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Expected vs Reported Chronic Hepatitis B Infection Cases in Persons with Active Tuberculosis – California, 2016–2020

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Abstract

Epidemiologic data regarding persons with active tuberculosis (TB) and chronic hepatitis B virus (cHBV) infection are limited because of lack of routine surveillance of cHBV in persons with TB. Potential underdiagnosis of cHBV in California among those with TB is concerning. We matched TB and cHBV registries to identify cHBV infections among persons diagnosed with TB during 2016–2020 and described their demographic characteristics. We calculated expected cHBV cases among persons with TB for each demographic characteristic using published cHBV prevalence estimates for the locations of birth for persons with TB. Estimates were from general or emigrant adult and teen populations. Reported cHBV infection among persons with TB were 23% lower than expected, particularly among Asian persons, persons living in the two healthiest Healthy

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Places Index quartiles, and residents of less populated jurisdictions in California. Results show the possibility exists for underdiagnosis of cHBV in persons with TB in California.

Keywords

hepatitis B; tuberculosis; underdiagnosis

Active tuberculosis (TB) and chronic hepatitis B virus (cHBV) infection are two preventable conditions that cause substantial morbidity and mortality and have multiple risk factors in common, including birth in regions where these conditions are more common than in the United States, male sex, and older age.[1] Current understanding of the epidemiology of TB with cHBV infection in the United States is not well characterized because national and state surveillance systems for TB and cHBV have not routinely collected information regarding the other condition.[1] As a result, available data on TB with cHBV infection are from limited-scale studies from local health departments and might not be representative of wider populations.[2] TB case reporting has been found to capture >99% of active TB cases, but only 34% of persons with cHBV in the United States are aware of their infection, largely due to lack of awareness of screening guidelines by health care providers and patients.[1,3,4] This raises the concern that cHBV could be undiagnosed in many persons with TB. Patients with TB and cHBV may be at increased risk for hepatotoxicity and other poor outcomes during TB treatment, so knowing cHBV status may help avoid poor outcomes through increased monitoring or treatment modification. To date, no analysis has been made assessing whether reported cases of cHBV infection among persons with TB meet expected case numbers of those with both conditions. Such information would be valuable in determining how well cHBV is being identified among persons with known TB disease in public health systems, and where to focus public health resources to improve screening, diagnosis, and linkage to care. TB surveillance in California collects country of birth, a common risk factor for both TB and cHBV, and literature on estimated cHBV prevalence by country and global region is available.[1,5–7] Therefore, we sought to assess underdiagnosis of cHBV among persons with TB in California using this information to estimate the expected number of cHBV infections among persons with TB.

Methods

We analyzed data obtained from California's Department of Public Health TB and cHBV registries, which include surveillance data collected from 61 local health jurisdictions. We restricted analyses to California residents aged ≥15 years who received a diagnosis of TB during January 1, 2016–December 31, 2020. We defined TB disease as a report of TB with microbiologic confirmation for *Mycobacterium tuberculosis*. We defined cHBV infection according to the Council of State Territorial Epidemiologists case definition for a confirmed or probable cHBV case.[8] We matched persons reported with TB during the study period to the cHBV registry (1989–2020) using a probabilistic matching algorithm in Match*Pro v2.0.6 to identify persons with both TB and cHBV in California based on first name, last name, date of birth, sex, and postal code (or local jurisdiction of residence if postal code was missing). After these persons were identified, we summarized the cases by demographic characteristics, including sex, race, age, and location of birth, and calculated corresponding 95% confidence intervals (CI) for reported case numbers of persons with TB and cHBV.

We calculated the expected number of cHBV cases among persons with TB for each demographic characteristic by multiplying published pooled cHBV prevalence estimates from 2009 to 2019 (2015–2018 for the United States prevalence) for each location of birth (reported by each person in the TB registry) by number of persons with TB born in those locations for each characteristic[6,7] (See Table, Supplemental Digital Content http://links.lww.com/JPHMP/B350). The published cHBV prevalence estimates were from general or emigrant adult and teen populations. We calculated number of expected cases within quartiles of California's Healthy Places Index (HPI), a measure of community health and access to care. Quartiles 1 and 2 represent the least healthy areas with the least resources, while quartiles 3 and 4 represent the healthiest areas.[9] We considered reported case numbers to have met expected case estimates if the expected case number was within the 95% CI of the reported case number. We used SAS® version 9.4 (SAS Institute, Incorporated, Cary, North Carolina) for all analyses.

