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Brief report

Large-scale synchronized replacement of Alpha (B.1.1.7) variant by the Delta (B.1.617.2) variant of SARS-COV-2 in the COVID-19 pandemic

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Abstract: In this work, we report a large-scale synchronized replacement pattern of the Alpha (B.1.1.7) variant by the Delta (B.1.617.2) variant of SARS-COV-2. We argue that this phenomenon is associated with the invasion timing and the transmissibility advantage of the Delta (B.1.617.2) variant. Alpha (B.1.1.7) variant skipped some countries/regions, e.g. India and neighboring countries/regions, which could have led to a mild first wave before the invasion of the Delta (B.1.617.2) variant, in term of reported COVID-deaths per capita.

Keywords: variants of concern; Delta (B.1.617.2) variant; Alpha (B.1.1.7) variant; synchronization; SARS-COV-2

1. Introduction

The coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) has seriously affected public health worldwide. As of February 2021, more than 100 million people had been diagnosed with SARS-COV-2 and more than 2 million deaths have been attributed to COVID-19 [1]. The virus evolved rapidly and several variants have emerged. In March 2021, the Alpha (B.1.1.7) variant, began to spread in Cambodia and Thailand, in some clusters in Thailand, the positive rate of SARS-CoV-2 testing is as much as 60–90% [2]. According to [3], besides a higher transmissibility than the previous wild strain, patients infected with the Alpha (B.1.1.7) variant were at a higher risk of hospitalization than those infected with the previous wild strain, reflecting the increased virulence of the Alpha (B.1.1.7) variant.

At the same time, Gamma (B.1.617.1) and Delta (B.1.617.2) variants appeared in Maharashtra, India and resulting in a resurgence of cases in the country. Different from Alpha (B.1.1.7) variant, the Delta (B.1.617.2) variant lineage is defined by eight non-synonymous mutations in S protein. The Delta (B.1.617.2) variant which spread around 200 countries/regions has been classified as a variant of concern by the CDC [4]. Besides a higher transmissibility than Alpha (B.1.1.7) variant, patients with the Delta (B.1.617.2) variant were more than twice as likely to be hospitalized as those with the Alpha (B.1.1.7) variant, according to [5]. The Delta (B.1.617.2) variant is replacing all the other SARS-COV-2 variants.

If the genome (ie, genetic code) of a virus contains one or more mutations (here a mutation refers to a single change in a genome of a virus) from its wild version, then it is called a variant. Samples were collected from patient and the genome of virus was sequenced via next-generation sequencing techniques to determine their classification. Comparing Alpha (B.1.1.7) and Delta (B.1.617.2) variants, the Alpha (B.1.1.7) variants, has 19 non-synonymous mutations, including replacement or deletion of 8 spike proteins. Liu et al. utilized reverse genetics approach to demonstrate only N501Y showed consistent fitness gain in the experimental model and the N501Y substitution summarizes the phenotype seen in combination with eight Alpha spike mutations for enhanced viral transmission, suggesting that it is the primary determinant of increased transmission of Alpha (B.1.1.7) variant [6]. The Delta (B.1617.2) variant has 23 mutations compared to Alpha (B.1.1.7) strain. Particularly significant are those residing in the spike protein, as they are alleged to posit the Delta's (B.1617.2) transmission advantage. The spike mutations in Delta (B.1.617.2) were T19R, L452R, T478K, D614G, P681R and D960N, with deletions at 157 and 158 sites. Most notable are mutations in L452R and P681R spike proteins. The L452R mutation replaced leucine at position 452 with arginine. This allows spike proteins to attach to ACE2 receptors with greater affinity, and helps antibodies that avoid vaccine stimulation bind to spike proteins [7]. And the P681R mutation replaces proline at position 681 with arginine, which allows the virus to better integrate into the host cell compared to variants without this mutation [8].

