The Role of Diabetes Mellitus in the Higher Prevalence of Tuberculosis among Hispanics

Ariel Pablos-Méndez, MD, MPH, Jan Blustein, MD, PhD, and Charles A. Knirsch, MD, PhD

Introduction

Tuberculosis in the United States is predominantly a disease of minorities.\textsuperscript{1,2} The incidence of tuberculosis among minority populations is three to five times that among non-Hispanic Whites.\textsuperscript{3} The increased incidence of active tuberculosis in these groups is attributed to a higher prevalence of infection with \textit{Mycobacterium tuberculosis},\textsuperscript{3} the exposure to which is conditioned by exogenous factors such as poverty and birth in areas with a high prevalence of tuberculosis.\textsuperscript{4,5}

An association between diabetes mellitus and tuberculosis was noted centuries ago.\textsuperscript{6} Early in the 20th century, diabetic patients who did not die in a coma were likely to die from tuberculosis.\textsuperscript{7} Even after the introduction of insulin therapy, pulmonary tuberculosis was reported three times more often among diabetic patients than among nondiabetic patients.\textsuperscript{8-10} However, the proportion of deaths attributable to tuberculosis among diabetic patients fell dramatically from the 1920s to the 1970s.\textsuperscript{11} As the tuberculosis epidemic became rare, the published record on the subject came to a virtual halt. Diabetes mellitus is not included in the surveillance information systems for tuberculosis in the United States,\textsuperscript{2} and experts find past evidence linking diabetes and tuberculosis unconvincing.\textsuperscript{12}

Hispanics, especially Mexican Americans, have higher rates of both tuberculosis and diabetes mellitus compared with non-Hispanic Whites.\textsuperscript{4,13} However, the epidemiological interrelation between diabetes mellitus and tuberculosis in Hispanic Americans has not been studied. Thus, the present case-control study was designed to address the relative contribution of diabetes mellitus to the high prevalence of tuberculosis among Hispanic Americans.

Methods

Study Sample and Data

California is the state with the largest reported number of tuberculosis cases in the United States,\textsuperscript{5} including 40% of all cases occurring among Hispanics.\textsuperscript{4} A secondary analysis was conducted of publicly available data on all discharges from civilian hospitals in California during 1991; these data were obtained from the Office of Statewide Health Planning and Development.

Study cases were patients with a discharge diagnosis of tuberculosis (codes 010 to 018 of the \textit{International Classification of Diseases}, 9th rev, \textit{Clinical Modification} [ICD-9-CM]),\textsuperscript{14} whether that diagnosis was entered in a primary or secondary position. The ICD-9-CM codes exclude a positive tuberculin skin test without active tuberculosis and late effects of the disease.

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Control patients were selected by a primary discharge diagnosis of deep venous thrombosis of the legs (ICD-9-CM codes 451.1, 451.2, and 451.9), pulmonary embolism (ICD-9-CM code 415.1), or acute appendicitis (ICD-9-CM codes 540 and 541)—three conditions that have not been associated with the risk factor of interest, diabetes mellitus.15 Having conditions not associated with the risk factor of interest as the reason for admission is the essential criterion for selecting control patients in hospital-based case-control studies. The age- and race-stratified prevalence of diabetes in the resulting control group was similar to that reported in the general population and among Hispanics in particular.13

Definition of Diabetes Mellitus and Other Covariates

In this analysis, the terms Blacks and Whites refer to non-Hispanic people. Those in insurance categories “self-pay,” “no charge,” and “indigent” were collapsed into “none”; patients with health maintenance organizations, Blue Cross, and private insurance companies, as well as those with workers’ compensation and other governmental and nongovernmental coverage, were collapsed into “other insurance.”

