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Toward a generation free of tuberculosis: TB disease and infection in individuals of college age in the United States

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Abstract

Objectives: To assess the magnitude of active TB disease and latent TB infection (LTBI) in young adults of college age.

Participants: Individuals who were aged 18–24 years in 2011 were used as a proxy for college students.

Methods: Active TB cases reported to the 2011 US National TB Surveillance System (NTSS) were included. LTBI prevalence was calculated from the 2011–2012 National Health and Nutrition Examination Survey. The 2011 American Community Survey was used to calculate population denominators. Analyses were stratified by nativity.

Results: Active TB disease incidence among persons aged 18–24 years was 2.82/100,000, 18.8/100,000 among foreign-born individuals and 0.9/100,000 among US-born individuals. In 2011, 878 TB cases were reported; 629 (71.6%) were foreign-born. LTBI prevalence among persons of 18–24 years was 2.5%: 8.7% and 1.3% among foreign-born and US-born, respectively.

Conclusion: Active screening and treatment programs for foreign-born young adults could identify TB cases earlier and provide an opportunity for prevention efforts.

Keywords

Students; TB screening; tuberculosis

Introduction

In 2015, 63% of the reported *Mycobacterium tuberculosis* (TB) cases in the United States were among individuals born outside the United States.¹ The majority of such cases are due to reactivation of latent TB infection (LTBI) after entering the United States.^{2,3} In 2015,

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approximately 11 million nonimmigrant-visa holders (NIVs) entered the United States; 6.2% of these individuals entered on a student visa.⁴ While the 500,000 immigrants and refugees applying for permanent residence in the United States annually are required to be screened for active TB disease as part of their visa process, NIVs are not required to undergo mandatory TB screening prior to entering the United States.⁵ From modeling calculations, foreign-born persons who enter on NIVs are estimated to contribute 58% of all TB cases among persons in the United States for less than 1 year.⁶ However, the extent of active TB disease incidence and LTBI among NIVs is unknown.

Because TB is transmitted from person to person via the airborne route, colleges present a unique environment for the spread of TB where congregate dormitory living can facilitate its spread. In 2014, more than 800,000 international students were studying in the United States.⁷ Approximately 43% of these students were from China or India, which have a high prevalence of TB and are two of the top five countries that contribute to TB cases in the United States.⁷ Although the Association of College Health recommends risk-based screening of students, a recent study showed only 55% of colleges have a TB screening policy.⁸ Because screening is not mandatory, the number of students with LTBI or active TB disease on arrival is unknown.⁹ Therefore a better understanding of TB in this population is needed.

The purpose of this analysis was to describe the epidemiology of active TB disease and LTBI in college-aged individuals in order to inform policy and opportunities for TB prevention.

Methods

We defined individuals of 18–24 years as a proxy for college students. TB cases between the ages of 18–24 years reported in 2011 from the 50 states or the District of Columbia to the US National TB Surveillance System database (NTSS) were included in the analysis. Cases in 2011 were analyzed to be consistent with data available from the National Health and Nutrition Examination Survey (NHANES), which was conducted in 2011–2012 and was used to calculate the prevalence of LTBI. All 50 states and the District of Columbia are required to report TB cases to NTSS using a standardized Report of Verified Case of Tuberculosis (RVCT), which includes demographic and clinical characteristics, and treatment outcomes. We used standard NTSS variable definitions.^{10,11} The NTSS defines a US-born individual as someone born in 1 of the 50 states or the District of Columbia, or someone born outside the United States to at least one parent who was a US citizen.^{10,11} All other individuals are classified as foreign-born. Visa options at first entry to the United States on the RVCT include immigrant, student, employment, tourist, family or finance, refugee, asylee or parolee, other, and unknown. The other visa category includes foreign-born persons who were not required to obtain a visa or those who entered the United States with no official immigration status and whose status it not unknown. We grouped refugee, asylee, parolee, and immigrant visas together in our analysis as these visa types require TB screening. Time in the United States prior to TB diagnosis was calculated using the date the patient first arrived and the date of TB diagnosis. Any individual with a culture result, including those with only extrapulmonary TB, were included in the analysis of

drug resistance. Infectiousness was defined as any individual with sputum culture-positive tuberculosis.

We used the public-use data from the 2011 American Community Survey (ACS) to derive population denominators to calculate active TB disease case rates.¹² The ACS is a series of monthly surveys that are conducted to produce annually updated estimates on demographic, social, economic, and housing information.¹³ Active TB disease case rates were reported as the annual number of cases from the NTSS per 100,000 persons. These rates were stratified by the country of origin.

