

New UK Variant of Coronavirus

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Abstract

A conference with the United Kingdom (UK) on December 8, 2020, about the new UK variant, has been announced by scientists and public health experts suspecting 70% more contagious amongst all the other variants. The emergence of this variant leads to stricter safety measures in the UK. It spread in 45 countries including Denmark, Netherlands, Italy, Japan, and Australia after hitting Europe. The researchers were originally suspicious about how important the modification of D614G mutation is which appeared independently in multiple locations and was found nearly in all sequences. But the appearance of the current "UK variant", lineage B.1.1.7, has raised widespread concern, and understanding why the variants are important involves an insight into the evolution of the virus and SARS-CoV-2 genomic epidemiology. This variant caused mayhem in the UK and elsewhere in Europe within 2 weeks of its announcement. Therefore in this review, we have enclosed completely how the new variant emerged, clear explanation of the terms strain, mutation, and variant. Apart from that, the review also includes how this variant was detected, its lineage and mutations, how harmful it is, and will the approved vaccines for SARS-CoV-2 be effective against this variant with a concluding remark and future directions.

Keywords: Coronavirus; SARS-CoV-2; Mutation; UK variant; B.1.1.7 lineage

Introduction

An outbreak of a severe form of pneumonia, named as novel coronavirus disease 2019 (COVID-19) epidemic, started at the end of the year 2019 in Wuhan, China [1]. The entire country was soon infected by the epidemic [1]. COVID-19 became a pandemic that spread to more than 219 nations and territories [2] due to the high contagiousness and dissemination rate of the virus during the pre-symptomatic period. The etiology of this outbreak was unknown but soon the Chinese government isolated the etiologic agent and described it as the new Severe Acute Respiratory Syndrome coronavirus-2 (SARS-CoV-2) or 2019-nCoV virus [3]. This virus has been declared as a "Public Health Emergency of International Concern (PHEIC)" on 31st January 2020 [3]. A significant and general characteristic of viruses, like SARS-CoV-2, is their reduced virulence and increased transmissibility.

SARS-CoV-2 is identified as one of the seven human infecting coronaviruses while severe acute respiratory syndrome coronavirus (SARS-CoV) and the Middle East Respiratory Syndrome coronavirus (MERS-CoV) are responsible for 10% to 30% of infections in the upper respiratory tract in adults [3]. The four other coronaviruses namely NL63, OC43, HKU1, and 229E are only responsible for minor infections of the upper respiratory tract with symptoms like headache and common cold [3].

Viruses continuously alter through mutation, and new forms of a virus are predicted to occur over time. One of such variants reported by the officials of the United Kingdom (UK) of Great Britain and Northern Ireland on 14 December 2020, to the World Health Organization (WHO) that, via viral genomic sequencing, a new form of SARS-CoV-2 was found. The new UK variant of SARS-CoV-2 is being snappily named VUI-202012/01 (the first "Variant under Investigation" in December 2020) [4]. This new UK variant is considered to have first appeared in September in Southeast England [5]. Ever since, it has become the dominant virus type and has also been detected in various countries namely Denmark, Japan, Australia, Netherlands, etc. [4]. Initially, the analysis of this variant indicates that it is highly contagious and can be readily spread between people. This variant bears 17 distinguishing mutations out of which eight in the spike protein which is responsible for the virus particles to penetrate in human cells [6]. The mutations occurring in SARS-CoV-2 tend to be around one to two changes each month. Researchers claim that they have never seen a virus acquiring dozens of mutations at a time. It is believed that due to long infection in a single patient the mutations have occurred [7].

In this review, we intend to enlighten the readers about how the new UK variant emerged and became dominant in entire Europe and took hold in several countries. This study is gathered from different sources, peer-reviewed studies, and incorporating news stories. Also, the article will discuss another target to develop a vaccine against mutations in the SARS-CoV-2 strain.

Strain, Variants, and Mutations

SARS-CoV-2 is considered the strain which further leads to the emergence of new variants like B.1.1.7 and various mutations. In science fiction, basically to mutate means to undergo a major transformation. New viral genetic variants are continuously produced because of the lack of proofreading action of RNA

virus polymerases [8]. Usually, RNA viruses have higher frequencies of mutations than DNA viruses. RNA viruses respond readily to changing circumstances in the world [8]. Each time, viruses mutate, and most of these variations do not change how lethal or contagious the virus is. Also, the mutations that have arisen by chance do not change the function of the virus [9]. The mutation rate of RNA viruses leads to viral adaptation, providing a balance between the integrity of genetic material and genome diversity.