Patients diagnosed with diabetes mellitus were identified by the corresponding ICD-9-CM code (250); fourth and fifth code digits were used to further classify the diabetes as type I or II and to ascertain whether the disease entailed complications or was poorly controlled. Acquired immunodeficiency syndrome (AIDS) or human immunodeficiency virus (HIV) infection was similarly noted (ICD-9-CM codes 042 to 044); patients with discharge diagnoses of Kaposi’s sarcoma (code 176), Pneumocystis carinii pneumonia (code 136.3), cryptococcosis (code 117.5), or acquired toxoplasmosis (code 130) were analyzed as HIV infected. Additional conditions in this analysis were chronic renal insufficiency (codes 585 and 586) and alcohol-related diagnoses (codes 291, 305.0, 303, 535.3, and 571.0 to 571.3). Cocaine and opiate dependence (codes 304.2 and 304.0) or abuse (codes 305.6 and 305.5) and unspecified drug dependence (304.9) were analyzed together as illegal drug use.

Data from the 1990 US Population Census were used to estimate the average income and educational attainment (percentage of subjects who had completed high school), as well as the proportion of those in the subjects’ zip codes of residence (using a total of 1508 zip codes) who were born outside the United States. Individuals with no zip codes (n = 144) or with zip codes outside California (n = 287) were assigned average values for the above socioeconomic measures from the rest of the data set stratified by age, sex, and race/ethnicity.

Statistical Analysis

Data management and statistical analysis were conducted in SPSS for Windows 6.0.16 All tests of significance (Student’s t, chi-squared) were two-tailed. Multiple logistic regression analysis was conducted following standard methods.17 All variables in Table I were entered in the multivariate models because they are clinically reasonable and not highly colinear (all pairwise kappa statistics were ≤.43). Given the large size of the study population, numerous pairwise interaction terms between diabetes and other covariates were found to be statistically significant; multivariate models to ascertain the association between diabetes and tuberculosis were run for each stratum of the clinically pertinent covariates of race/ethnicity, age group, foreign birth, and HIV status. The method recommended by Fleiss for retrospective studies was used to calculate population attributable risks: prevalence (odds ratio [OR] − 1)/(1 + prevalence [OR − 1]).18

Results

In 1991, there were 5290 discharges with active tuberculosis from all civilian hospitals in California; these included 1226 discharges (23.2%) with extrapulmonary disease. Tuberculosis was listed

<table>
<thead>
<tr>
<th>TABLE 1—Demographic and Clinical Characteristics of Study Subjects, among Patients Discharged from Civilian Hospitals in California during 1991</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases of Tuberculosis (n = 5 290)</td>
</tr>
<tr>
<td>---------------------------------</td>
</tr>
<tr>
<td>No.</td>
</tr>
<tr>
<td>---------------------------------</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Age, y</td>
</tr>
<tr>
<td>&lt;25</td>
</tr>
<tr>
<td>25–54</td>
</tr>
<tr>
<td>≥55</td>
</tr>
<tr>
<td>Race/ethnicity</td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Hispanic</td>
</tr>
<tr>
<td>Black</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Health insurance</td>
</tr>
<tr>
<td>Medicare</td>
</tr>
<tr>
<td>Medicaid</td>
</tr>
<tr>
<td>Other insuranceb</td>
</tr>
<tr>
<td>Uninsured</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td>HIV-related conditions</td>
</tr>
<tr>
<td>Chronic renal failure</td>
</tr>
<tr>
<td>Alcohol-related conditions</td>
</tr>
<tr>
<td>Drug use</td>
</tr>
<tr>
<td>Foreign birth, %c</td>
</tr>
<tr>
<td>Education, % without high schoolc</td>
</tr>
<tr>
<td>Median income, US $c</td>
</tr>
</tbody>
</table>

aPatients with a primary discharge diagnosis of deep venous thrombosis, pulmonary embolism, or acute appendicitis.
bHealth insurance other than Medicare or Medicaid.
cCensus-derived, median values (in brackets) in the zip code where patients resided.
as the primary diagnosis in 2514 discharges (47.5%). In the remaining cases, primary diagnoses included bacterial pneumonia (12.4%), heart failure and other cardiovascular disorders (7.1%), chronic lung diseases (3.7%), other lung disorders such as respiratory failure and pleurisy (5.3%), AIDS (3.0%), diabetes mellitus (2.5%), and other, less frequent conditions. The control group included 29,437 patients with acute appendicitis, 4624 patients with pulmonary embolism, and 3305 patients with deep venous thrombosis as the primary discharge diagnosis.

