

## Emerging Covid-19 Variants and Vaccine Efficacy, an Eye on the Future

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### ABSTRACT

When COVID-19 outbreak commenced in late 2019 and was fast spreading across the globe, all efforts of the global scientific community was targeted at finding prevent further spread and get a lasting cure. These efforts culminated in the emergence of several drugs and eventually vaccines. The vaccines have substantially slowed down the spread of the disease. While vaccines appear to have started having a firm grip on the disease, the emerging viral variants from the continued mutation of SARS-CoV-2 appear to have started responding differently to the vaccines licensed for Emergency Use Authorization (EUA) by the World Health Organization (WHO). It is clear from documented records that AstraZeneca, Moderna, Johnson & Johnson, Pfizer BioNTech, SinoVac, Sputnik, Soberana, Abdala, Novavax, and Cansino have all been effective against Alpha and Beta Kappa and Gamma variants of the virus among other variants and marginally with the Delta variant. Although, cases of breakthrough infection with other variants in fully vaccinated individuals have been rare so far, this is different with the Delta variant that has started showing visible signs of vaccine escape with high levels of breakthrough infections and evidence of severe morbidities and record of mortalities as well. Given that vaccine escape of some strains of Delta variant has already commenced; composition of newer vaccines should using computational modeling target variants of Delta which may even be more resistant and deadly.

**Keywords:** COVID-19, SARS-CoV-2, Resistance, Vaccine, Variant

### INTRODUCTION

All over the world, countries continue to mount mitigation efforts to stem the effects of COVID-19 as well reap the benefits associated with the COVID-19 pandemic through various public health, economic and legal frameworks and measures. Exploring the relative rate of mutations of COVID-19, several clinical trials and experimentation of virtually all classes of

drugs against the disease are still ongoing. The most desired outcomes are efficient preventive mechanisms and possible cure. Whilst effective vaccines have been developed, one of the greatest challenges to its success is the relative rate of mutation of the causative agent, coronavirus.<sup>1,2</sup>

It is clear through the spectrum of the different waves

from when COVID-19 was restricted to Wuhan in late December 2019 to when WHO declared COVID-19 a pandemic in March 2020 till date, the issues of variants of the SARS-Cov-2 are no longer negligible. So far, there have been at least 205 million cases with 4.33 million deaths worldwide.

### **Transmission of SARS-COV-2 from Animals to Man**

In the course of a year and half (January 2020 to June 2021), the virus has mutated into several variants that are currently circulating and causing spikes in different parts of the world. It has been difficult and almost impossible to identify the index case patient zero i.e. the first patient that demonstrated clinical features of COVID-19 in Wuhan China or from anywhere in the world. This would have given a veritable pointer to the source of the virus. Common impression based on comprehensive insight into the trend, frequency, scope, and spatial distribution of the various strains and variants of SARS-CoV-2 across the globe posits the virus came from the wild animal that mutated into human host. Even though, the Coronavirus precursors of SARS-CoV-2 that possibly mutated to infect humans have been identified in Bats and Pangolins,<sup>3,4</sup> the vital link between the epidemiology and virology of the virus is incomplete

### **Origin of SARS-COV-2 Variants**

Information available at present indicates that at the time COVID-19 outbreak was announced in Wuhan, China, the viral progenitors and precursor Coronaviruses of SARS-CoV-2 had already been circulating across the world for at least 6 weeks earlier especially in USA and China. Genetic sequencing analysis has shown significant differences between the earliest viral isolates in Wuhan in December 2019 and the earliest isolates in USA in January 2020. There is a closer similarity between the earliest isolates in China with those from most parts of Asia such as Indonesia and Philippines. It is interesting to note that COVID-19 was detected in persons with no travel history and contact with any known infected suspect cases in New York and

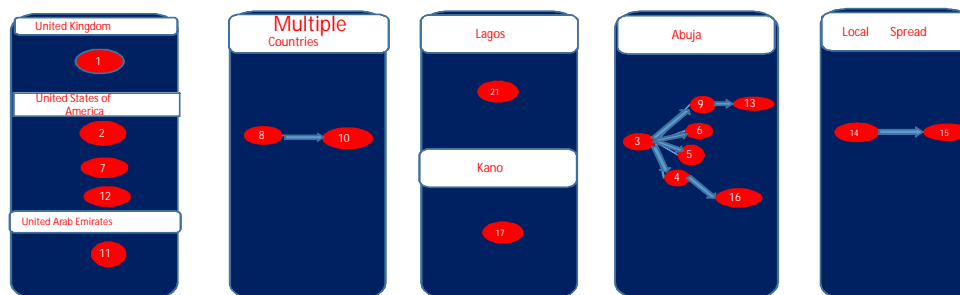
California. These isolated cases also had no contact with animals. SARS-CoV-2 was isolated in a zoo in New York city although the animals had been in prolonged captivity in the zoo. By the time international travels across countries was banned, most of the transmission had already taken place.<sup>5,6</sup> This picture was similarly observed in Nigeria in which there were several cases of local spread with no identifiable contact. See transmission tree in figure 1 below.

