Received: 13 October 2022 | Revised: 21 December 2022 | Accepted: 22 December 2022

DOI: 10.1111/phn.13170

PHN PUBLIC HEALTH NURSING WILEY

CASE STUDY

Correlates of SARS-CoV-2 anti-RBD IgG antibody titers among persons experiencing homelessness in Los Angeles

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Funding information
UCI Office of Research Craft-COVID

Abstract

Objectives: People experiencing homelessness (PEH) have been especially impacted by the COVID-19 pandemic, likely due to increased vulnerabilities stemming from chronic diseases, substance use, and mental health conditions.

Design: A case–control study to assess the presence of antibodies against SARS-CoV-2 among PEH and associations with key variables.

Sample: A convenience sample of 97 PEH in Skid Row, Los Angeles.

Measurements: A structured questionnaire assessing socio-demographic, mental health, drug and alcohol use, health care access, pandemic stress, and other COVID-19-specific questions.

Results: We found high anti-receptor binding domain (RBD) IgG titers among five of 15 PEH who reported no prior COVID-19 diagnosis or being vaccinated, suggesting undiagnosed and/or asymptomatic COVID-19. While anti-RBD IgG titers across vaccination categories were not statistically significant ($p = .069$), participants vaccinated with Janssen had the lowest mean anti-RBD IgG titers. In multivariable analysis, we found negative associations between level of SARS-CoV-2 antibody titers with the Janssen vaccine and depression; thus, a need for integrated care for PEH with depression and COVID-19.

Conclusions: Further research is warranted to confirm the immune response, initial and over time, to SARS-CoV-2 infection and to COVID-19 vaccinations, particularly among PEH whose immune systems may be impacted by multiple health conditions.

KEYWORDS
people experiencing homelessness, SARS-CoV-2 antibody seroprevalence, substance use

1 | INTRODUCTION

People experiencing homelessness (PEH) are particularly vulnerable to infectious diseases as they experience higher rates of chronic diseases and accelerated physical decline (Baggett et al., 2018; Self et al., 2021). Sociodemographic characteristics, such as sex, race, and ethnicity also factor into significant health risk outcomes for PEH with COVID-19 as compared to their counterparts in the general population (Porter et al., 2022). Specifically, mortality rate increases substantially for the female and Hispanic populations with COVID-19, and there is likewise greater vulnerability to infection with older age in LA County (Porter et al., 2022).

PEH who use substances to cope are particularly vulnerable during COVID-19, and the search for drugs or alcohol further increases the risk of exposure to SARS-CoV-2 (Nyamathi et al., 2022). Tobacco and alcohol effects on health also make PEH more susceptible to higher severity of COVID-19 due to its associated cardiopulmonary risk factors (Benzano et al., 2021).

As crowded housing presents an increased risk for SARS-CoV-2 exposure among PEH, the causative agent for COVID-19, increased spacing between beds and transfer of medically vulnerable PEH to single-room emergency hotels was implemented by shelter operators in Los Angeles County (LAC) in 2020 and 2021 in response to the COVID-19 pandemic (Chang et al., 2022; Los Angeles County, Department of Public Health [LADPH], 2022). However, for some PEH, transition to alternate housing, challenges in accessing necessary care and support (Adams et al., 2022), and the sudden change towards telehealth and remote social services often led to increased feelings of stress, depressed moods, feelings of loneliness, and for some, greater use of drugs and alcohol (Benzano et al., 2021; Nyamathi et al., 2022; Perri et al., 2020). Furthermore, lack of knowledge about COVID-19 exacerbated worries about the disease.

A key factor for protecting against SARS-CoV-2 infection and developing COVID-19 disease is COVID-19 vaccination. Estimates suggest that in LAC, by July 2021, 35.2% of PEH were fully vaccinated, with 44.3% receiving at least one dose (Montgomery et al., 2021).

1.1 | Prevalence of SARS-CoV-2 among PEH living in Skid Row

In the Skid Row (Central City East) area of LAC, as of July 30, 2022, an estimated 20,430 PEH have tested positive for SARS-CoV-2 since the beginning of the pandemic; of these, 355 have died (Los Angeles County, Department of Public Health, 2022). The majority of PEH who have tested positive for SARS-CoV-2 identify as Latinx (42%) and Black or African Americans (27%); this is similarly true for mortality rates.