The demographic and clinical characteristics of the study subjects are presented in Table 1. Important characteristics of control subjects are further detailed in Table 2 by each of the racial/ethnic groups. Hispanic control subjects were younger and more likely to be uninsured than the other control subjects. They also resided in communities with higher proportions of foreign-born people and of non-high school graduates. The prevalence of diabetes was highest among Blacks and Hispanics. The proportion of diabetic patients with poorly controlled or complicated disease was similar among all three racial/ethnic groups.

The multivariate adjusted risk of tuberculosis for patients with diabetes mellitus, along with that of other risk factors, is presented in Table 3. The effect of all variables except drug use was statistically different across race/ethnicity (P < 0.01 for each two-way interaction term). While an association between diabetes and tuberculosis was found for Whites (OR = 1.31; 95% confidence interval [95% CI] = 1.19, 1.45), the association was much higher for Hispanics (OR = 2.95; 95% CI = 2.61, 3.33). Diabetes was also associated with tuberculosis for the “other” race/ethnicity group (OR = 2.55; 95% CI = 2.15, 3.01 [not shown]) but not for Blacks (OR = 0.93; 95% CI = 0.78, 1.09).

Among subjects younger than 25 years, diabetes mellitus increased the risk of tuberculosis nearly eightfold (OR = 7.84; 95% CI = 4.72, 13.02), while among those aged 55 or more, its impact was relatively small (OR = 1.26; 95% CI = 1.17, 1.36). The risk of tuberculosis associated with diabetes was also more apparent among patients more likely to be foreign born, with an OR of 1.95 (95% CI = 1.80, 2.10) among those living in areas with above the median prevalence of foreign birth by zip code, vs an OR of 1.38 (95% CI = 1.23, 1.54) for those living in areas below that median prevalence. The multivariate adjusted association between diabetes and tuberculosis did not vary significantly across the likelihood of having completed high school or the average income in the zip code area where patients resided. In patients not identified as HIV infected, diabetes nearly doubled the risk of tuberculosis (OR = 1.72; 95% CI = 1.61, 1.83).

HIV infection was a significant risk factor for tuberculosis in all racial/ethnic groups, although the degree of the association was two to three times higher among Hispanics. HIV infection increased the risk of extrapulmonary location of tuberculosis in Whites (OR = 1.88; 95% CI = 1.58, 2.24) and Hispanics (OR = 1.39; 95% CI = 1.18, 1.64), but not in Blacks (OR = 0.92; 95% CI = 0.75, 1.12).

Table 4 shows the population-attributable risk for diabetes mellitus and HIV infection as measured for each of the three racial/ethnic and age groups of interest. Tuberculosis was attributable to HIV infection in 45.7% of the cases among middle-aged Whites and in 33.5% of the cases among middle-aged Blacks, while diabetes played a significant role among young Black individuals and a relatively minor one in middle-aged Whites. Among Hispanics, 10.8% of the overall risk of tuberculosis could be attributed to diabetes mellitus, while 13.8% of the tuberculosis cases were associated with HIV infection (not shown). Among middle-aged and older Hispanics, diabetes was as important as HIV in explaining the prevalence of tuberculosis.

**Discussion**

This study shows that diabetes mellitus remains an important risk factor for tuberculosis in the 1990s. Diabetes nearly tripled the risk of tuberculosis among Hispanics, even after adjustment is made for census-derived estimates of immigration and socioeconomic status. The risk of tuberculosis attributable to diabetes mellitus among middle-aged Hispanics (25.2%) was similar to that attributable to HIV infection (25.5%).

