

Perspective

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Ever−evolving SARS−CoV−2: Latest variant KP.2 is on the rise

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Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) emerged at the end of 2019 and is responsible for the coronavirus disease (COVID-19) pandemic which shook the healthcare system worldwide. Until April 2024, over 775 million positive cases and 7 million deaths have been reported globally[1]. Since its emergence, the virus is constantly accumulating mutations in its genome and evolving frequently over time. In the last 3 years, we have witnessed the emergence of numerous variants from Alpha to Omicron and other subvariants, and some of them are more virulent escaping the natural and/or vaccine induced immunity and some are much less virulent than earlier variants and contributed to the pandemic[2,3]. The World Health Organization (WHO) announced that the COVID-19 is no longer a public health emergency of international concern on May 5, 2023[4]. However, the emergence of new subvariants continues to pose significant challenges to global health.

In early 2024, JN.1 variant (BA.2.86.1.1) replaced XBB.1 lineage as the predominant variant. Recently, the new variant KP.2 derived from the parental JN.1 variant with R346T, F456L mutation in the spike region and a substitution in non-spike protein was detected and is spreading rapidly. The variant has been reported in at least 28 countries including the US, UK, Canada, Australia, India and Thailand[5−7]. This variant appears to be more transmissible and has been responsible for the surge in the number of cases in many of the countries over the past few days and garnered attention. Infections have increased in the US and the cases have soared in India as well. On 3 May, 2024, the WHO designated KP.2 as a "variant under monitoring"[8]. According to the data from the Centers for Disease Control and Prevention (CDC), KP.2 variant and its parental strain JN.1 contribute for 4% and 55% of the infections, respectively in the last week of March. In May 2024, the new variant accounts for 28% cases in the US in the span of two weeks (280April-11 May) which makes it a dominant variant in the US overtaking JN.1 variant accounting for 16% of cases in the same time span[5]. Due to the surging number of cases and possibility of immune evasion, the healthcare authorities are monitoring the variant closely. Preliminary research by Kaku *et al.* indicated higher viral fitness of KP.2, whereas its infectivity is 10.5 fold lower compared to JN.1. Furthermore, neutralization assay performed using monovalent XBB.1.5 vaccine sera showed KP.2 resistance to neutralization indicating the immune resistance ability of this variant[9].

Earlier in May 2023 and December 2023, the WHO advised the manufacturers to use monovalent XBB.1 descendant lineage as vaccine antigen. The JN.1 derived variants (*e.g.* JN.1.13.1, JN.1.11.1, KP.2) replaced the XBB.1 lineage variants and became the dominant variant in US in early 2024. Based on the data from global initiative on sharing all influenza database, >90% of the sequence in the publicly available databases are JN.1 as of 20 April, 2024. Hence, in April 2024, the WHO Technical Advisory Group suggested using JN.1 as the antigen formulation for future COVID-19 vaccines (GenBank: PP298019). Due to greater fitness of the JN.1 variant and it is likely that the future variants might evolve from the JN.1, updating the vaccine antigen composition with JN.1 could enhance the immune response to circulating strains. Notably, immunization of mice with JN.1 vaccine candidates elicit significantly higher neutralizing antibodies against co-circulating JN.1 variants compared to the responses induced by currently approved vaccines[10]. As the new vaccine development requires substantial time, vaccination programmes should continue to use currently approved vaccines which can provide considerable protection against severe disease[10]. Further research is necessary to assess the vaccine efficacy against this variant.

While KP.2 variant transmissibility is concerning, the symptoms and severity of infection caused by this variant is most likely similar to those of JN.1 and the cases of hospitalizations have not surged. Evidence so far suggests that vaccination prevents

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severe disease and fatalities. The new variant might pose a threat to vulnerable populations, hence booster doses confer better protection. In February 2024, the CDC recommended additional doses of COVID-19 vaccines for adults of 65 years or older due to the increased risk of severe disease[11]. While the risk posed by KP.2 is considerably low as of now, it cannot be guaranteed that it will remain so. There is not much data about this variant so far to draw any conclusion at this moment, hence the antigenic characteristics, surge in cases and severity of the symptoms, concerns about immune evasion remain to be seen as the situation evolves.

The fewer number of cases and mortality indicates that the pandemic has nearly ended. However, SARS-CoV-2 still poses a significant global health threat. The identification of new variants has shown that the SARS-CoV-2 is still circulating among the susceptible host and the virus is evolving to infect many individuals. As long as the virus is circulating, there is chance for the mutants to appear. Some mutations have little or no impact, but some mutations can increase viral fitness and infectivity. Hence, the emergence of new variants requires vigilance and prompt response[12]. The healthcare authorities are still monitoring the evolving variants in order to lessen their impact on public health. By increased surveillance, rapid diagnosis, vaccination coupled with other proactive health measures can curtail the infections and control the virus transmission that could eventually reduce the chance for the further virus evolution. If an individual is having the symptoms, it is advisable to isolate and stay home in order to avoid the spreading of virus. Furthermore, it is essential to create awareness, and people should take personal responsibility by understanding the situation, stay up to date with vaccinations, and follow precautionary measures. It is vital to remain vigilant and committed to prevent the virus spread with a goal of a pandemic free future.

Conflict of interest statement

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