Because reporting of LTBI is not required nationally, we used the 2011–2012 public-use NHANES data to estimate the prevalence of LTBI. NHANES is a series of cross-sectional, nationally representative surveys designed to assess the health and nutritional status of adults and children in the United States through interviews and physical examinations.¹⁴ The survey examines a nationally representative sample of about 5,000 persons each year selected using a complex, stratified, multistage probability cluster sampling design.¹⁵ They were tested with the QuantiFERON®-TB Gold In-Tube test (QFT-GIT) as part of the NHANES 2011–2012. A positive QFT-GIT was calculated based on the qualitative values and had to meet the following criteria:

- Nil value must be $= < 8.0$ international units (IU) gamma interferon (IF)/ml AND
- TB antigen value minus nil must be ≥ 0.35 IU gamma interferon (IF)/ml AND
- TB antigen value minus nil must be $\geq 25\%$ of the Nil value

TB infection prevalence estimates, using QFT-GIT results, from NHANES were applied to ACS denominator data to determine LTBI prevalence rates, which were stratified by the country of origin.

The protocol for this project was reviewed by the Centers for Disease Control and Prevention (CDC) and determined to be public health surveillance and not human subject research which would require oversight by an institutional review board.

Results

Active TB disease

Using ACS and NTSS data, the active TB disease incidence was 2.8 per 100,000 among individuals of 18–24 years. Stratified by nativity, active TB disease incidence among US-born 18- to 24-year olds was 0.9 per 100,000 and that among foreign-born 18- to 24-year olds was 18.8 per 100,000.

The total number of individuals with active TB disease reported among 18- to 24-year olds in 2011 was 878, constituting 8.3% of the total TB cases reported in 2011 ($n = 10,521$).¹⁰ Of these, 629 (71.6%) were among the foreign-born with 39.0% ($n = 245$) being diagnosed within 2 years of arrival into the United States of the foreign-born TB cases, 9.7% ($n = 61$) and 22.6% ($n = 142$) entered the United States on a student visa and other immigration status, respectively. Among foreign-born individuals, 19.9% ($n = 125$) were from Mexico

and 19.6% were from India, China, and the Philippines (n = 123, Table 1). Among all cases of 18- to 24-year olds, 26.7% (n = 234) were not seeking employment (a category that included full-time students). Clinically, 79% (n = 694) presented with an abnormal chest radiograph consistent with TB and 61.4% (n = 539) were considered infectious due to sputum culture-positive TB. Of those with a positive culture from any site of disease and reported drug susceptibility tests results (n=597), 85.6% (n = 511) had an *M. tuberculosis* isolate sensitive to all first-line drugs (isoniazid, rifampin, ethambutol, and pyrazinamide). Among foreign-born individuals reported in 2011, 80.1% (n = 504) had pulmonary or both pulmonary and extrapulmonary disease and of those with a positive culture and reported drug susceptibility tests results, 62.1% (n = 370) had an isolate sensitive to all first-line drugs (Table 1). The majority of individuals completed treatment (90.3% and 94.2% among foreign-born and US-born, respectively).

Latent tuberculosis infection

From NHANES data, the prevalence of TB infection among 18- to 24-year olds was 2.5% (95% confidence interval [CI] 1.7%, 3.6%, Table 2). Stratified by nativity, US-born individuals had a TB infection prevalence of 1.3% (95% CI: 0.6%, 2.9%) and foreign-born individuals had a TB infection prevalence of 8.7% (95% CI: 4.4%, 16.6%). Using NHANES prevalence estimates and ACS population data, a total of 778,979 (95% CI: 529,706–1,121,730) persons in the United States aged between 18 and 24 years were infected with TB in 2011. Stratified by nativity, 363,155 (95% CI: 167,610–810,116) and 291,568 (95% CI: 147,456–556,326) US-born and foreign-born individuals, respectively, were infected with TB.

Comment

The CDC Division of Tuberculosis Elimination is mandated to eliminate TB in the United States. The National TB Program Objective and Performance target is to decrease the TB incidence to 1.4 cases per 100,000 population by 2020: 11.1 cases per 100,000 among foreign-born individuals and 0.4 cases per 100,000 in US-born individuals.¹⁶ Our analysis showed a TB case incidence of 2.82 per 100,000 among all individuals between 18–24 years old. When stratified by nativity, foreign-born individuals in the same age group had a TB incidence of 18.8 cases per 100,000. Our estimate was lower than findings from a study of foreign-born college students from 2004 to 2007, which showed a TB case incidence of 48.1 cases per 100,000 person-years.¹⁷ Both estimates highlight the importance of TB prevention efforts in this population in order to reach the 2020 goals.