Our retrospective analysis cannot establish either a cause-and-effect relationship or the required time order between diabetes and tuberculosis. In the 1930s, tuberculosis occurred in 8% of diabetic patients within 3 years of recovery from diabetic coma (and in 20% of such

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**TABLE 2—Characteristics of Control Subjecta Discharged from Civilian Hospitals in California during 1991, by Race/Ethnicity**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Whites (n = 22,759)</th>
<th>Hispanics (n = 10,252)</th>
<th>Blacks (n = 1,792)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, %</td>
<td>54.5</td>
<td>63.3</td>
<td>52.5</td>
</tr>
<tr>
<td>Age group, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25 y</td>
<td>31.7</td>
<td>56.3</td>
<td>30.1</td>
</tr>
<tr>
<td>25–54 y</td>
<td>38.4</td>
<td>37.9</td>
<td>41.0</td>
</tr>
<tr>
<td>≥55 y</td>
<td>29.8</td>
<td>5.8</td>
<td>28.8</td>
</tr>
<tr>
<td>Health insurance, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other insuranceb</td>
<td>62.3</td>
<td>38.4</td>
<td>45.8</td>
</tr>
<tr>
<td>Medicare</td>
<td>20.6</td>
<td>14.4</td>
<td>21.7</td>
</tr>
<tr>
<td>Medicaid</td>
<td>7.6</td>
<td>25.7</td>
<td>21.1</td>
</tr>
<tr>
<td>Uninsured</td>
<td>9.3</td>
<td>21.3</td>
<td>11.2</td>
</tr>
<tr>
<td>Diabetes mellitusb</td>
<td>4.0</td>
<td>6.8</td>
<td>9.2</td>
</tr>
<tr>
<td>Uncomplicated type I</td>
<td>18.1</td>
<td>16.0</td>
<td>20.3</td>
</tr>
<tr>
<td>Uncomplicated type II</td>
<td>54.4</td>
<td>57.0</td>
<td>50.5</td>
</tr>
<tr>
<td>Complicated/poor control</td>
<td>27.5</td>
<td>27.1</td>
<td>29.2</td>
</tr>
<tr>
<td>HIV infection, %b</td>
<td>0.5</td>
<td>0.1</td>
<td>0.4</td>
</tr>
<tr>
<td>Foreign birth, %d</td>
<td>18.3</td>
<td>33.0</td>
<td>25.7</td>
</tr>
<tr>
<td>Education, % without high schoold</td>
<td>12.6</td>
<td>21.6</td>
<td>18.7</td>
</tr>
<tr>
<td>Median income, US $d</td>
<td>18 115</td>
<td>12 186</td>
<td>12 936</td>
</tr>
</tbody>
</table>

*a* All patients with a primary discharge diagnosis of deep venous thrombosis, pulmonary embolism, or acute appendicitis.

*b* Prevalence of factor standardized for age and sex using the direct method.

*c* Health insurance other than Medicare or Medicaid.

*d* Census-derived, median values in the zip code area where patients resided (standardized for age and sex using the direct method).
### TABLE 3—Adjusted Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for Tuberculosis among Patients Discharged from Civilian Hospitals in California during 1991, by Race/Ethnicity

