Vaccines vs Variants: What we know so far?

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KINIGUIDE | Since the beginning of the Covid-19 pandemic, scientists have been monitoring the genetic sequence of the virus behind the disease to help spot mutations that could spell problems in the future.

Now, the World Health Organization (WHO) has flagged four such SARS-CoV-2 variants for closer scrutiny.

More worryingly, some of these variants have been found circulating in the Malaysian population, including those that would reduce the effectiveness of Covid-19 vaccines.

In this instalment of KiniGuide, we look into what causes these variants and what it could mean for the vaccines in Malaysia's immunisation programme.

How did the variants come about?

As the SARS-CoV-2 virus spreads across the human population, it naturally accrues “errors” in making copies of its genetic code.

Most of these mutations are benign or even harmful to the virus, but by chance, a rare few may help it infect humans more efficiently.

This propels the new variants to spread further and faster across the population. The more people it infects, the more likely it is that variants with advantageous mutations would arise.

Scientists are constantly collecting samples from confirmed Covid-19 patients to undergo full genome sequencing. This is highly specialised work that would reveal the genetic code of the virus that is responsible for the patient’s infection.

A computer-generated image of the SARS-CoV-2 virus, with its spike proteins highlighted in red. Certain mutations to the spike protein, such as D614G and E484K, can significantly alter how the virus behaves.

The scientists are on the lookout for mutations that may help the virus evade detection through existing Covid-19 tests, increase its transmissibility or lethality, or even make vaccines less effective.

Different health authorities have slightly different definitions, but generally,

Covid-19 variants that carry mutations believed to confer such traits may be flagged as a “variant of interest”.

If there is evidence to confirm that a variant of interest is indeed more dangerous, then it may be redesignated as a “variant of concern”.

These designations mean a variant may need to be monitored more closely, and perhaps require more stringent measures to prevent its spread.

What are the variants of concern?

The WHO has identified four variants of concern so far.

B.1.1.7 was first identified in the UK in September 2020. It is associated with increased transmissibility, but vaccines are as effective against this variant as older variants.

According to the WHO, it has been reported in 149 countries as of May 11.

B.1.351 was first identified in South Africa in May 2020. It is associated with increased transmissibility as well as dampened vaccine efficacy, and an enhanced ability to infect Covid-19 survivors. This variant has been reported in 102

countries.

The B.1.1.28.1 (also known as P.1) variant was first detected in Japan in November 2020 among travellers arriving from Brazil. It shares similar traits as B.1.351. It has been reported in 60 countries.

A “family tree” of some of the SARS-CoV-2 samples collected all around the world highlights four variants of concern and traces its lineage to the earliest virus samples collected in Wuhan, China.

The B.1.617 variant was first detected in India in October 2020, but was only recognised as a variant of concern on Monday amid deadly outbreaks in the country.

It actually refers to three sub-variants – B.1.617.1, B.1.617.2 and B.1.617.3.

Little is certain about B.617, but it appears to spread even faster than B.1.1.7. Some reports also suggested it can cause more severe disease than older variants.

It may have some ability to evade antibodies induced by vaccines but not enough to render vaccines ineffective.

The B.1.617 has been reported in 44 countries as of May 11.

What about the D614G mutation I heard so much about last year?

An individual SARS-CoV-2 virus particle may contain many mutations compared to the ones first detected in Wuhan, China, at the onset of the Covid-19 pandemic.

The D614G mutation is just one of many possible mutations.

Indeed, each of the four variants of concern carries six to 12 "signature" mutations that distinguish it from other variants.

Some mutations are featured on several of these variants.

For example, the E484K mutation is found on the B.1.351 variant as well as the P.1 variant, giving them both some ability to evade vaccine-induced antibodies. The B.1.617.1 and B.1.617.3 subvariants carry a similar E484Q mutation.

The D614G mutation, meanwhile, is associated with increased transmissibility. It is the only "signature" mutation found on all four variants of concern.

Which variants have been found in Malaysia so far?

The local variant is known as B.1.524. This is neither considered a “variant of interest” nor a “variant of concern”. The same goes for the B.1.470 and B.1.466.2 variants also circulating in Malaysia.

More recently, however, three of the four variants of concern have been identified in the country.

These are B.1.1.7, B.1.351, and B.1.617. That leaves the P.1 variant - the one first detected in travellers from Brazil - the only variant not yet found circulating in Malaysia.

The most prominent of these is the B.1.351 variant that was first detected in South Africa.

Yesterday, Health Ministry director-general Dr Noor Hisham Abdullah said four more cases have been detected, bringing the total to 66 cases.

These have been found in Selangor, Kuala Lumpur, Perak, Kedah, Kelantan and Negeri Sembilan.

Most of these cases are linked to various clusters, but 19 are close contacts not linked to any cluster, and one turned up for screening after experiencing Covid-

19 symptoms.

One case involved a vaccinated person and another had already survived an earlier bout of Covid-19.

For the B.1.1.7 variant, a total of three cases have been detected locally – one in Selangor as part of the Lorong Megah Jaya cluster, another two in Sabah sampled during screening for close contacts.

Another five cases are imported cases.

For the B.1.617 variant, five cases have been detected. All of them had recent travel history to India, including three who were detected during quarantine upon arriving in Malaysia.

