Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Travel Medicine and Infectious Disease 35 (2020) 101667

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

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

What are the factors influencing the COVID-19 outbreak in Latin America?

Dear Editor,

Rodriguez-Morales AJ et al. [1] reported the implications of the first confirmed case in Brazil. In whole Latin America now, all countries are reporting cases of the novel coronavirus disease 2019 (COVID-19), hitting Brazil, Ecuador and Chile the most. The times are of globalization and huge digital connectivity, though there are intrinsic local community characteristics that are determined by some factors such as demographics, endemic infections and environmental conditions. How may all these factors influence and shape the outcome of the current SARS-CoV2 infection in Latin America?

1. Endemicity for other infections

Taking Brazil as a thermometer, this country has been dealing with important seasonal outbreaks of virus infections such as dengue, zika, chikungunya, and yellow fever. In Brazil more than 350′000 dengue cumulative cases have been reported since starting of this year. Therefore, it is important to consider this region as primed for these infections: Reconvalescent people keep some level of immunity as memory Cytotoxic $CD8^+$ T and or antibody producing Plasma B cells. Moreover, it has been shown that cross immunity is active in Flavivirus infections [2]. Even though the coronaviruses belong to another family, they may conserve some immunogenic epitopes. In murine models, prior immunity to distinct Flavivirus can somehow be protective to secondary challenges with other counterparts. In humans it is controversial if this cross immunity is beneficial or not. In the current outbreak it is difficult to analyze whether those levels of anti-Flavivirus antibodies and/or specific T-cells could cause a more severe or a mild disease. One way to address this question will be with cross-sectional studies comparing prevalence of antibody titers against many of those infections, with anti-SARS-CoV2, and also disease severity in different populations.

2. Immune regulation with other co-infections

The immune response against virus infections is usually Type I and it acts to clear the virus and virus-infected cells. It has been long known that in murine models Type I response is counterbalanced and inhibited by Type II response which is more directed against helminths. It was recently demonstrated in a murine model that the efficacy of vaccination against seasonal flu is impaired by concomitant helminth infection in an IL-10 dependent manner. Helminthic infection induced Type I regulatory (Tr1) cells that somehow impairs the efficacy of influenza vaccination, and even when the infection was cleared, the vaccination efficacy was not restored [3]. Thus, it is evidence that helminthic infections can influence how the immunity against virus infection is acquired. Considering the heterogeneity of the Brazilian population, this might influence mostly the poor populations infected who lack basic sanitation and proper nutrition.

3. BCG vaccination

Bacillus Calmette-Guérin (BCG) vaccine is implemented in many vaccine plans across Latin America, in Brazil, to induce protection against tuberculosis and leprosy. But BCG has another important effect which has been demonstrated in the last years by many clinical studies, that is a heterologous protection against non-related infections. Recent works have demonstrated that BCG might induce secretion of specific cytokines resulting in activation of $CD4^+$ and $CD8^+$ memory T cells [4]. Another proposed mechanism is to induce a more active innate immune response through several epigenetic modifications in *IL-6 and TNFA* genes, and activation of human monocytes that can protect against a non-related viral infection mediated by IL-1β [5]. BCG vaccination could be an important factor also to protect health professionals against SARS-CoV2 infection.

4. Population age

The Brazilian median age is 34 years, which is relatively young when comparing to other populations in which the epidemic is growing much faster: Italy's demographic data reports a median age of 47 years, China actually 38 years. During the current outbreak, like SARS-CoV1 outbreak, children infected have very low or no symptoms, and only very few cases of severe disease or even death. It is not clear yet, by which mechanism a younger immune system can faster control virus replication and barely cause a disease. Murine studies correlated a better SARS-CoV1 clearance with more T and B cells clones available to control the infection. While old mice have lost crucial clones to control viral replication and therefore are more susceptible to more severe disease. On the other hand, it was shown that old lungs have a less inflammatory environment in order to control inflammatory conditions such as asthma and allergies, and therefore this could create a more susceptible environment for the present virus proliferation [6].

5. How can we translate those factors into data to better understand what happens in the Latin America?

We now need accurate, standardizable data and factors gathered from (sub-)clinical data to be transferred without losing precious time to experts in immunology or virology. Age, lifestyle and climatic factors should be recorded or made available in future. Health status and medications shall be annotated. Mass-gatherings and interventional factors such as early lock-down measures shall be included into the analyses for developing a vaccine and deciding where to implement it

https://doi.org/10.1016/j.tmaid.2020.101667
Received 2 April 2020; Accepted 8 April 2020
Available online 11 April 2020

first. Epidemiologists and immunologists across Latin America should work together side-to-side and use the digital resources at their best, and it shall be increased, especially among people living in areas of difficult access. These factors shall be considered in studies in order to better understand how they will have influenced the outbreak dynamics in Latin America and to better help predicting new outbreaks.

Ethics approval and consent to participate

Not applicable.

Availability of data and materials

Not applicable.

Consent for publication

Not applicable.

Funding

This work was not funded.

Disclaimer

Not applicable.

Author' contributions

Both authors have read and approved the final version of the letter.

Declaration of competing interest

The authors declared no competing interests.

Acknowledgments

Not applicable.

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