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Clinical situation of Venezuelan migrants living with HIV in a hospital in Lima, Peru

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Abstract

Due to a huge crisis extensive to health services many Venezuelan people living with HIV (PLWH) had migrated abroad, including Peru where favorable laws were in place until June 2019. We describe the health status and epidemiological trends of PLWH from Venezuela at an HIV program in Lima. We analyzed baseline and follow-up data of all Venezuelan PLWH enrolled in our HIV program from January 2017 to December 2019. A cross-sectional study in a subsample served to describe ARV adherence and context of migration. Between 2017-2019 our HIV Program registered 398 Venezuelan PLWH, representing 20% of the 2018 annual enrollments; numbers decreased since mid-2019. The median age was 30 years (IQR 26;37) and 90.5% were men. Between 2017 and 2019, the proportion with diagnosis in Peru increased from 14.3% to 60.9%; of AIDS stage at entry, from 8.8% to 27.2%. By December 2019, 182/250 (72.8%) were still in care, and 43 (10.8%) had not started ART. Viral suppression evaluated in 195, was achieved in 71.8%. From 2017 to 2019, migrant PLWH arrived in worsened clinical conditions, with increasing diagnosis in Peru; the flow of migrant PLWH entering care diminished with less favorable laws. Viral suppression rates were suboptimal.

Keywords

Emigrants and immigrants, Peru, Latin America, Human migration, Venezuela, HIV infections

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Introduction

Massive migrations challenge the public health systems of host countries, which need to prioritize disease control and provide responsive health services for the migrant population. By June 2019, amid an escalating socioeconomic crisis, at least four million people had departed from Venezuela[1]; half of their 650,000 asylum claims were presented to Peru.[2] A Peruvian law enacted in 2017, and halted in June 2019, allowed that Venezuelan migrants could reside and work legally in the country for a year.[3]

The health system deterioration in Venezuela,[4,5] extensive to health information systems,[6] led to the reemergence of vaccine-preventable diseases and other infectious conditions, including HIV.[7] In 2016, UNAIDS estimated a 24% increase in new HIV infections compared to those reported in 2010 in Venezuela, and a total of 120 000 people living with HIV (PLWH). Shortages of tests for diagnosis and laboratory monitoring and drug supplies for antiretroviral therapy (ART) and of health practitioners further affected the continuum of care[5,8]: by 2016, 59% of PLWH in Venezuela had access to ART and only 7% were virally suppressed.[9] By 2019, approximately 8000 PLWH in Venezuela had migrated.[10]

At host countries, migrants encounter several challenges especially when trying to access health services.[11] In an HIV cohort in Italy, migrants were at greater risk of viral and treatment failure than residents.[12] According to a national survey directed to the Venezuelan population living in Peru, 93.3% lacked health insurance and half of them restrained from using health services.[13] By December 2018,

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approximately 1338 Venezuelan PLWH were receiving ART in Peru, 90% in the capital (Lima).[10,14]

In this study, we described the clinical and epidemiological characteristics of Venezuelan PLWH at the time of their entry to an HIV program in Lima and until 2 years afterward. In a subsample, we described adherence to ART, the reported reasons for nonadherence, and its impact on HIV outcomes.

Methods

Setting

Since 2008, most South American countries share a free transit policy with a waiver of visa requirements. In 2017, a Peruvian law allowed Venezuelan migrants to stay and work legally in Peru for a year; once it was reversed (June 2019), passports and permits were required for Venezuelan migrants who arrived at Peru.

ART and ART laboratory monitoring are provided free of charge to all PLWH enrolled in governmental-funded Peruvian HIV Programs. Until 2017, multidisciplinary appointments (medical, psychology, social services, and nurse evaluation) were mandatory to initiate ART. Between 2017 and 2018, a new Peruvian HIV guideline simplified such process, with only a mandatory physician appointment before ART initiation.[15,16] Additional medical tests and appointments are out-of-pocket expenses for PLWH without social/health insurance. The latter can be granted to migrants who obtain a resident status or are considered a vulnerable population, although the process can take a couple of months.[10,17]

