Rapid Reviews COVID-19

Review 3: "Emergence of a novel SARS-CoV-2 strain in Southern California, USA"

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RR:C19 Evidence Scale rating by reviewer:

- **Misleading.** Serious flaws and errors in the methods and data render the study conclusions misinformative. The results and conclusions of the ideal study are at least as likely to conclude the opposite of its results and conclusions than agree. Decision-makers should not consider this evidence in any decision.

General comments:

This report describes the appearance of a new SARS-CoV2 variant (CAL.20C) in Southern California that the authors claim contributed to the surge of COVID-19 that occurred in the region in fall 2020. The analysis is not very thorough and the conclusions do not support their main claim.

Specific comments:

1. This is a very small-sample study based on genome sequence analysis of only 181 viral samples. There is no description of the sources of these samples. The estimation of proportion of a single variant among such a collection can be greatly biased by local outbreaks in large congregate settings (e.g., college campus, long-term care facility, hospital, meat processing warehouse, etc), where an investigation happened to have been conducted and samples collected.
2. The authors claim that this variant has mutations in the Spike protein similar to those variants of concern reported from the UK and South Africa. This is not correct. The Spike protein mutation of concern in the UK's variant (B.1.1.7) is N501Y and those of SA's variant (B.1.351) are N501Y and E484K, which are also found in another variant of concern from Brazil (P.1). Cal.20C has neither but has a mutation in the receptor binding domain (L452R). The significance of this mutation with respect to viral neutralization by anti-Spike protein antibodies has not been determined.
3. The legend in Fig 2 has no detail. It is unclear what the viral variant data are based on. Are the CAL.20C data based on the sequences obtained from the GISAID database or are they from the analysis done by the authors? If they are based on the GISAID database, then the authors' observation shows nothing new.

In summary, this report is devoid of detail, misinterprets the significance of the mutations found in Cal,20C, and does not provide any convincing evidence that explains the reason for the surge of the epidemic in LA in fall 2020.