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Commentary

Altered demographic profile of hospitalizations during the second COVID-19 wave in Amazonas, Brazil

Charles Whittaker[1], Oliver Ratmann[2], Christopher Dye[3], Ester C. Sabino[4], Nuno R. Faria[1,3,4,*]

[1] MRC Centre for Global Infectious Disease Analysis; and the Abdul Latif Jameel Institute for Disease and Emergency Analytics (J-IDEA), School of Public Health, Imperial College London, United Kingdom.
[2] Department of Mathematics, Imperial College London, United Kingdom.
[3] Department of Zoology, University of Oxford, United Kingdom.
[4] Departamento de Moléstias Infecciosas e Parasitárias e Instituto de Medicina Tropical da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brasil.

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Recent months have seen the emergence of SARS-CoV-2 variants with altered epidemiological properties, including increased transmissibility and the ability to partially evade protection immunity from prior infection. These variants have frequently been associated with resurgence of transmission and COVID-19 mortality in settings where they have established. Detailed investigations into the epidemiology of variants of concern (VOC) are crucial to sustained, long-term control of SARS-CoV-2. Despite this, epidemiological studies remain scarce, particularly with regards to clinical outcomes and profiles of disease severity associated with VOC transmission.

In this issue of The Lancet Regional Health - Americas, Ribas-Freital et al. [1] leverage detailed COVID-19 clinical and mortality surveillance data from the city of Manaus, capital city of the Amazonas state in North Brazil, and find evidence of altered age and sex COVID-19 mortality profiles (deaths per population, per reported COVID-19 case and per hospitalised COVID-19 case) when comparing periods during the first epidemic wave (April to May 2020, when SARS-CoV-2 lineages B.1.1.28, B.1.1.29 and B.1.1.33 dominated), the interepidemic period (June to November 2020, pre-Gamma VOC period), and the second epidemic wave (January 2021, when the Gamma VOC – also known as P.1, 20J/501Y.V3 or GR/501Y.V3 lineage; dominated [2,3]). Specifically, they found evidence to suggest an increased risk of death from COVID-19 during the second wave compared to periods prior to the circulation of the Gamma VOC, and that this elevated risk is concentrated in younger individuals. This is most notably seen for case fatality ratios (CRF) among hospitalized cases aged 20–39 years old, which were 2.7–fold greater in the second wave compared to the first wave. By contrast, the CRF was less than 1.4 for individuals aged 60-79 years, and less than 1.3 for individuals aged over 80. The authors propose that the greater disease severity among young adults of both sexes is associated with the emergence and establishment of the SARS-CoV-2 Gamma VOC.

Whilst the ecological nature of this study means the authors are unable to demonstrate a causal connection, these results sit alongside a growing body of previous work that has demonstrated altered pathogenicity and severity of SARS-CoV-2 variants compared to other lineages. Early work characterising the variant Alpha (B.1.1.7) showed it to be ~60% more deadly than co-circulating non-variant lineages [4]. However, evidence of age-specific modification of disease severity remains unclear for Alpha. A cohort analysis of 839,278 COVID-19 patients in England found an overall

* Corresponding author: Dr. Nuno Rodrigues Faria, Imperial College London, Department of Infectious Disease Epidemiology, London, United Kingdom, University of Oxford, Department of Zoology, South Parks Road, United Kingdom, Tell: +441865281314.
E-mail addresses: nfaria@ic.ac.uk, nmrfaria@gmail.com (N.R. Faria).

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1.52–fold greater risk of hospitalization with the Alpha VOC compared to other lineages, with a greater risk of hospital admission in adults aged above 30 [5]. The later study suggested that the higher disease severity previously associated with circulation of the Alpha VOC was due to the increased risk of being hospitalised [5], rather than elevated rates of mortality in individuals already hospitalised [6]. The findings of Ribas-Freital et al. are therefore novel in two regards - firstly, because they show an increase in mortality among patients in hospitals with the Gamma VOC; and secondly because they show that elevations to mortality risk with the Gamma VOC are most concentrated in younger individuals, rather than the elderly. If these changes are indeed attributable to the Gamma VOC as the authors suggest, rather than to some aspect of hospital care, they highlight important plasticity in the nature and severity of disease that different SARS-CoV-2 variants can elicit.

