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Latent tuberculosis in migrants travelling through the northeast regions of Mexico

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ABSTRACT

Background: Latent tuberculosis infection (LTBI) affects nearly a quarter of the global population. Public health interventions aimed at interrupting tuberculosis transmission do not routinely include systematic screening of migrant populations for LTBI in Mexico, nor other high-income countries. However, early detection and treatment of LTBI in immigrant populations from high-burden countries are recommended by the World Health Organization.

Objective: The objective of this study was to determine the proportion of migrants with LTBI in shelters in northeastern Mexico.

Methods: In this cross-sectional study, blood samples were obtained from 455 migrants living in shelters in northeastern Mexico during January 2017 to October 2019. LTBI was diagnosed using the QuantiFERON®-TB Gold Plus test.

Results: Most of the migrants evaluated in this study were from Honduras; ~86% were male; the average age was 29 ± 10 years. LTBI was identified in 18.4% of those from Central America. Migrants from El Salvador and Nicaragua were more likely to have LTBI than those from Honduras or Guatemala. Overweight or obese persons and older persons had a higher prevalence of LTBI. We detected no significant differences with respect to LTBI when the results were compared based on gender, education, or marital status.

Conclusion: The LTBI rates amongst migrants from Central America recently screened in shelters in northeastern Mexico appears to be relatively low given recent estimates of LTBI prevalence in Mexico.

1. Introduction

According to the World Health Organization (WHO), latent tuberculosis infection (LTBI) affects 1.7 billion people, a number that represents ~ 23% of the global population [1], ~12% of whom will ultimately develop active disease [2–4].

In Mexico, in 2016, the most recent year for which published state-specific tuberculosis (TB) case rates are available, the published national incidence of TB was reported to be 13.8 cases per 100,000 persons [5]. In the states of Nuevo León and Coahuila on the Mexico-U.S. border, the comparable TB prevalence published by the same source was higher than the national average, with case rates of disease in 24.4 and 14.6 cases per 100,000 persons, respectively [5].

Interferon-Gamma Release Assays (IGRAs), including the commercially-available QuantiFERON®-TB Gold Plus (Qiagen, Hilden, Germany), are amongst the most widely used tests for detecting LTBI since the assay helps discriminate between those who have LTBI and those who do not have LTBI but have been vaccinated with Bacille Calmette Guérin (BCG), and, as a consequence, may react positively to a tuberculin skin test (TST) [6–9].

A large number of studies have shown that the QuantiFERON®-TB Gold Plus's sensitivity and specificity for detecting LTBI are equal or superior to those of the TST in evaluations carried out in children, adults, and those chronically-infected with human immunodeficiency virus (HIV) [8–12].

Reactivation of latent infection is a commonplace occurrence

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amongst immigrants; latent infection may remain undetected for several years after arrival in the new host country [13]. Early detection and treatment of LTBI in immigrant populations from high-burden countries have been recommended to reduce the prevalence of active TB as part of an overall strategy aimed at eliminating TB [14].

The principal aim of this study was to evaluate a population of migrants recently in transit through Northeast Mexico to determine what percentage test positive for LTBI using the QuantiFERON®-TB Gold Plus assay

2. Methods

2.1. Population

This study focused on migrants residing while in transit in two large shelters within the states of Nuevo Leon and Coahuila, respectively, during the period of January 2017 to October 2019. The study included 455 persons > 12 years old residing in the shelters temporarily and migrating to the United States from any part of Central America or Mexico. Persons with chronic cough and/or active TB, those with clinical characteristics compatible with a diagnosis of TB, or those with positive smears and/or positive cultures were excluded from the study. Persons who were unable to respond to the questionnaire or to participate in blood sampling, for reasons such as blindness or difficult venous access, were also excluded. Amongst those initially enrolled, persons who did not complete the questionnaire, or on whom blood was not drawn, or whose blood samples were insufficient in quantity for evaluation were removed from the study. After exclusions, everyone completed the questionnaire; however, blood samples were collected from only 316 persons. For the cross analysis, data for migrants from Costa Rica, Cuba, and Ecuador were sparse (each < 1%) and were excluded. Therefore, the cross-analysis tables only include data from 297 persons.