The initial suspect cases in red contact and transmission nodes clearly had contacts and epidemiological linkages and were contributions from Persons of Interest (POI) international travelers, Points of Entry (POE) i.e. suspects from neighbouring states/countries and contacts of suspected cases. By 11<sup>th</sup> of May, 2020, barely 2 weeks and beyond from the representation on figure 1a, there were multiple confirmed cases within the community with no form of exposure to any contact. The highlighted transmission nodes in white depict the isolated confirmed cases. All these further unfold the complex nature of the spread of this virus.

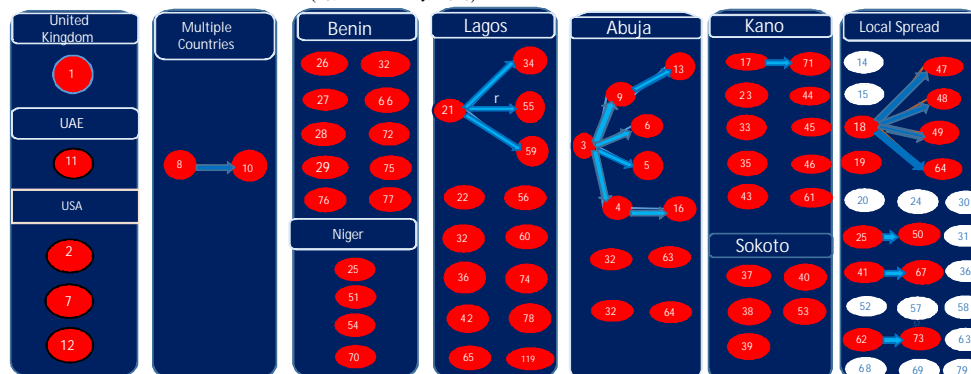
The most plausible hypothesis at present to unravel the early evolutionary history and track the global spread of SARS-CoV-2 is the Mutational Order Approach (MOA) which aims at reconstructing the ancestral sequence and mutational history. The progenitor genome of the index case COVID-19 is said to have evolved from the mutated tree of the Most Recent Common Ancestor (MRCA) of all the genomes of SARS-CoV-2, that have been analysed so far.

The two earliest Coronavirus lineages that MRCA genomes gave rise to were ? and ? and are referred to as ProCoV2 and the index case of COVID-19 is believed to have carried ProCoV2 virus genome. The Wuhan-1 genomes (EPI\_ISL 402123) as well as all other earliest genomes are believed to have evolved from ProCoV2 after the divergence of the ? and ? lineages. Coronavirus ? lineages were detected in Wuhan in early January, and the ? lineages in early February in USA. According to Professor Kumar of Temple University Philadelphia, SARS-CoV-2 acquires 25 mutations a year on average, and the present variants in Wuhan and across the globe

COVID-19 TRANSMISSION TREE IN AN EMERGENCY OPERATION CENTER (EOC) IN NIGERIA (20<sup>th</sup> – 25<sup>th</sup> APRIL, 2020)



COVID-19 TRANSMISSION TREE IN AN EMERGENCY OPERATION CENTER (EOC) IN NIGERIA (18<sup>th</sup> – 24<sup>th</sup> May, 2020)



Figures 1a and 1b: COVID-19 transmission tree in an Emergency Operation Center (EOC) in Nigeria

have replaced the earliest variants that triggered the outbreak of the disease.<sup>3,7,8</sup>

