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Commentary

Rapid Global Spread of the SARS-CoV-2 Delta (B.1.617.2) Variant: Spatiotemporal Variation and Public Health Impact

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Abstract

The COVID-19 pandemic has already affected human society for more than 1.5 years. As of August 8, 2021, this pandemic had caused more than 203 million infected and 4.3 million deaths worldwide. As an RNA virus, SARS-CoV-2 is prone to genetic evolution, thus resulting in development of mutations over time. Numerous variants of SARS-CoV-2 have been described globally, four of which are considered variants of concern (VOCs) by the WHO: Alpha (B.1.1.7), Beta (B.1.351), Gamma (P1) and Delta (B.1.617.2). The Delta VOC was first reported in India in December of 2020 and has since affected approximately 130 different countries and regions. Herein, the spatiotemporal spread of the Delta VOC during April to July 2021 in 20 selected countries with available data were analyzed. The prevalence of the Delta VOC sequences was maintained at low levels in the beginning of April, increased rapidly in the following 3 months and is now becoming the predominant viral strain in most regions of the world. We also discuss the effects of the Delta VOC on transmissibility, clinical severity and vaccine effectiveness according to the latest data. The Delta VOC has greater transmissibility and risk of hospitalization than the ancestral SARS-CoV-2 strains and the other three VOCs. The Delta VOC places partially or unvaccinated sub-populations at high risk. Currently authorized vaccines, regardless of vaccine type, still have reliable effectiveness against symptomatic infections and hospitalizations due to the Delta VOC.

Key words: SARS-CoV-2, COVID-19, Delta VOC, spread, impact

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BACKGROUND

Since the emergence of COVID-19, variations in SARS-CoV-2 have been a matter of great concern. The WHO has classified the variants into variants of concern (VOCs) and variants of interest (VOIs) on the basis of transmissibility, clinical severity and possible effects on therapeutic and prophylactic measures. VOCs are variants with evidence of greater transmissibility, which cause more severe diseases (such as greater hospitalization or death rates) and show significantly less neutralization by antibodies generated during previous infections or vaccinations, less effectiveness of treatments or vaccines, or diagnostic detection failures. In contrast, VOIs are variants with specific genetic markers associated with changes in receptor binding, diminished neutralization by antibodies generated against previous infections or vaccinations, lower treatment efficacy, potential diagnostic effects, or greater predicted transmissibility or disease severity. Furthermore, the US Center

for Disease Control and Prevention (CDC) has proposed a third class, variants of high consequence (VOHCs), for which preventive measures or medical countermeasures have significantly less effectiveness than those toward previously circulating variants. Currently, no SARS-CoV-2 variant has been classified as a VOHC [1].

The Delta VOC (B.1.617.2) was first identified in India in December of 2020 [2]. It was considered a VOI on Apr 4, 2021 and designated a VOC on May 11, 2021 [3]. By the end of July 2021, approximately 130 different countries and regions had reported identification and/or transmission of the Delta variant. Herein, we performed a spatiotemporal analysis of the spread of the Delta VOC in selected countries, on the basis of public data issued by international organizations [4], national departments, and several professional agencies [5-7] and websites [8-11]. Effects of the Delta VOC on transmissibility, clinical severity and immune escape are also summarized.

Spatiotemporal spread of the Delta VOC

Before March 2021, the Delta variant circulated relatively silently in the global context, mainly in India and several European countries, such as Italy and the UK. In India, the proportions of the Delta variant ranged from 0.5% to less than 5% of all identified SARS-CoV-2 sequences nationally during the period from the beginning of January to the end of February of 2021. The proportion of the Delta VOC increased rapidly in India from approximately 3.7% in the beginning of March to 22.2% in the beginning of April. Meanwhile, 7.0%, 6.1% and 2.6% of SARS-CoV-2 sequences in Indonesia, South Africa and Australia were the Delta VOC; moreover, Mexico (0.11%), the UK (0.09%), Japan (0.07%), the USA (0.04%), Canada (0.03%), Italy (0.03%) and Germany (0.01%) also reported small proportions of the Delta VOC sequences (Fig 1).

The circulation of the Delta VOC increased after May 2021. At the end of May, 94.1% of SARS-CoV-2 sequences involved the Delta variant in India, and the Delta VOC became the predominant strain in the UK (73.3%) and Russia (70.3%). The proportions of the Delta VOC sequences were also substantial in Kenya (46.8%), Bangladesh (45.8%), Indonesia (30.9%), Thailand (30.8%), South Africa (21.8%), Australia (17.1%), Malaysia (17.0%) and Canada (15.6%). One month later (at the end of June), all countries examined in this study reported the Delta VOC; among them, the proportions of Delta VOC sequences exceeded 90% in four countries (98.1% in the UK, 95.1% in Russia, 91.4% in India and 91.4% in Bangladesh) and exceeded 50% in another seven countries (88.4% in Indonesia, 88.0% in Kenya, 84.9% in Australia, 77.7% in South Africa, 73.9% in Malaysia, 54.4% in the USA and 50.8% in Turkey).