1.2 | Seroprevalence of antibodies to SARS-CoV-2 among PEH

Although LAC implemented an aggressive screening testing strategy in homeless settings, case detection is unlikely to have been completed. Measurement of antibody levels against SARS-CoV-2 can help assess immune protection against future infection. Currently, based on a few studies, SARS-CoV-2 IgG and IgM antibody prevalence among PEH has ranged from 1.5% to 54.7% and 2.1% to 15.2%, respectively (do Couto et al., 2021; Loubiere et al., 2021; Rowan et al., 2022). No studies have been conducted among PEH living in Skid Row, Los Angeles in assessing vaccine history or considered antibody response of the most vulnerable population. This information can help inform the design and development of infection control and prevention strategies (Lai, Wang & Hseuh, 2020).

1.3 | Theoretical framework

The Comprehensive Health Seeking and Coping Paradigm (Nyamathi, 1989) has provided a view of factors that might impact the health of vulnerable populations. These included sociodemographic, psychosocial, and behavioral factors. Sociodemographic factors included age, race/ethnicity, and country of birth. Psychosocial factors included mood, generalized anxiety, depressive symptoms, and post-traumatic stress disorder. In addition, social factors included social isolation and social support, while behavioral responses included drug and alcohol use.

1.4 | Purpose

We explored SARS-CoV-2 antibody response among PEH with and without prior COVID-19 diagnosis and vaccination history and examined evidence of undetected SARS-CoV-2 infections among PEH. Moreover, we explored the associations between sociodemographic, psychosocial, and behavioral factors with SARS-CoV-2 antibody response.

2 | METHODS

2.1 | Design

We conducted a case–control study to assess the presence of antibodies against SARS-CoV-2 among PEH with and without prior history of laboratory-confirmed COVID-19 diagnosis; data were collected between April 2021 and July 2021. Additionally, we assessed associations with sociodemographic, psychosocial, and behavioral factors. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guideline was followed to ensure a systematic reporting of the cross-sectional aspects of the study. Our study was approved by the Human Subjects Protection Committee at the University of California, Irvine.

2.2 | Sample and setting

A convenience sample of 97 PEH in Skid Row, Los Angeles were enrolled in the study. The Skid Row is a 54-block area wherein the

most vulnerable of the homeless populations live. Eligibility criteria included (1) age 18 years and older; (2) self-reported being homeless during the previous night; and (3) self-reported having used illicit substances or alcohol during the past year. PEH excluded were those who (1) exclusively spoke languages other than English or Spanish; or (2) were unable to understand informed consent.

PEH residing in one of three homeless shelters or two drug treatment sites in Skid Row, as well as from tents on the street in Skid Row during the COVID-19 pandemic, were enrolled. We aimed to enroll half of the sample among PEH previously diagnosed with laboratory-confirmed COVID-19, and the other half among those who never tested for SARS-CoV-2 or tested negative for SARS-CoV-2.

2.3 | Procedures

Trained research staff visited the recruitment sites wherein approved flyers were posted. Prearranged informational sessions were held for PEH who were interested in the study. If interest continued, research staff met privately with the PEH and presented more details about the study and answered all questions posed. Once completed, an informed consent was read and understanding assessed. Upon completion, the individual signed the consent.

The research staff then administered a structured questionnaire, which lasted about 45 min, assessing socio-demographic information, as well as mental health, drug and alcohol use, health care access, pandemic stress, and other COVID-19-specific questions. Snacks and breaks were offered. Data were entered into REDCap, and all participants were paid $3 for the screening questionnaire, and $30 for the structured questionnaire.

3 | SELF-REPORTED MEASURES

3.1 | Sociodemographic characteristics

Measures assessed include age, gender, race/ethnicity, county of birth, history of substance use, personal health, history of physical and mental illness, and days in shelter/street over the past 2 weeks.

3.2 | Psychosocial factors

Anxiety was assessed by the Generalized Anxiety Disorder-7 (GAD-7), a self-report 7-item measure (Spitzer et al., 2006) of symptoms of anxiety. Scores were summed. Severity of anxiety was determined with cut-off scores of five (mild anxiety), 10 (moderate anxiety), and 15 (severe anxiety). Reliability was $\alpha = .87$.