2.2. Study design

The present study was observational, descriptive, and cross-sectional. This was registered with the University of Monterrey Research Committee, after which appropriate permits were obtained from the migrant home administrators, and study visits were made every 15 days. Two shelters were reviewed; they are located in the states of Coahuila and Nuevo Leon and have a population that changes on a daily basis. The shelters offer food and housing to migrants in transit for a period of 3–5 days. The study visits were conducted on random days throughout a given week, and all eligible persons in the shelters at that time were invited to participate in the study. Those who agreed to participate provided written informed consent. Written informed consent was also obtained from parents of participants aged 12–17 years (inclusive).

2.3. Questionnaire

Following receipt of informed consent, a standardized questionnaire was administered by trained public health personnel. This questionnaire collected sociodemographic data and medical history including participant age, gender, marital status, country of origin, and status whether travelling alone or accompanied by others, and data related to health and comorbidities, such as diabetes.

2.4. Procedures

All participants (n = 455) who completed the questionnaire underwent a somatometric evaluation that included weight and height measurements used to calculate a body mass index (BMI). They then were given an option of having blood drawn for glucose level and QuantiFERON®-TB Gold Plus (QFT®-Plus) testing. If consent was provided, blood samples were drawn. Participants who chose to have blood samples drawn were asked to fast for at least 8 h prior to blood drawing.

After authorization for blood collection was obtained, approximately 4 ml blood that was needed to fill the QuantiFERON tubes was obtained by direct peripheral venipuncture. The QFT®-Plus test was performed by qualified laboratory personnel who were blinded with respect to the participants' clinical details. Blood was placed in each of the 4 different collection tubes included in the QFT®-Plus kit at 1 ml per tube. Tube number 1 was the negative control and contained no antigens; tubes numbered 2 and 3 contained antigenic peptides TB1 and TB2, which are associated with the *Mycobacterium tuberculosis* complex, and tube number 4 contained mitogen as a positive control. The tubes, with each participant's blood samples, were incubated for 16–24 h at 37 °C. Gamma-interferon (IFN-γ) produced (UI/ml) in response to the TB antigens was determined using an ELISA plate contained in the kit and read on an ELISA plate reader. A positive QFT®-Plus test is one in which the IFN-γ (IU/ml) response to either TB antigen is significantly higher than the response measured in the negative control tube. A diagnosis of LTBI was made according to the results of the QFT®-Plus test. The results were considered positive, negative or undetermined according to criteria established by the manufacturer's software (QIAGEN, Hilden, Germany).

2.5. Statistical analysis

All questionnaire data were maintained in a Microsoft Office Excel database. Statistical analysis was performed using the statistical package of SPSS version 25.0. For the statistical analysis, the proportions were calculated by dividing the value obtained from the total of the participants who answered the questionnaire or took the measurement. For the cross analysis, the data of migrants from Costa Rica, Cuba and Ecuador were excluded because of sparse data. Frequency differences, identified in the crossover analysis, were evaluated using chi-square test with Yates correction, while mean differences were determined using Student's *t*-test. Statistical significance was defined as $p \leq 0.05$.

3. Results

Our study enrolled 455 migrants; their countries of origin are included in Table 1. Most of the participants were from Honduras (71%). Only 6.4% of the migrants were Mexicans and one migrant (0.2%) was from South America. A large fraction (88.5%) of the participants who answered the survey was male; the vast majority was unmarried with only a primary education (Table 2). The mean age was 29 ± 10 years, mean weight was 67.5 ± 12.9 kg and mean height was 1.66 ± 0.08 m. Mean values for blood glucose, BMI and blood pressure were within normal ranges (data not shown).