The HIV program at our study center, in Lima, provides clinical care to the largest HIV cohort in Peru. When PLWH are enrolled in the HIV program, nurses fill out a structured questionnaire regarding past medical history, date of HIV diagnosis, and previous use of ART; a medical questionnaire filled out by infectious diseases specialists lists the clinical diagnoses at entry. Whenever available, the physicians attach documents from previous medical reports. Nurses register the dates of visit and the ART regimen at each ART pickup appointment, as well as $CD4^+$ count and viral load results. As part of the standard of care, nurses make efforts to contact patients identified as ART abandonment or those who became lost to follow-up before ART start by phone call or home visits, aiming to facilitate their return to care. PLWH in need of admission are hospitalized at the Infectious Disease Unit of the study center. At discharge, a physician fills out a structured form that summarizes the period of hospitalization, diagnoses, and vital status.

The information generated by all these procedures is entered into an anonymized database whose use and data management is supported by the Caribbean, Central and South America network for HIV Epidemiology.[18]

Study design and study population

For the secondary data analysis, we considered all HIV program files and hospital discharge forms of patients aged 18 or more with Venezuelan nationality that entered the HIV program at the study center from January 2017 to December 2019.

For the cross-sectional component of this study, we contacted PLWH who attended the HIV Program between September 2019 to December 2019 for ART pickup or ART restart.

Study procedures

For the secondary data analysis, we used a digital data collection form to retrieve the epidemiological (age, sex, sexual orientation, and level of education), clinical (baseline $CD4^+$ count and viral load, HIV/TB coinfection, and previous ART treatment), ART (drug combination and ART changes), admissions (hospitalizations and diagnoses), and HIV outcomes (viral suppression, ART abandonment, and death) information. We contrasted these data with the datasets from the routine HIV program database. Additional data quality control was done in a random selection of 50% of the files; discrepancies were solved by review of the original forms. Information about previous HIV diagnosis and ARV treatment was obtained by a nurse or physician and registered in their respective questionnaire including the medical report from Venezuela when available.

For the cross-sectional component, the nursing HIV program staff contacted eligible participants during either their visits to the HIV program or via phone calls or home visits because of abandonment or lost to follow-up. PLWH who provided informed consent, responded to the study questionnaire. The questionnaire inquired about HIV clinical information in Venezuela, the itinerary to access health care in Peru, the SMAQ questionnaire[19] for adherence, and information on the reasons for abandonment and nonadherence. This information was entered into a study database.

Variable definitions

We defined baseline $CD4^+$ count and viral load as the first measure taken in Peru; TB coinfection by the initiation of TB treatment; and for those who had started ART, ART abandonment was the lack of ART pickup visits for more than 90 consecutive days. We defined viral suppression as $\leq$ 40 copies/ml and virologic failure as $>$ 200 copies/ml; in both cases, we considered the last viral load test performed between 3 and 9 months after ART initiation at our study center. Thus, these outcomes are presented for PLWH with at least 3 months of follow-up.

We defined ART nonadherence either by (i) a positive response in any of the questions of the SMAQ questionnaire; or the loss of (ii) more than two ART doses during the

last week; or (iii) for more than two consecutive days in the last 3 months.[19]

Statistical analysis

For quality control, we carried double digitation for 20% of the data to check for typing or content errors. We calculated mean and standard deviation for quantitative variables with normal distribution and median and interquartile range for those with nonparametric distribution. For categorical variables, we reported absolute and relative frequencies. Baseline and follow-up characteristics were analyzed by the year of enrollment in the HIV Program to determine trends over time of the clinical conditions at entry. We used STATA 15 (Stata Statistical Software; Stata Corporation, College Station, TX, licensed by Universidad Peruana Cayetano Heredia) for data management and statistical analyses.

Ethics

The study protocol, including the informed consent for the cross-sectional component, was approved by the Institutional Review Boards of the Universidad Peruana Cayetano Heredia and the Hospital Cayetano Heredia.

Results

From January 2017 to December 2019, the HIV program at our center registered 398 Venezuelan PLWH (Figure 1); this represented 4.4% of new enrollments in 2017, 20% in 2018, and 18.7% in 2019. The peak of new enrollments of PLWH migrating from Venezuela to Peru was observed in the second trimester of 2018 (65 new enrollments), and it decreased to 38 in 2019, after more restricted Peruvian border control laws came into force (Figure 2).