Depression was measured by the Patient Health Questionnaire-9 (PHQ-9). We used the PHQ-9, a brief, 9-item depression module from the full 26-item PHQ (Kroenke et al., 2001). PHQ-9 makes criteria-based diagnoses of depressive disorders, and can also determine severity, with scoring cut-offs for minimal (1–4), mild (5–9), moderate (10–14), moderately severe (15–19) and severe (20–27) depression. Reliability of the PHQ-9 in the PHQ Primary Care study was $\alpha = .89$.

Post-Traumatic Stress Disorder (PTSD) was assessed using the Primary Care PTSD Screen for DSM-5 (PC-PTSD), a 5-item questionnaire formatted to screen for possible PTSD in primary care settings (Prins et al., 2016), and reflects the DSM-5 criteria for PTSD (Prins et al., 2016). Participants were asked to respond "yes" or "no" to a question regarding prior traumas experienced by the participant. If a participant answered "no" to the initial question, their screen total was zero. If a participant answered "yes" to the initial question, they then answered 5 "yes" or "no" questions pertaining to how the trauma affected them in the past month. A positive screening was determined by a "yes" response to any three of the five items. The PC-PTSD-5 showed high diagnostic accuracy (AUC = 0.941; 95% CI: 0.912–−.969) (Prins et al., 2016).

Social support was measured by the Medical Outcome Study (MOS) Social Support Survey (Sherbourne & Stewart, 1991). The MOS is a 19-item instrument and includes four subscales: emotional/informational support; tangible support; positive social interaction; and affectionate support. The MOS uses a Likert-scale, with endpoints 1 (none of the time) to 5 (all of the time) that assesses availability of social support, with higher scores indicating more social support. An overall support index was also calculated.

3.3 | Behavioral factors

Drug and alcohol use was measured by the Texas Christian University (TCU) Screen V (Knight et al., 2018), a 17-item measure screening for mild to severe substance use disorder (SUD) based on self-reported use during the past three months. Participants indicated "yes" or "no" responses to substance dependency questions and the frequency of drug use based on a 5-point scale from 1 (never) to 5 (daily). The TCU Screen V is scored on a point-system ranging from 0 to 11. Participant scores correspond to the number of symptoms endorsed by the participant and the severity of SUD: mild disorder (2–3 points), moderate disorder (4–5 points), or severe disorder (6 or more points).

3.4 | Health factors

Chronic Health Conditions was assessed by the self-reported comorbidity index (SCQ) for medical problem, treatment, and limitations (Sangha et al., 2003). PEH were asked to respond if they have chronic health conditions (e.g., heart disease, high blood pressure, diabetes, osteoarthritis; Sangha et al., 2003). Responses include "yes or no" (Sangha et al., 2003). In a previous PEH sample ($N = 150$), Cronbach's $\alpha = .91$ (Salem et al., 2013).

Frailty was assessed using the Tilburg Frailty Indicator (TFI), a 15-item self-report instrument with three subscales which focus on physical (eight items), psychological (four items), and social frailty (three items) domains (Gobbens et al., 2015). An individual who scores 5/15 is considered frail (Gobbens et al., 2015).

3.5 | COVID-19 history

Participants were asked if they were ever diagnosed with COVID-19. Those who responded "yes" were confirmed by documented laboratory reports provided by the participant or, with permission, confirmed testing was reported by the facility staff. Moreover, vaccination history was confirmed by a documented vaccination record. Vaccination dates and manufacturer information were collected for each vaccine dose received.

3.6 | COVID-19 serology

Anti-RBD and Anti-NP IgG End-Point Titers—The anti-SARS-CoV-2 S1 (Spike Protein) RBD (Receptor Binding Domain) and NP (nucleocapsid protein) IgG ELISA is a highly specific enzyme immunoassay for the detection of IgG antibodies directed at the SARS-CoV-2 S1 RBD and NP in human blood. Anti-RBD IgG is expected to be elevated among people with prior history of SARS-CoV-2 infection and/or vaccination. Anti-NP IgG would only be elevated among people with prior SARS-CoV-2 infection as current vaccines do not include the NP target. This assay presents a useful tool to assess the individual's exposure to SARS-CoV-2. Anti-RBD and anti-NP IgG end-point titers were performed as described previously (Sureshchandra et al., 2021).