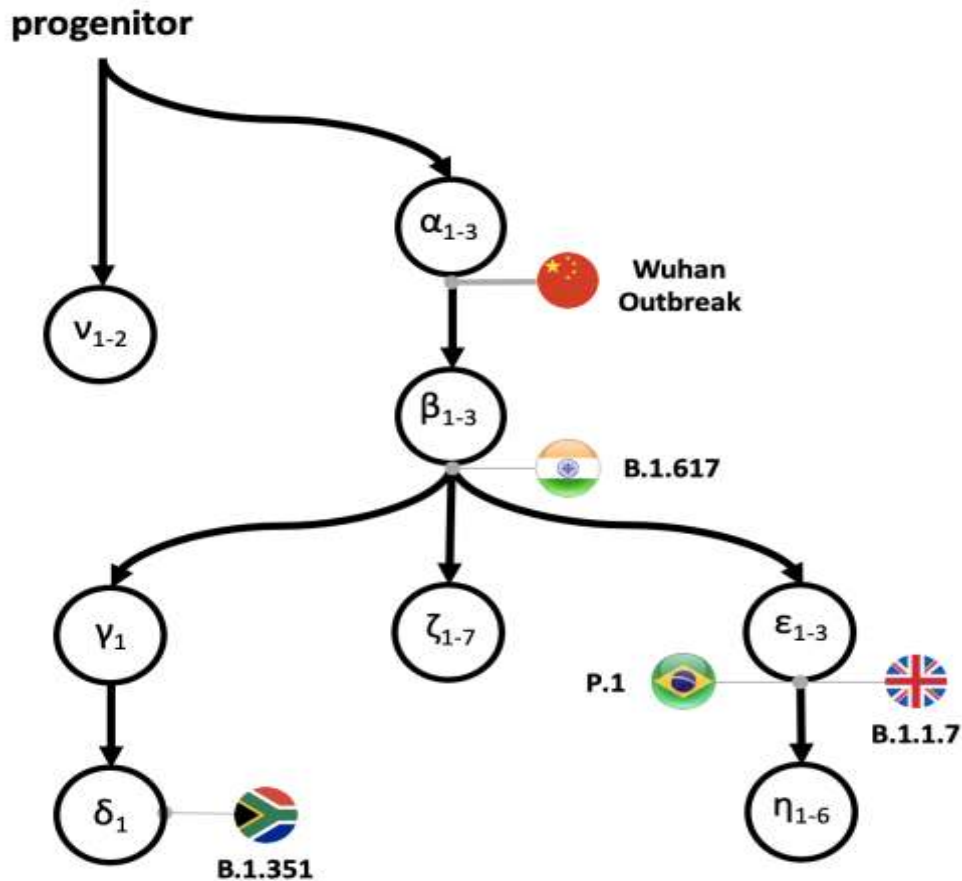
**SARS-COV-2 Variants<sup>9,10</sup>**

While retaining the GISAID, Nextstrain and Pango naming systems, World Health Organization (WHO) has re-named the various SARS-CoV-2 variants to have more scientific identification. These include:

- a. Variants of Interest- These possess specific genetic markers for immune escape and propensity to cause unique outbreak clusters and are: (B.1.427, and B.1.429 California), B.1.525 Eta UK and Nigeria, B.1.526 Iota New York, (B.1.617.1, and B.1.617.3 Kappa India).
- b. Variants of Concern- These have increased disease transmissibility and increased disease severity with reduced induced-vaccine protection from severe disease.

These include: B.1.1.7 Alpha of UK, (B.1.351, B.1.351.2, and B.1.351.3 Beta of South Africa), (B.1.617.2, AY.1, AY.2, and AY.3 Delta of India), (P.1, P.1.1, P.1.1.2 Gamma of Japan/Brazil).

c. Variants of High Consequence- These cause more severe disease, are more difficult to diagnose and treat and less susceptible to available vaccines. No variant is yet to be grouped here.



**Figure 2: Pictorial schema on evolution of SARS-CoV-2 from progenitor Coronavirus in animals and subsequent mutation and infection of humans. (Kumar S, et al, 2021).**

**Table 1: Names of some SARS-CoV-2 variants presently causing epidemic waves across the globe. (WHO, May & August 2021)**

<b>Alpha</b>	B.1.1.7	GRY	20I/S:501Y.V1	UK, Sept 2020
<b>Beta</b>	B.1.351	GH/501Y.V2	20H/S:501Y.V2	South Africa, May 2020
<b>Gamma</b>	P.1	GR/501Y.V3	20J/S:501Y.V3	Brazil, Nov 2020
<b>Delta</b>	B.1.617.2	G/452R.V3	21A/S:478K	India, Oct 2020

Due to the relatively unstable nature of the Coronavirus with its continued mutations, more variants are anticipated and the major source of worry is the continued susceptibility of the new variants to the current vaccines in use.

### SARS-COV-2 Variants of & Vaccine Susceptibility

AstraZeneca, Moderna, Johnson & Johnson, Pfizer BioNTech, SinoVac, Sputnik, Soberana, Abdala, Novavax, and Cansino have all been well effective against Alpha and Beta Kappa and Gamma variants of the virus among other variants except the Delta variant. Cases of breakthrough infection with other variants in fully vaccinated individuals are extremely rare so far. This is however not the same with the Delta variant that is fast spreading with new epidemic waves. The delta variant appears less susceptible to most of the vaccines presently in use.

The susceptibility of Kappa, Gamma, Iota and other variants to available vaccines is also much higher compared to the Delta variant as documented in UK and France. Studies from France have demonstrated that 12 months after vaccination with full dose of Pfizer or AstraZeneca, the neutralizing antibody are no longer effective against the Delta variant.<sup>11,12</sup>

Studies have already starting showing vaccine escape with the Delta variant owing to why fully vaccinated individuals with any of the above vaccines have and can still be infected with severe COVID-19 symptoms. Although, outcomes and vaccine behavior in the phase IV clinical trials can be unpredictable, the rising possibility of newer variants undergoing vaccine escape is a tenable cause for concern.

### CONCLUSION

COVID-19 trajectory is complex and our knowledge at present could still be limited. Every measure of control of infection needs to be a major consideration for adoption since the control of COVID-19 by the available vaccines is already being challenged by vaccine escape in newer variants of SARS-CoV-2. There is a high probability that

prospective newer variants may prove more resistant and subsequently render the available vaccines ineffective. Newer formulated vaccines therefore should have the ability to block escape property of Delta and newer SARS-CoV-2 variants.<sup>13-15</sup> This should be a major factor in all future vaccine formulations towards the control of the disease.

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