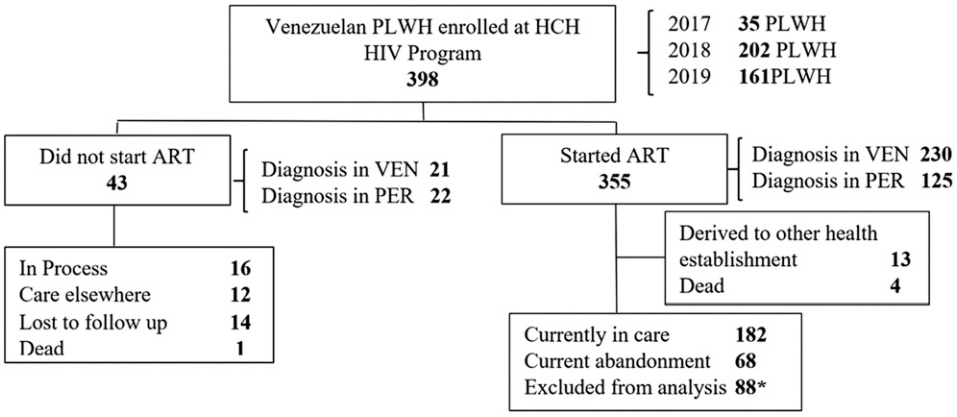

Figure 1. Patients flowchart. *Reasons for follow-up exclusion: 19 started after 30 November 2019; 69 had no information of antiretroviral therapy pick up. PLWH: People living with HIV; ART: antiretroviral therapy; VEN: Venezuela; PER: Peru; HCH: Hospital Cayetano Heredia.

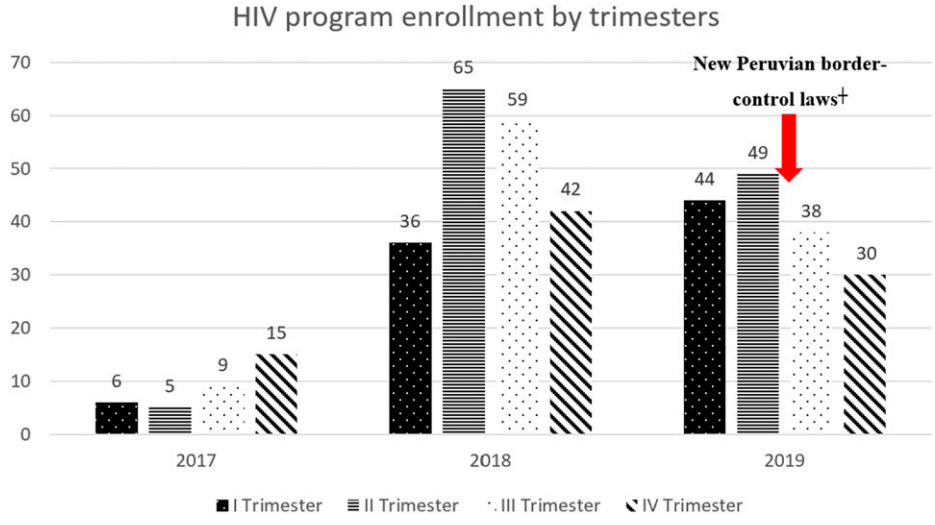

Figure 2. Number of enrollment of HIV positive Venezuelen patients in HCH HIV program by trimesters. †In June 2019 new border-control laws were enforced for Venezuelen immigrants, adding requirements to enter the country.

The median age of Venezuelan PLWH enrolled at our center was 30 years (IQR 26; 37); 90.5% were male. By time of enrollment, seven out of 38 women were pregnant and two in postpartum period. Most of our study population had higher education (71.3%), were single (77.4%), and identified themselves as men who have sex with men (52.9%). One-third of the study population was diagnosed with HIV infection in Peru and 19% had a $CD4^+$ count below 200 cells/mm^3. Table 1 presents baseline characteristics of our study population.

Table 1. Baseline characteristics (n = 398).