Briefly, 100 ul/well of 500 ng/ml SARS-CoV-2 S1 RBD and NP (GenScript) in dPBS (type of saline) were plated in clear 96-well high-binding plates. Plasma samples were heat-inactivated at 55°C and plated in duplicate at a 1:30 starting dilution with a threefold dilution thereafter. Horseradish peroxidase (HRP-conjugated anti-human IgG (BD Pharmingen) and *o*-phenylenediamine dihydrochloride (OPD) substrate were used to visualize responses before plates were read at 490 nm on a VICTOR3 Multilabel plate reader (PerkinElmer). A positive-control sample included with each assay was used to standardize titers.

3.7 | Statistical analysis

We calculated frequencies and percentages to describe categorical variables and mean and standard deviation to describe continuous variables. The primary outcome variable was log-transformed IgG titers against SARS-CoV-2 receptor binding domain (RBD). The outcome for samples with optical density indicative of no immune response was set to 0. Vaccination status was categorized as: unvaccinated, partially vaccinated (one dose of Moderna or Pfizer-Biontech), and fully vaccinated (two doses of Moderna or Pfizer-Biontech or one dose of Janssen). The Fisher's exact test and one-way analysis of variance (ANOVA) were used to compare categorical and continuous variables, respectively, across immune status categories.

We used linear regression models to estimate the association between participant characteristics and level of IgG titers among vaccinated participants to determine predictors of post-vaccination immune response among PEH. First, we ran separate bivariate models for each participant characteristic with IgG titers as the outcome variable. We then selected variables with $p < .1$ in the bivariate models for placement in the multivariable model. Variables with $p < .05$ was considered statistically significant and retained in the final model. R version 4.2.0 was used for all analyses.

4 | RESULTS

4.1 | Sample characteristics and reported prior COVID-19 diagnosis and vaccination status

Among the 105 screened, three did not meet eligibility criteria. Of the remaining 102 eligible individuals, we excluded five (4.9%) who did not have complete immunity status information and 28 (27.5%) who had unknown vaccination history. Sociodemographic characteristics of the 69 enrolled participants are presented in Table 1, separated by mutually exclusive categories based on vaccination status consisting of: "Unvaccinated" ($n = 22$), "Partially Vaccinated" ($n = 6$), "Fully Vaccinated (Janssen)" ($n = 6$), "Fully Vaccinated (Moderna)" ($n = 26$), and "Fully Vaccinated Pfizer-Biontech" ($n = 9$). The mean number of days since vaccination was 56.8 (SD 32.6), ranging from a mean of 27.3 days among partially vaccinated participants to 67.0 days among participants fully vaccinated with Pfizer-Biontech. Thirty-seven (53.6%) participants reported prior COVID-19 diagnosis, with different proportions across vaccination categories ($p = .037$). Prior COVID-19 diagnosis ranged from 16.7% among fully vaccinated participants with Janssen to 77.8% among fully vaccinated participants with Pfizer-Biontech.

Mean age of the participants was 47.4 (SD 12.5), with the majority being male (73.9%), Latinx (52.2%) or Black (24.6%), and US born (87.0%). Sociodemographic characteristics were similar across vaccination categories.

4.2 | Behavioral characteristics

About one fourth of the sample reported having a drug use disorder during the past three months, including 8.7% reporting severe drug use disorder. Greater numbers reported alcohol use (42.6%) or marijuana use (49.3%). Any drug or alcohol use was reported by the majority of participants (89.9%), while the use of more serious drugs, such as cocaine, amphetamine, methamphetamine, and heroin/opiate use was less than 5%. Behavioral characteristics were similar across vaccination categories.

4.3 | Self-reported chronic diseases

Self-reported prevalence of heart disease, diabetes, osteoarthritis, and chronic obstructive lung disease (COPD) was less than 10%, while high blood pressure was slightly higher at 13.0%. Chronic diseases were reported at similar frequencies across vaccination status categories.

