SARS-CoV-2 in Rural Latin America. A Population-based Study in Coastal Ecuador

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Antibodies to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) were detected in 303/673 rural Ecuadorian adults (45%), 77% of whom had compatible clinical manifestations. Seropositivity was associated with the use of open latrines. Our findings support the fears of mass spread of SARS-CoV-2 in rural Latin America and cannot exclude a contributing role for fecal-oral transmission.

Keywords. SARS-CoV-2; coronavirus-19; population study; rural setting; Ecuador.

The global severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has spread to rural areas of developing countries [1, 2]. These people are likely to be especially vulnerable to this pandemic because of factors inherent to underdevelopment [3]. However, there is little or no evidence of the burden and profile of SARS-CoV-2 infections in remote rural settings.

The Atahualpa Project is a population-based prospective cohort studying individuals aged 40 years or older in rural Ecuador, starting on 2012 [4]. An abrupt increase in deaths in the village was noticed in April and May 2020 (overall mortality rate, 21.6 per 1,000 of the population, almost three-quarters of it attributable to SARS-CoV-2, representing 266% of excess mortality), that coincided with the peak of this pandemic in Ecuador, suggesting an outbreak of SARS-CoV-2 infection. Taking the opportunity of the above-mentioned well-established cohort, we assessed the prevalence, distribution, and risk factors associated with SARS-CoV-2 seropositivity in middle-aged and older adults living in this closed population.

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Atahualpa is located in coastal Ecuador. The village has electricity and almost all houses have piped water. A sizable proportion of houses do not have flushing toilet systems and still use open latrines. Inhabitants are homogeneous regarding race/ethnicity (Amerindian ancestry), lifestyles, and diet. Almost all men belong to the blue-collar class (artisan carpenters) and most women are homemakers. Atahualpa has a low index of migration and the adherence of the population to the Atahualpa Project has been high, which makes it an optimal setting for conducting population-based studies [5].

For the present study, field personnel (including medical doctors) visited all houses of Atahualpa Project participants. Demographic data and risk factors were updated during house visits. Individuals were examined to assess current or past (prior 2 months) clinical manifestations suggestive of coronavirus disease 2019 (COVID-19), according to the recommendations of the World Health Organization [6]. Detection of SARS-CoV-2 immunoglobulin (Ig) M and IgG antibodies was performed using a lateral flow antibody test (BIOHIT Health Care Ltd, Cheshire, United Kingdom) in finger-prick blood samples. The manufacturer reports 97.5% sensitivity with 99.5% specificity for IgM and 97.5% sensitivity with 100% specificity for IgG detection of this kit. Results of those tests were independently reviewed by 2 readers, with excellent κ coefficients for interrater agreement (0.91). Discrepancies were resolved by consensus.

The study followed the STROBE (Standards for Reporting of Observational Studies in Epidemiology) guidelines [7], and the Independent Review Board of Universidad Espiritu Santo (IORG: 0010320; FWA: 00028878) approved the study protocol and informed-consent forms.

Covariates were selected if they were suggested to play a role in disease acquisition or spread, or in the development of clinical manifestations, and included age, gender, level of education, alcohol intake, number of individuals living in the house, number of bedrooms, having an open latrine, home confinement during the past 2 months, and cardiovascular health status, according to the American Heart Association criteria (smoking status, diet, physical activity, body mass index, blood pressure, fasting glucose, and total cholesterol blood levels) [8].

Data analyses were carried out by using STATA version 16 (StataCorp, College Station, TX). In univariate analyses, continuous variables were compared by linear models and categorical variables by the chi-square or Fisher’s exact test as appropriate. Mixed logistic regression models, where subjects were clustered within blocks and each block was considered a panel of random intercept, were fitted using seropositivity to...
SARS-CoV-2 antibodies as the dependent variable, adjusted for the above-mentioned covariates.

**RESULTS**

From 730 individuals aged 40 years or older who were actively enrolled in the Atahualpa Project as of 31 May 2019, 39 had either died (n = 24) or emigrated (n = 15) in the past 12 months. Thus, 691 were living in the village as of 25 May 2020, and of these, 18 declined participation in the current survey (coverage, 97.4%).

The mean age of the 673 participants was 59.2 ± 12.8 years, 381 (57%) were women, 354 (53%) had primary school education only, and 142 (21%) disclosed heavy alcohol intake. A poor cardiovascular health status was noticed in 453 (67%) participants, and the mean number of metrics in the poor range was 1.1 ± 1 per person. A total of 238 (35%) individuals had been confined at home during the past 2 months. The 673 participants inhabited a total of 411 houses, with a mean of 6.6 ± 4.7 persons per house (including young adults and children), and the houses had a mean of 2.6 ± 1.1 bedrooms. Open latrines were used by 137 (20%) individuals.