Of the 878 TB cases diagnosed in college-aged individuals in 2011, 539 were infectious, translating to the potential of at least one TB exposure on a college campus in the United States every day. For each person with infectious TB, previous data estimates an average of 10 contacts.¹⁸ Of these 10 contacts, on average 20–30% are found to have LTBI, and one infected person will progress to active TB disease, thereby potentially perpetuating the cycle of TB on college campuses and potential transmission.¹⁸ A recent study found that TB cases among students identified by a screening program were less likely to have a positive sputum smear and, therefore, were less likely to be infectious than unscreened students diagnosed

with active TB disease.¹⁷ These findings suggest that transmission of TB on US college campuses can be decreased with earlier case finding through screening programs.

The current pre-departure overseas immigration screening requirements do not include students and are not focused on preventing active TB disease. However, cost-effectiveness analysis has shown that implementing overseas screening and treatment programs to detect active TB disease prior to entry into the United States among those coming from high-incidence countries would be cost-saving and reduce the public health impact of TB in the United States.¹⁹ Furthermore, as expected, and consistent with recently published NHANES TB data,²⁰ foreign-born individuals had a higher prevalence of TB infection than their US-born counterparts in this age category. In addition to overseas screening for active TB disease, increased treatment of individuals with LTBI will decrease the reservoir of individuals who can progress to active TB disease. Since most colleges require international students to have health insurance and new US Preventive Services Task Force recommendations are to screen persons who were born in, or are former residents of, countries with increased TB prevalence for TB without cost sharing, screening foreign-born students may be feasible from a cost perspective.^{21,22}

Limitations

Our analysis provides an estimate of TB incidence in an important group, young adults, both college-bound, and those who are not college-bound, who should be evaluated for TB prevention efforts. We used 18–24 years old as a proxy for individuals who are likely to be students and therefore our cohort may be different and likely larger from those actually enrolled, as we were unable to directly measure the fraction of enrolled students sampled in this age group. Our estimates of TB incidence are lower than recently reported data, possibly due to the above described denominator limitation, suggesting we may be underestimating the magnitude of infection and disease among this population. Further, the publicly available data on students from the National Center for Education Statistics (NCES) does not have data available by nativity, making denominator estimates challenging. Nevertheless, according to NCES data, 42% of individuals 18–24 years old were enrolled in a degree-granting institution.^{23,24} The NCES suggests that our analysis is likely an underestimate of the magnitude of infection and disease in college students. Though TB surveillance data only reported 9.7% of persons aged 18–24 years entering the United States on a student visa, data for an individual's visa status are not always completed by local TB programs, and thus analysis of this variable may result in an underestimate. Lastly, given the low prevalence of TB in the United States, there may be a higher proportion of false-positive QFT-GIT results among US-born individuals, leading to an overestimation of LTBI prevalence for the US-born young adults in our analysis.²⁵

Conclusions

Our analysis reports the magnitude of active TB disease among young adults of college age in the United States and estimates the prevalence of LTBI in this group. The high incidence of active TB disease and LTBI prevalence among foreign-born individuals suggest a need for targeted TB screening efforts in this population. Both the CDC strategic plan and the CDC's Antibiotic Resistance Solutions Initiative call for extending medical exams and treatment

overseas to persons who are likely to remain in the United States for 6 months or longer such as students and temporary workers.^{16,26} Additionally, a recent cost analysis study showed that overseas TB screening and treatment of individuals from high and medium incidence countries who intend to study in US colleges and universities prior to entry into the United States, is cost-saving.¹⁹ Already many colleges in the United States, require TB screening for all international students. The shorter courses for LTBI treatment, such as 12-doses of weekly isoniazid and rifapentine or 4 months of daily rifampin, are likely to increase treatment acceptance and enhance treatment completion among students. Data from a CDC-led post-marketing surveillance project of the 12-dose regimen have shown that 95% of students starting the 12-dose LTBI regimen completed therapy.²⁷ The completion rate of the 12-dose regimen at the University of California, San Diego, was 91%, far exceeding the 59% completion rate previously reported among students treated with 9 months of isoniazid.^{28,29}

In order to reach TB elimination, we will need to address the high incidence of active TB disease and prevalence of LTBI among the foreign-born persons living in the United States. Collaboration with colleges and universities to focus on the foreign-born college-aged population in the United States provides an opportunity to reach a population with a high prevalence of LTBI prior to progression to infectious disease, and when individuals are young and usually healthy. With the shorter course LTBI treatment regimens, the new recommendation from the US Preventive Services Task Force, and potential new strategies for screening students prior to entry or at entry to the United States, we may be able to speed the decline of TB in young adults.

