

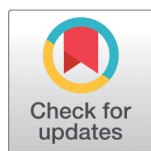
Coronavirus new variants: The mutations cause and the effect on the treatment and vaccination

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ABSTRACT

Background: The world has watched with growing alarm as scientists in the U.K. Identified a new coronavirus variant that appears to be more contagious than, and genetically distinct from, other established variants. The scientists keep collecting the facts about the new variant and its impact on symptom, severity, mortality, and vaccine efficacy.

Objectives: This review shed light on the SARS-CoV-2, 2020 virus, that appeared in Britain and South Africa in December 2020, known as B.1.1.7. Furthermore, it highlights the main differences between the new COVID-19 version (B.1.1.7) and the other strains of the virus.

Conclusions: Mutations are still happening in the SARS-CoV-2 virus as the RNA viruses cause many changes in the proteins of the spikes of the virus and other parts. The British variant has 23 mutations, compared with the version that erupted in Wuhan, that renders the virus more contagious; however, these mutations do not change the disease's severity.

Keywords coronavirus, COVID-19 strains, genomics, mutations, SARS-CoV-2, U.K. variant

INTRODUCTION

RNA virus SARS- CoV-2 is one of the RNA viruses that have a genetic proofreading mechanism. The mechanism is complex molecular machinery that can maintain the genome by preventing and preparing the mutations.^{1,2} However, mutations occur due to natural selection of the species improving mutations, genetic drifts, or epidemiological factors.³ Compared with HIV, SARS-CoV-2 is changing much more slowly as it spreads. However, one mutation appears to cause a significant change in the transmission of B.1.1.7 strain detected in the U.K.⁴

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B.1.1.7 strain is not the first mutation that happened. A total of 149 mutations have already been found in 103 sequenced strains that evolved from the early stage of the pandemic till May 2020.⁵ Most of these new mutations affect the spikes of the virus, which are used by the virus to enter the human cell through the angiotensin-converting enzyme 2(ACE2) receptor.⁶

The first notable strain, and it is now the predominant globally, is the D614G variant, also referred to as G614, resulting from an Aspartic Acid (A)-to- Glycine (G) amino acid change caused by a single nucleotide mutation at position 23,403 of S1 subunit of the virus spikes. This mutation changed the original Wuhan strain (D614). The mutation emerged in Europe and spread within a month to the globe. D614G variant SARS-CoV-2 is transmitted more rapidly than the Wuhan strain and the other strains.⁷

The B.1.1.7 strain coronavirus variant is different from the D614G variant in many points; it tends to spread faster (up to 70%). Although The virus tends to be more readily spread, it also renders people sicker and raises the risk of death.^{8,9}

DIFFERENCES IN (B.1.1.7) STRAIN

Mutations happened in all RNA viruses, and Coronavirus is one of them. As a result, multiple SARS-CoV-2 variants are circulating globally. In December 2020, samples from southern England showed what is known today as 20I/501Y.V1, VOC 202012/01, or B.1.1.7. The variant came to researchers' notice since it started to spread rapidly. When researchers took a close look at its genome, they were struck by the relatively large number of mutations which was 23 (including 13 non-synonymous mutations, four deletions, and six synonymous mutations).¹⁰

Many coronavirus mutations have either adverse effect on the virus or have little effect in one way or another. However, the mutations in B.1.1.7 strain potentially affect how the virus spread. A series of tiny mutations found in many British coronavirus samples may help spread the virus more easily.¹¹

One of the most important changes in B.1.1.7 seems to be N501Y, a change from asparagine (N) to tyrosine (Y) at amino-acid site 501.¹² This is because of its position inside the spike glycoprotein's receptor-binding domain (RBD)—more specifically inside the receptor-binding motif (RBM), a part of the RBD,¹³ which binds human ACE2.

Filip Fratev and his group have found that this mutation causes conformational changes in the N501Y mutated S1 RBD-ACE2.¹⁴ The study shows a significant decrease of the free energy binding between the N501Y strain and the wild type about 161 times lower than the wild type.¹⁴ This decrease in energy binding increases the ability of the spike to bind to the ACE2 receptor, which can increase the viral load and the spread of the virus.