<table>
<thead>
<tr>
<th>Variable</th>
<th>Whites</th>
<th>Hispanics</th>
<th>Blacks</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjusted OR 95% CI</td>
<td>Adjusted OR 95% CI</td>
<td>Adjusted OR 95% CI</td>
</tr>
<tr>
<td>Sex (male vs female)</td>
<td>1.51 (1.42, 1.61)</td>
<td>1.02 (0.96, 1.10)</td>
<td>1.87 (1.68, 2.08)</td>
</tr>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25 (reference)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25–54</td>
<td>4.98 (4.35, 5.70)</td>
<td>2.87 (2.66, 3.10)</td>
<td>5.92 (5.02, 6.98)</td>
</tr>
<tr>
<td>&gt;54</td>
<td>12.71 (11.02, 14.65)</td>
<td>9.98 (8.93, 11.15)</td>
<td>4.90 (4.00, 6.01)</td>
</tr>
<tr>
<td>Foreign borna</td>
<td>1.18 (1.15, 1.21)</td>
<td>1.14 (1.11, 1.19)</td>
<td>0.94 (0.90, 0.99)</td>
</tr>
<tr>
<td>Poor educationb</td>
<td>1.40 (1.31, 1.50)</td>
<td>0.96 (0.88, 1.05)</td>
<td>2.33 (2.02, 2.68)</td>
</tr>
<tr>
<td>Median incomec</td>
<td>0.99 (0.98, 0.99)</td>
<td>1.00 (0.99, 1.01)</td>
<td>0.97 (0.95, 0.99)</td>
</tr>
<tr>
<td>Health insurance Other (reference)d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medicaid</td>
<td>2.22 (2.04, 2.42)</td>
<td>1.78 (1.54, 2.06)</td>
<td>2.58 (2.17, 3.07)</td>
</tr>
<tr>
<td>Medicare</td>
<td>5.87 (5.33, 6.46)</td>
<td>3.71 (3.39, 4.05)</td>
<td>5.21 (4.50, 6.02)</td>
</tr>
<tr>
<td>None</td>
<td>2.10 (1.88, 2.36)</td>
<td>2.51 (2.29, 2.76)</td>
<td>5.39 (4.61, 6.29)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type II, uncomplicated</td>
<td>1.31 (1.19, 1.45)</td>
<td>2.95 (2.61, 3.33)</td>
<td>0.93 (0.78, 1.09)</td>
</tr>
<tr>
<td>Type I, uncomplicated</td>
<td>0.99 (0.87, 1.15)</td>
<td>1.67 (1.39, 2.01)</td>
<td>0.63 (0.49, 0.82)</td>
</tr>
<tr>
<td>Poor control/complicated</td>
<td>1.49 (1.17, 1.88)</td>
<td>2.22 (1.66, 3.00)</td>
<td>0.80 (0.56, 1.13)</td>
</tr>
<tr>
<td>HIV-related conditions</td>
<td>54.26 (47.66, 61.77)</td>
<td>237.81 (160.81, 351.56)</td>
<td>79.37 (52.64, 119.67)</td>
</tr>
<tr>
<td>Chronic renal insufficiency</td>
<td>4.11 (3.30, 5.11)</td>
<td>10.92 (7.50, 15.89)</td>
<td>2.23 (1.61, 3.09)</td>
</tr>
<tr>
<td>Alcohol-related conditions</td>
<td>10.19 (8.87, 11.70)</td>
<td>24.49 (18.95, 31.64)</td>
<td>9.29 (6.92, 12.47)</td>
</tr>
<tr>
<td>Drug use</td>
<td>4.63 (3.26, 6.58)</td>
<td>9.51 (6.36, 14.20)</td>
<td>9.26 (6.26, 13.70)</td>
</tr>
</tbody>
</table>

*Race stratified models containing all the variables listed in the table. The odds ratios for all variables, except drug use, were statistically different across race/ethnicity (P<.01 for each two-way interaction term).

*bRisk associated with a 10% increase in the prevalence of foreign-born people or the proportion not completing high school in the zip code area where patients resided.

*cRisk associated with a $1000 decrease in the mean income per capita in the zip code area where patients resided.

*dHealth insurance other than Medicare or Medicaid.

### TABLE 4—Risk of Tuberculosis Attributable to Diabetes Mellitus (DM) and Recognized HIV Infection for Different Ethnoracial and Age Groups in California, 1991, Based on Hospital Discharge Data

