Tuberculosis Among Participants in an Academic Global Health Medical Exchange Program

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BACKGROUND: Although individuals from low tuberculosis (TB) burden countries experience an increased risk of TB infection when traveling to high burden countries for medical training or service, the degree of risk has not been well quantified.

OBJECTIVE: Improved knowledge will aid development of guidelines for TB screening, pre/post-travel education, and risk reduction.

DESIGN: Retrospective survey including questions on demographic characteristics, pre-travel TB counseling, in-country activities, and post-travel TB testing.

PARTICIPANTS: Six hundred eight individuals who traveled to Eldoret, Kenya with the Academic Model Providing Access to Healthcare (AMPATH) medical exchange program between July 2004 and June 2009 were invited to complete an online survey in January 2010.

MAIN MEASURES: The percentage of participants with a tuberculin skin test (TST) conversion and percentage reporting pre-travel and post-travel counseling and testing for TB were examined.

KEY RESULTS: Four hundred thirteen out of 608 (68%) responded with sufficient information to be included in the analysis. Two hundred thirty-nine individuals (58%) reported that TB prevention was discussed in pre-travel preparations. One hundred thirteen (27%) of the survey participants reported "ideal" care [definition: pre-travel TST (within 1 year of travel), pre-travel counseling, and a post-travel TST specifically related to their travel]. Out of 267 participants at risk for TST conversion, 11 (4.1%; 95% CI: 2.2–7.3) had a conversion. TST conversion was not associated with longer duration of stay or participation in direct medical care.

CONCLUSIONS: Travelers to TB-endemic areas with international medical exchange programs are at risk for TB infection, regardless of their length of stay or whether or not they participate in direct medical care. Many receive inadequate pre- and post-travel TB counseling and testing. Efforts should be made to improve TB education for program participants.

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BACKGROUND

Tuberculosis (TB) is one of the most common infectious diseases in the world. The World Health Organization (WHO) estimates over 9 million new cases and nearly 2 million deaths attributable to TB each year.[1] Many regions with the highest burden of TB disease also continue to report a rise in the incidence of drug-resistant TB.[2]

Interest among US medical trainees for on-site health experiences in the developing world has grown in recent years. A recent survey of pediatric residency programs found that more than half offered a global health elective, an increase from 25% reporting similar programs 10 years earlier.[3,4] In a 2009 survey of medical students conducted by the Association of American Medical Colleges, 30% of students indicated participation in a global health experience on an elective or volunteer basis during medical school.[5] Recognition of this interest in global health has prompted many medical educators and researchers to establish formal opportunities for trainees to gain experience in health care facilities in the developing world.

Trainees in these settings may experience increased risk of exposure to infectious diseases such as TB, malaria, and HIV. While universal precautions and appropriate prophylactic medications can significantly reduce the risk of acquiring HIV and malaria, adequate infection control measures to minimize the spread of airborne pathogens such as TB are lacking in many health care facilities in the developing world. Reports of US Peace Corps volunteers and long-term (>3 months) Dutch travelers to areas of TB endemicity demonstrate that the incidence of TB infection and disease is higher than in the travelers' country of origin.[6,7] Furthermore, the risk of exposure to highly drug-resistant TB in many of these settings [especially in locations where nosocomial spread of multidrug (MDR) and extensively (XDR) drug-resistant TB has been documented[8]] heightens the urgency for measures to prevent transmission.

The Indiana University Kenya medical exchange program (now AMPATH Consortium Medical Exchange Program) was established in 1990 between Indiana University School of Medicine (Indiana) and Moi University Faculty of Health Sciences (now renamed Moi University School of Medicine) in Eldoret, Kenya.

The history and philosophical underpinnings of this relationship have been described previously.[9] Over the past 20 years, the partnership has grown to include a number of North American academic partners and a variety of care, teaching, and research initiatives. The medical exchange program facilitates the travel of over 300 individuals to Eldoret annually. Eldoret is located within Uasin Gishu District where a TB intensified case-finding program screened over 36,000 individuals in the community from 2005–2009 and revealed an average acid-fast bacillus (AFB) smear positivity rate of 12% among those with a positive symptom screen (unpublished data). The Moi Teaching and Referral Hospital is a District Referral hospital with a catchment population of 13 million. The hospital has crowded, shared, open-air wards where multiple patients often share beds. Infection control efforts include: placement of TB suspects and smear-positive patients near windows and encouraging cough hygiene, opening of windows during ward rounds, and early diagnosis and initiation of treatment through an intensified case finding strategy. There are no isolation facilities for TB patients; personal respirators are not routinely available. The medical exchange program is "family friendly;" it is not uncommon for spouses and children to accompany program participants to Kenya. Many spouses and children volunteer in various affiliated programs such as the hospital pediatric education center and local orphanages.