One case arrived on April 7, then tested negative for Covid-19 on the same day and on April 12. On April 21, however, the patient was admitted to hospital with severe Covid-19 symptoms and later died on May 1.

On May 12, Noor Hisham reported that the case involved the B.1.617.2 variant.

For the other case, Noor Hisham said yesterday the case was detected through

screening of people with Covid-19 symptoms.

However, the above information should be read with caution, since only a small fraction of the cases has been sequenced, and the cases described here are only those that have been genomically confirmed (details below).

How well do vaccines hold up against these variants?

A study in Qatar found the Pfizer-BioNTech vaccine to be 75 percent effective in preventing a B.1.351 infection, and 100 percent effective against severe illness and death.

For comparison, earlier trials showed the vaccine to have 95 percent efficacy against symptomatic Covid-19.

A trial on the AstraZeneca vaccine in South Africa found that its efficacy dropped to as low as 10.4 percent against mild-to-moderate B.1.351 infections.

However, the study is beset with several problems.

Firstly, its small size means the estimate could be far off the mark.

Second, no one in the study got severely ill or died of Covid-19 - whether they were vaccinated or not - meaning no conclusions could be drawn on whether the vaccine still protects against severe illness or death. Again, this is due to the small size of the study.

Nevertheless, this study and an earlier but similarly disappointing study is enough to prompt the South African government to abandon the AstraZeneca vaccine.

AstraZeneca is reportedly working on an updated vaccine that would work against all variants, and expects this to be ready for use in late-2021.

Meanwhile, a Reuters report quoted sources claiming that the AstraZeneca vaccine remains effective against the P.1 variant.

The Sinovac vaccine was 50.38 percent efficacious in a clinical trial in Brazil and 49.6 percent effective in a “real world” study there in terms of preventing Covid-19 symptoms, where the P.1 variant is prevalent.

As of February, no one who received the vaccine in the Brazil trials developed the moderate or severe disease, compared to seven among those who didn’t get the vaccine.

In comparison, the same vaccine was 94 percent effective in Indonesia, where SARS-CoV-2 variants of concern are not yet prevalent.

The makers of the Sputnik V vaccine claim it is reduced efficacy against the B.1.351 variant, but said it still performs better than other vaccines. It has yet to release data to back its claims.

The CanSino Biologics vaccine's performance against SARS-CoV-2 variants has not been publicly announced.

With regard to the B.1.1.7 variant, all vaccines tested against it appear to work as well as they did against older coronavirus variants.

However, the very fact that it is more transmissible would mean more people would have to be vaccinated to achieve herd immunity. This applies to other highly transmissible variants as well.

As for the B.1.617 variant, it may be too soon to be sure but there are promising signs that vaccines will remain effective.

Laboratory tests found that antibodies induced by various vaccines have reduced potency against B.1.617, but the drop is reportedly not as sharp as those seen in

the B.1.315 variant.

However, what such tests mean for real-world effectiveness is unclear for several reasons. For one, antibodies are only one component of a complex immune response.

Meanwhile, in the UK yesterday, where the country is seeing a rise in B.1.617 infections, Health Secretary Matt Hancock reportedly told the House of Commons that the majority of those hospitalised for the variant are those eligible for a vaccine but have yet to be vaccinated.

“This shows the new variant is not tending to penetrate into older, vaccinated groups and it underlines again the importance of getting the jab especially - but not only - among the vulnerable age groups,” he said, based on a video recording of his address.

The UK currently uses vaccines from Pfizer-BioNTech (11.4 million doses as of May 5), AstraZeneca (23.3 million doses) and Moderna (about 100,000 doses).

Do we really know where are SARS-CoV-2 variants cropping up?

The short answer is: No.

As alluded to before, genomic sequencing of the coronavirus is highly specialised work. Only a handful of countries have the capacity to do this routinely and sequence a significant portion of samples collected in their territory.

Of the more than 160 million confirmed Covid-19 cases reported all over the world, only about 1.5 million are ever sequenced and shared on the Gisaid platform.

Gisaid is used by researchers to quickly share genomic information of influenza viruses, but has since been used to monitor SARS-CoV-2 sequences as well.

Nearly half of the SARS-CoV-2 submissions on Gisaid are from the UK and the US, while most countries submitted far fewer samples.

Malaysia, in particular, only managed to sequence and share 683 genome sequences with the rest of the world up to May 17, which amounts to 0.14 percent of its confirmed cases up to that point.

Neighbouring Singapore managed to sequence and share 3.91 percent of its cases, while Indonesia managed 0.10 percent.

The number could go as high as 77.6 percent in Iceland and 59.1 percent in

Australia – both advanced economies that have relatively few Covid-19 cases to begin with.

On the other hand, about 50 countries and territories did not submit any genomic sequences to Gisaid at all, even though some such as Honduras have reported hundreds of thousands of cases.

This leaves humanity with significant blind spots all over the world when it comes to monitoring the spread of variants of concern and spotting the emergence of new variants.

Moreover, identifying SARS-CoV-2 mutations through sequencing is only the beginning of the work needed to determine if the mutations made any meaningful difference in how the coronavirus behaves.

Malaysia has allocated a portion of the budget under the National Covid-19 Immunisation Programme to ramp up its genomic surveillance of the coronavirus, in order to ensure Malaysia's vaccine portfolio would work against variants circulating in the country.

Source: https://www.malaysiakini.com/news/575060