Reinfections are more frequent than currently considered in countries with high incidence of COVID-19 cases due to stringent definitions

Luis Pampa-Espinoza<sup>1</sup>, Javier Silva-Valencia<sup>1</sup>, Manuel Fernández<sup>1</sup>, Carlos Padilla-Rojas<sup>1</sup>, Lely Solari<sup>1</sup>

Instituto Nacional de Salud, Lima, Peru

Corresponding author:

Lely Solari (Corresponding author) lelysol@hotmail.com Telephone: 051999128241 Instituto Nacional de Salud, Lima Peru

Alternate Corresponding author:

Luis Pampa-Espinoza (First author, alternate corresponding author)
Luchopampa26@gmail.com
Telephone: 051943726240
Instituto Nacional de Salud, Lima Peru

Keywords: COVID-19, reinfection, diagnosis, research report

## **Dear Editor**

In a recently published review and analysis of reinfections due to SARS-COV-2, Choudhary finds 20 cases in 16 published reports [1]. According to the selected criteria, 273 publications were excluded. In the aforementioned publication, oriented to the genomic analysis of the infections, relatively stringent inclusion criteria were correctly applied; however, for public health purposes, an alternative approach could be considered.

CDC proposed a working definition of reinfection by SARS-CoV-2 based on genomic studies evidencing infection caused by different strains, with 90-day interval between them, as opposed the 30 days used by Choudhary [2]. This proposal takes into account the possibility that some patients may have a prolonged viral shedding of up to 82 days and correspond to persistent infections [3]. However, this approach underestimates the real magnitude of the sanitary problem and limits our understanding of the virus behavior and of the impact of the circulation of new variants. This is because, in order to be able to register reinfections as such, countries should have wide availability of genomic testing. In addition, huge bio banks to keep samples with positive results to have them available for sequencing if the patient presents a second infection would be needed. Finally, as antigenic testing for case detection scale up in many countries, special considerations should be implemented to allow subsequent genomic sequencing of these samples [4].

Let us examine Perú's situation. Peru has been one of the countries most affected by the SARS-CoV-2 pandemic, ranking top in estimated deaths per capita [5], According to data from the Information System of the National Laboratory Network (NETLABv2) until the end of July 2021, Perú had 3,444,304 people with a positive test (serological, antigenic or molecular) for COVID-19. Of these, 47,924 are likely to have had 2 episodes of infection but cannot be considered as reinfections with current standards (Figure 1A). Therefore, we propose a new approach to reporting reinfections from a public health perspective, taking into account the diverse testing capabilities of the countries, as follows (Figure 1B):

- -Possible reinfection due to SARS-Cov-2: Patient with a positive test (serological (if not vaccinated), antigenic or molecular) and after >90 days a second positive test (antigenic or molecular).
- -Probable reinfection by SARS-Cov-2: Patient with a positive molecular test and after >90 days a second positive molecular test.
- -Confirmed reinfection: Patient with different clades of SARS-CoV-2 as defined in Nextstrain and GISAID between the first and second samples, with >90 days between them. Each of these categories would complementary and provide key clues about the dynamics of

actual reinfections in a country. This approach would also change how we conceive reinfections, allowing us to better track them through the successive waves of the disease. Integration with virological, clinical, inmunological (including vaccination status) and epidemiological studies of these cases should complement the picture and provide better understanding about the impact of the waning immunity due to previous infections and vaccines, of the immune escape to the novel circulating variants, or the suboptimal immunity in special groups, among the main implications [6].

None of the authors has any conflicts of interest to disclose.

## References

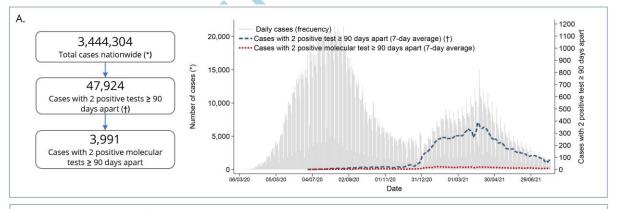
- 1. Choudhary MC, Crain CR, Qiu X, Hanage W, Li JZ. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Sequence Characteristics of Coronavirus Disease 2019 (COVID-19) Persistence and Reinfection. Clinical Infectious Diseases 2021; Available at: https://doi.org/10.1093/cid/ciab380. Accessed 9 August 2021.
- 2. CDC. Health Departments. 2020. Available at: https://www.cdc.gov/coronavirus/2019-ncov/php/invest-criteria.html. Accessed 24 June 2021.
- 3. Mukherjee A, Anand T, Agarwal A, et al. SARS-CoV-2 re-infection: development of an epidemiological definition from India. Epidemiology & Infection 2021; 149. Available at: https://www.cambridge.org/core/journals/epidemiology-and-infection/article/sarscov2-reinfection-development-of-an-epidemiological-definition-from-india/2140E6F272E50BD8613776BCCC047447. Accessed 24 June 2021.
- 4. Peeling RW, Olliaro PL, Boeras DI, Fongwen N. Scaling up COVID-19 rapid antigen tests: promises and challenges. The Lancet Infectious Diseases 2021; 0. Available at: https://www.thelancet.com/journals/laninf/article/PIIS1473-3099(21)00048-7/abstract. Accessed 7 July 2021.
- 5. COVID-19 Map. Available at: https://coronavirus.jhu.edu/map.html. Accessed 7 July 2021.
- 6. Harvey WT, Carabelli AM, Jackson B, et al. SARS-CoV-2 variants, spike mutations and immune escape. Nat Rev Microbiol 2021; 19:409–424. Available at: https://www.nature.com/articles/s41579-021-00573-0. Accessed 11 August 2021.

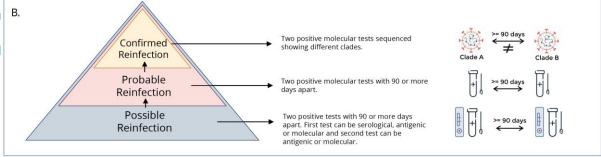
## Figure Legend:

- A) Number of cases in Peru until July 2021
- B) Operational definitions for COVID-19 reinfection



Figure 1





A. Number of cases in Perú until July 2021. B. Operational definitions for COVID-19 reinfection. (\*) Number of people with a positive test (serological, antigenic or molecular) throughout the country since the start of the pandemic. Only serological tests in the 2020 period were considered due to access to vaccination. (†) Cases with Two positive tests 90 or more days apart in which the first test can be serological, antigenic or molecular and second test can be antigenic or molecular.