Guidelines exist for management of TB risk among travelers from low burden countries who are visiting TB-endemic areas.[10–12] These include recommendations for pre- and post-travel testing for TB infection, counseling travelers to avoid exposure to known TB patients in crowded environments, and consideration of BCG vaccination in selected populations. Guidelines vary slightly in identification of which individuals are at increased risk and suggest that the specific location visited, duration of stay, and in-country activities should all be considered as important variables. The US Center for Disease Control and Prevention's *Health Information for International Travel* suggests that a subset of travelers anticipating "prolonged or routine exposure to TB (hospitals, prisons, homeless shelters) or those who plan an extended stay over a period of years in an endemic country" should be advised to have pre- and post-travel TB skin testing (TST), including a two-step TST or interferon gamma release assay (IGRA) prior to departure.[11] The Public Health Agency of Canada suggests a similar strategy for travelers visiting high-incidence countries for 3 months or longer, and for travelers engaged in health care work in such countries.[12] The particular emphasis on screening of health care workers is justified by the higher risk of TB exposure in health care settings in the developing world, and the implications for US and Canadian hospitals if trainees and health care workers develop active TB upon return. [13]

We evaluated the risk of TB infection among travelers participating in an academic, international medical exchange program. Improved knowledge defining high-risk individuals and activities will aid the development of guidelines for TB screening, pre/post-travel education, and risk reduction.

METHODS

A survey was administered in January 2010 to individuals who traveled to Eldoret, Kenya in association with the Academic Model Providing Access to Healthcare (AMPATH) program between July 2004–June 2009. Participants were identified through review of housing records and through communication with program directors at each of the seven North American academic institutions that participate in the AMPATH Consortium medical exchange program. We attempted to obtain contact information for all participants—this was possible for 608 of 728 (84%) identified participants. While the survey was not restricted to clinicians, the majority of participants in the program were medical trainees active in clinical care (senior medical students, senior residents). The study was approved by the Lifespan Institutional Review Board.

Survey

The survey consisted of 20 questions designed to collect the following information: participants' baseline demographic and medical characteristics, pre-travel TB counseling and testing, in-country activities, and post-travel TB testing. TST conversion was by self-report, and participants were asked to include the size of their post-travel TST. Travelers younger than 18 years of age were not invited to complete the survey; however, the survey included questions about children accompanying participants during their visit. The survey was administered via an online survey tool (SurveyMonkey.com®) and by hard copy upon request.

Analysis

The risk of TB infection (TST conversion or active TB) was calculated among all respondents who reported a negative baseline TST and who had a post-travel TST. Chi-square or Fischer's exact test was utilized to examine for associations between TST conversion and the following categorical variables: duration of stay and participation in direct medical care. We defined "ideal" care as the presence of pre-travel TST (within 1 year of travel), any pre-travel counseling concerning TB prevention, and a repeat post-travel TST related to travel. This definition is consistent with recommendations of the Center for Disease Control and Prevention and facilitates timely diagnosis and management of latent TB infection.

RESULTS

Baseline Characteristics

Of 608 participants who received the survey, 413 (68%) responded with sufficient information for inclusion. Baseline characteristics of the survey respondents are displayed in Table 1. Most participants were ≤40 years old (273, 66%). Few had chronic medical conditions that predispose to TB. Three hundred thirty-three (80.6%) respondents reported that their last test for TB infection was negative by TST or IGRA. Forty-three (10.4%) respondents were unaware of their TB infection status or had never been tested.

Table 1. Baseline Characteristics of Medical Exchange Participants

Demographic characteristics	Number (%)
Age (years)	
18–21	6 (1.4)
22–30	168 (40.7)
31–40	99 (24.0)
41–50	54 (13.1)
51–60	48 (11.6)
>60	38 (9.2)
Sex	
Female	227 (55.0)
Medical history	N=369
No chronic medical illness	341 (92.4)
HIV	1 (0.3)
Silicosis	1 (0.3)
Diabetes mellitus	6 (1.6)
Autoimmune disease	8 (2.2)
Cigarette smoking	5 (1.4)
>10% below ideal body weight	3 (0.8)
Immunomodulatory medication*	3 (0.8)
Current pregnancy	1 (0.3)
TB history prior to travel	
Negative test for LTBI	333 (80.6)
History of LTBI	37 (9.0)
Never tested for LTBI/unknown	43 (10.4)

Non-exclusive (1 TNF-a inhibitor, 1 methotrexate, 2 prednisone >20 mg/day for 30 days in last year), 1 azathioprine)

Pre-Travel Counseling and Testing

Participants sought pre-travel medical advice from a variety and number of different sources; overall, 393 (95%) sought some pre-travel medical advice. Two hundred nineteen (54%) attended a travel clinic, and 129 (31%) sought advice from the Centers for Disease Control and Prevention website or other travel websites. Sixty-three (15.2%) relied exclusively on their local medical exchange program director or University Health Services for travel advice. Other sources included primary care physicians, local health centers, and previous travelers to this site. Nineteen (4.6%) respondents did not seek any pre-travel medical advice. Among those who sought pre-travel medical advice, 239 (58.3%) respondents reported that TB prevention was discussed.