The existence of a newly emerging mutation is, in most cases, defined by natural selection. Coronaviruses belong to a group of related RNA viruses and therefore, for expressing the epidemiology of SARS-CoV-2 these terms mutation, strain and variant are frequently used interchangeably [10]. In general, mutation means the actual change occurred in the sequence for example, at the 614th amino-acid position of the spike glycoprotein, the amino acid aspartate (D) is regularly being substituted by the amino-acid glycine (G) due to the copying fault that altered the single nucleotide in the coronavirus RNA naming it as a D614G mutation [11]. This mutation was majorly found in the United States and is considered more transmissible which is emerged as a product of natural selection [11]. There are already more questions than responses from experts about coronavirus mutations, and no improvement in SARS-CoV-2 has yet been identified that could increase public-health issues. But for managing the pandemic, researching mutations in depth may be significant [11]

The UK Variant

Emerging of the new variant

The new variant of strain SARS-CoV-2 was first detected in Kent County in England on September 21, 2020. It then took off and between October and the end of December, it affected more than 60% population in the UK according to WHO [5]. The government officials say that this new strain is likely more able to transmit than the other variants. When the virus begins to spread like wildfire, the UK authority named it SARS-CoV-2 VUI-202012/01 (the first 'Variant under investigation' in December 2020) [12]. But on 14 December 2020, the UK authority reported the variant to WHO as SARS-CoV-2 VOC 202012/01 (Variant of Concern, the year 2020, month 12, variant 01) [4]. This variant is not related to the SARS-CoV-2 virus phylogenetically and contains about 23 substitutions of nucleotides [4].

Preliminary epidemiologic analysis, phylogenetic, and clinical studies have indicated that the new variant has enhanced transmissibility [4,13]. According to some scientists and The Imperial College of London, the new variant is 70% more transmissible than previous versions that occurred in the UK in the first wave [14,15]. The researchers now suspect that the variant has developed inside an immuno-compromised person who has been chronically infected for a long time [15]. Even though it is uncertain why this variant is more transmissible, the Government's NERVTAG (New and Emerging Respiratory Virus Threats Advisory Group) has observed that individuals infected with this variant have higher viral loads in their throats and may

thus shed more infectious particles [15]. To date, the variant has already spread in 45 countries [16].

How was the variant detected?

In genomic surveillance, the variant was identified by the Covid-19 Genomics UK (COG-UK) consortium, which undertakes random genetic sequencing across the UK of positive Covid-19 samples [12]. The consortium is a collaboration of four public health organizations in the UK, as well as 12 research institutions and the Wellcome Sanger Institute [12]. Genetic sequencing has confirmed that the new variant has infected at least one person who received the virus in the first wave. Scientists reported that there was a "rapid increase" in cases in areas where previous rates of infection were considered to be very high [15]. They also mentioned that the individuals who were previously exposed to the virus are at increased risk of reinfection.

Lineage B.1.1.7 and its mutation (N501Y.V1)

The lineage B.1.1.7 carries a mutation (N501Y.V1) that changes the conformation of the receptor-binding domain in the S (spike) protein [17]. It is named N501Y.V1 because it was first found in the UK and the one found in South Africa is called N501Y.V2 [4]. The variant has 23 other B.1.1.7 lineage mutations after detecting it in September. It means it has achieved mutations in a chronically infected host as mentioned earlier [10].

Most of the mutations are in S protein which includes N501Y.V1 in the receptor-binding domain, deletion 69-70, and P681H. They are described further as follows –

1. The N501Y mutation, which is at the tip of spike protein, binds the human angiotensin-converting enzyme-2 (ACE2) receptor (Figure 1) with higher affinity and is one of the key receptor-binding-domain amino acids. In this case, the amino acid Asparagine (N) is replaced by Tyrosine (Y). Errors in this part of the spike protein can cause the virus to become more contagious and more quickly spread between individuals [5,10,12,18-20]. Better binding may contribute to greater transmission [21].

2. The P681H is right next to the "furin cleavage" site, which is considered to be the gateway to penetrate human cells by the virus [5].

3. The other one is including a deletion at position 69/70 del causing S-gene target failure (SGTF) in PCR-based diagnostic assay i.e., the B.1.1.7 lineage and other lineages with del69-70 generate a negative result for the S-gene target and a positive result for the other two targets with the Thermo Fisher TaqPath COVID-19 assay [19,20].