Moreover, A series of tiny mutations found in many British samples of the coronavirus may help the virus spread more easily. The B.1.1.7 variant has 23 mutations, compared with the version that erupted in Wuhan, China, 2019. However, 17 of those mutations appeared suddenly after the virus diverged from its most recent ancestor.¹⁵ Figure 1 and Table 1 sum-

marize the total mutations that took place in B.1.1.7 lineage.

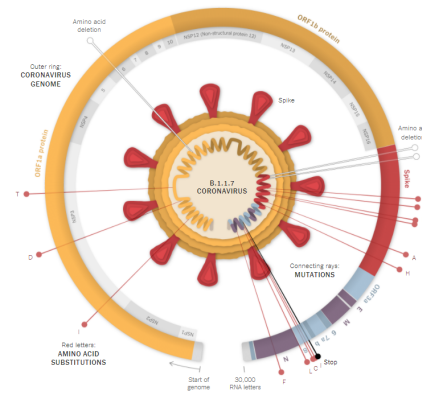


Figure 1 Mutations in B.1.1.7 SARS-CoV-2 virus (six other mutations are not showing above as they did not change the amino acid). (Rees-Spear, C. et al., 2021)¹⁶

Table 1 Non-synonymous mutations and deletions inferred to occur on the branch leading to lineage B.1.1.7 lineage.¹⁷

Gene	Nucleotide	Amino acid
ORF1ab	C3267T	T1001I
	C5388A	A1708D
	T6954C	I2230T
	11288-11296 deletion	SGF 3675-3677 deletion
spike	21765-21770 deletion	HV 69-70 deletion
	21991-21993 deletion	Y144 deletion
	A23063T	N501Y
	C23271A	A570D
	C23604A	P681H
	C23709T	T716I
	T24506G	S982A
	G24914C	D1118H
Orf8	C27972T	Q27stop
	G28048T	R52I
N	A28111G	Y73C
	28280 GAT->CTA	D3L
	C28977T	S235F

Note: There are six synonymous mutations with 5 in ORF1ab (C913T, C5986T, C14676T, C15279T, T16176C), and one in the M gene (T26801C)

THE DIFFERENCE IN THE SYMPTOMS OF B.1.1.7.

Primary symptoms are still the same as the old version consisting mainly of fever, chest pain, continuous cough, headache, loss of taste and smell, diarrhoea, and skin rash. There

is no strong evidence so far that B.1.1.7 has different or severe symptoms. However, South Africa, another lineage B.1.1.7. coronavirus has one mutation that is also found in B.1.1.7. This variant is spreading quickly. Moreover, it has been found that people infected with this variant carry a high viral load which translates to be a higher concentration of the virus in the upper respiratory tract.¹⁸

However, A publication released by scientists on the New and Emerging Respiratory Virus Threats Advisory Group in the U.K¹⁵ suggests that the new variant B.1.1.7 may be associated with an increased risk of death. The study showed that the risk of death after 28 days might be significantly higher, with some studies citing 35-36% increased rate, and one up to 91%, compared to people infected with non-B.1.1.7 viruses. This increased risk is based on the actual lethality of the virus per infection and not on the fact that higher transmission may lead to more hospitalizations and the potential for overwhelming health care resources.¹⁵

As with the previous variants, a person immunocompromised and who became chronically infected with the Coronavirus are the most affected people. Such people have been given multiple rounds of treatment with antibody and antiviral drugs. According to the British scientific reports, four of about 1,000 people infected by the new variant previously had covid-19.¹⁹ The re-infection with a different variant has been reported. Many cases reported that the re-infection also occurred with the same strain;²⁰⁻²² the scientist does not know if the re-infection happened because of the scant antibody response after the first infection.²⁰ Other reports verify re-infections with different variants with different symptom severity.^{21,23,24} In addition, one of the important cases that have been reported in Brazil was the co-infection with two strains which represent a rare case and a possible scenario.²⁵

The infections have been raised possibly due to its ability to infect children, which several researchers have posed. Some scientists also proposed that infection occurs by travelling through an animal population, including minks; before re-entering the human population, the virus may have developed new mutations. When more livestock pathogens have been identified, certain "animal reservoirs" have become a subject of intense concern.²⁶

NOW, WHERE IS THAT STRAIN?