Starting from June 2020, India has implemented 11 stages of unlocking, phase 11 of which was announced at the end of March, 2020 and remains in effect until April 30, 2020. But since mid-April, 2020, India has seen a severe surge in the pandemic. As of May 10, 2020, more than 388,000 people had been affected [9]. And according to another report [10], characteristic mutations of the Delta (B.1.617.2) variant were observed in sequences obtained in India in April and May 2021, and the Delta (B.1.617.2) variant became the dominant transmission variant in May and June, 2021 in India.

2. Methods and result

In this work, we visualize the replacement of previous strain with Alpha (B.1.1.7) variant and the replacement of Alpha (B.1.1.7) variant with Delta (B.1.617.2) variants globally. We find that the Alpha (B.1.1.7) variant only dominated for a short period of 3–4 months and the replacement of Alpha (B.1.1.7) with Delta (B.1.617.2) show surprisingly synchronous pattern in a large number of countries/regions.

Proportions of the different variants of concern confirmed over time (https://ourworldindata.org) We downloaded biweekly aggregated variant proportion data from "The Our World in Data" who obtained their data originally from GISAID Initiative [11–13].

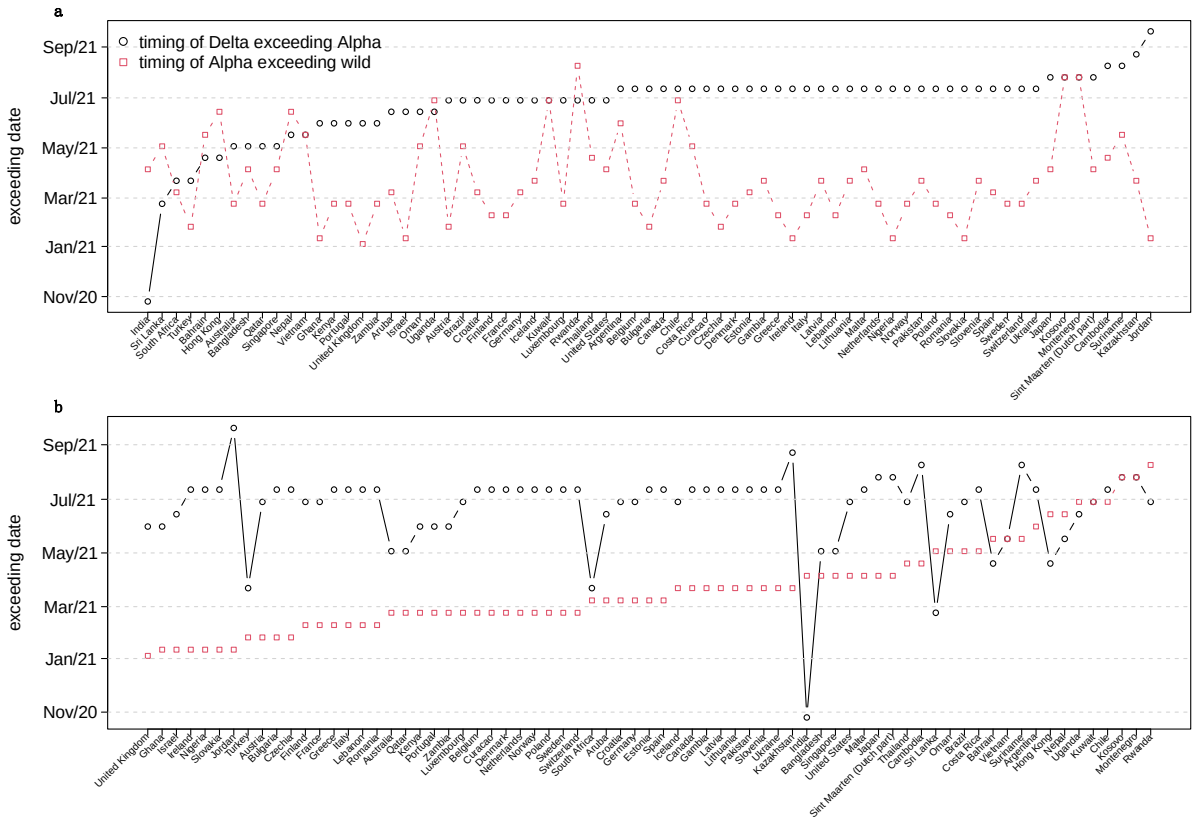

Figure 1. Timing of the confirmations of Delta (B.1.617.2) variant exceeding Alpha (B.1.1.7) variant. The first time that the proportion of B.1.617.2 (Delta variant) > the proportion of B.1.1.7 (Alpha variant), denoted as $T_{A\to\Delta}$ in 71 countries/regions, versus timing of the confirmations of Alpha (B.1.1.7) variant exceeding the previous strain $T_{W\to\alpha}$. (a) countries/regions are ordered from left to right according to $T_{A\to\Delta}$. (b) countries/regions are ordered from left to right according to $T_{W\to A}$.

