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Reaching the theoretical herd immunity threshold in Iquitos, Peru: are seroprevalence data enough?



Since the beginning of the COVID-19 pandemic, there has been serious concern over monitoring and predicting transmission of the virus. Because of the disease's clinical profile, with many asymptomatic infections, passive surveillance only accounts for a fraction of all cases. Seroprevalence studies are an alternative method to estimate the proportions of infected and susceptible individuals in the population. Nevertheless, performance of serological assays can hinder the findings of these studies. Moreover, previous studies have shown that the target population is important for an accurate test selection, as reactivity could vary geographically and might be in part related to previous human coronavirus exposure.¹⁻³

In *The Lancet Global Health*, Carlos Álvarez-Antonio and colleagues⁴ report the findings of a seroprevalence study of COVID-19 infections that was done just after the first wave of the pandemic in Iquitos, Peru. In Latin America, Peru was one of the countries most affected by COVID-19, despite its strict lockdown in the early stage of the pandemic. The first COVID-19 case in Peru was detected on March 5, 2020. 12 days later, Iquitos, a city of approximately 467 000 habitants situated in the northeastern Amazon forest of Peru, had its first case, leading to devastating consequences as infection spread, reaching 26 404 cases and 1802 deaths at the end of 2020.⁵ Iquitos, a main hub for commerce, with both urban and rural areas and a high prevalence of tropical infectious diseases, proved to have increased risk of transmission compared with other regions in Peru.

The population-based cohort study presented by Álvarez-Antonio and colleagues,⁴ done in July and August, 2020, included 716 participants distributed across 40 strata (four districts, two genders, and five age groups). To detect IgG and IgM antibodies, the investigators used the COVID-19 IgG/IgM Rapid Test (Zhejiang Orient Gene, Biotech, China) immunochromatographic assay (which detects anti-spike protein antibodies). A very high seroprevalence of 70% (95% CI 67–73) at baseline in July, 2020, and a 1-month retest positivity of 65% (61–68) were found, after adjusting for the study sampling effects and sensitivity and specificity of the test. Moreover, the

authors noticed an incidence of new exposures upon retesting of 2% (95% CI 1–3). One of their key findings is the short timeframe in which Iquitos reached such a high seroprevalence in all of its four districts, which suggests that either the mandatory lockdown was not thoroughly followed, or it was not enough to slow down transmission.

Previous SARS-CoV-2 studies reported seroprevalence values ranging from less than 0.1% to greater than 30%,^{6,7} which differ remarkably from the 70% value reported in Iquitos by Álvarez-Antonio and colleagues. In addition, COVID-19 infection was equally distributed across genders, and the authors reported that some of the highest seroprevalence values were among children aged younger than 12 years (70% [95% CI 63–77]) and adults aged 60 years or older (74% [60–85]). These results contradict what has been found in Lima, Peru, where children aged younger than 12 years had almost the same seroprevalence as other age groups,⁸ and what has been reported in Europe and the USA, where children had the lowest seroprevalence.⁶ The reasons why children had such a high prevalence in Iquitos remain unclear. A possible explanation could be the presence of previous human coronavirus antibodies cross-reacting with SARS-CoV-2. A previous study in the UK using pre-pandemic serum samples from children aged younger than 16 years reported detectable levels of SARS-CoV-2 IgG antibodies.¹ It would have been valuable to know how the rapid test used in Iquitos was validated using pre-COVID-19 specimens to determine any potential cross-reactivity, as various studies indicate the presence of high levels of other human coronavirus antibodies in other populations.¹⁻³ For example, using samples from a unique cohort of patients collected before the pandemic and during the pandemic in the USA, it was clearly shown that approximately 20% of 431 human serum samples collected in 2017 cross-reacted with SARS-CoV-2.³ It is possible that SARS-CoV-2 reactive antibodies could have been circulating before the pandemic due to other coronavirus infections in cities such as Iquitos, where respiratory infections are common. Further clarification of this hypothesis will strengthen the results obtained in this study.

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The duration of antibodies in COVID-19 convalescent individuals and whether the circulation of different SARS-CoV-2 variants will indeed have an effect on COVID-19 infection dynamics are not yet known. It is now imperative to do studies that include molecular testing, stratify results by clinical presentation (eg, asymptomatic vs presymptomatic individuals), and measure neutralising antibodies after ongoing COVID-19 vaccination campaigns. Findings from these studies will allow for a broader understanding of the transmission of the disease and the potential role of immune protection after vaccination and natural infections. Finally, the current disease dissemination trends, with increasing numbers of cases and the occurrence and spread of new variants, namely the SARS-CoV-2 P1 variant first identified in Brazil, suggest that herd immunity is unlikely to be reached through natural exposure alone. Vaccination should be the main target for COVID-19 transmission control, and will hopefully help reach high levels of protective antibodies and herd immunity.

We declare no competing interests.

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