<table>
<thead>
<tr>
<th>Ethnoracial and Age Groups</th>
<th>Age Distribution, %</th>
<th>Prevalence of DM in Controls, %</th>
<th>Odds Ratio for DM</th>
<th>DM-Population Attribute Risk, %</th>
<th>Prevalence of HIV in Controls, %</th>
<th>Odds Ratio for HIV</th>
<th>HIV-Population Attribute Risk, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whites (n = 24 501)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25 y</td>
<td>29.8</td>
<td>0.27</td>
<td>0.0335</td>
<td>...</td>
<td>0.000</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>25–54 y</td>
<td>38.5</td>
<td>2.28</td>
<td>2.0816</td>
<td>2.41</td>
<td>0.847</td>
<td>100.406</td>
<td>45.71</td>
</tr>
<tr>
<td>≥55 y</td>
<td>31.7</td>
<td>10.24</td>
<td>1.0991</td>
<td>1.00</td>
<td>0.544</td>
<td>6.320</td>
<td>2.81</td>
</tr>
<tr>
<td>Hispanics (n = 11 864)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25 y</td>
<td>51.6</td>
<td>0.07</td>
<td>4.8215</td>
<td>0.27</td>
<td>0.017</td>
<td>438.692</td>
<td>6.93</td>
</tr>
<tr>
<td>25–54 y</td>
<td>40.0</td>
<td>6.18</td>
<td>6.4530</td>
<td>25.21</td>
<td>0.128</td>
<td>268.962</td>
<td>25.54</td>
</tr>
<tr>
<td>≥55 y</td>
<td>8.4</td>
<td>19.76</td>
<td>1.4160</td>
<td>7.80</td>
<td>0.169</td>
<td>29.958</td>
<td>4.67</td>
</tr>
<tr>
<td>Blacks (n = 2849)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;25 y</td>
<td>31.5</td>
<td>0.37</td>
<td>0.1412</td>
<td>7.60</td>
<td>0.000</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>25–54 y</td>
<td>41.3</td>
<td>6.25</td>
<td>0.9222</td>
<td>...</td>
<td>0.816</td>
<td>62.681</td>
<td>33.48</td>
</tr>
<tr>
<td>≥55 y</td>
<td>27.2</td>
<td>22.63</td>
<td>0.7556</td>
<td>...</td>
<td>0.193</td>
<td>45.313</td>
<td>7.88</td>
</tr>
</tbody>
</table>

*aProportion of all cases in a given population that can be attributed to a given risk factor (i.e., DM or HIV infection).

*bDM was protective in this subgroup.

*cHIV prevalence was near zero in this subgroup, and coefficients were unstable.
patients within 5 years), and the development of tuberculosis appeared to follow the onset of diabetes in 85% of the cases.9 Also, the risk of tuberculosis is correlated with the severity of diabetes.

Tuberculosis infection depends mostly on circumstances exogenous to the exposed host, such as overcrowding and birth in regions with a high prevalence. Progression of latent infection to active disease, on the other hand, is primarily determined by endogenous host factors.3 Diabetic patients are not necessarily at higher risk of acquiring \( M \) tuberculosis infection,19 and a case–control study among American Indians suggested that diabetes is associated with reactivation of dormant tuberculosis.20

This is the first study on the relative contribution of diabetes mellitus to the increased prevalence of tuberculosis in Hispanic Americans. Although the risk of tuberculosis associated with HIV is more than 50 times that conferred by diabetes, the prevalence of diabetes is 20 times higher. The explanation for the heightened risk of tuberculosis among Hispanic patients with diabetes, compared with diabetic patients in other racial groups, cannot be addressed directly by our data. Possible explanations include differential exposure to \( M \) tuberculosis in hospitals and clinics, genetic factors predisposing individuals to both diabetes and tuberculosis, and unmeasured environmental or other socioeconomic factors. Differential hospitalization rates for some Hispanic patients—many of them undocumented aliens—is another possibility, although adjustment for health insurance makes this explanation less plausible.

Poor glucose control in diabetics confers a higher risk of tuberculosis,21 but the duration and pharmacological treatment of diabetes have been found to be similar across ethnicity.22 This study found no significant difference across racial/ethnic groups in the proportion of diabetic patients who had complications or in whom the disease was poorly controlled. In addition, the risk of tuberculosis for complicated or poorly controlled diabetes was still higher among Hispanics than among the other racial/ethnic groups. Thus, poor diabetes control is unlikely to explain the varying risk of tuberculosis for diabetics across racial/ethnic groups.

