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BRIEF REPORT

Bartonella Seroreactivity Among Persons Experiencing Homelessness During an Outbreak of *Bartonella quintana* in Denver, Colorado, 2020

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During a recent outbreak of *Bartonella quintana* disease in Denver, 15% of 241 persons experiencing homelessness who presented for severe acute respiratory syndrome coronavirus 2 testing were seroreactive for *Bartonella*. Improved recognition of *B quintana* disease and prevention of louse infestation are critical for this vulnerable population.

Keywords. *Bartonella quintana*; health disparities; homelessness; SARS-CoV-2; vector-borne disease.

The louse-borne bacterium *Bartonella quintana* is the most frequent cause of vector-borne disease among persons experiencing homelessness (PEH) in the United States and Europe [1]. *Bartonella quintana* disease is characterized by a wide range of clinical presentations, including a distinctive febrile illness and culture-negative endocarditis; many individuals may have asymptomatic or mildly symptomatic infections [2]. Serology can assist with the diagnosis of *B quintana* infection, but *Bartonella* seroreactivity does not necessarily indicate active disease and does not differentiate between *Bartonella* species [3]. Individuals infected with *B quintana* can remain seroreactive for years, even after effective treatment [3].

During the summer of 2020, an outbreak of *B quintana* disease was identified among PEH in the Denver, Colorado metropolitan area [4]. To estimate the prevalence of past exposure to *B quintana* among this population, we evaluated seroreactivity to *Bartonella* among PEH in Denver using residual serum samples obtained for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) serology testing.

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METHODS

Study Design and Sample Collection

Residual serum samples after SARS-CoV-2 antibody testing among people living homeless in Denver, Colorado collected during June–July 2020 were sent to Centers for Disease Control and Prevention (CDC) in Fort Collins, Colorado for *Bartonella* antibody testing after deidentification. Only information on age, gender, collection setting (shelter or encampment), race/ethnicity, and SARS-CoV-2 antibody result was retained.

Patient Consent Statement

This project was deemed a nonresearch activity by the CDC Human Subjects Review Board under provision of public health surveillance. Because this analysis involved residual, deidentified samples, consent for *Bartonella* serology testing was not obtained.

Laboratory Methods

Bartonella serologic testing was performed by indirect fluorescence antibody (IFA) assay. For antigen preparation, *B quintana* strain OK90-268 was cocultured with Vero cells. Cells were harvested and the resulting antigen preparation was spotted onto microscope slides and acetone fixed. Participant serum was applied at 2-fold dilutions from 1:128 to 1:4096, incubated, and washed. Goat antihuman immunoglobulin (Ig)G labeled with DyLight 488 (SeraCare, Milford, MA) was used as a secondary antibody with an Evans Blue counterstain (Sigma Aldrich, St. Louis, MO). After staining and washing, slides were examined with a fluorescent microscope and scored by 2 operators who did not have access to participant information. A reactive titer of ≥1:512 was chosen as the cutoff for positivity based on results in sera ($n = 479$) from the following: (1) polymerase chain reaction and/or culture-confirmed *B quintana* cases, the majority of which were collected during the postacute phase; (2) patients with other *Bartonella* infections or other diseases/conditions; and (3) healthy blood donors. At this titer cutoff and among this sample population, the sensitivity and specificity of this assay for *B quintana* infections are 95.7% and 96.5%, whereas the sensitivity and specificity for all *Bartonella* infections are 80.0% and 99.7%, respectively. For healthy blood donors the specificity at this cutoff is 100% (0 of 244). Serologic testing for SARS-CoV-2 was performed using either the Thunderbolt (Gold Standard Diagnostics, Davis, CA) or Access (Beckman Coulter, Brea, CA) assays according to manufacturers' instructions.

Statistical Methods

We described continuous variables using median and interquartile ranges (IQRs) and categorial data using counts

and percentages. *Bartonella* seroreactivity was defined as a titer ≥1:512. We used the Mann-Whitney *U* test to compare age between seroreactive and non-seroreactive persons and the χ^2 test or Fisher's exact test to examine associations between categorical variables and seroreactivity status. All statistical tests were 2-sided and we considered a $P \leq .05$ statistically significant. Statistical calculations were performed using R version 4.0.3 (R Foundation for Statistical Computing) [5].

We used logistic regression to examine the strength of association between available demographic variables and seroreactivity to *Bartonella*. We included self-identified gender, self-identified race/ethnicity, age, collection setting, and SARS-CoV-2 serostatus in a multivariable model. To examine for an effect due to cross-reactivity between SARS-CoV-2 and *Bartonella* antibodies, we repeated the analyses after censoring all PEH who tested positive for SARS-CoV-2.

RESULTS

Residual serum samples were available from 241 participants at encampments (n = 141; 59%) or overnight shelters (n = 100; 41%). Most participants identified as male (203 of 230, 88%). The median age was 45 years (IQR, 35–55 years). Among 223 persons who provided information on self-identified race/ethnicity, 105 (47%) were white, non-Hispanic persons, 37 (17%) were black, non-Hispanic persons, and 53 (24%) were Hispanic persons. Thirty-eight participants (16%) were SARS-CoV-2 seropositive. Approximately 15% (37 of 241) of participants were *Bartonella* seroreactive; of these, 6 (16%) at a titer of 1:512, 13 (35%) at 1:1024, 9 (24%) at 1:2048, and 9 (24%) at ≥1:4096.

Persons who were seroreactive to *Bartonella* were significantly older (median age 50.5 years; IQR, 40–57 years) than persons who were not seroreactive (median age 43 years; IQR, 34–54 years; P = .04) (Table 1). Seroreactive persons had similar gender and race/ethnicity distributions compared with those who were not seroreactive. In the adjusted logistic regression model, gender, race/ethnicity, collection setting, or age were not significantly associated with *Bartonella* seroreactivity (Supplemental Table 1). After censoring persons who tested positive for SARS-CoV-2, a similar proportion were *Bartonella* seroreactive (Supplemental Table 2).