Characteristic	N (%); median (IQR)
Male	360 (90.5)
Age (years)	30 (26; 37)
Level of education[a]	
Primary school	18 (4.5)
Secondary school	96 (24.2)
Higher education	283 (71.3)
Marital status	
Married or cohabitant	82 (20.6)
Divorced or separated	8 (2)
Single	308 (77.4)
Sexual orientation[a]	
Bisexual	104 (26.2)
Heterosexual	83 (20.9)
Homosexual	210 (52.9)
Place of diagnosis	
Venezuela	251 (63.1)
Peru	147 (36.9)
Previous ART in Venezuela[a]	235 (93.6)
First $CD4^+$ count (cell/ml)[a]	395.5 (233; 612)
>500	132 (35.7)
350–499	78 (21.1)
200–349	90 (24.3)
50–199	45 (12.1)
<50	25 (6.8)
First viral load (copies/ml)[a]	20500 (75.1; 143000)
<40	89 (23.1)
40–500	31 (8)
500–10000	43 (11.1)
>10000	223 (57.8)
HIV/TB coinfection	10 (2.5)
Pregnancy (n = 38)	9 (23.7)
Year enrolled in HIV program	
2017	35 (8.8)
2018	202 (50.7)
2019	161 (40.5)

[a]Variables can add up to less than 398 due to missing data.

Throughout the study period, the proportion of migrants enrolled in our HIV program with a previous HIV diagnosis in Venezuela decreased from 85.7% (2017) to 39.8% (2019); the median baseline $CD4^+$ count also decreased: from 488 [IQR 294–633]) in 2017 to 346 [IQR 161–588]) in 2019. In 2017, the majority of patients were on viral suppression at baseline (63%) in comparison with 11.2% in 2019. The comparison of clinical characteristics by year of enrollment is summarized in Table 2. Overall, the group diagnosed in Venezuela (251) was less compromised at entry in our HIV program, with higher median baseline $CD4^+$, lower percentage of AIDS cases, and higher frequency of ART start (250, 91.6%) (Table 3). In the cross-sectional study (n = 137), the median time between the arrival to Peru to the first encounter with our hospital was 121 days [IQR 24; 315] for all participants and 52.5 days [IQR 7; 109] for the participants with HIV diagnosed in Venezuela.

Follow-up information

The median time since the enrollment to the HIV program until the initiation of ART was 22 days (IQR 14; 43); it was 24.5 days (IQR 16; 47) for those diagnosed in Peru and 21 days (IQR 10; 38) for those diagnosed in Venezuela. Among PLWH whose baseline $CD4^+$ count was below 50 cells/mm^3, the median time to ART initiation was 19.5 days (IQR 14.5; 30). Out of 191 with information on the last ART combination used in Venezuela, 120 (62.8%) maintained such ART combination in our HIV program, with TDF/FTC/EFV as the most frequent (71, 59.2%).

Until the end of follow-up, ART combinations prescribed at our HIV program were modified in 18 PLWH due to adverse drug reactions (8 cases) predominantly cutaneous; virologic failure (4 cases); and pregnancy, renal disease, and TB treatment (2 cases per each category). After a moderate or severe adverse drug reaction to 2NRTIs + NNRTI, the usual treatment modification was 2NRTIs + PI.

Table 2. Clinical characteristic by year of enrollment.

	2017 (n = 35)	2018 (n = 202)	2019 (n = 161)
Characteristic	N (%); median (IQR)		
$CD4^+$ count	488 (294; 633)	407 (259; 617)	346 (161; 588)
AIDS	3 (8.8)	27 (14.3)	40 (27.2)
Viral suppression at start of ART at study center[a]	20 (63)	54 (26.4)	15 (11.2)
HIV diagnosis in Venezuela	30 (85.7)	157 (77.7)	64 (39.8)

[a]Variables with missing data (>5%).

Table 3. Clinical characteristic by place of diagnosis and year of enrollment.

