Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Battle against the pandemic: Emergence of SARS-CoV2 variants and global challenge

Dear editor,

Over the course of the pandemic, SARS-CoV2 encounters the host immune system driven by diverse genetic variation across the globe and altered cellular microenvironment due to monoclonal antibody (mAb) and immunomodulators resulting in selective pressure, which favored the viruses for acquiring mutations [1]. A variant is an altered strain with mutations in the genetic sequence leading to distinguishable phenotypic properties such as virus antigenicity, transmissibility, or virulence, etc. [2]. The emerging SARS-CoV2 variants were classified into three categories [3,4]. First, the one which is of global concern, called VOC. The second one is designated as a variants of interest (VOI) and the third one as a high consequence variants. A SARS-CoV2 variant is considered a VOC when it is found to be associated with change at global public health significance consisting of one or more of the criteria drawn by WHO. This includes an increased transmission rate or any harmful alteration affecting global health, or increased virulence ability or altered medical presentation, or reduction in the effectiveness of vaccines, therapeutics, and diagnostics available to the public. As per WHO, the VOCs includes Alpha variant (Pango: B.1.1.7; also called 501Y.V1) initially documented in the United Kingdom in the month of September 2020 [1,3]. The Beta (Pango: B.1.351, B.1.351.2/3; also called 501Y.V2) variant was identified in May 2020 in South Africa [3]. The Gamma (Pango: P.1, P.1.1/2; also called 501Y.V3) variant was discovered later in November 2020 in Brazil [3]. The Delta (Pango: B.1.617.2, AY.1/2/3; also called G/478K.V1) variant was detected first in India in October 2020 (Fig. 1) [3]. The three (Alpha, Beta and Gamma) variants pose spike protein mutation N501Y at position 501 in the RBD. Also, there are two additional mutations (K417N/T and E484K) in Beta and Gamma variants [1]. However, Delta variants lack mutation at E484Q but carry T478K, L452R, P681R and D950N modifications [5]. All the variants share one common mutation, i.e., D614G which is a non-synonymous mutation reported in the early phase of pandemic, leading to a replacement of aspartic acid (614D) with glycine (614G) at position 614 of the SARS-CoV2 spike (S) glycoprotein [1]. These mutations can enhance the binding of spike protein to the host receptor (ACE2). A variant with altered genetic markers which lead to the alteration to receptor binding capacity, reduced neutralization capacity by antibodies developed due to past infection or immunization, reduced responsiveness towards therapeutics and increased transmissibility or severity of the disease is known as variants of Interest (VOI) [4]. VOIs of SARS-CoV2 are Eta (Pango: B.1.525) documented from multiple countries in December 2020, Iota (Pango: B.1.526) reported from the United States in November 2020, Kappa (Pango: B.1.617.1) isolated from India in Oct 2020 and Lambda (C.37) documented from Peru in Dec 2020, and Mu (Pango: B.1.621) earliest documented in January 2021 from Colombia [3]. All VOIs displayed characteristic features of the potential reduction in neutralization by convalescent and immunized sera or therapeutics utilizing mAb treatments [1]. SARS-CoV2 variants of high consequences are the variants of concerns with some additional features such as alteration of antigenicity to a large extent which significantly reduce vaccine efficiency leading to a large number of breakthrough infections, significantly severe clinical manifestation and hospitalization, decreased susceptibility to available therapeutics and failure of existing diagnostic assays. However, as per the CDC, no SARS-CoV2 variants have been reported to rise to the level of high consequence [4].

During this pandemic of the SARS-CoV2, both the clinical and the scientific community had a tough time responding to the continuous emergence of new variants. Interestingly, the Covid-19 RNA viruses undergo lesser mutations compared to most RNA viruses. This is because of the presence of an enzyme that corrects the errors at the time of viral replication [6]. The resultant mutants may have competitive advantages and disadvantages. Those confirming advantages (in the form of replication, transmissibility, and escape from the host immunity) will eventually have increased frequency. In comparison, those reducing the viral fitness are likely to be eliminated from the population [2].

These new variants pose a significant threat to humanity, potentially compromising the efforts made by scientists towards the development of vaccines and other treatment strategies. Vaccine development is the most effective way to neutralize the variants of SARS-CoV2. However, the primary concern is the continuous mutation in SARS-CoV2, which leads to the origin of resistant strains [1]. Also, most of the new variants resist neutralization by convalescent plasma and sera of patients who received attenuated vaccines. Some new variants, such as B.1.1.7, named Alpha variant, were linked with higher viral load. This strain was moderately resistant to treatment with mAb. A variant of lineage B.1.351, named Beta variant, possesses high transmissibility and is more resistant to neutralization by mAb and convalescent plasma. Variant P.1, also referred to as the Gamma variant, can escape from immunosurveillance and was reported to cause reinfection in patients. Similar to other variants, this variant is also more resistant to neutralization by mAb. The variant of lineage B.1.617.2, named Delta variant, possesses high transmissibility and severity. Presently available Covid-19 vaccines are based on earlier identified Covid-19 strain before mutations in spike proteins. The currently available vaccines (first-generation Covid-19 vaccines) are somehow less effective in combating new emerging variants. Therefore, there is an urgent need to redesign vaccines and work for an effective multivalent vaccine that can effectively neutralize various variants of SARS-CoV2.

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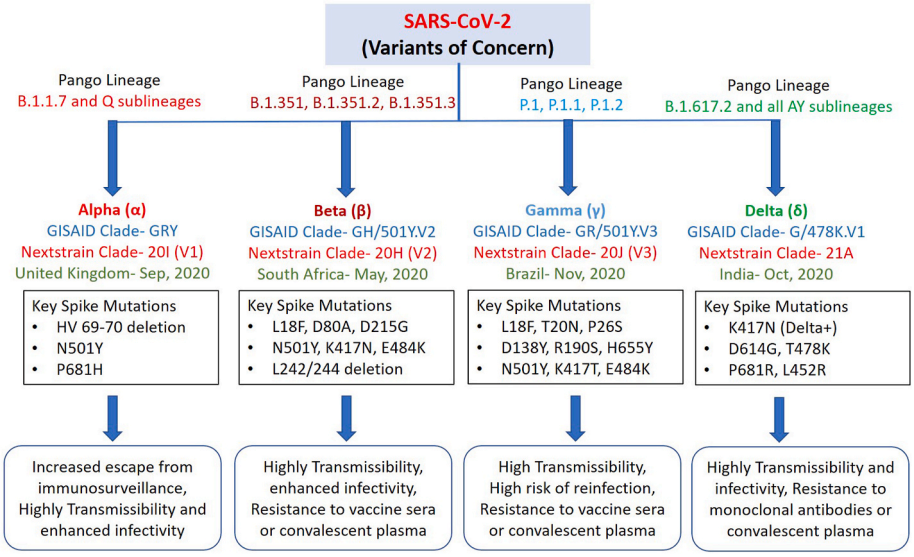

Fig. 1. Summary and characteristics of SARS-CoV2 variants of concern (as of September 19, 2021; references referred for the compilation includes WHO [3], CDC [4], Janik et al. [1]).

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Declaration of competing interest

We declare no conflict of interest.

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