.^{6,7}

2. In future, corona virus may evade vaccines/treatments

Slow vaccine rollout, mutated strain which is 50% more contagious, may undermine diagnostic testing, antibody treatment and vaccine efficacy. At present the 2 Covid-19 vaccines for use in the US remain highly effective for now. A high level of immunity appears to last for 8 months or more as per research. Researchers around the world agree that the threat of vaccine evading mutations are possible though not necessarily imminent but all also agree that urgent action is required to prevent such a situation. Hence solution is to double down on public health measures to quickly roll out the vaccines.

3. Increased transmission can increase mutations

The mutated variant that originated in the U.K., called B.1.1.7 allows the spikes on the virus to bind easily with receptors on human cells. B-117 is not a deadly virus, but because of its high infectivity it kills more people than the original strain would have. B-117 has the capability to grow in communities where SARS-CoV-2 is kept under control. Till date the two most notable mutated strains B-117 and 501. V2, from South Africa do not seem to sidestep vaccines or natural immunity. Pfizer announced that a preliminary study finds its vaccine holds up against the B-117 mutations, noting that the nature of the vaccine's construction should allow adjustments to meet the challenge of corona virus mutations.

4. Slow progress

One of the major reasons which can give the virus time to mutate its spike protein and escape the vaccine in some countries is the slow vaccine rollout. As per scientists, some vaccines could even start to exacerbate Covid-19 infections via a phenomenon known as antibody dependent enhancement, where certain antibodies end up contributing to the severity of the disease. Vaccine producers like Moderna is developing a booster dose to better tackle emerging SARS-CoV-2 strains. AstraZeneca quoted that in 6–9 months they may come out with a vaccine for new strains. German biotech Cure Vac recently has collaborated with GlaxoSmithKline to develop messenger RNA (mRNA) vaccines.

The new generation of vaccines for Covid-19 are being given all over the world, but the new strains are a big challenge for them. As per reports, the Oxford vaccine is less effective against a variant common in South Africa than against other strains, causing the country to halt the distribution of that vaccine. A study assessing Israel's vaccination⁸ showed that 2 doses of Prizer–Bio Tech vaccine reduces symptomatic cases by 94%, hospital admission by 87% and severe Covid-19 by 92%. As per the article the vaccine was also effective against B.1.1.7. Single dose Covid-19 vaccine made by Johnson and Johnson has been given emergency use authorization US FDA.⁹ Based on analysis, data on 39,321 adults

with no previous signs of infection reported the efficacy as 66.1% for preventing moderate to severe Covid-19, 28 days after vaccination. The company initially reported that the vaccine provided 72% protection against moderate to severe Covid-19 but proportion fell to 66% in Latin America and 57% in South Africa. There is no evidence suggesting vaccines will be any less effective against the new variant. As per experts they are not seeing any increased virulence spike protein, that may reduce vaccine effectiveness so Covid-19 vaccines appears to be adequate in generating an immune response to the variant of the corona virus.

5. Redesigning of Covid-19 vaccines

The immediate way to combat the threat of emerging variants is probably to quickly vaccinate as many people as possible with current shots. Researchers are of the opinion that new updated vaccines may be required in the future. South African variant called 501Y.V2 (also known as variant B.1.351), is of concern since it carries mutations that sap the potency of virus-inactivating 'neutralizing antibodies' that were made by people who received either the Pfizer/Moderna RNA vaccines. It is not clear if these changes are enough to lower the effectiveness of those vaccines. Other immune responses that vaccines prompt may help to protect against the effects of variants. Data released by Novavax concluded that experimental vaccine, designed to combat the original virus, was 85% effective against a United Kingdom and 50% effective against 501Y.V2. Hence drop in vaccines effectiveness is of high concern. According to the year, the flu vaccine has to be updated as the influenza virus mutates and adapts to escape the immunity already present in the population. If the corona virus shows similar capabilities, the vaccines may have to regularly updated. Vaccines like Moderna, Pfizer and AstraZeneca instruct cells to produce the virus's spike protein. Variants including 501Y.V2 carry spike mutations that alter regions targeted by neutralizing antibodies. Another possibility is to change older versions identified in Wuhan, China for an updated molecule with specific amino-acid changes that hinder antibody responses. It also needs to be determined whether any such changes would have knock-on effects that alter how the immune system reacts to the vaccine. Other options is to include both new and old forms of the spike protein in a single jab (multivalent vaccine).

6. Universal Covid-19 vaccine

Solution is to develop a universal vaccine that is future-proof against the evolving corona virus. Clue lies in examining vaccines for other viral infections that have stayed effective for decades. Yellow fever has a weakened form of yellow fever virus. Just like Covid-19, yellow fever is caused by an RNA virus. As per research, T cells largely ignore the surface antigens of the yellow fever virus. Instead, they recognize antigens within the virus. Influenza viruses mutate faster than Corona virus. They have a step in their replication process that proofreads the copied genetic code for errors, slowing the introduction of mutations. All depends on how quickly we can

get the pandemic under control. The likelihood of mutations depends on how much virus is circulating,^{10,11} It is uncertain, how long immunity from the Covid-19 vaccine will last. A flu vaccine is needed every year not only because the flu virus mutates quickly but also because the antibody response wanes over time.¹² The present Covid-19 vaccines are expected to provide some protection against new virus variants, because they elicit a broad immune response. Hence changes/mutations in the virus should not make vaccines completely ineffective. If these vaccines prove to be less effective against one or more variants, it will be possible to change the composition of the vaccines to protect against these variants hence, in future vaccines may need to incorporate more than one strain when in development or booster shots may be required. Stopping Measures to reduce transmission including frequent hand washing, wearing a mask, physical distancing, good ventilation and avoiding crowded places or closed settings continue to work against new variants by reducing viral transmission thereby also reducing opportunities for the virus to mutate. High-risk groups have to be prioritized to maximize global protection against new variants and minimize the risk of transmission. Ensuring equitable access to Covid-19 vaccines is more critical than ever to address the evolving pandemic.

7. People's future response to revaccination with the updated vaccine

As per research, people tend to have more robust immune responses to the first variant of a pathogen that they encounter than subsequent variants. Hence updated vaccines may trigger lower immune responses as compared to the first one. As per evidence, RNA vaccines may not fall prey to this trend. But some RNA vaccines trigger surprisingly complex immune responses, yielding antibodies that target regions of viral proteins that are often not detected in responses to other kinds of vaccines which means that RNA vaccines will also be better able to target the changes present in a variant. Many US companies are planning to update their vaccines in the near future. A French company is working on an inactivated vaccine using the complete virus, to potentially form a response to all possible epitopes, a term for the portions of the virus's proteins that the immune system can recognize. It also combines the inactivated virus with an adjuvant. As more people get vaccinated, it is expected that the virus circulation should decrease, which will further lead to fewer mutations.

Conflicts of interest

The authors have none to declare.

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