	HIV diagnosis					
	Venezuela (n = 251)			Peru (n = 147)		
	N (%); median (IQR)			N (%); median (IQR)		
Characteristic	2017 (30)	2018 (157)	2019 (64)	2017 (5)	2018 (45)	2019 (97)
Baseline						
Age	31.7 (27.4–37.8)	33.0 (27.5–38.6)	31.3 (25.8–29.5)	31.0 (22.5–32.3)	28.3 (24.4–31.4)	28.1 (24.4–30.2)
Female	4 (13.3)	8 (5.1)	10 (15.6)	0	5 (11.1)	11 (11.3)
$CD4^+$ count[a]	531 (323–673)	450.5 (296–630.5)	319.5 (118.5–627.5)	305.5 (273.5–354.5)	344 (203–476)	362 (204–538)
AIDS stage[a]	3 (10)	18 (12.2)	18 (32.1)	0	9 (22.0)	22 (24.2)
Started ART	28 (93.3)	145 (92.4)	57 (89.1)	5 (100)	39 (86.7)	81 (83.5)
Follow-up	Venezuela (n = 133)			Peru (n = 62)		
Achieved viral suppression[a]	14 (87.5)	67 (70.5)	13 (59.1)	3 (100)	23 (74.2)	20 (71.4)
Virologic failure[a]	0	17 (17.9)	5 (22.7)	0	3 (9.7)	4 (14.3)

[a]Variables with missing data.

According to the cross-sectional study ($n = 137$), 67.2% showed nonadherence to ART; the main reported reasons were forgetfulness to take pills (22.6%) and conflicting schedules (21.9%).

Of those who initiated ART during the study period, 250 were included in our final analysis for retention in care: 182 (72.8%) were considered in care and 68 (27.2%) as abandonment, which included 12 PLWVH (17.6%) who had already left Peru. Out of 195 (61.0%) with a viral load measure between 3 and 9 months, 140 (71.8%) achieved viral suppression and 29 (14.9%) had virologic failure. PLWH diagnosed in Venezuela had higher percentage of virologic failure despite better baseline clinical characteristics (Table 3). Most PLWH diagnosed in Venezuela who entered with baseline viral suppression remained in such status on follow-up (39/42, 92.9%). Among those who entered without viral suppression, higher percentage of viral suppression on follow-up corresponded to those diagnosed in Venezuela (74.6% vs. 60.4%).

In our study population, we identified 22 hospital admissions: 13 occurred in PLWH who had not yet started ART and nine occurred after ART start. The most frequent diagnoses were tuberculosis (7 PLWH), cytomegalovirus (3 PLWH), and histoplasmosis (2 PLWH).

By December 2019, 43 (10.8%) Venezuelan PLWH had not started ART at the study center (Figure 1): 16 were still in the process to start ART at the study center, given that economical and time limitations had hampered the completion of the laboratory or medical appointments; 12 had transferred their HIV care to an other health establishment in Peru. We identified five deaths: three occurred within the first month after enrollment in PWLH whose baseline $CD4^+$ counts were below 200 cell/ml and one corresponded to someone who had not started ART. Causes of death were tuberculous meningitis (1 PLWH), *Pneumocystis jiroveci* pneumonia (PJP) (1 PLWH), Kaposi's sarcoma (1 PLWH), and unknown (2 PLWH).

Discussion

Conducted at the largest HIV program in Peru, this study reports, first, a sustained increase in the number of Venezuelan PLWH attended by such program, which reaches a peak of 20% of new enrollments in 2018 but ceased since mid-2019, once modifications in Peruvian law restricted such migration. A second major finding is the increasing proportions in time of Venezuelan migrants who entered into care in AIDS stage and with HIV diagnosed in Peru.

The profile of the initial migrants who entered the HIV Program were men who have sex with men diagnosed in Venezuela, without AIDS, and with a high proportion of viral suppression at enrollment. As our results showed, the number of PLWH whose HIV diagnosis was made in Peru increased in later periods in parallel with the cases in AIDS stage at diagnosis. Compared to native citizens, migrant populations tend to present with advanced HIV disease at their initial healthcare encounter at host countries.[12,20,21]

Our findings also are consistent with an initial "healthy migrant effect"[22]: the initial migrants usually have better conditions than those that migrate later, especially those virally suppressed at baseline. Interestingly, despite baseline characteristics, migrant PLWH diagnosed in Peru had better results for viral suppression (74.2% vs 70.7%) and virologic failure (6.9% vs 16.5%) compared with those diagnosed

in Venezuela, which might respond to a differential risk of ART interruptions and viral resistance by time of enrollment.