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Conflict of interest disclosure

The authors have no conflicts of interest to report. The authors confirm that the research presented in this article met the ethical guidelines, including adherence to the legal requirements, of the United States. The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention.

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Demographics and clinical characteristics of TB cases among young adults of 18–24 years old by nativity, United States, 2011.

Table 1.

Characteristic	Total		U.S.-born		Foreign-born	
	N	%	N	%	n	%
Total	878		249	28.4	629	71.6
Male	497		142	57.0	355	56.4
Race and/or ethnicity						
White, Non-Hispanic/Latino	54		35	14.1	19	3.0
Hispanic/Latino	325		96	38.6	229	36.4
Black/Non-Hispanic/Latino	196		83	33.3	113	18.0
Asian/Pacific Islander	268		17	6.8	251	39.9
Other ¹	35		18	7.2	17	2.7
Occupation						
Employed	373		96	38.6	277	44.0
Not seeking employment	234		64	25.7	170	27.0
Unemployed	252		87	34.9	165	26.2
Unknown	19		2	0.8	17	2.7
Years in US at TB diagnosis						
<2 years	245		N/A		245	39.0
2–5 years	231		N/A		231	36.7
>5 years	110		N/A		110	17.5
Missing	43		N/A		43	6.8
Visa status ²						
Immigrant, refugee, asylee, or parolee	140		N/A		140	22.3
Student	61		N/A		61	9.7
Tourist or family/france	18		N/A		18	2.9
Employment	6		N/A		6	1.0
Other	142		N/A		142	22.6
Unknown	262		N/A		262	41.7
Location of birth						

Characteristic	Total N		U.S.-born		Foreign-born	
	N	%	N	%	n	%
Mexico	125	N/A	125	19.9		
Guatemala	46	N/A	46	7.3		
India	43	N/A	43	6.8		
China	40	N/A	40	6.4		
Philippines	40	N/A	40	6.4		
Vietnam	36	N/A	36	5.7		
Other	299	N/A	299	47.5		
Culture positive						
Culture positive other than sputum	338	98	39.4	38.2	240	
Sputum culture positive (infectious) ³	539	150	60.2	61.8	389	
Sputum smear positive	346	111	44.6	37.4	235	
Sputum smear negative	193	39	15.7	24.5	154	
Site of disease						
Extrapulmonary only	165	41	16.5	19.7	124	
Pulmonary only	616	183	73.5	68.8	433	
Both extrapulmonary and pulmonary	95	25	10.0	11.3	71	
Abnormal chest radiograph consistent with TB	694	204	81.9	77.9	490	
Cavitary chest radiograph ⁴	278	96	47.1	37.1	182	
Pan-sensitive TB ⁵	511	141	23.6	62.1	370	
Treatment outcomes						
Completed	798	230	94.2	90.3	568	
Lost	14	4	1.6	1.6	10	
Died	7	2	0.8	0.8	5	
Refused/other ⁶	49	11	4.4	6.0	38	

Note.

¹This group includes: multiple race, native Hawaiian, American Indian/Alaska native, and unknown.

²Other group includes those who were not required to obtain a visa or those who entered the United States with no official immigration status. Unknown group includes missing, unknown, and N/A.

³Defined for analysis as sputum culture-positive tuberculosis.

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⁴ Of those cases with an abnormal chest X-ray or abnormal CT scan (n = 753).

⁵ Of those tested to all four first-line anti-TB drugs (isoniazid, rifampin, ethambutol, and pyrazinamide, total n = 597) and found to be susceptible to all. Included anyone with a positive culture.

⁶ Includes: unknown, adverse reaction, other, and refused.

Interferon gamma release assay positive pPrevalence in the civilian, noninstitutionalized US population aged 18–24 years, National Health and Nutrition Examination Survey, 2011–2012.

Table 2.

Characteristic	IGRA positive prevalence % (95% CI)	Estimated # IGRA positive N (95% CI) × 1000
Total	2.5 (1.7–3.6)	778 (530–1,122)
US-born	1.3 (0.6–2.9) [†]	363 (168–810)
Foreign-born	8.7 (4.4–16.6) [†]	292 (147–556)

Note.

[†] Estimates and 95% CIs may be unreliable because the relative standard error is > 30%.