

Tuberculosis in the Foreign-Born Population of Tarrant County, Texas by Immigration Status

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The epidemiology of tuberculosis is changing in the United States as a result of immigration, yet the extent to which different classes of immigrants contribute to overall morbidity is unknown. Tuberculosis in nonimmigrant visitors is of particular interest as they are currently exempt from screening requirements. We conducted a prospective survey of all culture-positive tuberculosis patients in Tarrant County, Texas from 1/98 to 12/00. Immigration status of foreign-born patients was classified as permanent residents, undocumented, or nonimmigrant visitors. Of 274 eligible participants, 114 (42%) were foreign-born; of these, 67 (59%) were permanent residents, 28 (25%) were undocumented, and 19 (17%) were nonimmigrant visitors. Among the foreign-born, we observed significant differences by immigration status in multidrug resistance ($p = 0.02$), human immunodeficiency virus (HIV) infection ($p = 0.0007$), and hospitalization ($p = 0.03$ for ever/never, 0.01 for duration). Compared with other immigrants, more non-immigrant visitors were multi-drug-resistant (16% versus 11% of undocumented residents and 1% of permanent residents), were HIV-positive (32% versus 0% of undocumented and 5% of permanent residents), were hospitalized (47% versus 36% of undocumented and 19% of permanent residents), and had lengthy hospitalizations (median [midspread] days = 87 [25 to 153] versus 8.5 [4 to 28] for undocumented and 10 [7 to 24 d] for permanent residents). We found nonimmigrant visitors to be an important source of tuberculosis morbidity in Tarrant County. Further studies in other regions of the U.S. are needed to determine if screening and treatment recommendations of persons who spend extended periods in the U.S. should be raised to the standards set for permanent residents.

Keywords: tuberculosis; foreign-born; HIV

Immigration is changing the epidemiology of tuberculosis in the developed world (1–4). Similar trends are occurring in the U.S. with an increasing proportion of tuberculosis morbidity occurring in the foreign-born population (5–6). The World Health Organization (WHO) has identified the movement of people from high prevalence areas to industrialized nations as one of the causes of the worldwide increase in tuberculosis prevalence (7). WHO estimates that one-third of the world population is infected with *Mycobacterium tuberculosis* (MTB) (8). Prevalence of infection varies with country of origin and is as high as 50% in some groups, such as refugees (9). This has important implications for tuberculosis control in the U.S., where the overall foreign-born population has increased from 5% in 1970 to 10% in 2000 (10) and where certain areas attract large numbers of immigrants; for example, 40% of the New York City population is foreign-born (11).

Tuberculosis incidence in the U.S. is highest among recent arrivals to the country (12). Whereas immigrants and refugees are required to be screened for tuberculosis before entry, persons entering the U.S. on nonimmigrant visas (students, tourists, diplomats, and temporary workers) are not screened unless they apply for permanent residence status (13). Because data on immigration status are not collected by the Centers for Disease Control and Prevention (CDC) on its case report form (6), the extent to which different classes of immigrants contribute to tuberculosis morbidity is unknown (6,13). The American Medical Association recently recommended studying the epidemiology of tuberculosis in nonimmigrant visitors and researching the feasibility of tuberculosis screening in this group (13). This report presents data on tuberculosis in the foreign-born population of Tarrant County, Texas by immigration status.

METHODS

Data were collected prospectively on all cases reported to the Tarrant County, Texas Health Department between January 1, 1998 and December 1, 2000. The health department serves the western portion of the Fort Worth–Dallas metropolitan area and includes a population of approximately 1.3 million (14). The Fort Worth–Dallas metroplex is the ninth largest metropolitan area in the United States (15). To be eligible for inclusion, patients had to be culture-positive for MTB. Children with recent positive skin tests, abnormal chest X-rays consistent with tuberculosis, and contact with a culture-proven tuberculosis patients were also included. The institutional review board of the University of North Texas Health Science Center at Fort Worth, Texas approved the study.

Eligible patients participated in a structured interview designed to obtain demographic and life history data and, as part of their initial medical evaluation, to determine the presence of adult human immunodeficiency virus (HIV) risk factors. Foreign-born patients were asked their current visa status. All interviews were administered by one of us (S.E.W.). When face-to-face interviews were not possible, data were obtained from medical records and interviews with family members.