The lack of an association between diabetes and tuberculosis among Blacks is puzzling. Except among Blacks, our estimates of the prevalence of HIV infection was higher among nondiabetic than among diabetic control subjects.

Black control subjects also had a lower rate of HIV infection, as measured, than did White control subjects (0.4 vs 0.5%, Table 2). The HIV seroprevalence among military recruits in California, however, is higher among Blacks (0.6% vs 0.2% in all races).23 Also, several serosurveys in emergency departments24 and among tuberculosis cases25 have documented higher rates of unrecognized HIV infection among Black compared with White patients (relative risk = 2.4; 95% CI = 1.2, 4.7).

Thus, unidentified HIV infection among nondiabetic Black patients could have attenuated an association between diabetes and tuberculosis in this subgroup.

Large electronic data sets are increasingly being used in medical research.26,27 Diabetes mellitus has been shown to be reliably and validly coded in hospital discharge data.28 Race has been shown to be reasonably reliably coded,29 although to our knowledge there have been no studies validating codes with patient self-classification of race; similar limitations apply to Hispanicity. Census-derived socioeconomic data according to zip code are also widely used.30 Although the combination of census-derived socioeconomic characteristics and individual clinical data has been previously validated,31 mixing zip code (ecological) and individual data does present special problems.32 Residual socioeconomic heterogeneity within zip codes could confound the reported association between diabetes and tuberculosis.33 However, our approach is not handicapped by the small number of group units (1508 zip codes in total), and excluding zip code data from our analysis does not change the estimate of risk of tuberculosis for diabetic patients.

Most patients with tuberculosis are initially hospitalized, and the decision to hospitalize is not known to be influenced by a concomitant diagnosis of diabetes mellitus. Although the accuracy of discharge coding for tuberculosis has not been studied, the number of cases reported from California in 1992 (5382)33 was very close to the figure recorded in this study (5290); still, multiple unrelated hospitalizations cannot be excluded. For half the cases of tuberculosis in our study, tuberculosis was listed as the primary discharge diagnosis; an analysis of that subgroup returned estimates of relative and attributable risks similar to those in the whole group. The estimate of the prevalence of HIV infection among tuberculosis cases and controls (17.2% and 0.4%, respectively, as shown in Table 1) are also within expectations.23–25 The prevalence of diabetes mellitus among US tuberculosis patients is not known.

The role of diabetes in tuberculosis observed in the present study is likely to vary from one Hispanic subgroup to another. The incidence of tuberculosis and the prevalence of diabetes mellitus are both higher among Mexican Americans, whereas Cuban Americans have rates similar to those of Whites in the United States.41 Olmos et al. reported a 10-year cumulative incidence of tuberculosis of 4.8% in diabetic patients compared with 0.8% in the general population of Chile.34 Finally, the risk of tuberculosis is lower among older diabetic patients. This could represent not only milder forms of diabetes or remote tuberculosis infection, but also accumulated opportunities for screening and prophylaxis.

The American Thoracic Society has long recommended tuberculin skin testing of all diabetic patients. Those with a positive skin test (induration of 10 mm or more to purified protein derivative) who have never been treated should receive isoniazid and pyridoxine for 6 to 12 months, regardless of their age.35 The high prevalence of diabetes among patients with tuberculosis in this study suggests that the implementation of this policy is deficient. Lack of awareness of the association between diabetes and tuberculosis, and the possibility of anergy among diabetic subjects,36 may contribute to the failure to comply with this recommendation.37 Studies need to be done to ascertain what the appropriate threshold is for tuberculin skin test induration in diabetic patients, and whether some anergic diabetic patients would benefit from isoniazid prophylaxis. Regardless of the mechanism underlying the association between diabetes and tuberculosis, diabetic patients—especially Hispanics and, probably, recent immigrants from areas with a high prevalence of tuberculosis5—should be the target of tuberculosis screening efforts.

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