SARS-CoV-2 variant in the United Kingdom (UK)

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In news

The Ministry of Health's top advisory body will meet urgently to discuss the new strain of the novel coronavirus in the United Kingdom, which has triggered concern and prompted several European countries to stop incoming flights from the UK.

What is the new SARS-CoV-2 variant?

- Referred to as SARS-CoV-2 VUI 202012/01 (Variant Under Investigation, year 2020, month 12, variant 01), has been identified through viral genomic sequencing in the United Kingdom (UK). It is also known as lineage B.1.1.7
- It is defined by multiple spike protein mutations (deletion 69-70, deletion 144, N501Y, A570D, D614G, P681H, T716I, S982A, D1118H) present.
- Over the last few weeks, the UK has faced a rapid increase in COVID-19 cases
- It is correlated with a significant increase in the rate of COVID-19 infection in England; this increase is thought to be at least partly because of mutation N501Y inside the spike glycoprotein's receptor-binding domain, which binds to the ACE2 receptor in humans.
- The Covid-19 Genomics UK (COG-UK) consortium said one of the most important mutations, N501Y, occurs in the region of the spike protein, the receptor-binding domain (RBD), which the virus uses to bind to the human ACE2 receptor.
    - Changes in this region of the spike protein can result in the virus changing its ACE2 binding

specificity and alter antibody recognition

- This increase was pronounced in South East England, with an increase in the 14-day case notification rate from 100 cases per 100 000 population in week 41/2020 to over 400 per 100 000 in week 50/2020
- This increase led to an enhanced epidemiological and virological investigation. Analysis using viral genome sequence data identified a large proportion (>50%) of cases belonged to a new single phylogenetic cluster
- This variant is referred to in the UK as SARS-CoV-2 VUI 202012/01 (Variant Under Investigation, year 2020, month 12, variant 01).
- Overall, around 5 to 10% of all COVID-19 cases are regularly sequenced in the UK, with a sequencing coverage in Kent, the part of South East England that was most affected, of around 4%. As of 13 December 2020, 1 108 individuals had been identified with this virus variant in England, with the earliest case identified from 20 September 2020.
- The observed rapid increase in COVID-19 cases overall was temporally associated with the emergence of the new variant in this area in November 2020.
- The reported COVID-19 cases related to the VUI 202012/01 variant are concentrated in Kent and wider South East England, including the regions of London and the East of England, but there are indications of a more widespread occurrence of cases across the UK as well as small numbers of cases detected in other countries.
- Additionally, Denmark has reported nine cases [2], the Netherlands reported one case [3], and one case from Australia was identified through the GISAID EpiCov database.

Age group affected

- The cases with the new variant are predominantly identified in people younger than 60 years, but the

increase of overall COVID-19 cases in England is similarly driven by this age group (Figure 2).

- Preliminary modelling results show a strong association between the presence of the new variant in the Kent/South East England region and increasing incidence of COVID-19.
- Among the SARS-CoV-2 cases identified in Wales, cases have a median age of 41 years (range 11-71 years), and are mainly located in South Wales, where incidences are also rising

Genomic properties of the new SARS-CoV-2 variant

- This new SARS-CoV-2 virus variant is referred to in the UK as SARS-CoV-2 VUI 202012/01.
- It is defined by multiple spike protein mutations present as well as mutations in other genomic regions
- One of the mutations is located within the receptor binding domain.
- The variant belongs to Nextstrain clade 20B [9,10], GISAID (GISAID is a global science initiative and primary source that provides open-access to genomic data of influenza viruses and the novel coronavirus responsible for COVID-19)clade GR, lineage
- Phylogenetic analysis reveals that there are very few intermediary forms between this variant
- The cluster differs by 29 nucleotide substitutions from the original Wuhan strain, which is higher than current molecular clock estimates of around two substitutions per genome per month.
- The fraction of non-synonymous mutations in the spike protein for the variant is much higher than expected from random mutations
    - 27% of the 22 substitutions acquired since the Nextstrain clade 20B common ancestor are located in the S-gene, which comprises 13% of the viral genome, and all of these substitutions are

nonsynonymous

Possible sources of SARS-CoV-2 virus variants with a high number of mutations in the spike protein

- The unusually high number of spike protein mutations, other genomic properties of the variant, and the high sequencing coverage in the UK suggest that the variant has not emerged through gradual accumulation of mutations in the UK.
- It is also unlikely that the variant could have arisen through selection pressure from ongoing vaccination programmes as the observed increase does not match the timing of such activities.
- One possible explanation for the emergence of the variant is prolonged SARS-CoV-2 infection in a single patient, **potentially with reduced immunocompetence,** similar to what has previously been described
- Such prolonged infection can lead to accumulation of immune escape mutations at an elevated rate.
- Another possible explanation could be **adaptation processes in a virus that occur in a different susceptible animal species** and is then transmitted back to humans from the animal hosts.
- This led to the emergence of a variant with multiple spike protein mutations in Denmark during transmission among mink
- Several different spike protein mutations associated with mink have also been described in the Netherlands
- The UK has reported to ECDC and the WHO Regional Office for Europe that there is no clear epidemiological link to animals for VUI 202012/01, so this explanation is less likely for this variant
- Lastly, it is also possible that the variant has emerged through circulation in countries with no or very low sequencing coverage.