We should remark that the increasing trend of enrollments in our HIV program started to diminish in late 2018 and was clearly reduced in 2019, after the imposition of new border control laws[23] which also increased documentation requirements. Although our study did not directly assess the implications of those border control laws, our findings suggest their potential effect on limiting access to HIV care, a situation that implies a higher risk of HIV-related complications. Relatedly, an increase of morbidity of various diseases has been reported in the Colombia and Brazil borders.[20]

Ten percent of our study population had not started ART until the end of follow-up, mainly restrained by economic and time reasons; in addition, only 61% had viral load measures to assess viral suppression, without differences comparing PLWH diagnosed in Peru and Venezuela. In a situation well described which ultimately affects HIV care,[11,22,24] direct and indirect costs (medical appointment, laboratory tests, transport, and day of work missed) could be unaffordable for migrant PLWH, even though the HIV program provides free ART drugs and ART laboratory monitoring. Poverty, social support, mental health problems, and legal status need to be addressed as major barriers for the continuity of HIV care of migrants.[12,25]

Women are particularly vulnerable to the violence and disparities of migration processes.[25] According to a local study, 17.8% of Venezuelan women in Peru reported being victims of harassment and 2.9% knew a victim of sexual assault.[26] In our study, women represented a minority (9.5%) throughout the whole period, but the percentage of women in 2019 exceeded that of the two previous years combined. According to the International Organization for Migration, from July to December 2019, the percentage of Venezuelan women crossing the Peruvian border was, for the first time, slightly higher than men.[23,27] Given that migrants might face a high-risk environment for HIV transmission[25] determined by the confluence of poverty, violence, and at-risk sexual behaviors, it is important to understand if sexual violence and/or sexual work is driving the increase of HIV cases among Venezuelan women.

The barriers for obtaining a legal status contribute to informal and "under the table" workers' status, limiting healthcare access.[28,29] Moreover, once the Venezuelan migration in Peru became noticeable, migrants might have encountered an increasing wave of xenophobia and discrimination.[30,31] Thus, beyond the burden of HIV stigma, Venezuelan PLWH might have faced xenophobia and negative context reception,[32] which directly affect their mental health[33,34] and hamper linkage to health services and retention in care. In this context, it is possible that, through a snowball effect, migrant PLWH could share information about certain HIV health services as "safer places" for peers. Although not addressed in this study, such circumstance could contribute to the preferential enrollment of migrants at specific centers. Indeed, the experiences that migrants face to access health services and treatment for different health conditions merit additional research.

Incomplete or missing information was an expected limitation for our secondary data analysis, considering that Peruvian health information systems lack integration of patient health information across health centers and that death is not consistently reported in the case of undocumented migrants.[35] Thus, with data of death and hospitalizations restricted to our study center, our reports could underestimate the real numbers; however, careful revision and contrast of different sources improved the quality of our data. There could be information bias on denying a previous HIV diagnosis/treatment in Venezuela possibly to avoid possible further discrimination or facilitate access to health services. A selection bias can affect our cross-sectional component which focused on a nonrandom sample of the population who were actively receiving ART, as the group that abandoned ART were not localized to answer the questionnaire despite home visits and telephone calls. Finally, our study is previous to the COVID-19 pandemic; lockdowns and closure of international borders might further aggravate the context here presented.

Conclusions

In conclusion, there was a major entry of Venezuelan PLWH to our HIV Program in Lima between 2017 and 2019, although it diminished after suspension of a favorable law for Venezuelan migration to Peru. Throughout such period, both HIV diagnosis in Peru and worsening clinical situation at entry increased over time. To foster HIV continuity of care in migrants, we suggest expanding the access to diagnostic tests for early HIV diagnosis and improve the engagement to health services to prevent disease progression. Interventions to strengthen patient-centered HIV services, such as reducing waiting times, wider periods between medication pickup, more opportunities for viral load and CD4 count measurements, can benefit HIV care continuity of migrant population. Migration policies and regulations that facilitate legal status and appropriate medical attention for special cases might strategically contribute to global HIV control.

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Author contributions

Genesis S Huerta-Vera completed the data collection, formal analysis, and did the original draft preparation. Manuel A Amarista was responsible for conceptualization and methodology. Fernando

A Mejía was responsible for conceptualization and supervision. Ana B Graña was responsible for the project administration, resources, and conceptualization. Elsa V Gonzalez-Lagos supervised the study and did the review and editing of the manuscript. Eduardo Gotuzzo was responsible for conceptualization, methodology, funding acquisition, study supervision, manuscript review, and editing.

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