It is important to note that other factors may contribute to the observed shifts in the age distribution of COVID-19 deaths. As Ribas-Freital et al. note, a smaller proportion of severe acute respiratory infection patients were hospitalised during the second wave compared to the first, suggesting more significant strain on the healthcare system than during the first wave, and possible alterations to triaging and admission practices. Manaus' second wave led to extensive healthcare collapse and well-documented shortages of essential healthcare resources such as beds, oxygen and staff [7]. Previous work has highlighted the impact that both increased healthcare utilization [8] and a shortage of resources [9] can have in elevating in-hospital COVID-19 mortality rates, although it remains to be investigated whether these effects are equally distributed across age-groups or disproportionately elevated in younger individuals.

Previous analyses of COVID-19 disease severity have shown that mortality risk increases significantly with age [10]. On a per case basis, this may have reduced the overall risk in low- and lower-middle income settings where populations are typically younger, although recent events in Brazil, India, Indonesia and South Africa have sadly illustrated the limits of demography's mitigative effect. Marked increases in case fatality rates in younger age-groups during the period where Gamma VOC predominated (a finding similarly observed in an analysis of COVID-19 mortality in the South Brazil state of Parana [8]) threatens to erode this demographic effect even further, and poses a significant risk to settings that are often less well equipped to manage growing epidemics and deal with the healthcare pressures that high levels of SARS-CoV-2 transmission can generate [11]. These considerations underscore the urgent need for widespread, globally equitable vaccine allocation and access in order to ensure the largest number of individuals benefit from the protection they offer.

Contributions

Literature search (CW, OR, NRF), data interpretation (CW, OR, CD, EC, NRF), writing (CW, OR, CD, NRF)

Declaration of interests

Authors declare nothing to disclose.

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References

[1] Freitas ARR, Beckedorff OA, Cavalcanti LPdG, et al. The emergence of novel SARS-CoV-2 variant P.1 in Amazonas (Brazil) was temporally associated with a change in the age and sex profile of COVID-19 mortality: A population based ecological study. The Lancet Regional Health – Americas, https://doi.org/10.1016/j.lana.2021.100021.
[2] Faria NR, Mellan TA, Whittaker C, et al. Genomics and epidemiology of the P.1 SARS-CoV-2 lineage in Manaus, Brazil. Science 2021;372(6544):815–21.
[3] FioCruz RG. REDE GENÔMICA FIOCRUZ. Homepage Rede Genômica 2021 Available at: <http://www.genomahcov.fiocruz.br/>Accessed in 21 July 2021. 2021.
[4] Davies NG, Jarvis CI, Group CC-W, et al. Increased mortality in community-tested cases of SARS-CoV-2 lineage B.1.1.7. medRxiv 2021.
[5] Nyberg T, Twohig KA, Harris RJ, et al. Risk of hospital admission for patients with SARS-CoV-2 variant B.1.1.7: cohort analysis. Bmj 2021;373:n1412.
[6] Frampton D, Rampling T, Cross A, et al. Genomic characteristics and clinical effect of the emergent SARS-CoV-2 B.1.1.7 lineage in London, UK: a whole-genome sequencing and hospital-based cohort study. The Lancet infectious diseases 2021.
[7] Covid-19Brazil hospitals 'run out of oxygen' for virus patients. BBC 2021. published online Jan 15 https://www.bbc.co.uk/news/world-latin-america-55670318 (accessed July 20, 2021). BBC News. 2021.
[8] de Oliveira MHS, Lippi G, Henry BM. Sudden rise in COVID-19 case fatality among young and middle-aged adults in the south of Brazil after identification of the novel B.1.1.28.1 (P.1) SARS-CoV-2 strain: analysis of data from the state of Parana. medRxiv 2021 2021.03.24.21254046.
[9] African C-CCOSIPatient care and clinical outcomes for patients with COVID-19 infection admitted to African high-care or intensive care units (ACCCOS): a multicentre, prospective, observational cohort study. Lancet 2021;397(10288):1885–94.
[10] O'Driscoll M, Ribeiro Dos Santos G, Wang L, et al. Age-specific mortality and immunity patterns of SARS-CoV-2. Nature 2021;590(7844):140–5.
[11] Walker PGT, Whittaker C, Watson OJ, et al. The impact of COVID-19 and strategies for mitigation and suppression in low- and middle-income countries. Science 2020;369(6502):413–22.