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SARS–CoV–2 variants: A continuing threat to global health

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Coronavirus disease 2019 (COVID-19) is an acute respiratory illness caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). COVID-19 pandemic has an unprecedented impact on economy, trade and human lifestyle globally. Since the emergence of SARS-CoV-2, more than 266 million infections and 5 260 888 deaths were reported globally over the last two years[1]. The scientific achievements particularly in last two years yielded effective vaccines against COVID-19. A variety of platform technologies including protein subunit, viral vector, RNA, inactivated and DNA are being employed to develop effective vaccines. To date, vaccines that have been approved against COVID-19 include the Pfizer BioNTech (mRNA vaccine), Oxford-AstraZeneca (viral vector vaccine), Moderna (mRNA vaccine), Janssen Ad26.COVS.2 (viral vector), Sinopharm, Sinovac-CoronaVac, Bharat Biotech's Covaxin (inactivated virus vaccines), etc. As of December 2021, over 8 billion doses of COVID-19 vaccines have been administered globally[1]. The details on the number of COVID-19 confirmed cases and global vaccination coverage are provided in Figure 1.

SARS-CoV-2 virus has been rapidly evolving and several variants of SARS-CoV-2 with diverse mutations in the spike protein have been identified causing a significant health concern worldwide. In common, the mutations in the spike protein were identified in all variants which enhance viral virulence, transmission frequency, and exhibit resistance to the action of antibodies. The World Health Organization (WHO) designated mutant SARS-CoV-2 either as 'variants of interest (VOI)' or 'variants of concern (VOC)'. At least 14 variants have been reported so far including 5 VOCs and 2 VOIs. VOC includes the alpha variant (B.1.1.7 lineage) that was first identified in UK in September 2020, the Beta variant (B.1.351 lineage) identified in South Africa in May 2020, the gamma variant (P.1 lineage) identified in Brazil in November 2020 and the delta (B.1.617 lineage) variant identified in India in October 2020. All these VOCs share multiple mutations with each other and other

SARS-CoV-2 VOIs (covdb.stanford.edu). VOI includes lambda (C.37), first identified in Peru in December 2020 and mu (B.1.621), first identified in Colombia in January 2021[2].

A highly mutated variant B.1.1.529 has been identified in South Africa in November, 2021. The first sequence of this new variant B.1.1.529 was uploaded in GISAID EpiCoV on November 22, 2021[3]. On November 26, 2021, the WHO declared B.1.1.529 as VOC and named the omicron variant[2]. Omicron cases were reported in several countries in early December this year, which were linked to travel history to some African countries, but the community transmission is also reported in several countries[4]. It is too early to predict whether the omicron variant will outpace the highly transmissible dominant delta variant. Currently, research is underway to study this variant transmissibility, clinical severity, and vaccine effectiveness. Though much information about this variant is currently not available, the cluster of mutations in its genome and the concurrent rise in the number of infections due to this variant in South Africa fuels global fear on this variant. Large number of mutations (>30) were reported in spike region which is an immunodominant region targeted by most of the neutralizing antibodies. Some of the identified mutations in omicron were also reported in other previously identified variants that are known to be involved in

