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Respiratory Physiology & Neurobiology 279 (2020) 103448

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

journal homepage: www.elsevier.com/locate/resphysiol

Propagation by COVID-19 at high altitude: Cusco case

Dear Editor

We have read with interest the article published by Arias-Reyes C. et al. (2020) in Respiratory Physiology & Neurobiology that suggests that high-altitude may provide protection from pathogenesis of SAR-COV-2 infection. While we basically support this hypothesis on a potential variation of pathophysiological severity in residents living at high altitude, we would like to add some additional considerations to this epidemiological study from a Peruvian perspective.

Peru is a country with several cities at high altitudes, such as Cusco (3300 masl). Cusco is a tourist city and the outbreak for COVID-19 started in the tourist population. At present, Cusco has 196 COVID-19 positive cases in population and 3 (1.5 %) cases needed to be transferred to intensive care units (ICU). There have been four deaths, three foreign tourists and one native from Cusco with risk factors (0.5 % fatality rate for the native population). For Peru there were 651 ICU patients, 1.7 % of all cases, and the case fatality was 2.8 % (Stand April 28, 2020). This difference, may support the hypothesis that life in high altitude may provide some protection from severe COVID-19.

However, from epidemiological perspective the spread of a disease depends, among other things, on the level of social interaction and the protection measures implemented. Cusco has a low demographic density (18.9 inhabitants per km^2, while Lima has 269 inhabitants per km^2). The ratio of urban to rural areas in Cusco is 1.2/1 and thus as quarantine may be more effective because there is natural social distancing in the rural area (Instituto Nacional de Estadística y Demografía, Perú. Peru: Department population density, 1961 – 2015. Access date: April 26, 2020).

Indeed, cities with rural characteristics have less logistics to face the pandemic, for this reason there is a high risk of under-registration of cases, so the statistics do not it would correspond to what would happen in reality. In Cusco we have 1.4 cases /1000 inhabitants and 2.7 cases*1000/km^2, compared to Lima which has 17.5/1000 inhabitants and 470*1000/km^2. However, in comparison to cities in Peru that have health, demographic conditions and potential under-registration similar to Cusco, we can see that the altitude postulate may be not as influential in Peru, as it was suggested for the epidemiological analysis for countries such as Ecuador, Bolivia and Tibet. For example, cities on the coast of Peru such as Piura (29 masl) have 0.4 cases/1000 inhabitants and 2.1 cases*1000/km^2, and Tacna (560masl) has 2.0 and 5.0 respectively.

This discrepancy of epidemiological data can have several explanations. Cities at high altitudes in Peru have a higher underreporting of cases due to weaknesses in their health systems and limitations of geographic accessibility. Furthermore, there are differences in risk factors in high altitude populations that could act as confounding variables. For example, Pajuelo-Ramírez J et al. (2019) reported that in Cusco, 6.7 % of men are obese, compared to Lima, where 24.4 % are. In the same study, altitude is associated with a lower proportion of obesity in Peru. Without studies that can resolve this bias, it is not possible to affirm the correct dynamics of the spread of the pandemic in Cusco.

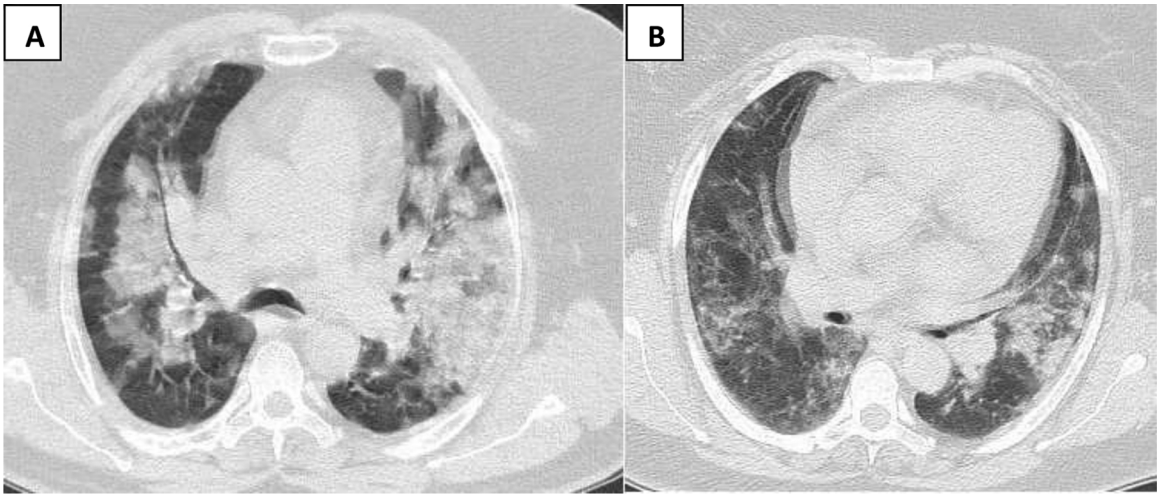

Fig. 1. Example of two cases COVID-19 positive treated in Cusco, Peru (3300msnm). Case A) 53 years old male-patient, morbid obese, required ICU care, CT with diffuse consolidation. B) 58-year-old female patient, morbid obese, hospitalized without requiring ICU care, CT with increased extent and density of bilateral lung opacities, with ground glass.

https://doi.org/10.1016/j.resp.2020.103448
Received 30 April 2020
Available online 08 May 2020
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Finally, regarding to pathogenesis of SAR-COV-2 infection, we present two chest tomography images of patients hospitalized by COVID-19 positive and who are natives from Cusco with risks factor (obesity) in Fig. 1. Both show the typical characteristics (Case A, severe stage: diffuse consolidation. Case B, advanced stage: increased extent and density of bilateral lung opacities, with ground glass) of COVID-19 described for Ye Z et al. (2020) Although we have few cases of Cusco natives requiring an ICU, those who require it have similar clinical manifestations. Therefore, we cannot conclude that the disease symptoms are different in residents at high altitude.

In summary we support the hypotheses presented by Arias-Reyes C. et al. because they have a biological plausibility. However, we believe it is still premature to conclude on the impact of high-altitude on severity and progression of COVID -19 without further evaluation of other social, demographic, risk factors or health variables.

References

Arias-Reyes, C., Zubieta-DeUrioste, N., Poma-Machicao, L., Aliaga-Raudan, F., Carvajal-Rodriguez, F., Dutschmann, M., Schneider-Gasser, E., Zubieta-Calleja, G., Soliz, J., 2020. Does the pathogenesis of SAR-CoV-2 virus decrease at high-altitude? Respir. Physiol. Neurobiol. 277, 1–4. https://doi.org/10.1016/j.resp.2020.103443. 1034433.

Pajuelo-Ramírez, J., Torres-Aparcana, L., Agüero-Zamora, R., Bernui-Leo, I., 2019. El sobrepeso, la obesidad y la obesidad abdominal en la población adulta del Perú. Anales de la Facultad de Medicina 80 (1), 21–27. https://doi.org/10.15381/anales.v80i1.15863.

Ye, Z., Zhang, Y., Wang, Y., Huang, Z., Song, B., 2020. Chest CT manifestations of new coronavirus disease 2019 (COVID-19): a pictorial review. Eur. Radiol. 1–9. https://doi.org/10.1007/s00330-020-06801-0.

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