By the end of July, the Delta VOC had spread in all continents globally. Proportions of the Delta VOC sequences approached 100% in Kenya, the UK and Australia; above 90% in India, Russia, South Africa, Indonesia, Spain, the USA, Germany and Italy; and above 70% in France, Mexico, Poland and Japan. In the context of continental regions, the areas most affected by the Delta variant were South and Southeastern Asia, Western Europe and North and Central America, as well as some countries in Africa; some countries in Eastern Europe and Far East Asia were slightly less affected, while South America was least affected.

EFFECTS OF DELTA VOC ON TRANSMISSIBILITY, CLINICAL SEVERITY AND VACCINATION

Like other variants of SARS-CoV-2, the Delta VOC has already been found to affect transmissibility, clinical characteristics and the efficacy of currently used vaccines to various degrees, thus greatly influencing the strategies and measures for control and prevention.

Transmissibility

Relatively early studies proposed that the Delta VOC might greatly affect transmissibility. On the basis of the sequences uploaded to the Global Initiative on Sharing All Influenza Data (GISAID)-hCoV-19 Variants, the effective reproductive number of the Delta VOC was estimated to be 55% (95%*CI*: 43–68%), a value higher than that of the Alpha VOC and 97% (95%*CI*: 76–117%) higher than that of non-VOC/VOI [12]. The basic reproduction number (R_0) of SARS-CoV-2 ancestral strains was estimated to range from 1.5 to 3.5, according to different studies [13-17]. However, the R_0 of the Delta VOC appeared to be higher [18], possibly reaching 5 to 6. The secondary attack rates (SARs) of various SARS-CoV-2 strains were evaluated in the UK [19]. Among the contacts of infected people without a travel history, the SAR was 11.4% (95%*CI*: 11.1–11.7%) for the Delta VOC but 8.0% (95%*CI*: 7.8–8.1%) for the Alpha VOC [20]. Direct estimation of the reproduction numbers for these two variants suggested that the Delta VOC has 50–100% greater transmissibility than the Alpha VOC (B.1.1.7) [21]. A more recent study released on medRxiv has highlighted that the viral load of the first positive test of Delta infections was approximately 1,000 times higher than that of the strains in the initial epidemic wave of 2020, on the basis of the daily sequential PCR testing of quarantined people [22]. In the USA, COVID-19 cases increased approximately 300%, driven by the highly transmissible Delta variant, and resulted in increases in hospitalizations and deaths from June 19 to July 23, 2021 [23]. In France, rapid growth of the Delta VOC was observed in 3 of the 13 metropolitan regions in June 2021, and 79% (95% *CI*: 52–110%) greater transmission than that of the Alpha VOC was estimated [24].

Clinical severity

The potential effects of the Delta variant on the clinical severity of COVID-19 appear to vary substantially. Early data from Scotland showed a greater risk of hospitalization (1.85-fold; 95%*CI*:1.39–2.47) among people infected with the Delta VOC than with the Alpha VOC [25]. A similar study in England revealed an increased risk of hospitalization among individuals infected with the Delta VOC (2.26-fold;