However, most PCR assays search for three distinct regions of the spike protein, so those assays will not be affected, said the WHO [5]. Many scientists have compared that other SARS-CoV-2 variants circulating in the United Kingdom, they suggest that B. 1.1.7 is transmitted more effectively [17]. A German virologist Drosten states "in another viral gene, ORF8, the new mutant also carries a deletion that previous studies indicate a reduction

in the ability of the virus to spread" [20]. Faster epidemic growth has been seen in the UK, than in other areas and patients having B.1.1.7 lineage infections were found more than any other lineages.

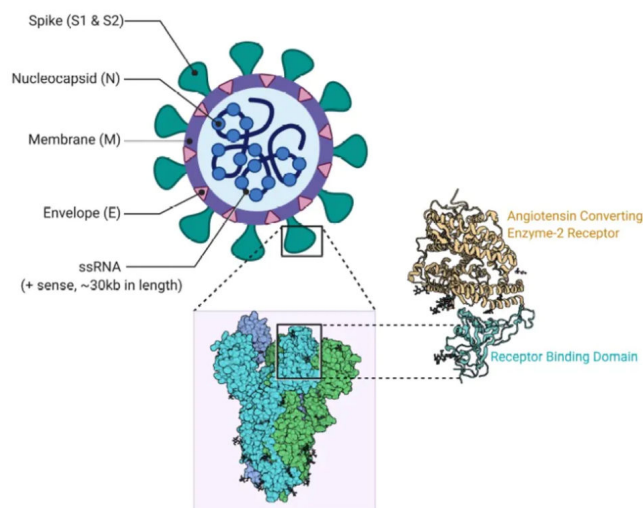


Figure 1 Structure of SARS-CoV-2 (18)

How much harmful the new variant is?

Although the transmissibility of this variant is found to be 70%, we do not know for sure how deadly the new variant is [9]. If the spread of the virus is rapid then a large number of people will be hospitalized which will lead to an increase in the death rate [5]. Nervtag analyzed that the reproduction number of the variant affecting people could go up to 0.93 [13]. The mutated strain may infect children and young people more rapidly, and therefore in the second wave, many younger individuals are hospitalized. Tentative research indicates that this is due to its 'stickiness' as well [15]. Children have fewer receptors than the older strain of coronavirus needed to get into cells, so they were less likely to catch it, but by being stickier, scientists said, the new variant could compensate for lower receptor levels or the entrance of the virus in children [15].

COG-UK states that the spike protein contains about 4000 mutations [12]. Not inherently, mutations that make viruses more contagious make them more harmful. The N501Y mutation is just as vulnerable to our defenses as the initial virus, suggests a microbiologist at University of Texas Medical Branch (UTMB) [20]. Some of the mutations have already been shown to improve the virus's capacity to infect cells in the laboratory [14].

Effectiveness of vaccines against the new variant

Currently, researchers are developing new vaccines as well as evaluating existing vaccines for the treatment of COVID-19 and this new variant. It is not yet known that if the COVID-19 vaccines that are now worldwide introduced will be successful against the mutations. The vaccine operates by revealing a portion of the genetic code of the virus to the body. SARS-CoV-2 variant genomic research has mainly concentrated on mutations in the spike glycoprotein, which facilitates cell attachment and is a primary target of neutralizing antibodies [10]. However,

vaccines develop antibodies to several regions of the spike protein, so it is difficult that a single alteration will make the vaccine less efficient. It is still not clearly shown that spike protein mutations make the UK variant more contagious but the spike locks on the human protein in order to allow infection [22]. There is a chance that a mutation that improves one viral property, such as receptor binding, may often decrease another property, such as the escape of antibodies from the host. The latest variant has spike protein mutations that are targeted by the three leading vaccines from Oxford/AstraZeneca, Pfizer/BioNTech, and Moderna [22]. Professor John Kaldor from the University of New South Wales (UNSW) said the revolutionary mRNA technology used to develop coronavirus vaccine was best suited for the virus that can rapidly alter and mutate [9]. Pfizer and Moderna assured that in spite of the emerging mutations, the vaccine will still be effective [22]. Even if vaccines work there is no certainty that there will not be any further mutations that won't make available vaccinations futile. Therefore, there is a need to focus on a new target other than S protein to develop an effective vaccine.

Future Directions

Currently, the UK variant is thought to be lethal but if a new strain or variant shows up that is both more infectious and more harmful then we have to hold our guard against anything like that. Even a more transmissible virus that causes the same degree of disease would be a really bad thing

So, alterations need to be done in the vaccine over time as more mutations occur like the seasonal flu which mutates every year, and the vaccine is manipulated accordingly. But there might be some risk that if the spike sequence varies too much, then it will need new vaccines [10]. This may be similar to the existing requirement to amend influenza vaccines annually. However, vaccines that have a component targeting the N protein are expected to be successful for longer since the N protein sequence is far more constant than the spike protein. Future vaccines are expected to rely on more than just the SARS-CoV-2 spike protein, and the N protein is a promising target to be applied to the existing techniques that are being explored [22].