While it was first seen in Britain in September 2020, by the week of 9th December in London, 62 % of COVID-19 cases were due to the B.1.1.7 B.1.1.7. variant compared with 28 % of cases three weeks earlier.²⁷

The governments of Australia, Italy and the Netherlands also announced that cases of this strain had been identified. Iceland and Denmark have also identified a few cases of COVID-19 with the B.1.1.7 version to the ECDC, the European Disease Monitoring Organization. In Belgium, media reports suggest cases have been identified there as well.

This strain has spread to over 50 countries, indicating that it may be more virulent.^{17,28,29} However, Iraq is still detecting the virus without gene sequencing. Some central laboratories started using qPCR kits to detect the new strain with other positive cases.³⁰⁻³² The need to

sequence SARS-CoV-2 virus isolates is crucial to identify new variants like the U.K. variant. Iraqi people be selected for sequencing based on population and geographic location of infections to identify emerging variants and assess their spread.

CAN THE VARIANT MAKE THE NEW VACCINES INEFFECTIVE?

The WHO states that laboratory studies are ongoing to determine whether the new virus has different biological properties or could alter vaccine efficacy. The mutations include changes to the spike protein that the virus uses to infect human cells;⁷ simultaneously, these spike proteins are the most significant target for the most current vaccine.

Messenger RNA, or mRNA, technology is used by both Pfizer and Moderna vaccines that have been approved for use in the U.S. Both vaccines create immunity to the Coronavirus by teaching our immune systems to make antibodies to a protein that sits on the surface of the virus, called spike protein.¹⁵ The spike protein latches onto cells and opens a passageway inside. Antibodies produced in response to the vaccines stick to the tip of the spike preventing the virus from getting inside the cell. Scientists are examining the variant and expect to know whether vaccines might not work against it.

Pfizer and scientists from the University of Texas Medical Branch³³ show only a small reduction in the neutralization titer observed with 3 of the changes found in the South Africa variant (50YY.V2). The study showed a better neutralization profile for the Pfizer vaccine than Moderna's.³³ Another study by Wuk et al.,³⁴ showed the same results, that the neutralization activity of Moderna's vaccine is significantly diminished (6.4 fold average) when assessed with pseudoviruses carrying the full set of mutations of the South African variant (B.1.351) and the U.K. variant (B.1.1.7.).³⁴

Moreover, San Diego researchers revealed an important study where they showed that the T cell (CD4+ and CD8+) responses in individuals infected with ancestral SARS-CoV-2 strains, or individuals vaccinated with the Moderna or Pfizer vaccines (based on the Wuhan-1 strain), the responses display minimal changes against peptides in the new variants from U.K. (B.1.17), South Africa (B.1.351), Brazil (P1) or California (Cal.20C). Indeed, 93% of CD4+ and 98% of T cell epitopes were conserved in the protein sequences of the new variants. Thus, they suggest that the T cell responses in these individuals could play an important role in recognizing the new variants, even though some of these strains can still escape the antibody (humoral) responses.³⁵

In conclusion, the SARS-CoV-2 virus as other RNA viruses mutates continually due to their genetic proofreading mechanism. So, mutations continue to be happened in SARS-CoV-2 virus. Which causes many changes in the spikes of the virus and other parts. The British variant has 23 mutations, compared with the Wuhan version make it more contagious, but no change in the severity of the disease. However, B.1.1.7 did increase the mortality rate; moreover no study shows vaccines ineffectiveness against the B.1.1.7 strain.

Finally, the new technology nowadays helps to provide a plethora of publications and research on SARS-COV-2, making humanity know more about the new pandemic than pre-

vious pandemics like cholera and plague. And the discovery and the follow up of the virus mutations and strains are tremendous and impressive. We can add to that the number of vaccines that have been developed and the diversity of the techniques and the methodology of creating them. Unfortunately, Iraq stays till the time of writing this review (May 2021) away from the advanced techniques to detect the virus strains like gene sequencing, neutralization techniques, CRISPR/Cas, and others; rely on the qPCR as the only technique to detect the virus.

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DECLARATIONS

Authors' contributions

All authors have equally contributed to this review.

Conflict of interest

The authors declare no conflict of interest.

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Data availability

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