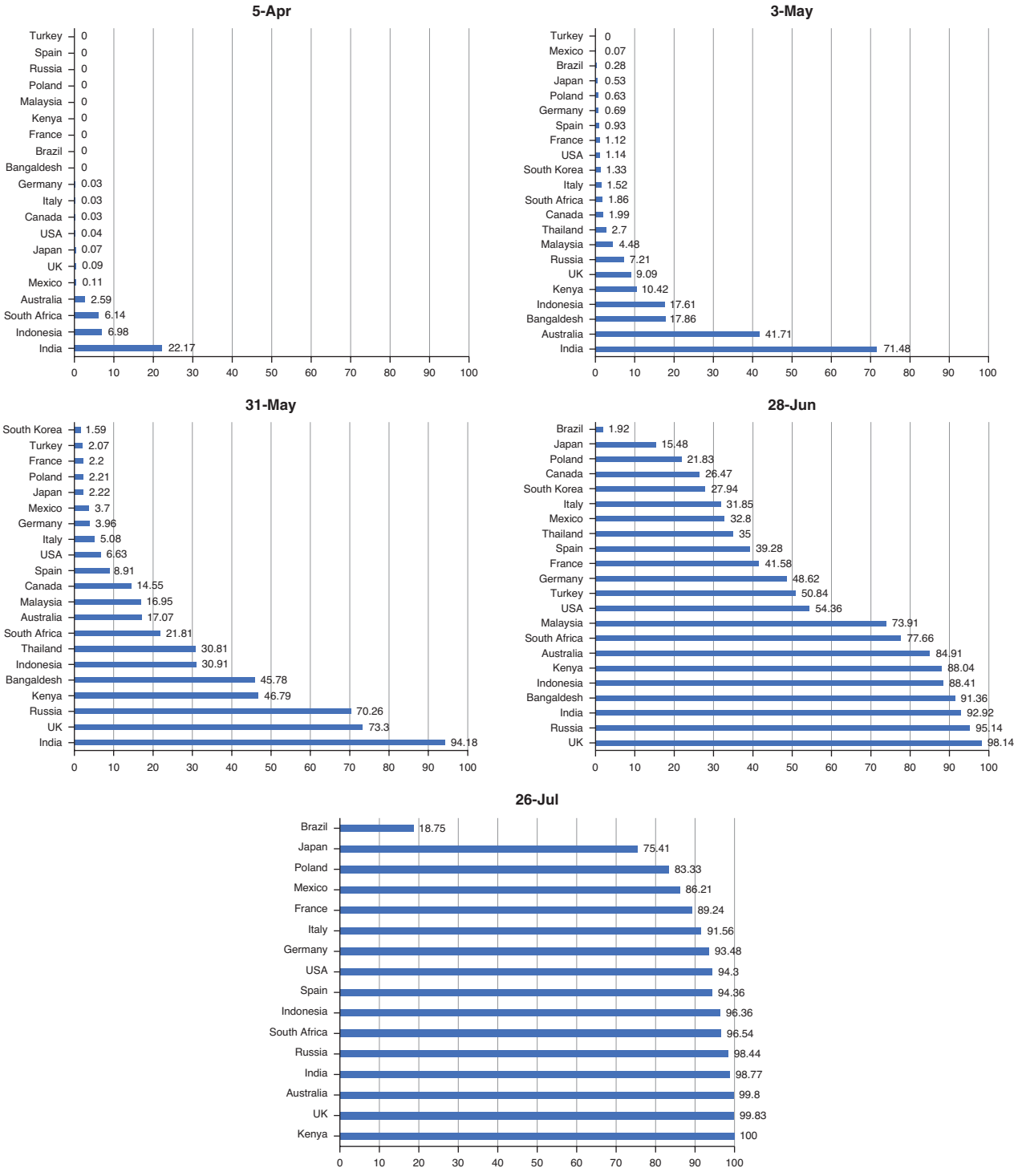

FIGURE 1 | Spatiotemporal alterations in the proportions of the Delta VOC in 22 selected countries with available data. The dates include April 5, May 3, May 31, June 28 and July 26, as highlighted at the top each graph. Some countries lack relevant data at some time points.

95%*CI*: 1.32–3.89) rather than the Alpha VOC [26]. A modeling study in South Korea has predicted increases in ICU hospitalizations (77.6) and deaths (35.1) per 10,000 people without vaccination over 150 days after the emergence of the Delta variant [27].

Another important issue is the effects of SARS-CoV-2 variants on critical and fatal illness. The Alpha VOC has been reported to influence the fatality ratio [28,29]. A large cohort study in the UK has reported that the mortality hazard ratio (*HR*) among patients infected with the Alpha variant was 1.64 (95% *CI*: 1.32 to 2.04) that in patients with previously circulating strains [30]. Another study has described greater mortality among the individuals infected with the Alpha VOC rather than other SARS-CoV-2 variants (*HR* = 1.61, 95% *CI*: 1.42–1.82) and non-Alpha SARS-CoV-2 (*HR* = 1.67, 95% *CI*: 1.34–2.09) [31].

The case fatality rate remains unclear among patients infected with the Delta VOC. An early evaluation in the UK has suggested a case-fatality rate of 0.3% (95% *CI*: 0.2–0.5%) for the Delta VOC after 28 days of follow-up. However, the European CDC (ECDC) has emphasized that this finding should be carefully interpreted, given the relatively short follow-up period [32]. Large-scale vaccination will apparently also influence the evaluation of the case fatality of the Delta VOC in European countries. Additionally, current data do not support the association between the emergence of the Delta VOC and possible reinfections among recovered patients infected with previously circulating SARS-CoV-2 strains [25,32].