Drug susceptibility patterns of MTB isolates were determined by the Mycobacteriology Laboratory at the Texas Department of Health using a Bactec radiometric system (Becton Dickinson, Paramus, NJ) and, in cases where the isolate showed resistance, testing was performed by the proportion method on Middlebrook 7H10 medium (Fisher Scientific, Houston, TX). We analyzed the following resistance patterns: initial, multidrug (MDR; at least isoniazid and rifampin), isoniazid (isoniazid alone or with anything other than rifampin), and streptomycin.

Patients born in the U.S. (or one of its territories) were considered U.S. natives; all others were considered foreign-born. Each foreign-born patient was classified into one of three categorical groups: permanent, nonimmigrant visitor, and undocumented. By convention, “permanent residents” are aliens admitted to the U.S. as lawful, permanent residents, including immigrants and refugees. “Nonimmigrant visitors” are aliens admitted for a specified purpose and for a temporary period of time, including visitors, temporary workers, asylum seekers, and students (16). “Undocumented persons” are aliens who enter the U.S. without entry documents.

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TABLE 1. BIRTH COUNTRIES OF FOREIGN-BORN TUBERCULOSIS PATIENTS

Birth Country	Permanent* (n = 67)		Undocu- mented (n = 28)		Nonimmigrant Visitor† (n = 19)	
	(n)	(%)	(n)	(%)	(n)	(%)
Mexico	17	25	27	96	3	17
Southeast Asia‡	22	33	0	0	0	0
Sub-Saharan Africa§	9	13	0	0	9	50
South Asia¶	3	4	0	0	5	28
Philippines	4	6	0	0	1	6
Central America¶	3	4	1	4	0	0
China/Taiwan	3	4	0	0	0	0
Europe **	4	6	0	0	0	0
Iraq	1	0	0	0	0	0
Japan	1	0	0	0	0	0

* Citizens, immigrants, and refugees.

† Work, student, and visitor visas (unscreened).

‡ Cambodia, Laos, and Vietnam.

§ Cameroon, Congo, Ethiopia, Ghana, Kenya, Liberia, Somalia, Nigeria, Sudan, Togo, Uganda, and Zaire.

¶ India, Pakistan.

¶ El Salvador, Guatemala, and Honduras.

** Bosnia, England, Poland, and Macedonia.

Statistical Analysis

Global comparisons among groups were done using Fisher exact test for categorical variables and analysis of variance for continuous variables. For the latter, nonparametric analyses were done using the Wilcoxon rank sum (2 groups) or Kruskal-Wallis (3 groups) test. In these instances, we report medians and midspreads (25th to 75th percentiles) for descriptive purposes. For categorical variables, logistic regression was used to compute maximum likelihood estimates of odds ratios (OR) and 95% confidence intervals (CI) associated with specific groups. For continuous variables, planned comparisons between nonimmigrant visitors and all other foreign-born subjects were done using analysis of variance with orthogonal contrasts. Subjects with missing data were excluded from relevant analyses. All tests were nondirectional with a 0.05 significance level.

RESULTS

Direct interview data were available for 253 of 274 eligible patients (92%); for the remaining 21 patients, data were from medical records and family interviews. 114 (42%) patients were foreign-born; of these, 67 (59%) were permanent residents, 28 (25%) were undocumented residents, and 19 (17%) were nonimmigrant visitors. Of the 19 nonimmigrant visitors, seven entered the U.S. with student visas, seven with visitor vi-

sas, and five with temporary work visas. Birth country was quite varied among permanent residents, whereas 96% of undocumented residents were from Mexico and 50% of nonimmigrant visitors were from sub-Saharan Africa (Table 1). Median number of months in the U.S. before diagnosis was 108 (midspread = 36 to 210) for permanent residents, 24 (midspread = 12 to 60) for undocumented residents, and 15 (midspread = 3 to 36) for nonimmigrant visitors. Foreign-born patients were significantly younger than natives [mean (SD) years = 38 (17) versus 48 (16); $p < 0.0001$] and, among foreign-born patients, age significantly differed by immigration status [mean (SD) years = 43 (19) for permanent, 30 (12) for undocumented, and 34 (13) for nonimmigrant visitors; $p = 0.001$].