This activity was reviewed by the Centers for Disease Control and Prevention (CDC) and was conducted consistent with applicable federal law and CDC policy.* It was determined to be a non-research public health activity that did not require Institutional Review Board approval.

Results

In total, 8435 persons were identified with TB during the study period, with 316 (4%) reporting cHBV infection (95% CI: 282, 350). All persons with TB and cHBV had locations of birth reported. We calculated 409 expected cases of cHBV among TB patients during the study period. Lower than expected case numbers were observed across all genders and most age groups (Table). When California HPI quartiles were evaluated, those in quartile 3 (reported: 80, 95% CI: 63, 97; expected: 110) and quartile 4 (reported: 53, 95% CI: 39, 67; expected: 85) had lower than expected cHBV. In total, 259 (95% CI: 228, 290) reported cHBV cases were among Asian persons with TB, compared with 345 expected cases. When individual countries of birth were evaluated, those from the Philippines had the largest absolute difference with 60 (95% CI: 45, 75) reported cases and 116 expected cases (Table). When geographic regions of California were evaluated, Central California jurisdictions (reported: 26, 95% CI: 16, 36; expected: 42), jurisdictions bordering Mexico (reported: 23, 95% CI: 14, 32; expected: 42), and Southern California jurisdictions excluding Los Angeles County (reported: 53, 95% CI: 39, 67; expected: 87) reported cHBV case numbers among persons with TB that were lower than expected (Table).

Discussion and Conclusion

This is among the first analyses to estimate expected case numbers of cHBV infection among persons with TB. Given that surveillance systems have not routinely collected data

*§See e.g., 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.

on coinfection, expected case numbers cannot be estimated from prior data on persons with both conditions. Our analysis revealed that across California, reported cHBV case counts among persons with TB were approximately 23% lower than expected, based on current cHBV prevalence estimates. Furthermore, reported cHBV case numbers for Asian persons with TB were 25% lower than expected, including 48% lower than expected cases reported among those born in the Philippines. Additionally, jurisdictions in central California, along the Mexican border, and in southern California (excluding Los Angeles County) also reported lower than expected cases. The gap between the number of reported and expected cHBV cases in this analysis showed that cHBV might be underdiagnosed among persons with TB, which might affect linkage to appropriate care. This is consistent with prior literature showing underscreening of those at risk for TB or cHBV, such as those born in countries with high rates of these infections.[1,10] California law mandates reporting of cHBV infections by laboratories, therefore underre-porting seems less likely in this analysis.[11] The geographic differences might be because of a combination of less access to care in less populated, rural areas (especially among racial and ethnic minority groups) and robust cHBV prevention programs in metropolitan areas of California, which work to improve screening and identify those with cHBV for treatment.[12,13] This might also explain the HPI findings showing lower than expected cases in the healthiest quartiles, which might be a reflection of improved prevention or decreased health disparities in these more advantaged areas.[12,13] Programs such as Hep B Free in the San Francisco Bay Area have screened over 27,000 persons with over 50% of these found to be unprotected and candidates for vaccination.[13]

The main limitations of our findings are the assumptions used to obtain our expected estimates. The pooled cHBV prevalence estimates from non-US countries and immigrants across the United States might not necessarily reflect the true prevalence of cHBV in California. Furthermore, the cHBV prevalence in those with TB may be different than in the general population for any country given the shared risk factors for the two conditions, but prevalence estimates among people with TB in locations of birth are unavailable to us. However, the general estimates were based on a random effects analysis that assumed heterogeneity among different studies in different populations. Therefore, we believed these data reflected the best available estimates of cHBV. Additionally, given the match process was based on probability, it is possible to have either missed persons with both conditions or incorrectly classified persons as having both conditions. However, we used standard matching variables and the cut-off utilized maximized the likelihood of true matches. Lastly, the analysis cannot determine if the lower-than-expected case numbers we observed were because of underscreening or underdiagnosis of cHBV, or current prevention efforts that are reducing the number of cHBV cases among this population.

