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Brief communication

Social and clinical predictors of drug-resistant tuberculosis in a public hospital, Monterrey, Mexico

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ABSTRACT

Purpose: Drug-resistant tuberculosis (DRTB) is steadily increasing in Mexico, but little is known of patient risk factors in the Mexico–United States border region. This preliminary case-control study included 95 patients with active pulmonary TB with drug susceptibility results attending the José E. González University Hospital in the urban hub of Nuevo León—the Monterrey Metropolitan Area. We report potential social and clinical risk factors of DRTB among this hospital-based sample.
Methods: We collected data through face-to-face interviews and medical record reviews from 25 cases with DRTB and 70 drug-sensitive controls. DNA was collected to assess an effect of genetic ancestry on DRTB by using a panel of 291,917 genomic markers. We calculated crude and multivariate logistic regression.
Results: After adjusting for potential confounding factors, we found that prior TB treatment (odds ratio, 4.5; 95% confidence interval, 0.9–21.1) and use of crack cocaine (odds ratio, 4.6; 95% confidence interval, 1.1–18.7) were associated with DRTB. No other variables, including genetic ancestry and comorbidities, were predictive.
Conclusions: Health care providers may benefit from recognizing predictors of DRTB in regions where routine drug susceptibility testing is limited. Prior TB treatment and illicit drug use, specifically crack cocaine, may be important risk factors for DRTB in this region.

Introduction

Drug-resistant tuberculosis (DRTB) is increasing along the Mexico–United States border region, but little is known about patient risk factors [1,2]. Previous research has highlighted the concern of DRTB in this region and called for a better understanding of the predictors of drug resistance [1,3,4]. Nuevo León, one of six Mexican states bordering the United States, has the second highest prevalence of DRTB cases [5]. More than 90% of TB cases in Nuevo León occur in its urban center, the Monterrey Metropolitan Area (MMA), located 140 miles southwest of Laredo, Texas. The MMA is the third most populous metropolitan area in Mexico with approximately 4 million inhabitants. Recent studies have reported extensive drug resistance in the MMA [6], particularly among cases that have been previously treated with anti-TB drugs [3].

Because of the selective use of resources in Mexico, testing of suspect TB cases in the general population is limited to acid-fast bacilli smears. In most hospitals, routine cultures and drug susceptibility testing are not conducted, rather, they are often reserved for special case situations, such as if drug resistance is suspected from initial treatment failure [7]. Given financial constraints that prohibit routine cultures and drug susceptibility testing (DST) within most hospitals, health care providers may benefit from identifying patient risk factors for drug resistance. To this end, we explored the role of social factors and clinical measures on DRTB among a hospital-based sample of pulmonary TB patients in the MMA.

Conflicts of interest: None.

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Methods

Study population

We conducted a case-control study from January 2010 to February 2011 at the public José E. González University Hospital in Monterrey. This 500-bed teaching, research, and assistance facility treats approximately 25% of new TB cases in the MMA each year. As part of the Autonomous University of Nuevo León, the University Hospital receives University-based resources to conduct cultures on all suspect TB patients and the first-line DST for cases with positive cultures. The hospital's "open-door policy" treats all patients regardless of insurance status or income, and primarily serves a low socioeconomic status population [6].

The study sample was recruited from the hospital's TB clinic and included 95 adult individuals with culture-confirmed pulmonary TB disease who were being seen for diagnosis, treatment, or follow-up. Participants were recruited for the study by the TB-clinic nurse; individuals who declined enrollment did not differ from participants in terms of sex, age, or socioeconomic status.

Selection of cases and controls

DRTB cases ($n = 25$) were confirmed through mycobacteriology DST and included patients with a TB isolate that was resistant to the action of one or more first-line TB drugs: isoniazid (INH), rifampin (RIF), ethambutol (EMB), and pyrazinamide (PZA). Although streptomycin (SM) is used only in cases that did not respond to the other first-line drugs, it is still considered a first-line anti-TB drug in Mexico [2,8]. Twenty-three DRTB patients (92%) had been previously treated for 30 days or more, known as secondary or acquired resistance, and 2 (8%) had never been treated or had received less than 30 days of treatment, known as primary or initial resistance. A total of 17 DRTB cases (68%) were multidrug-resistant tuberculosis (MDR-TB), defined as drug resistance to at least INH and RIF.