The principal comorbidities reported by the participants in this study were being overweight, obesity, and diabetes. The proportion of participants reporting these disorders is shown in Table 2.

Only 316 of the 455 participants gave blood samples for testing.

Table 1
Countries of origin of migrants in shelters participating in evaluation for latent tuberculosis infection, Coahuila and Nuevo Leon, Mexico, 2017–2019.

Country	Frequency (n)	Percentage (%)
Honduras	323	71.0
El Salvador	27	5.9
Nicaragua	24	5.3
Guatemala	25	5.5
Mexico	29	6.4
Costa Rica	2	0.4
Cuba	3	0.7
Ecuador	1	0.2
No response	21	4.6
	455	100.0

Table 2
Sociodemographic characteristics of migrants in shelters participating in evaluation for latent tuberculosis infection, Coahuila and Nuevo Leon, Mexico, 2017–2019.

Characteristic		Frequency (n)	Percentage (%)
Sex	Male	394	88.5
	Female	51	11.5
	No response	10	
Marital status	Single	274	63.8
	Married	62	14.5
	Consensual union	85	19.8
	Separated/divorced	8	1.8
	No response	26	
Education	Primary school	205	49.8
	Secondary school	117	28.5
	High school	48	11.7
	College/university	21	5.1
	No education	20	4.8
	No response	44	
[a]Diabetes	Yes	22	5.8
	No	353	94.2
	No tested	80	
[b]Overweight	Yes	115	26.5
	No	318	73.5
	No tested	22	
[c]Obesity	Yes	47	10.8
	No	386	89.2
	No tested	22	

[a] Diabetes: Fasting blood glucose levels > 120 mg/dL.
[b] Overweight: BMI > 25 kg/M^2 SC.
[c] Obesity: BMI > 30 kg/M^2 SC

Table 3
Cross-analysis of QuantiFERON TB Gold Plus results of migrants in shelters participating in evaluation for latent tuberculosis infection, Coahuila and Nuevo Leon, Mexico, 2017–2019.

Variable		Positive QFT®-Plus	Negative QFT®-Plus	p
Age		34.31 ± 9.94	29.13 ± 9.63	0.001
Country of origin	Honduras	30 (13.9%)	186 (86.1%)	0.001
	El Salvador	10 (41.7%)	14 (58.3%)	
	Nicaragua	7 (43.8%)	9 (56.3%)	
	Guatemala	4 (19.0%)	17 (81.0%)	
	Mexico	6 (30.0%)	14 (70.0%)	
Sex	Male	49 (19.1%)	208 (80.9%)	0.955
	Female	7 (19.4%)	29 (80.6%)	
Marital status	Single	32 (17.9%)	147 (82.1%)	0.602
	Married	10 (27.0%)	27 (73.0%)	
	Consensual union	12 (17.9%)	55 (82.1%)	
	Separated/divorced	2 (33.3%)	4 (66.7%)	
Education	Primary school	22 (16.8%)	109 (83.2%)	0.710
	Secondary school	20 (24.1%)	63 (75.9%)	
	High school	7 (17.9%)	32 (82.1%)	
	College/university	4 (26.7%)	11 (73.3%)	
	No education	2 (12.5%)	11 (84.6%)	
[a]*Diabetes*	Yes	4 (26.7%)	11 (73.3%)	0.610
	No	45 (18.0%)	205 (82.0%)	
[b]*Overweight or* [c]*Obesity*	Yes	33 (27.0%)	89 (73.0%)	0.003
	No	20 (12.4%)	141 (87.6%)	

p = The chi-square statistic with Yates correction for qualitative variables, Student's *t*-test for quantitative variables.
[a] Diabetes: Fasting blood glucose levels > 120 mg/dL.
[b] Overweight: BMI > 25 kg/M^2 SC.
[c] Obesity: BMI > 30 kg/M^2 SC.