In conclusion, reported numbers of cHBV infection among persons with TB were lower, compared with the expected case numbers calculated, indicating an underdiagnosis of cHBV might be occurring in persons with TB in certain California communities. Our identification of specific populations with fewer cases than expected might guide future efforts to determine the reasons for these findings in these groups and improve cHBV screening in the TB population. New efforts are underway to increase cHBV screening in the general population and these efforts might improve cHBV screening practices among people at risk for TB. For example, California recently passed legislation requiring primary care providers to offer HBV screening for patients who meet US Preventive Services Task Force criteria.[14] Nationally, in March 2023, CDC recommended that all adults be screened for cHBV at least once in their lifetime.[15] Additionally, a field to capture viral hepatitis infection was recently added to the national TB surveillance system, which might enable similar assessment of underdiagnosis outside of California and raise awareness for more cHBV screening in patients with TB.[5]

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Implications for Policy & Practice

- Study results showed lower than expected HBV cases among persons with TB, particularly among Asian persons, those living in the two healthiest Healthy Places Index quartiles, and residents of less populated jurisdictions in California. These findings are concerning for underdiagnosis of cHBV in these California communities in persons with TB.
- These data can guide future efforts to improve cHBV screening in persons with TB in these communities and help reduce disparities in preventative care in vulnerable populations.
- Screening for HBV among all patients diagnosed with active TB should be encouraged in accordance with CDC recommendations and recent California state law for universal one-time testing of all adults.

TABLE

Expected Vs Reported Chronic Hepatitis B Virus (cHBV) Infections in Persons with Active Tuberculosis (TB) – California, 2016–2020

	Reported			
Characteristic	**Reported cHBV Cases**	**95% CI**	**Expected cHBV Cases**	**Total Number of TB Cases**
Total	**316**	**282, 350**	**409**	**8435**
Sex				
Male	**204**	**177, 231**	**248**	**5246**
Female	**112**	**92, 132**	**161**	**3189**
Race [a]				
American Indian or Native Alaskan	**0**	**NA**	**0**	**7**
Non-Hispanic Asian	**259**	**228, 290**	**345**	**4595**
Non-Hispanic Black	**18**	**10, 26**	**17**	**373**
Hispanic	**27**	**17, 37**	**27**	**2881**
Non-Hispanic Pacific Islander	**3**	**0,6**	**1**	**54**
Non-Hispanic White	**9**	**3, 15**	**14**	**507**
Age (yrs)				
15–24	**4**	**0, 8**	**25**	**670**
25–44	**53**	**39, 67**	**78**	**1986**
45–64	**132**	**110, 154**	**134**	**2655**
≥65	**127**	**105, 149**	**171**	**3124**
Location of birth [b]				
Africa	**8**	**3, 13**	**13**	**146**
Australia	**0**	**NA**	**0**	**1**
Canada	**0**	**NA**	**0**	**2**
China	**49**	**36, 62**	**50**	**591**
Europe	**1**	**0,3**	**1**	**62**
India	**4**	**0, 8**	**13**	**502**
Mexico	**16**	**8, 24**	**7**	**1809**
Other Asia (except Southeast)	**22**	**13, 31**	**34**	**573**
Other Southeast Asia	**33**	**22, 44**	**32**	**380**
Other Latin America	**5**	**1, 9**	**3**	**478**