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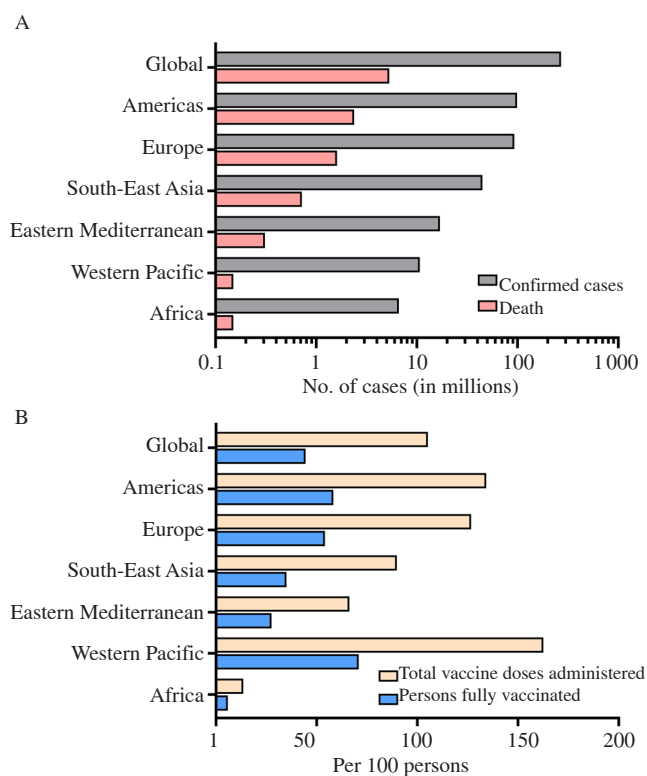


Figure 1. Data on confirmed COVID-19 cases and deaths reported worldwide (A) and vaccine doses administered and persons fully vaccinated per 100 persons (B) (data as of December 15, 2021; data from: <https://covid19.who.int>).

immune escape and enhanced ACE2 affinity. Researchers have been racing to study the virus properties and the risk associated with this variant. Preliminary results suggested that omicron variant showed resistance to convalescent or vaccine sera neutralization compared to other variants and wild type strain which showed that this variant is likely to compromise vaccine induced protection[5,6]. Further, neutralization sensitivity of convalescent sera was decreased dramatically against pseudotyped SARS-CoV-2 omicron variant when tested *in vitro*[7]. Another study showed that the booster dose of BNT162b2 vaccination greatly reduces the virus escape and enhance the neutralization capacity against omicron[8]. However, more detailed results on viral fitness, growth rate, vaccine escape, disease severity and real-world data will emerge in the coming weeks.

The emergence of new variants complicates the virus control and preventive measures, and challenges the human healthcare system[2]. South Asian countries in particular, are facing more challenging situation due to their high population, overcrowded lifestyle, lack of infrastructure, poor healthcare system, high poverty rates and financial constraints. Although the pandemic was kept in control during the initial months, the more contagious delta variant made a drastic impact and led to a massive second wave of infection in South Asia. All the countries are managing to control the virus spread and save the human lives at the expense of high economic

cost. After the devastating impact of delta variant and its associated complications[9], the world is now in the grip of highly mutated omicron variant. Due to the rise of omicron cases in South Asian countries, governments have again imposed a partial lockdown with travel restrictions, screening and enforced quarantine for international travelers to control the virus spread. The rapid implementation of active and intensive surveillance systems associated with timely detection, contact tracing, isolation, risk assessment, vaccination, outbreak control management and early warning of new variants emergence are the effective ways to control the virus transmission.

Still, we need more information regarding the efficacy of available vaccines against the existing and newly emerging VOCs. The efficacy of vaccine was reported to be reduced against VOCs including omicron; hence, the development of variant-specific vaccines and monoclonal antibodies might be required to treat the infection caused by variants. Prevention and controlling the virus spread is a global public health priority now. Hence, there is now an urgent need to examine the virus characteristics, effect of the mutations on vaccine efficacy or severity of the disease and follow the control measures to reduce virus transmission which could prevent the new waves of infection. Further more, addressing the vaccine inequity, enhancing vaccine effectiveness against SARS-CoV-2 variants and development of variant specific vaccines that can induce durable immune responses can keep the virus spread under control[10]. In particular, equal access to vaccines would reduce the emergence of new variants, helps to achieve herd immunity that eventually could end the pandemic.

Conflict of interest statement

WP from Chulalongkorn University is a co-founder/shareholder of Baiya Phytopharm Co., Ltd. Thailand. The other authors declare that there are no conflict of interest

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Authors' contributions

BS and WP conceptualized the study. BS performed the literature review and wrote the original draft. BS, NK and WP contributed to writing, review and editing the manuscript. WP provided funding acquisition. All authors have read and agreed to the published version of the manuscript.

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