It has been suggested that applying N-protein to SARS-CoV-2 vaccines may also be beneficial because N protein is very close amongst different coronaviruses, even more so than the spike protein [22]. But it has been a longtime mystery how N protein antibodies will protect us from infection and so have largely been overlooked. Therefore, researchers are exploring this further and suggest that if the vaccines induce both N-protein, as well as S-protein, can be more valuable as they can stimulate an immune response that can eliminate SARS-CoV-2.

Conclusion

A growing new UK variant of the SARS-CoV-2 virus that causes COVID-19 was identified. The above information suggests that the virus is continuously evolving and may lead to new different mutations. The scientists say that the vaccines will still work against the new UK variant but unsure how long developed

vaccines will work against emerging mutations. Therefore, learning the immunopathological response of the host would greatly enhance our ability to formulate vaccines and reduce the burden of disease. Finally, we speculate that the UK variant is been more transmissible but is less prone to death so far.

Authors Contribution

Shefali Khisty: Abstract, Introduction, Strain Variants and Mutations, Effectiveness of vaccines against the new variant

Pranjal Somvanshi: The UK variant – Emerging of the new variant, How was the variant detected, Lineage B.1.1.7 and its mutation, How much harmful the new variant is?

Both authors: Future Directions, Conclusion

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Conflict of Interests

The authors declare no conflict of interests

References

1. SARS-CoV-2 Variant – United Kingdom of Great Britain and Northern Ireland [Internet]. World Health Organization. 21 December 2020.
2. Countries where COVID-19 has spread. Worldometer. January 16, 2021.
3. Candra H. A Mini Review of Coronavirus Disease 2019(COVID-19) Therapeutics2020.
4. Organization WH. SARS-CoV-2 Variants. In: WHO, editor. US: WHO; 2020.
5. Ghose T. (2020) Fast-spreading UK coronavirus variant: All your questions answered. Live Science.
6. There's a new coronavirus variant. This is what we know so far. ABC News. 21 December 2020.
7. Terry M. (2020) Research Roundup: UK Strain of COVID-19 and More. BioSpace.
8. Elena SF, Sanjuán R (2005) Adaptive Value of High Mutation Rates of RNA Viruses: Separating Causes from Consequences. *J of Virology*. 79(18): 11555-8.
9. Saunokonoko M. (2021) What the super strain mutants mean for the world in 2021. *9 News*.
10. Luring AS, Hodcroft EB. (2021) Genetic Variants of SARS-CoV-2- What Do They Mean? *J American Med Asso*. 325(6): 529-531.
11. Callaway E. (2020) The coronavirus is mutating -does it matter? *Nature*. 585(7824): 174-7.
12. Wise J. Covid-19: New coronavirus variant is identified in UK. *BMJ*. 2020: m4857.
13. M KS (2021) Explained: How rapidly does the new coronavirus strain spread? Will it affect vaccination? *The Indian Express*.
14. Gallagher J. (2020) New coronavirus variant: What do we know? *BBC News*.
15. Knapton S (2021) Brazilian variant: what is the new Covid strain and should I be worried? *The Telegraph*.
16. Willis O (2021) How much more contagious is the new strain of COVID B117 detected in the UK? *ABC News*.
17. Summer E. Galloway PPP, PhD1; Duncan R. MacCannell, PhD2; Michael A. Johansson, PhD1; John T. Brooks, MD1; Adam MacNeil, PhD1; Rachel B. Slayton, PhD1; Suxiang Tong, PhD1; Benjamin J. Silk, PhD1; Gregory L. Armstrong, MD2; Matthew Biggerstaff, ScD1; Vivien G. Dugan, PhD1. Emergence of SARS-CoV-2 B.1.1.7 Lineage United States, December 29, 2020 January 12, 2021. Centers for Disease Control and Prevention. 15 January, 2021.
18. Bamford C (2020) New coronavirus variant: what is the spike protein and why are mutations on it important? *The Conversation*.
19. Lowe D (2020) The New Mutations. *Science*.
20. Kupferschmidt K (2020) Mutant coronavirus in the United Kingdom sets off alarms, but its importance remains unclear. *Science*.
21. Reardon S (2020) The U.K. Coronavirus Mutation Is Worrying but Not Terrifying. *Scientific American*.
22. Caddy SL (2020) COVID vaccines focus on the spike protein – but here's another target. *The Conversation*.