Table 1. Association Between Demographic Characteristics or SARS-CoV-2 Antibody Status and *Bartonella* Seroreactivity

Characteristics	*Bartonella* Seroreactive (N = 37)	*Bartonella* Nonreactive (N = 204)	P Value*
Age (N = 241, median, IQR)	50.5, 40–57	43, 34–54	.04
Gender (N = 230)			
Female (n, %)	2 (6%)	25 (13%)	.39
Male (n, %)	31 (94%)	172 (87%)	
Race/Ethnicity (N = 223)			
Black, non-Hispanic (n, %)	3 (9%)	34 (18%)	.46
White, non-Hispanic (n, %)	17 (52%)	88 (46%)	
Hispanic (n, %)	7 (21%)	46 (24%)	
Other (n, %)	6 (18%)	22 (12%)	
Collection Setting (N = 241)			
Shelter (n, %)	18 (49%)	82 (40%)	.37
Encampment (n, %)	19 (51%)	122 (60%)	
SARS-CoV-2 Antibody Result (N = 238)			
Negative (n, %)	28 (86%)	172 (76%)	.20
Positive (n, %)	9 (14%)	29 (24%)	

Abbreviations: IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

*Calculated using Wilcoxon rank-sum test (age), χ^2 test (SARS-CoV-2 antibody result), or Fisher's exact test (gender, race/ethnicity, collection setting).

DISCUSSION

We identified a high proportion of *Bartonella* seroreactivity among PEH in Denver, Colorado during June–July 2020 in the context of a recently recognized outbreak of *B quintana* disease. These findings in Denver are consistent with prior studies in urban settings and indicate that *B quintana* disease remains a concern in PEH in the United States. In 1996, an outbreak of *B quintana* endocarditis among PEH in Seattle prompted a serologic study of PEH presenting for clinical care at a single clinic, 20% were seroreactive compared with 2% of blood donor controls [6]; another study reported that 9.5% of a convenience sample of persons who sought care at a free clinic in Los Angeles in 2002 were seroreactive [7]. Studies examining seroreactivity to *Bartonella* in the United States among persons who inject drugs found seroreactivity to *B quintana* antigens in 10% of individuals in Baltimore (1996) [8] and 2% in New York (2001) [9]. During 2012–2014, there were 6 confirmed cases of *B quintana* endocarditis among PEH in Alaska. Body lice positive for *B quintana* were collected from 2 of these patients [10]. More recent data on seroprevalence in the United States is lacking.

It is difficult to directly compare our results to other studies given different serological assays/test reagents and subjectivity in determining titers [11, 12]. The ≥1:512 titer used to define *Bartonella* seroreactivity was chosen for this serosurvey to optimize specificity. Although this high titer threshold may have resulted in misclassifying some persons with very recent *Bartonella* infection as non-seroreactive, it allows for high confidence that persons classified as seroreactive in this study truly represent those with prior or current *Bartonella* infection. Prior studies suggest that high titers are present in active, recent, or recurrent infection [11, 12].

Older age was associated with seroreactivity in this study, which may reflect higher prevalence of risk factors for *Bartonella* infection. Risk factors associated with *Bartonella* seroreactivity in previous studies included alcohol abuse, tobacco abuse, intravenous drug use, and homelessness [6]. Body lice infestation is a well recognized risk factor for *B quintana* infection among PEH [2, 13], and body lice infestation among PEH in San

Francisco was associated with sleeping outdoors, male gender, and black, non-Hispanic race/ethnicity [14].

This study is subject to at least 4 limitations. First, the presence of serum IgG does not distinguish between current and past infections; thus, these results in the absence of clinical symptoms, epidemiologic data, or other laboratory evidence are insufficient to confirm recent infections or a common source of *B quintana* infection among these participants. The *Bartonella* IFA is not specific to *B quintana* and cross-reacts with antibodies to other *Bartonella* species. Thus, the true rate of seroreactivity due to infection with *B quintana* among PEH in Denver may be lower than presented here. Second, our findings might not be representative of PEH in Denver or in other urban areas, given the risk for selection bias due to use of residual specimens from a convenience sampling strategy. Third, health and behavioral risk factor data were not collected, making it impossible to evaluate critical determinants of health, such as access to hygienic services and behavioral and medical healthcare services. Fourth, we did not have information regarding shelter or encampments where participants may have visited or slept. This information could provide useful insights as to common sources of lice exposure or settings where access to hygiene and lice mitigation are more challenging.

CONCLUSIONS

The high proportion of seroreactive participants in this report suggests that *B quintana* infection is of concern among PEH in Denver. Overcrowded living conditions and limited access to hygienic services for people without stable housing are likely to continue to drive this disease of poverty [2]. Active surveillance and treatment of body lice infestation, especially among at-risk individuals and in communities where *B quintana* infections or outbreaks are detected, can be implemented to prevent infection. Clinicians should be vigilant for symptoms among PEH that might suggest *B quintana* disease such as nonspecific febrile syndromes or symptoms of endocarditis and consider sending clinical specimens for *B quintana* molecular diagnostic testing. If culture is ordered, the microbiology laboratory should be notified that *B quintana* infection is suspected to optimize culture techniques, including extending the incubation period for ≥21 days [3]. These results underscore the need for heightened clinical awareness of *B quintana* infection and improved access to hygienic services in this population given louse-borne transmission of this bacterium [2].

Supplementary Data

Supplementary materials are available at Open Forum Infectious Diseases online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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