Duration of Stay and In-Country Activities

The duration of stay was reported by category (n=409). Respondents who had visited repeatedly during the study period were asked to report cumulative time spent in Kenya: 185 (45%) respondents were on site for<4 weeks, 151 (37%) were on site for 4–12 weeks, and 73 (18%) were on site for >12 weeks. The most commonly reported non-clinical activities included visiting a Kenyan home (266, 65%), using public transportation (162, 40%), participating in non-direct patient care activities within the hospital or laboratory (156, 38%), and visiting the child-life center adjacent to the hospital pediatric ward (153, 37%). Two hundred forty-nine (61%) individuals provided direct medical care on inpatient wards or in outpatient clinics. (Table 2)

Table 2. Commonly Reported In-Country Activities

Clinical	Non-clinical
Direct medical care on hospital wards or clinics	Visiting Kenyan home
Direct medical care in rural HIV clinics	Riding public transportation
Work in AMPATH pharmacy	Non-patient care activities within hospital or laboratory
	Volunteering in child-life center adjacent to pediatric ward
	Frequenting downtown restaurants, clubs
	Visiting local orphanages
	Conducting research surveys in rural households and villages
	Participating in tourist activities
	Teaching students and meeting with university administrators

Post-Travel Testing and Risk of TB Infection

One hundred thirteen (27.4%) survey participants reported "ideal" care. In total, 187 (49.7%) eligible respondents had a post-travel TST or IGRA that was specifically related to their travel; 189 did not. Of those who were not tested specifically related to their travel, 80 had a test for annual surveillance at their place of employment leaving 109 that did not have any post-travel TB testing at the time of survey response. Excluding those with a known history of positive TST pre-travel, those who reported no participation in direct medical care were less likely to have obtained a post-travel TST/IGRA (64/152= 42.1%) than those who reported participation in direct medical care (203/224=90.6%; p<0.001).

Eleven of 267 (4.1%; 95% CI 2.2-7.3%) adult respondents with documented absence of infection prior to travel and sufficient post-travel testing to identify incident infection were newly diagnosed with TB infection after their rotation in Kenya. Nine of 11 reported being offered treatment for LTBI: 7 reported completing treatment and 1 individual who did not receive LTBI treatment reported development of active TB. None of the infected individuals reported a chronic medical condition or travel to other TB-endemic areas that could account for their TB infection. We did not find a significant relationship between the risk of TB infection and either (1) duration of stay or (2) the type of work done while in Kenya (defined by participation in direct medical care or not) (Table 3).

Children

Overall, 50 respondents reported that they were accompanied by a total of 69 children under the age of 18 years. Twenty-one (30%) children had a TST/IGRA upon return from travel. Ten of these children had a known baseline negative TST; of these ten, one converted. In total, three children had positive post-travel TSTs (ages 8, 12, and 15), but two of them had unknown baselines—both subsequently had IGRA testing, and both were negative. All three were on site for 1 month each at different times during the 5-year study period. Children's activities were not solicited as part of the survey; however, it

Table 3. TB Risk Among Adults by Duration of Stay and Participation in Direct Medical Care

Duration of stay in Kenya	Direct medical care	No direct medical care	p - value
<4 weeks	3/74 (4.1%)	1/30 (3.3%)	0.86
4–12 weeks	3/104 (2.9%)	1/17 (5.9%)	0.52
>12 weeks	2/25 (8.0%)	1/17 (5.9%)	0.79
Total	8/203 (3.9%)	3/64 (4.7%)	0.79

is common for visiting children to spend time in the child-life center next to the pediatric medical ward within the hospital.