A total of 303 (45%) individuals were seropositive to SARS-CoV-2 antibodies (including 247 who were reactive to both IgM and IgG, 9 to only IgM, and 47 to only IgG). Seropositive individuals were spread across the village (Figure 1). As IgM and IgG responses in SARS-CoV-2 develop with only a few days of difference, we defined seropositivity as a positive response to any of them. COVID-19–related clinical manifestations were recalled by 232 (77%) seropositive and 55 (15%) seronegative individuals. Twelve symptomatic seropositive patients required oxygen therapy, and another 3 needed artificial ventilator support. No patient died during the survey.

In univariate analyses, seropositive individuals presented more often with COVID-19–related symptomatology, used more often open latrines than their seronegative counterparts, and fewer of them had been confined at home (Table 1). Multivariate analyses confirmed independent associations between seropositivity to SARS-CoV-2 antibodies and compatible symptomatology (odds ratio [OR], 24.3; 95% confidence interval [CI], 15.3–38.8; *P* < .001) as well as use of open latrines (OR, 2.14; 95% CI, 1.23–3.72; *P* = .007).

**DISCUSSION**

This study demonstrates a high (45%) seroprevalence of SARS-CoV-2, disseminated across the entire village, confirming fears of mass spread of the disease in rural populations of Latin America [9]. Despite almost no migration into Atahualpa, many men travel to neighboring towns to trade the furniture they build as artisan carpenters. Atahualpa's scenario is typical of closed populations where inhabitants are immunologically naive to a rapidly spreading pathogen. Rural populations of Latin America are additionally burdened by poor social determinants of health and inadequate access to medical care and do not seem to be prepared for this pandemic [3].

Most available data on COVID-19–related predisposing factors derive from clinical series in health centers, with only few urban community surveys covering sampling proportions of the target population [10, 11]. There are no similar community-wide studies reported from remote rural settings. In these settings, living conditions, risk factors, and access to healthcare are different from those in urban centers or in developed countries.

Factors associated with SARS-CoV-2 seropositivity in univariate analyses included the presence of COVID-19–related symptomatology and the use of open latrines. In contrast, confinement...
to home was inversely associated with seropositivity. A multivariate model confirmed the associations of seropositivity with clinical manifestations and the use of latrines. We cannot conclude that the presence of asymptomatic seropositive patients points to true asymptomatic cases. This was a cross-sectional survey, and both recall bias and the occurrence of other infections could have contributed to our finding. Also, higher rates of asymptomatic infections than in our study were reported in Veneto, Italy [10]. Likewise, a Swiss study found a seroprevalence of approximately 11% after 5 weeks of the first demonstrated case, with most individuals being asymptomatic [11].

On the basis of the demonstration of SARS-CoV-2 in feces [12], it has been suggested that the fecal–oral route may contribute to the transmission of this pathogen in rural areas of the developing world [3]. The present study provides indirect support to the above-mentioned hypothesis. Open latrines are often associated with inadequate handling of human feces, which may facilitate SARS-CoV-2 transmission. However, we cannot rule out the possibility that latrines are acting as a proxy for other unknown interacting variables. Further studies are needed to confirm the role of the fecal–oral route as a source of SARS-CoV-2 infection in rural settings.

Our study is the first to demonstrate the magnitude of the expansion of SARS-CoV-2 and the factors associated with seropositivity in a remote rural village. Another strength of this study includes the high coverage and unbiased inclusion of long-term participants in the Atahualpa Project cohort, in whom several risk factors and conditions have been well characterized. This will provide grounds for the conduct of ambispective studies to assess long-term consequences of COVID-19 infection.

Nevertheless, the study has limitations. The study population was limited to individuals aged 40 years or older. As such, we missed the infection status of the younger villagers and how it could have influenced the overall seroprevalence. Individuals recently infected could be in the process of building their antibody response and would have tested negative. In addition, we cannot rule out a small degree of misclassification due to false-positive or false-negative results. The number of individuals with COVID-19–related clinical manifestations may be an overestimation due to poor specificity of the variable or recall bias.

In conclusion, this study demonstrates a high prevalence of seropositivity to SARS-CoV-2 in a closed rural population, as well as the independent association between seropositivity and COVID-19–related symptoms and the use of open latrines. Our findings confirm assumptions of mass dissemination of COVID-19 disease in immunologically naive rural settings and depict the initially devastating consequences of this infection.

**Notes**

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