Vaccine effectiveness

Numerous studies have provided evidence that sera from convalescent patients with COVID-19 who were infected with ancestral viral strains in 2020 and other variants, sera from individuals immunized with different vaccines, and various panels of generated monoclonal antibodies show different degrees of reduction of the *in vitro* neutralizing titers to the Delta VOC [33-37]. However, the sera from convalescent or vaccinated patients still have efficient neutralizing activity toward the Delta VOC *in vitro*. On the basis of the currently available evidence, the ECDC believes that individuals who have received only the first dose of a two-dose vaccination schedule are less protected against infections with the Delta VOC than other variants, regardless of the vaccine type; however, full vaccination provides comparable protection against the Delta VOC and the Alpha VOC. A study has found that the vaccine effectiveness among individuals with symptomatic Delta VOC infections after the first dose (33.5%, 95% *CI*: 20.6–44.3%) is slightly lower than that among individuals with symptomatic Alpha VOC infections after a single dose (51.1%, 95% *CI*: 47.3–54.7%). Following the second dose of either vaccine (Comirnaty and Vaxzevria), the vaccine effectiveness markedly increases against both two variants [38]. The vaccine effectiveness regarding hospitalization has been satisfactory for the Delta VOC: 71–94% after the first dose and 92–96% after two doses. A study from Scotland has also verified that both the Oxford–AstraZeneca and Pfizer–BioNTech COVID-19 vaccines are effective in reducing the risk of SARS-CoV-2 infection and hospitalization in people infected with the Delta VOC, although their protection against infections appears to be lower than that in people infected with the Alpha VOC [19]. The US CDC COVID-19 response team has concluded that the authorized vaccines in the USA provide high levels of protection against severe illness and death from infections with the Delta VOC and other currently circulating variants [23]. However, a study with a test-negative case-control design has reported lower effectiveness after one dose of vaccine (BNT162b2 or ChAdOx1 nCoV-19) among people with the Delta VOC (30.7%, 95% *CI*: 25.2–35.7) than the Alpha VOC (48.7%, 95% *CI*: 45.5–51.7%) [39]. Relatively lower effectiveness of those vaccines toward the Delta VOC has also been reported after two doses [39].

OUR CONCERNS

On June 23, 2021, the ECDC issued a risk assessment for infections with Delta VOC [32], proposing two essential items: (1) the overall risk of SARS-CoV-2 infection associated with the expected increase in circulation of the Delta VOC for the general population is considered low for fully vaccinated sub-populations and high to very high for partially vaccinated or unvaccinated sub-populations, and (2) the overall risk of SARS-CoV-2 infection associated with the expected increase in circulation of the Delta VOC for vulnerable populations is considered low to moderate for fully vaccinated sub-populations and very high for partially vaccinated or unvaccinated sub-populations. On August 6, 2021, the US CDC updated guidance for fully vaccinated people according to new evidence regarding the Delta variant [40], emphasizing that: (1) the Delta variant causes more infections and spreads more rapidly than early forms SARS-CoV-2, (2) vaccines in the US are highly effective against strains including the Delta variant, and (3) given current knowledge regarding the Delta variant, vaccine effectiveness and current vaccine coverage, layered prevention strategies, such as wearing masks, are necessary to decrease the transmission of this variant. In interim guidance posted online on July 23, 2021, the WHO concluded that new SARS-CoV-2 variants are likely to continue to emerge as the COVID-19 pandemic evolves [41]. Assessing how vaccines perform against these new variants will be essential to inform immunization programs, policy makers and vaccine developers. Critical evidence to evaluate performance will probably come from post-introduction observational vaccine effectiveness studies.

CONCLUSIONS

In summary, the Delta VOC has already demonstrated higher transmissibility and faster spread, thus making it the predominant strain currently circulating in most regions of the world. This variant is also associated with a greater risk of hospitalization than the initial SARS-CoV-2 strains and the other three known VOCs. However, the effects of infections with the Delta VOC on critical and fatal illness are unclear. More well-designed clinical cohort studies are needed, particularly to assess the effects on populations at high risk, such as people who are older or pregnant, or have various underlying medical conditions. An active and efficient global surveillance-response system based on viral genome sequencing will be critical to monitor the potential evolution and changes in the Delta VOC and the emergence of new VOCs. The Delta VOC places partially or unvaccinated sub-populations at a high risk. Currently authorized vaccines, probably regardless of vaccine types, show reliable effectiveness against symptomatic infections and hospitalization due to the Delta VOC. Therefore, rapid rollout of COVID-19 vaccines with the target of reaching full vaccination of all groups at a high risk of severe COVID-19 in the shortest time is urgently needed. In addition, non-pharmaceutical interventions should also continue to be

tailored, including mask wearing, social distancing, quarantine, and closure of public gathering places.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

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