From Figure 1, we can see that Delta (B.1.617.2) variant was first found in India and spread first in neighboring countries/regions, gradually to other countries/regions. Alpha (B.1.1.7) variant was first found in United Kingdom and spread first in neighboring countries/regions, gradually to the rest of the world. $T_{A\to\Delta}$ (Black circle) has a surprisingly synchrony patten across a large number of countries/regions (ie, a horizontal line across a large number of countries/regions in July 2021). This synchrony pattern is less evident in the $T_{W\to A}$ (red squares). In other words, the timing of Delta (B.1.617.2) variant replacing Alpha (B.1.1.7) variant occurred simultaneously in many countries/regions. In contrast, the timing of Alpha (B.1.1.7) variant replacing the previous wild strain did not show a strong synchronous substitution trend. This could be related to a higher transmissibility of Delta (B.1.617.2) variant compared to other previous strains. Delta (B.1.617.2) variant also possesses shortened incubation period and increased viral load. In particular, the viral load is about 1000 times higher in patient who was infected with Delta (B.1.617.2) variant than patient who was infected with the original strain. And the first detectable time for Delta (B.1.617.2) variant is 4 days after infection which is longer than the average detectable time of original strain (6 days) [14].

Also, the invasion time of Delta (B.1.617.2) variant happened at the tail of the wave of Alpha (B.1.1.7) variant and coincided with a relax of social distancing in many countries (see Figure 2).