Using the QuantiFERON TB Gold, 18.4% (51/277) of the migrants from Central America (excluding migrants from Mexico, Costa Rica, Cuba and Ecuador) were diagnosed with LTBI. In the cross analysis (Table 3), we found that participants originally from El Salvador and Nicaragua were more likely to test positive for LTBI; those originally from Honduras and Guatemala were less likely to test positive, and LTBI rates were lower who those determined for migrants who were originally from Mexico. These differences were statistically significant ($p < 0.001$). Older people and migrant people with some degree of obesity also showed a higher LTBI prevalence. Finally, no statistically significant differences were found when the results were evaluated according to participants' gender, education, diabetes, or marital status (Table 3).

4. Discussion

The overall LTBI rate amongst Central American migrants in this study was 18.4%. Those who had recently arrived from Central America exhibited lower LTBI rates than those who were from Mexico. Migrants from Nicaragua and El Salvador had the highest percentages with LTBI, at 43.8% and 41.7%, respectively; migrants from Honduras had the lowest percentage (13.9%). However, relatively few of the migrants who participated in our study came from El Salvador or Nicaragua (only 11.3% of the total migrant population), while a large percentage (71%) of the migrants in the shelters we assessed came from Honduras. The percentages of Central American migrants in relation to their countries of origin were similar to those previously reported at the border of Mexico and Guatemala by Santiago et al. in 2014 [15]. The relative rates of LTBI amongst these migrants were not consistent with the relative annual rates of active TB observed in their countries of origin. The 2018 WHO annual TB case rate estimates were 70 per 100,000 for El Salvador, and 41, 37, and 23 per 100,000 for Nicaragua, Honduras and Mexico, respectively [1].

Although there have been some studies on the prevalence of LTBI in specific populations in Mexico [16–17], there have been no regional studies focusing on LTBI in Mexico or Central America. One recent study featured a mathematical model that suggested a high LTBI prevalence in Mexico but not for Central America; with estimated percentages of LTBI of 27% in Mexico, 15.1% Honduras, 10.5% Guatemala, 3.8% Nicaragua, and 6.5% El Salvador [18]. In our study population from the Mexico-United States border, Central American migrants had lower rates of LTBI than did Mexican migrants [16,19–20].

In our data, overweight or obese people and older people had a higher prevalence of LTBI. Body mass index has been correlated with having LTBI in at least two other studies [21–22]. The correlation of having LTBI with age is easily explained as older populations have had more time and exposure to acquire TB infection. In general, the migrants in this study were young people with little comorbidity; for this reason, although a cross analysis was performed, some of the cross analysis boxes had data too sparse to observe or infer statistically significant differences between populations."

Screening of refugees in travel is neither carried out on a routine basis in Mexico, nor is it standard procedure in other high income countries [23–24]. This study presents a unique picture of a select population of refugees in Mexico on which few current data exist; this population may go on to influence TB case rates both in Mexico and in the United States. The results of this study suggest that consideration be given to monitoring migrants from El Salvador and Nicaragua more closely than from other Central American countries due to the high rates of LTBI observed in this sample population, travelling under conditions that may also predispose them to disease reactivation. However, the LTBI rates amongst migrants from Central America recently screened in shelters in northeastern Mexico appears to be relatively low given recent estimates of LTBI prevalence in Mexico.

CRediT authorship contribution statement

Obed Medina-Macías: Conceptualization, Methodology, Software. **Philippé Stoessle:** Conceptualization, Supervision. **Leonardo E. Perales-Rendón:** Software. **Jorge E. Moreno-Cuevas:** Conceptualization. **Francisco González-Salazar:** Conceptualization, Software.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethical considerations

This work complies with established general health laws on research in Mexico and the Declaration of Helsinki for human research.

This work has been approved by the Research Ethics Committees of the University of Monterrey, Nuevo León, Mexico, with the number 042016-ClE. All participants provided their written informed consent before being included in the study.

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