TABLE 1 Sample characteristics of people experiencing homelessness by prior COVID-19 and vaccination status

	Unvaccinated (*N* = 22)	Partially vaccinated (*N* = 6)	Fully vaccinated (Janssen) (*N* = 6)	Fully vaccinated (Moderna) (*N* = 26)	Fully vaccinated (Pfizer-BNT) (*N* = 9)	Overall (*N* = 69)	*p*-value
Vaccination and COVID-19 history							
Days since vaccination							
Mean (SD)	Not applicable	27.3 (26.0)	53.2 (22.5)	60.8 (31.4)	67.0 (38.1)	56.8 (32.6)	.135
Prior COVID							
No prior COVID iagnosis	15 (68.2%)	2 (33.3%)	5 (83.3%)	8 (30.8%)	2 (22.2%)	32 (46.4%)	.037
Prior COVID iagnosis	7 (31.8%)	4 (66.7%)	1 (16.7%)	18 (69.2%)	7 (77.8%)	37 (53.6%)	
Sociodemographics							
Age							
Mean (SD)	47.3 (14.0)	43.2 (11.4)	40.5 (10.9)	50.6 (11.7)	45.6 (12.5)	47.4 (12.5)	.388
Median [Min, Max]	49.0 [18.0, 70.0]	42.0 [32.0, 63.0]	37.0 [32.0, 62.0]	53.5 [31.0, 67.0]	44.0 [23.0, 62.0]	49.0 [18.0, 70.0]	
Gender							
Male	11 (50.0%)	5 (83.3%)	6 (100%)	22 (84.6%)	7 (77.8%)	51 (73.9%)	.132
Female	10 (45.5%)	1 (16.7%)	0 (0%)	4 (15.4%)	2 (22.2%)	17 (24.6%)	
Transgender	1 (4.5%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1.4%)	
Race/Ethnicity							
Latino	8 (36.4%)	4 (66.7%)	3 (50.0%)	14 (53.8%)	7 (77.8%)	36 (52.2%)	.785
Black	8 (36.4%)	1 (16.7%)	1 (16.7%)	5 (19.2%)	2 (22.2%)	17 (24.6%)	
White	2 (9.1%)	0 (0%)	2 (33.3%)	5 (19.2%)	0 (0%)	9 (13.0%)	
Other	4 (18.2%)	1 (16.7%)	0 (0%)	2 (7.7%)	0 (0%)	7 (10.1%)	
Country of Birth							
United Statues	20 (90.9%)	4 (66.7%)	6 (100%)	22 (84.6%)	8 (88.9%)	60 (87.0%)	.354
Mexico	2 (9.1%)	0 (0%)	0 (0%)	3 (11.5%)	0 (0%)	5 (7.2%)	
Other	0 (0%)	2 (33.3%)	0 (0%)	1 (3.8%)	1 (11.1%)	4 (5.8%)	
Behavioral factors							
Drug use disorder							
No	13 (59.1%)	6 (100%)	6 (100%)	21 (80.8%)	7 (77.8%)	53 (76.8%)	.153
Yes	9 (40.9%)	0 (0%)	0 (0%)	5 (19.2%)	2 (22.2%)	16 (23.2%)	
Drug use category							
No disorder	13 (59.1%)	6 (100%)	6 (100%)	21 (80.8%)	7 (77.8%)	53 (76.8%)	.545
Mild/moderate	5 (22.7%)	0 (0%)	0 (0%)	4 (15.4%)	1 (11.1%)	10 (14.5%)	
Severe	4 (18.2%)	0 (0%)	0 (0%)	1 (3.8%)	1 (11.1%)	6 (8.7%)	
Alcohol use							
No	14 (56.0%)	13 (59.1%)	4 (66.7%)	2 (33.3%)	6 (66.7%)	39 (57.4%)	.852
Yes	11 (44.0%)	9 (40.9%)	2 (33.3%)	4 (66.7%)	3 (33.3%)	29 (42.6%)	
Marijuana use							
No	15 (62.5%)	10 (45.5%)	2 (33.3%)	4 (66.7%)	3 (33.3%)	34 (50.7%)	.607
Yes	9 (37.5%)	12 (54.5%)	4 (66.7%)	2 (33.3%)	6 (66.7%)	33 (49.3%)	
Cocaine Use							
No	24 (100%)	19 (86.4%)	6 (100%)	6 (100%)	9 (100%)	64 (95.5%)	.28
Yes	0 (0%)	3 (13.6%)	0 (0%)	0 (0%)	0 (0%)	3 (4.48%)	
Amphetamine use							
No	24 (100%)	20 (90.9%)	6 (100%)	5 (83.3%)	9 (100%)	64 (95.5%)	.232
Yes	0 (0%)	2 (9.09%)	0 (0%)	1 (16.7%)	0 (0%)	3 (4.48%)	

(Continues)

TABLE 1 (Continued)