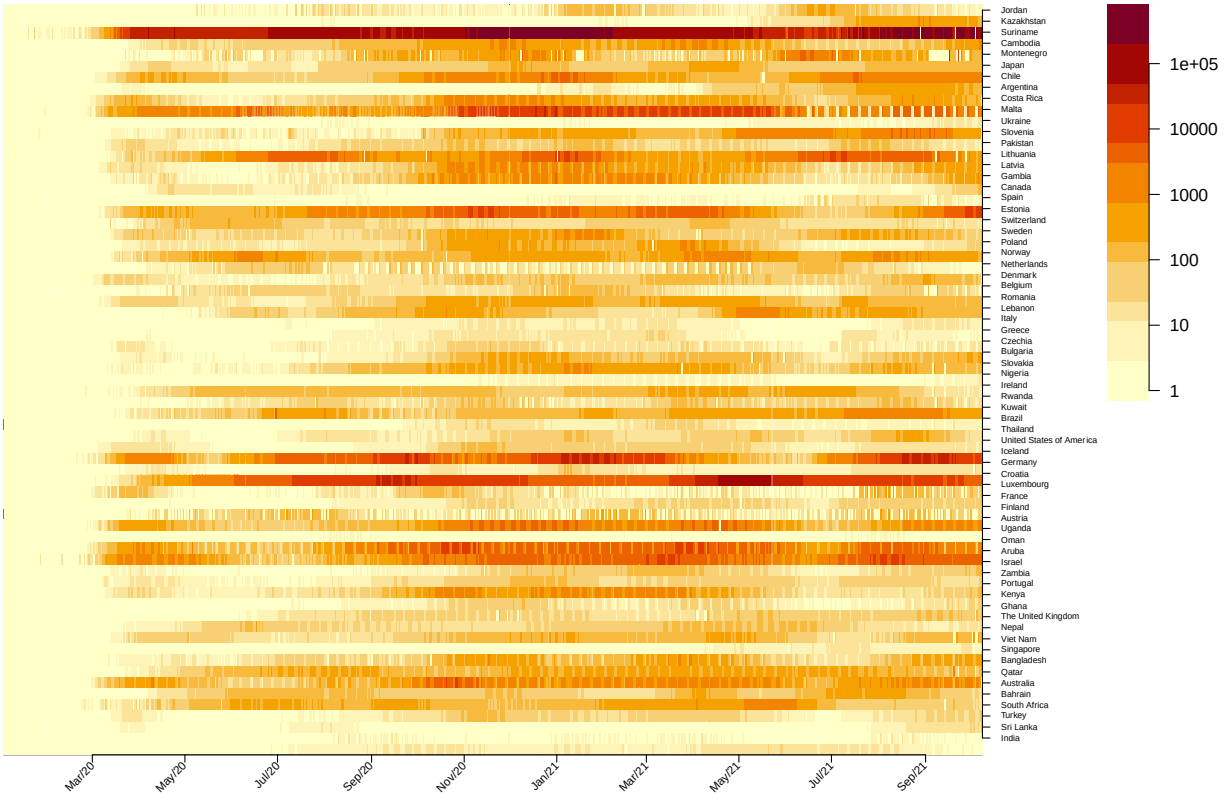

Figure 2. The population standardized daily reported COVID-19 deaths in these countries/regions listed in Figure 1. The countries/regions skipped by Alpha (B.1.1.7) variant (e.g., India) had a mild 2020 year. The synchronized $T_{\alpha\to\delta}$ coincided by a trough of deaths in European countries. Here we show population standardized daily data (daily reported COVID-19 per 1 million population). A bright band (low deaths) can be seen in June-July 2021, when Delta (B.1.617.2) invaded. Data are obtained from https://covid19.who.int/info/.

3. Discussion and Conclusion

The dominance time of the Alpha (B.1.1.7) variant is between $T_{W\to A}$ and $T_{A\to\Delta}$. In South and Southeast Asia, e.g. India, the Alpha (B.1.1.7) variant failed to dominate, which could be associated to a mild first wave (with low deaths per capita in India in 2020).

In Scotland, BNT162b2 and Astrazeneca vaccines were 79% and 60% effective at preventing SARS-COV-2 Delta (B.1.617.2) variant infection after two doses, respectively. However, the Pfizer-Biontech and Astrazeneca vaccines maintain a high degree of protection against any infection similar to Alpha (B.1.1.7) variant [15].

In summary, we reported a large-scale synchronized replacement of Alpha (B.1.1.7) variant by the Delta (B.1.617.2) variant which could be due to the invasion timing of Delta (B.1.617.2) variant and its relatively high transmissibility. Also, we note that these countries/regions in South and Southeast Asia experienced a mild 2020 year was largely skipped by the Alpha (B.1.1.7) variant. Modelling simulation can be done using model framework similar to those in previous works [16,17].

Ethics approval and consent to participate

This study only reanalyzed publicly available data which were carried out in accordance with relevant guidelines and regulations.

Availability of data and materials

All data are publicly available. https://ourworldindata.org/grapher/covid-variants-area

Competing Conflict of interests

The authors declare that they have no competing interests.

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Authors' contributions

All authors conceived the study, carried out the analysis, wrote the draft, revised the manuscript critically, and approved it for publishing.

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