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Tuberculosis screening at a diabetes clinic in the Republic of the Marshall Islands

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ABSTRACT

Setting: Tuberculosis (TB) and diabetes mellitus (DM) are prominent public health problems in the Republic of the Marshall Islands, a small island nation with high rates of tuberculosis and diabetes.
Objective: Evaluate the rate of active and latent TB in a Pacific Island DM clinic.
Design: In one DM clinic on the island of Ebeye, 213 adult patients aged 27–86 years completed tuberculin skin testing and TB work-up between April 2010 and March 2012.
Results: Screening for TB led to the diagnosis of 77 patients with TB infection and 11 patients with TB disease. From these data, the prevalence of TB disease among DM patients in the clinic exceeded 5% (95% CI 2.2%–8.1%). All patients who completed TB screening were at high risk of TB disease, and those with DM aged ≤ 50 years had a higher risk of TB disease than those with DM over age 50 (RR 3.1, C.I. 1.0–9.7, $p = 0.05$).
Conclusion: The experience at the Ebeye Diabetes Clinic demonstrates that screening DM patients for TB can identify significant rates of TB infection and TB disease, and should be considered for other settings with a high background TB incidence. Further assessment of TB risks should explore age, gender, and level of diabetes control.

1. Introduction

Tuberculosis (TB) and diabetes mellitus (DM) are highly prevalent in the U.S. Affiliated Pacific Islands (USAPI) which include American Samoa, Commonwealth of the Northern Mariana Islands, Federated States of Micronesia, Guam, Palau, and Republic of the Marshall Islands (RMI). Despite recent improvements in regional TB control, the reported 2013 TB incidence rate in the USAPI was 76.6 cases per 100,000 persons, compared to the overall U.S. national TB case rate (for the 50 States and the District of Columbia, exclusive of territories) of 3.0 per 100,000 [1]. The prevalence of TB in the RMI is the highest in the USAPI at 215 per 100,000 [1]. To add to this, the prevalence of type 2 diabetes among adults in the Marshall Islands is 41%, one of the highest reported DM rates in the world [2].

In response to growing awareness of the convergence of DM and TB in USAPI, the Pacific Island TB Controllers Association (PITCA) has adopted a set of clinical practice standards, the *USAPI Standards for the Management of Tuberculosis & Diabetes* [3]. These standards were proposed in 2006, were reviewed by regional experts, and were formally adopted by USAPI public health authorities in December 2010. In parallel to the overarching *WHO Collaborative Framework for Care and Control of Tuberculosis and Diabetes* [4], the USAPI TB-DM Standards include recommendations for bidirectional TB and DM screening, strategies for glucose control during TB treatment, DM education during TB treatment, and clinical practices to improve TB-DM patient outcomes.

The USAPI TB-DM Standards are being followed in several locations, including the RMI. Ebeye is a remote island of 9614 people in RMI's Kwajalein Atoll in the North Pacific, and it represents one of two population centers in RMI [5]. This study assesses the impact of TB screening in Ebeye among DM patients presenting for routine DM care. The screening paradigm used by the program is

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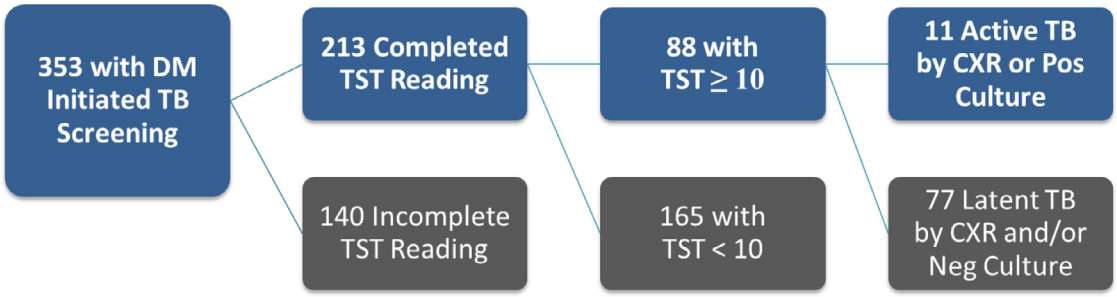

Fig. 1. Tuberculosis (TB) screening results among people with diabetes mellitus, Ebeye Island, 2010–2012 ($N = 353$).

described, and results of TB screening for finding latent TB infection (LTBI) and TB disease are discussed.

2. Study population and methods

Ethics approval was obtained from the Institutional Review Board (IRB) in the RMI Ministry of Health. The study also underwent ethical review at the Centers for Disease Control (CDC) and was determined to be research that was exempt from CDC IRB review on the basis of this being limited to a program evaluation activity.