DISCUSSION

Incidence of TB Infection

The overall risk of TB infection (4.1%) was calculated by dividing the number of respondents who converted their TST or IGRA by the number of respondents "at risk" of being called a converter (i.e., had a negative pre-travel TST/IGRA and had a post-travel TST/IGRA). Our estimate is slightly higher than that documented in other populations of travelers.[6,7] In the study of Dutch travelers, health care work involving direct patient contact was a significant and independent risk factor for TB infection.[7] A recent meta-analysis of the risk of latent tuberculosis infection (LTBI) among military and long-term civilian travelers concluded that the overall cumulative incidence was 2.0%.[14]

In our study, there was no significant relationship between the risk of TB infection and participants' duration of stay or work type (direct involvement in clinical care or not), suggesting that even short-term, non-clinical rotators in medical exchange programs may be at risk for TB infection. Our survey only asked about laboratory work in general—it is possible that a more specific assessment of exposure (e.g., work in a mycobacterial laboratory) would have better identified high-risk non-clinical activities. Kenya is ranked 13th on the WHO list of high-TB-burden countries, with an estimated 142 new smear-positive cases per 100,000 annually.[15] Participants in this program, regardless of whether providing clinical care or not, reported a number of activities that involve interaction with the local populace including visiting local homes and utilizing public transportation (Table 2). These activities probably place individuals at higher risk of TB exposure than the activities of typical vacation travelers. Our findings may not be generalizable to exchange programs in which participants do not participate in such activities.

It is possible that the small number of outcomes in our study did not allow for sufficient power to detect a difference in risk of TB infection based on duration of stay or work type. Also, since those who reported no participation in direct medical care were less likely to have a post-travel TST or IGRA, it is possible that those participating in higher risk, non-clinical activities were more likely to pursue post-travel TB testing. This could have masked a true association between work type and risk of TB infection. Our estimate of the risk of TST conversion may be overestimated due to non-response bias if participants not infected with TB were less likely to respond to the survey.

The validity of our results depends on the quality of self-reported data on TST conversion (outcome) and work type and duration of stay (exposures). The reliability of these self-reports may be less accurate for those traveling in the earlier years of our study since recall over a longer period of time may be compromised. If those experiencing TST conversion differentially remember exposures, this may introduce recall bias.

Medical Exchange Program Issues

A growing number of academic institutions and medical training programs have established international partnerships that encourage clinicians (including trainees), researchers, and others to conduct work in TB-endemic areas of the world. As far as we are aware, this is the first study of the assessment of TB-specific counseling and TB infection risk in such a program. Our findings indicate that many participants in this program are not receiving appropriate pre-travel counseling about the risk of TB and ways to minimize exposure. Only 58.3% of respondents noted that they received any pre-travel counseling about TB. Less than 30% of participants who responded to the survey met the criteria for "ideal" care consistent with current CDC recommendations.[11] While students and trainees in our study sought pre-travel counseling in a variety of settings, we suggest that program directors coordinate with local travel clinics and provide supplementary counseling on issues related to TB prior to participants' departure for their international site. Facilitating post-travel testing for program participants may result in timely diagnosis of TB infection and the opportunity to be treated for LTBI. Ultimately, faculty leaders of these programs need to engage with their counterparts in TB-endemic areas to improve infection control practices in hospitals and clinics in order to protect all medical staff. The World Health Organization has clear, published guidelines that discuss the most effective administrative interventions and outline an approach to implementation.[16] Often, implementation of such changes requires investment of resources and a change in hospital culture that can only be achieved with long-term commitment and trust.

Most clinicians had some post-travel testing for TB either specifically related to their travel or for annual surveillance in their home institution. In contrast, non-clinical researchers and volunteers are not routinely tested. Unless specific efforts are made to discuss and offer post-travel testing to these individuals, they may not appreciate the need to pursue testing. This was clear in some of the informal comments we received from non-respondents who claimed they did not consider a TB risk survey relevant to them since they were not involved in direct medical care.

Another issue raised in our study is the lack of post-travel testing among family members who travel with medical rotators, particularly children. A number of children accompanied their parents, but only a few received pre- and post-travel TB testing. The small number in our study makes it difficult to produce a reliable estimate of risk, but clearly children are at risk for TB infection. Children who travel to TB-

endemic areas may be exposed to infectious adults in communal living environments, personal childcare settings, child play areas within the hospital, or in the community at large. These types of interactions are common among children who accompany medical rotators.

CONCLUSIONS

Health care workers, researchers, trainees, and travelers to western Kenya within this academic international medical exchange program are at risk for TB infection, and many do not receive adequate pre- and post-travel counseling and testing. Education and counseling of this population should be improved. There are challenges in making sweeping policy recommendations for TB screening in travelers; further study is needed to accurately quantify the risk of TB infection. The broad gradient of TB incidence around the world makes it difficult to make a "one policy fits all" recommendation. Our study was of travelers to a highly endemic country within the context of a medical exchange program. Many of the participants in this program work in health care facilities—those who become infected and subsequently develop pulmonary TB disease may be at risk of exposing large numbers of susceptible individuals in their US workplace. Participants not working in health care who travel with our program and become infected have the potential to be the source of community transmission as they are unlikely to be suspected of having TB and are thus at risk for late diagnosis. In the context of our exchange program to a highly endemic area, a strategy of TST coupled with therapy for latent infection is warranted.

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