Differences in drug resistance patterns by immigration status are shown in Table 2. Foreign-born patients were significantly more likely than natives to have initial drug resistance ($p = 0.00002$), MDR ($p = 0.002$), and isoniazid resistance ($p = 0.01$). Among foreign-born patients, MDR significantly differed by immigration status ($p = 0.02$); specifically, nonimmigrant visitors were more likely than permanent residents to be MDR (OR = 12.4, CI = 1.2, 127.0). Birth country was highly correlated with MDR status, with six of seven MDR patients originating from Mexico. Age was unrelated to MDR and primary resistance status. Neither initial nor isoniazid resistance differed by immigration status in foreign-born patients.

HIV screening results were available for 263 (96%) patients. Differences in HIV-related variables are shown in Table 3. HIV coinfection was comparable between native and foreign-born patients; however, natives were significantly more likely to have had adult HIV risk factors: intravenous drug use ($p < 0.00001$); bisexuality or homosexuality ($p = 0.003$); multiple sex partners ($p = 0.00002$); and sex with intravenous drug users ($p < 0.00001$), homosexual males ($p = 0.006$), or someone with HIV ($p = 0.03$). Among foreign-born patients, nonimmigrant visitors were significantly more likely to be HIV coinfecting (32%) than were undocumented (0%) or permanent (5%) residents ($p < 0.0001$). Exposure to HIV risk factors did not differ by immigration status. All nonimmigrant visitors with HIV coinfection were from sub-Saharan Africa. However, after controlling for sub-Saharan African countries of origin, the rate of HIV coinfection among nonimmigrant visitors remained significantly higher than in undocumented and permanent residents ($p = 0.004$). This was because eight of the nine permanent residents who had emigrated from sub-Saharan African countries were not HIV coinfecting.

Hospitalization for tuberculosis by immigration status is shown in Table 4. Native and foreign-born patients were

TABLE 2. DRUG RESISTANCE BY IMMIGRATION STATUS

Resistance Pattern	Immigration Status								p Values	
	U.S. Native (n = 160)		Permanent* (n = 67)		Undocu- mented (n = 28)		Nonimmigrant Visitor† (n = 19)			
	(n)	(%)	(n)	(%)	(n)	(%)	(n)	(%)	N versus FB‡	FB Groups§
Primary resistance	9	6	16	24	7	25	4	21	0.00002	1.00
Multidrug resistance¶	0	0	1	1	3	11	3	16	0.002	0.02
Isoniazid resistance¶	1	1	4	6	2	7	1	5	0.01	1.00
Streptomycin mono-resistance	7	4	7	10	2	7	0	0	0.30	0.49

* Citizens, immigrants, and refugees.

† Work, student, and visitor visas (unscreened).

‡ Native versus foreign-born.

§ Comparison among three foreign-born groups.

¶ Resistant to at least isoniazid and rifampin.

¶ Resistant to isoniazid alone or isoniazid in combination with anything other than rifampin.

TABLE 3. HIV INFECTION AND RISK FACTORS BY IMMIGRATION STATUS

	Immigration Status								p Values	
	U.S. Native (n = 160)		Permanent* (n = 67)		Undocu- mented (n = 28)		Nonimmigrant Visitor [†] (n = 19)		N versus FB [§]	FB Groups
	(n)	(%) [‡]	(n)	(%) [‡]	(n)	(%) [‡]	(n)	(%) [‡]		
HIV-infected	17	11	3	5	0	0	6	32	0.41	0.0007
HIV risk factor										
Used IV drugs	26	17	0	0	1	4	0	0	< 0.00001	0.41
Bisexual or homosexual	11	7	0	0	0	0	0	0	0.003	—
Number of sex partners [¶]										
None	19	14	15	24	5	20	1	5	0.00002	0.08
1 – 2	77	55	46	73	17	68	15	79		
3 – 4	19	14	1	2	2	8	1	5		
> 5	24	17	0	0	1	4	2	11		
Ever had sex with:										
IV drug user	28	20	0	(0)	0	(0)	1	(5)	< 0.00001	0.17
Prostitutes	17	12	4	(6)	1	(4)	2	(11)	0.19	0.74
Someone with HIV	10	7	0	(0)	0	(0)	1	(5)	0.03	0.18
Homosexual male	9	6	0	(0)	0	(0)	0	(0)	0.006	—

* Citizens, immigrants, and refugees.