Over a 24-month period between April 2010 and March 2012, 353 DM patients were offered a tuberculin skin test (TST). All testing was done at the Ebeye Diabetes Clinic as part of routine DM management. TB program staff visited the weekly half-day DM clinics to provide TB skin-testing. TB staff encouraged DM patients to participate in TB screening, but patient participation was voluntary.

Clinic nurses administered TSTs and recorded results in the DM clinic logbook and patient records. Patients were scheduled to return to the DM clinic 48–72 h later for skin test interpretation. Patients with a TST ≥ 10 mm were referred to the Ebeye TB Clinic for chest x-ray (CXR) and further examination. The Ebeye TB clinician interpreted the CXR and, if consistent with TB disease, ordered sputum for acid-fast bacillus (AFB) smear microscopy in Ebeye. Sputum specimens were also sent to Diagnostic Laboratory Services in Honolulu for AFB culture. Drug susceptibility testing (DST) was obtained on all samples with a positive *Mycobacterium tuberculosis* culture. Spoligotype and 24-locus Mycobacterial interspersed repetitive units (24-locus MIRU-VNTR was performed on culture confirmed TB isolates that were submitted using the National Tuberculosis Genotyping Service [6]. Follow-up and management for TB were directed through the Ebeye TB Program. Preventive treatment (principally with 9 months of isoniazid) was offered to patients with diabetes who were diagnosed with LTBI.

For patients completing TB screening, rates of active TB were compared for patients age ≤ 50 years and those >50 years old using Epi-Info 7 [7] to obtain the risk ratio (RR) and the 95% confidence interval (CI); Fischer's two-tailed exact test was used to determine the probability [8]. The significance level for statistical analyses was p ≤ 05.

3. Results

A diagram of the screening methodology is depicted in Fig. 1. A total of 353 patients with DM aged 27–86 years received a TST from April 2010 to March 2012. Of the total, only 213 (60%) had the TST read and documented. Among those who completed initial TB screening, 88 (41%) had a positive result, i.e., TST induration ≥10 mm. All these patients underwent CXR, and those with abnormal CXR findings underwent sputum collection for acid-fast bacillus (AFB) smear and culture. Among the 88 patients with a positive TST result, 11 cases of TB disease and 77 cases of LTBI were diagnosed. The isolate from one patient was multi-drug resistant (MDR) TB and the rest of the isolates were susceptible to isoniazid, rifampin, ethambutol and pyrazinamide. Five of the 11 cases (45%) were smear positive and six of the TB cases (54%) were culture positive. Genotype results were available for three out of the six (50%) culture positive cases, and all three had the same Lineage 2 (East-Asian, formerly known as Beijing) genotype (GENType G00017) [9].

Table 1
Tuberculosis (TB) screening compliance among adults with diabetes mellitus by gender and age, Ebeye Island, 2010–2012 ($N = 353$).

Category	Completed TB screening	Did not complete TB screening	*p* value
Number	213	140	–
Age	56.4	54.7	$p = 0.11$
% Male	32%	22%	$p = 0.04$

Of the five culture-negative cases, 4 (36%) were clinically diagnosed with radiographic changes. Overall, 10 cases were pulmonary TB and one case (9%) was both pulmonary and extrapulmonary TB. From this screening effort, the rate of TB disease among DM patients on Ebeye was 5200 per 100,000 (5.2%; 95% CI 2.2%–8.1%), based on 11 TB cases identified and treated from among the 213 patients who completed the initial screening.

Differences in patient characteristics among those who completed TST screening and those who failed to complete TST screening are listed in Table 1. There was no difference in age between the compliant and non-compliant groups, but the percentage of males who completed screening was significantly higher than females.

Further assessment of the TB case rate among patients with DM on Ebeye reveals an association with age among the 210 individuals who completed screening and for whom age data were available (Table 2). Although TB disease was highly prevalent among all adults who completed screening (11/210, or 5200 per 100,000), adults with DM ≤ 50 years of age had greater prevalence (6/56, or 10,700 per 100,000) than those >50 years (5/154, or 3200 per 100,000) (RR 3.1, C.I. 1.0–9.7, p = 0.05).

4. Discussion

In the Ebeye Diabetes Clinic over a 2-year period, 213 patients were tuberculin skin tested, which resulted in diagnosing 77 with LTBI and 11 with TB disease. Recent reviews have underscored the synergistic effect of TB and DM, particularly the effect of DM on progression of TB infection to TB disease, the complexity of treatment when both diseases are present, and the potential value of bidirectional screening [10]. Systematic reviews and meta-analyses of observational studies have demonstrated a relative risk of TB disease developing in DM patients of 3.1 in populations with high