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CLINICAL RESEARCH STUDY

TB in a Low-Incidence Country: Differences Between New Immigrants, Foreign-Born Residents and Native Residents

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ABSTRACT

BACKGROUND: New immigrants and foreign-born residents add to the burden of pulmonary tuberculosis (TB) in low-incidence countries. The highest TB rates have been found among recent immigrants. Active screening programs are likely to change the clinical presentation of TB, but the extent of the difference between immigrant and resident populations has not been studied prospectively.

METHODS: Adult new immigrants were screened upon entry to 1 of 5 immigration centers in Switzerland. Immigrants with abnormal chest radiographs were enrolled and compared in a cohort study to consecutive admitted foreign-born residents from moderate-to-high incidence countries and native residents presenting with suspected TB.

RESULTS: Of 42,601 new immigrants screened, 112 had chest radiographs suspicious for TB. They were compared with foreign-born residents (n = 118) and native residents (n = 155) with suspected TB (n = 385 patients included). Active TB was confirmed in 40.5% of all patients (immigrants 38.4%, foreign-born residents 50%, native residents 34.8%). Clinical signs and symptoms of TB and laboratory markers of inflammation were significantly less common in immigrants than in the other groups with normal results in >70%. The proportion of positive results on rapid testing to detect *M. tuberculosis* (MTB) in 3 respiratory specimens was significantly lower in immigrants (34.9% for acid-fast staining; 55.8% for polymerase chain reaction) compared with foreign-born residents (76.2% and 89.1%, respectively) and native residents (83.3% and 90.9%, respectively). Isoniazid resistance and multi-drug resistance were more prevalent in immigrants.

CONCLUSION: New immigrants with TB detected in a screening program are often asymptomatic and have a low yield of rapid diagnostic tests but are at higher risk for resistant MTB strains. Postmigration follow-up of pulmonary infiltrates is essential in order to control TB among immigrants, even in the absence of clinical and laboratory signs of infection.

KEYWORDS: Foreign-born; Clinical presentation; Immigrants; Residents; Screening; Tuberculosis

More than one-third of the world's population is estimated to be infected with *Mycobacterium tuberculosis* complex (MTB). Eight million new cases of pulmonary tuberculosis (TB) and approximately 2 million deaths attributable to TB are reported each year.[1] In many developed countries, new immigrants and foreign-born residents are increasingly contributing to the burden of TB in the host country. The proportion of TB cases in these 2 groups exceeds 50% in the US and parts of Europe.[2-4] In particular, new immigrants who are screened for TB as they enter a country show high TB prevalences (256-504/100,000 population per year).[3,5-8] Consistently high incidences (33-85/100,000 population per year) also have been reported for foreign-born residents in low-prevalence countries.[3,6,9,10] Among the native residents in these countries, the TB incidence is below 10/100,000 population per year.[3,10] The risk of disease for foreign-born

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residents is highest in the first 5 years after arrival, with 50% of cases occurring in this period.[11]

Prompt identification, early effective treatment, and isolation of TB patients are important strategies in preventing an increase in the occurrence of TB in the general population of a low-incidence country. The most important criteria for establishing an early diagnosis are positive results in rapid diagnostic tests on respiratory specimens (acid-fast smear and polymerase chain reaction) and a case definition that is based on clinical and radiographic signs and risk factors. Although scoring systems and decision trees have been developed to more adequately predict patients at high risk for active TB,[12-15] they are difficult to apply in clinical practice.

The clinical presentation of TB depends largely on how far the disease has progressed in an individual. The diagnosis is particularly challenging in immigrants who are actively screened upon entry to their host country. We hypothesized that active screening changes the presentation of TB compared with passive case detection and that many actively screened immigrants presenting with TB are asymptomatic. The extent of this difference in comparison with the resident population has not been investigated in prospective studies before.

Active screening programs are currently under debate because of their costs and the limited evidence of a reduction in transmitting TB in the host country. If most immigrants with TB are asymptomatic, and thus cannot be diagnosed by passive case detection, active screening programs should be reinforced. This would aid in identification of large numbers of individuals who will benefit from therapeutic interventions and limit the transmission at least within the migrant community living under crowded conditions.

CLINICAL SIGNIFICANCE

- Immigrants add substantially to the burden of tuberculosis (TB) in low-incidence countries.
- Screening programs to detect TB in immigrants are recommended as a measure to support TB elimination efforts.
- Postmigration follow-up of pulmonary infiltrates is essential in order to control TB among immigrants, even in the absence of clinical signs of infection.

METHODS

Patient Population

From January 1997 through July 2004, all patients admitted to our hospital who were placed in respiratory isolation for suspected TB were included in this cohort study. The University Hospital Basel is a 780-bed primary and tertiary care center with approximately 23,000 admissions annually. The patients were categorized into new immigrants who were actively screened for TB upon entry into Switzerland, foreign-born residents who emigrated from countries with a moderate to high prevalence of TB, and native Swiss residents. Immigrants were referred to our hospital if the screening chest radiograph was suspect for TB upon entry to 1 of the 5 State immigration centers (Basel) in Switzerland (active screening). Foreign-born residents (ie, persons with work permit in Switzerland and their families, students and tourists) are not actively screened for tuberculosis in Switzerland. Like the native residents, they were referred at the discretion of the general practitioners (passive case detection). Demographic data (age, sex, country of origin), duration of isolation, laboratory results, and microbiological data were collected prospectively and recorded in a database. Additional data (fever, weight loss, night sweats, cough, sputum production, dyspnea, and auscultatory findings) were extracted by chart review. Countries of origin were categorized into those with a low notification rate of TB (<24/100,000 population per year) and those with a moderate to high notification rate of TB (≥24/100,000 population per year), as reported by the 1998 report of the World Health Organization (WHO). The study was reviewed and approved by the Ethics Committee of the University of Basel.

Microbiology

Respiratory specimens were digested, decontaminated, concentrated, and stained with auramine-rhodamine and then examined with fluorescent microscopy. Ziehl-Neelsen acid-fast staining (AFS) was used to confirm the presence of acid-fast bacilli. Mycobacterial cultures were performed by sample-inoculation on to Loewenstein-Jensen media and into liquid media (radiometric Bactec 460 TB system, Becton Dickinson, Franklin Lakes, NJ, used from 1997 to 2000; BacT/ALERT 3D system, BioMérieux Inc., Durham, NC, used from 2001 through 2004) according to the manufacturers' instructions and incubated at 37°C for 8 weeks. Polymerase chain reaction (PCR) testing for MTB was performed by using the Roche Amplicor *Mycobacterium* test with a Cobas Amplicor analyzer (Roche Diagnostics Systems, Basel, Switzerland) according to the manufacturer's instructions on concentrated decontaminated specimens.

Study Definitions

Active TB was defined as one or more positive cultures of respiratory specimens for MTB (proven TB), or as culture-negative with a compatible abnormal chest radiograph and clinical and radiological improvement after therapy for 2-3 months with a standard combination therapy and without any alternative diagnosis (probable TB needing treatment). *Inactive TB* was defined as negative cultures and an abnormal chest radiograph, which was stable after a standard