[†] Work, student, and visitor visas (unscreened).[‡] Percentages are of subjects with available data.[§] Native versus foreign-born.^{||} Comparison among three foreign-born groups.[¶] Maximum number of sex partners in any one year in the last 10 yrs.

equally as likely to be hospitalized for tuberculosis and to have been hospitalized for similar lengths of time. Among foreign-born patients, hospitalization significantly differed by immigration status ($p = 0.03$); specifically, nonimmigrant visitors were more likely to be hospitalized for tuberculosis than permanent residents (OR = 3.7, CI = 1.3, 11.1). Further, duration of hospitalization for tuberculosis significantly differed among foreign-born patients ($p = 0.01$), with nonimmigrant visitors having significantly longer hospitalizations (median = 87 d) than undocumented (median = 8.5 d) or permanent (median = 10 d) residents ($p = 0.002$).

Differences in foreign travel in the 2 yr before diagnosis by immigration status are shown in Table 4. Foreign-born patients were significantly more likely than natives to have traveled outside of the U.S. in the 2 yr before diagnosis (23% versus 4%, $p < 0.00001$), and foreign-born travelers had significantly lengthier travel than natives (median = 42 d [midspread = 28 to 112 d] versus 14 d [midspread = 7 to 30 d], re-

spectively; $p = 0.02$). Travel destinations of the foreign-born were exclusively regions of high tuberculosis prevalence.

DISCUSSION

There are no available data on the relative contribution of immigrants, undocumented immigrants, and nonimmigrant visitors to U.S. tuberculosis morbidity. Ours is the first report on the differences among groups of foreign-born tuberculosis patients by immigration status. We found that nearly one in five foreign-born persons with tuberculosis were nonimmigrant visitors (students, tourists, and temporary workers), who are not currently required to be screened for tuberculosis. In addition, nonimmigrant visitors were more likely to be HIV-infected and to have multi-drug-resistant tuberculosis (though based on small numbers) than permanent residents and undocumented immigrants. Hospitalizations for tuberculosis treatment were more likely and were significantly lengthier among

TABLE 4. HOSPITALIZATIONS FOR TUBERCULOSIS AND FOREIGN TRAVEL BY IMMIGRATION STATUS

	Immigration Status				p Values	
	U.S. Native (n = 160)	Permanent* (n = 67)	Undocumented (n = 28)	Nonpermanent [†] (n = 19)	N versus FB [‡]	FB Groups [§]
No. (%) [¶] ever hospitalized	61 (38)	13 (19)	10 (36)	9 (47)	0.09	0.03
Median (midspread) duration of hospitalization, days [¶]	15 (8–32)	10 (7–24)	8.5 (4–28)	87 (25–153)	0.88	0.01
No. (%) who traveled abroad within 2 yr of diagnosis	6 (4)	18 (28)	6 (23)	1 (5)	< 0.00001	0.13
Median (midspread) duration of travel, days ^{**}	14 (7–30)	38.5 (28–112)	73 (21–180)	28 —	0.02	0.66

* Citizens, immigrants, and refugees.

[†] Work, student, and visitor visas (unscreened).[‡] Native versus foreign-born.[§] Comparison among three foreign-born groups.[¶] Percentages are of subjects with available data; all subjects had available hospitalization data; number of subjects with missing travel data = four U.S. natives, two permanent residents, and two undocumented residents; all subjects who traveled had available data on duration of travel.[¶] Of those hospitalized.^{**} Of those ever traveled.

nonimmigrant visitors compared with permanent residents and undocumented immigrants. We showed that, although 50% of nonimmigrant visitors with tuberculosis were from sub-Saharan Africa, these results could not be entirely explained by their country of origin. These findings have important implications for immigrant screening programs.