Characteristic	Reported		Expected cHBV Cases	Total Number of TB Cases
	Reported cHBV Cases	95% CI		
Other Pacific Islands	**3**	**0, 6**	**1**	**34**
Philippines	**60**	**45, 75**	**116**	**1655**
United States	**23**	**14, 32**	**31**	**1257**
Vietnam	**92**	**74, 110**	**108**	**920**
California regions [c]				
San Francisco Bay Area	**117**	**104, 146**	**142**	**2368**
Mexican Border	**23**	**14, 32**	**42**	**1171**
Central	**26**	**16, 36**	**42**	**941**
Los Angeles County	**95**	**76, 114**	**92**	**2147**
Northern	**2**	**0,4**	**1**	**56**
Southern (Except Los Angeles County)	**53**	**39, 67**	**87**	**1727**
HPI quartile [d]				
1: <25th percentile	**63**	**48, 78**	**78**	**2478**
2: 25th–50th percentile	**103**	**84, 122**	**121**	**2289**
3: 51st–75th percentile	**80**	**63, 97**	**110**	**1878**
4: >75th percentile	**53**	**39, 67**	**85**	**1462**

Abbreviations: cHBV, chronic hepatitis B virus; CI, confidence intervals; TB, tuberculosis; HPI, Healthy Places Index.

[a] Self reported.

[b] Africa: Burundi, Benin, Botswana, Central African Republic, Côte D'Ivoire, Cameroon, Congo, Algeria, Egypt, Ethiopia, Eritrea, Western Sahara, Ghana, Guinea, Gambia, Kenya, Libya, Mauritania, Nigeria, Rwanda, Sudan, Senegal, Sierra Leone, Somalia, Togo, Tunisia, Tanzania, Uganda, South Africa, Zimbabwe, Liberia, and Zaire.

Europe: Belgium, Bulgaria, Bosnia and Herzegovina, Belarus, Germany, Denmark, Spain, France, United Kingdom, Greece, Croatia, Hungary, Iceland, Italy, Lithuania, Latvia, Moldova, Netherlands, Poland, Portugal, Romania, Serbia, Sweden, and Russia.

Other Asia: Afghanistan, Armenia, Azerbaijan, Bangladesh, Bhutan, Georgia, Hong Kong, Iran, Iraq, Israel, Jordan, Japan, Kazakhstan, Kyrgyzstan, North Korea, South Korea, Lebanon, Sri Lanka, Macao, Madagascar, Nepal, Oman, Pakistan, Saudi Arabia, Syria, Turkey, Taiwan, Ukraine, Uzbekistan, Yemen, Mongolia, and British Indian Ocean Territory.

Other Southeast Asia: Cambodia, Thailand, Laos, Burma, Malaysia, Brunei, Indonesia, and Singapore.

Other Latin America: Argentina, Belize, Bolivia, Brazil, Chile, Columbia, Cuba, Ecuador, Guatemala, Honduras, Haiti, Jamaica, Nicaragua, Peru, Puerto Rico, El Salvador, Suriname, Trinidad and Tobago, Venezuela, and Costa Rica.

Other Pacific Islands: American Samoa, Fiji, Micronesia, Guam, Marshall Islands, Solomon Islands, Tonga, United States Minor Outlying Islands, and Samoa.

[c] San Francisco Bay Area: Alameda, Contra Costa, Marin, Monterey, Napa, San Benito, San Francisco, San Mateo, Santa Clara, Santa Cruz, Solano, Sonoma, and Berkeley. Mexican Border: San Diego and Imperial; Central: Alpine, Amador, Calavera, El Dorado, Fresno, Inyo, Kings, Madera, Merced, Mariposa, Mono, Placer, Sacramento, San Joaquin, Stanislaus, Sutter, Yuba, Tulare, Tuolumne, and Yolo; Northern: Butte, Colusa, Del Norte, Glenn, Humboldt, Lake, Lasse, Mendocino, Modoc, Nevada, Plumas, Shasta, Sierra, Siskiyou, Tehama, and Trinity; Southern: Kern, Orange, Riverside, San Bernardino, San Luis Obispo, Santa Barbara, Ventura, Long Beach City, and Pasadena City.

[d] Healthy Places Index. The two lower quartiles (<25th and 35th–50th percentiles) represent less healthy areas and the higher quartiles (51st–75th and >75th percentiles) represent healthier areas.