Controls ($n = 70$) represented individuals with culture-confirmed pulmonary TB disease that responded to first-line medications, also known as pan-susceptible. Controls were not matched to cases with respect to clinical or demographic characteristics. Exclusion criteria were extrapulmonary TB and human immunodeficiency virus (HIV) because patients with these characteristics represented too small a subset for stratified analysis. HIV among this study population is considered to be low, as seen with a previous study of pulmonary TB patients sampled from January 31, 1996 to March 31, 1998 from the University Hospital's TB clinic that showed HIV seropositivity in only three of 103 patients aged younger than 40 years, and no clinically suspect cases or risk factors for HIV among 83 TB patients aged older than 40 years [6].

Mycobacteriology

The University Hospital's laboratory performed all mycobacteriology testing for the study. Cultures were conducted with specimens on Löwenstein–Jensen slants and identified as positive for *Mycobacterium tuberculosis* based on a positive niacin test. DST was conducted on initial isolates using the proportion method [9]. Drug concentrations (microgram per milliliter) were used to test the susceptibility for INH (0.2), RIF (40), SM (4), and EMB (2), and resistance was defined by 1% or more of growth on the drug-containing medium compared with the control medium.

Data collection and analysis

To investigate patient risk factors for DRTB, we conducted face-to-face interviews, reviewed medical records, and assayed Native American, European, and African genetic ancestry from 291,917 single nucleotide polymorphisms [10]. The interview questions were derived from established Mexican and other Latin American questionnaires and hospital risk assessments [11,12]. Interviews were conducted based on patient availability at random points during the treatment process. Comorbidities, such as diabetes, were queried in the interview and confirmed by reviewing medical records.

Crude associations between DRTB and the social, clinical, and genetic ancestry variables were assessed using Pearson's chi-square tests, Fisher's exact tests, and *t*-tests. Potential risk factors of DRTB were introduced into multivariate logistic regression models and retained based on a significance level of 0.1 [13]. Multicollinearity of variables was assessed using a variance inflation factor cutoff of 2.5. We reported crude and adjusted odds ratios (OR) and 95% confidence intervals (CI) for the full and final models. Statistical analyses were performed in SAS 9.3 (SAS Institute Inc., Cary, NC, 2008).

This project was approved by the Institutional Review Boards of the University of New Mexico (No. 09-318) and the Autonomous University of Nuevo León (No.IN09-001). Participation was voluntary and participants gave informed, written consent.

Results

Sample characteristics

The mean age of the sample was 44.9 years (SD, 17.1), 54% were male, 72% had an education level of secondary or less, and 74% were unemployed or had nonprofessional employment for most of their life. Most participants reported nonindigenous ethnicity and did not speak an indigenous language (82%). Genetic ancestry proportions estimated from the polymorphisms ranged from 1.5% to 57.8% European, 39.6% to 98.5% Native American, and 0% to 8.1% African. Mean sample ancestry estimates were 37.2% (SD, 11.7), 58.2% (SD, 12.7), and 4.3% (SD, 2.0) for European, Native American, and African, respectively. Participants represented all MMA municipalities, with the highest proportion from Monterrey (39%).

The drug resistance patterns for the 25 DRTB cases are displayed in Table 1. Five patients (20%) had monoresistance to INH or SM, and three (12%) had polyresistance to INH + SM, and INH + SM + PZA. There were 17 cases (68%) with multidrug resistance, three of which were resistant to all five drugs (Table 1). DST results for PZA were

Table 1
Drug resistance patterns to the first-line anti-TB drugs among the 25 DRTB cases recruited at the José E. González University Hospital, Monterrey, Mexico, 2010–2011

Drug resistance patterns	*N*	%
Monoresistant		
RIF	0	0
INH	2	8
EMB	0	0
PZA*	0	0
SM	3	12
Subtotal	5	20
Polyresistant		
INH + SM	2	8
INH + SM + PZA	1	4
Subtotal	3	12
Multidrug resistant		
INH + RIF	2	8
INH + RIF + EMB	7	28
INH + RIF + SM	1	4
INH + RIF + SM + EMB	3	12
INH + RIF + SM + PZA	1	4
INH + RIF + EMB + PZA + SM	3	12
Subtotal	17	68
Total	25	100

EMB = ethambutol.
* PZA susceptibility results were unavailable for 20 cases.