A recent report from the Institute of Medicine (IOM) recognized that strategies for dealing with undocumented immigrants from high tuberculosis prevalence countries would be necessary to achieve elimination of this disease in the United States (17). Among its recommendations were treatment of latent tuberculosis with isoniazid as a cost-effective approach for reducing incidence in the foreign-born population, and requiring tuberculosis screening as a condition of receiving permanent residency or "green cards." (17). However, the report made no recommendations for screening of nonimmigrant visitors, which, in this study, comprised 17% of the tuberculosis morbidity. Our data suggest that screening requirements similar to those for permanent residents should be considered for nonpermanent residents who will be spending extended periods in the U.S.

Using chest X-rays to screen for tuberculosis in nonimmigrant visitors is unlikely to be successful. This approach has resulted in very low yield among new arrivals to Canada (13, 18), and it has been observed that 23% of persons developing tuberculosis within 1 yr of arrival to the United States had a "normal" chest X-ray before their arrival (19). In our study, the median duration of time in the U.S. before diagnosis among nonimmigrant visitors was 15 mo. It is probable that some and perhaps most of these patients had normal chest X-rays at the time of their entry into the U.S. These data suggest that an effective program would require chest X-rays, tuberculosis skin tests, and some inducement for completing either preventative therapy or a period of surveillance.

Our findings differ from those of earlier studies. In Manitoba, Canada, surveillance of foreign-born groups between 1981 and 1985 at high risk for developing active tuberculosis based on abnormal chest X-rays failed to identify any student or visitor who later developed the disease (1). A 1992–1993 study in Hawaii found that students and visitors accounted for 4.4% of foreign-born tuberculosis patients (19). In our study, visitors and students comprised 12.5% of foreign-born tuberculosis patients. One approach to the identification and treatment of students might be school screening. However, a CDC study of tuberculosis screening practices at colleges and universities found that these procedures were inconsistent and problematic (20). Only one of the seven students with tuberculosis in our study was identified through a school-screening program. These students attended not only colleges and universities, but also seminaries and technical schools. Our data suggest that the epidemiology of tuberculosis in students is changing, with more foreign-born students developing the disease, and therefore, support the need for school-based screening with tuberculosis skin tests and chest X-rays and treatment programs.

It has been suggested that screening of nonimmigrant visitors would be prohibitively expensive (18). In order to evaluate cost-benefit fairly, however, costs of medical care for these patients must also be assessed. Although tuberculosis is considered an ambulatory disease, the majority of treatment costs result from inpatient rather than outpatient therapy (21). Nonpermanent residents with tuberculosis were more likely to be hospitalized for tuberculosis and were hospitalized for longer durations than undocumented or permanent residents with tuberculosis. Among the 19 nonimmigrant visitors, comorbid conditions that resulted in prolonged inpatient ther-

apy were common: six had coinfection with HIV (all from sub-Saharan Africa) and three were infected with MDR-TB (two from Mexico, one from India), one of whom remains smear-positive and culture-positive after 360 d of inpatient therapy. Nine of the nonimmigrant visitors were hospitalized during the study period for a total of 1,119 d. Only 104 of these days were covered by health insurance; all other inpatient care days and other medical expenses were paid for by the health care system of Tarrant County and the State of Texas. Of the 1,015 nonreimbursed days, 49 were from private hospitals, 372 were from the county hospital system, and 594 were from the state hospital system. The average cost for a hospital stay in the U.S. in 1997 was \$1,033 per day (22). It can be estimated from these data that the cost of treating these patients was in excess of 1 million dollars. These costs must be considered when evaluating the usefulness of screening programs for nonimmigrant visitors.

We found no evidence of longer hospitalization stays among nonimmigrant visitors owing to travel to the U.S. for purposes of medical treatment. Only four foreign-born patients indicated that they had come to the U.S. for medical evaluation: two for unexplained weight loss, one for back pain, and one specifically for MDR-TB treatment. Only one of these patients was a nonimmigrant visitor (visitor's visa); two were permanent residents and one was undocumented. The longer hospital treatment duration of the nonimmigrant visitors was related to their comorbidities of HIV or MDR-TB, which have been shown to result in more frequent and longer hospitalizations (23, 24). The median CD4 count of the HIV coinfecting nonimmigrant visitors was less than 50/mm³ at the time they presented with tuberculosis.

In a nationwide CDC survey of tuberculosis patients from 1993 to 1998, 6.9% were HIV-positive (6). We observed a similar prevalence of HIV coinfection among all foreign-born patients (8%) but substantially higher prevalence in nonimmigrant visitors (32%). Recent immigrants and refugees may have a lower prevalence of HIV infection than the native population as a positive test for HIV is an exclusion for admission to the U.S. (25). Although foreign-born and native patients in our study had similar HIV prevalence, foreign-born patients were less likely than natives to have reported typical HIV risk factors, such as intravenous drug use and high-risk sexual practices. Among the foreign-born, exposure to HIV risk factors did not differ by immigration status. After controlling for sub-Saharan African countries of origin, the rate of HIV coinfection among nonimmigrant visitors remained significantly higher than in undocumented and legal permanent residents ($p = 0.004$). In other words, the relatively high proportion of HIV in nonimmigrant visitors compared with other foreign-born patients could not be explained solely by their country of origin. Rather, the lack of screening in this group was likely a contributing factor. Because all HIV-positive nonimmigrant visitors were from sub-Saharan Africa, it appears that the most important HIV risk factor in the nonimmigrant visitor group was originating from a country with high prevalence of HIV infection.

The drug susceptibility patterns we observed have important implications for treatment of latent and active tuberculosis. Isoniazid has been established through clinical trials in multiple settings to be an effective agent and is the recommended treatment for latent tuberculosis (8). Isoniazid resistance, either alone or in combination with other agents, was present in 12% of foreign-born patients in our study; i.e., approximately one in eight would be expected to receive no benefit from isoniazid treatment of latent tuberculosis due to drug resistance. Of even more concern, based on our data, one in 16

foreign-born tuberculosis patients would be expected to fail treatment with the present standard four first-line drug regime (26). These data suggest the need for additional trials of treatments for latent tuberculosis which do not include isoniazid and for changes in the suggested treatment algorithms for tuberculosis in foreign-born patients.

Recently, international travel to areas of high tuberculosis endemicity has been identified as a risk for acquiring tuberculosis (27, 28). We identified return travel to the country of origin as a previously underappreciated risk for tuberculosis in the foreign-born. Nearly one in four foreign-born patients had traveled to area of high tuberculosis prevalence during the 2 yr before their diagnosis. Several patients gave histories of staying in the same household as persons with active tuberculosis while traveling abroad; others gave histories of onset of symptoms that started during or soon after returning from foreign travel.

These data underestimate the extent of imported tuberculosis treated in Tarrant County as they include only culture-positive cases. During the study time period, we also treated clinical cases of tuberculosis in foreign-born patients that were not culture-positive. A potential source of bias is the possibility that nonimmigrant visitors with tuberculosis or HIV infection preferentially migrated to Tarrant County, although we found no evidence of this. Each temporary worker and student came from different organizations. Nonetheless, our results need to be replicated in other areas of the United States to determine if they are generalizable.

Elimination of tuberculosis in the United States will require global control of the epidemic. Further reductions in tuberculosis rates in the U.S. can occur with improvements in the present system of screening and treatment as suggested by the IOM. These include such measures as participation in tuberculosis screening as a condition of permanent residency and either completing treatment for latent tuberculosis or a period of tuberculosis surveillance. We found that nonimmigrant visitors contributed substantially to tuberculosis morbidity in Tarrant County. This suggests that consideration should be given to raising the standards for screening and treatment recommendations for nonimmigrant visitors to those set for permanent residents. However, because the size of the nonimmigrant population at risk in Tarrant County is unavailable, the feasibility and cost-effectiveness of this strategy is uncertain. Further studies in different parts of the United States are needed to address these issues and to determine the most cost-effective screening and treatment programs for this subgroup of the foreign-born population, which should include determining the minimum length of visits to target.

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