	Unvaccinated (*N* = 22)	Partially vaccinated (*N* = 6)	Fully vaccinated (Janssen) (*N* = 6)	Fully vaccinated (Moderna) (*N* = 26)	Fully vaccinated (Pfizer-BNT) (*N* = 9)	Overall (*N* = 69)	*p*-value
Methamphetamine use							
No	22 (91.7%)	21 (95.5%)	6 (100%)	6 (100%)	9 (100%)	64 (95.5%)	.92
Yes	2 (8.33%)	1 (4.55%)	0 (0%)	0 (0%)	0 (0%)	3 (4.48%)	
Heroin/Opiate use							
No	22 (91.7%)	21 (95.5%)	5 (83.3%)	6 (100%)	9 (100%)	63 (94.0%)	.713
Yes	2 (8.33%)	1 (4.55%)	1 (16.7%)	0 (0%)	0 (0%)	4 (5.97%)	
Any drug use							
No	6 (27.3%)	2 (33.3%)	3 (50.0%)	14 (53.8%)	3 (33.3%)	28 (40.6%)	.435
Yes	16 (72.7%)	4 (66.7%)	3 (50.0%)	12 (46.2%)	6 (66.7%)	41 (59.4%)	
Any drug or alcohol							
No	1 (4.5%)	0 (0%)	0 (0%)	5 (19.2%)	1 (11.1%)	7 (10.1%)	.509
Yes	21 (95.5%)	6 (100%)	6 (100%)	21 (80.8%)	8 (88.9%)	62 (89.9%)	
Health factors							
Heart disease							
No	20 (90.9%)	5 (83.3%)	6 (100%)	26 (100%)	9 (100%)	66 (95.7%)	.239
Yes	2 (9.1%)	1 (16.7%)	0 (0%)	0 (0%)	0 (0%)	3 (4.3%)	
High BP							
No	20 (90.9%)	3 (50.0%)	6 (100%)	23 (88.5%)	8 (88.9%)	60 (87.0%)	.165
Yes	2 (9.1%)	3 (50.0%)	0 (0%)	3 (11.5%)	1 (11.1%)	9 (13.0%)	
Diabetes							
No	21 (95.5%)	5 (83.3%)	6 (100%)	25 (96.2%)	8 (88.9%)	65 (94.2%)	.705
Yes	1 (4.5%)	1 (16.7%)	0 (0%)	1 (3.8%)	1 (11.1%)	4 (5.8%)	
Osteoarthritis							
No	19 (86.4%)	6 (100%)	6 (100%)	25 (96.2%)	8 (88.9%)	64 (92.8%)	.754
Yes	3 (13.6%)	0 (0%)	0 (0%)	1 (3.8%)	1 (11.1%)	5 (7.2%)	
COPD							
No	21 (95.5%)	6 (100%)	6 (100%)	25 (96.2%)	9 (100%)	67 (97.1%)	.875
Yes	1 (4.5%)	0 (0%)	0 (0%)	1 (3.8%)	0 (0%)	2 (2.9%)	
Psychosocial factors							
Drug treatment motivation							
Mean (SD)	1.68 (1.25)	1.00 (0)	1.17 (0.408)	1.69 (1.38)	1.11 (0.333)	1.51 (1.13)	.606
Median [Min, Max]	1.00 [1.00, 5.00]	1.00 [1.00, 1.00]	1.00 [1.00, 2.00]	1.00 [1.00, 5.00]	1.00 [1.00, 2.00]	1.00 [1.00, 5.00]	
Social support							
Mean (SD)	35.9 (32.8)	34.4 (33.4)	62.7 (45.9)	46.7 (32.0)	33.6 (34.9)	41.9 (34.1)	.453
Median [Min, Max]	26.3 [0, 100]	27.0 [7.89, 100]	85.5 [2.63, 100]	42.1 [0, 96.1]	31.6 [0, 100]	31.6 [0, 100]	
Depression							
Mean (SD)	3.73 (4.95)	1.00 (1.55)	1.50 (1.22)	3.15 (3.98)	3.78 (6.18)	3.09 (4.35)	.594
Median [Min, Max]	1.00 [0, 16.0]	0.500 [0, 4.00]	1.00 [0, 3.00]	1.50 [0, 13.0]	0 [0, 18.0]	1.00 [0, 18.0]	
Anxiety							
Mean (SD)	4.68 (5.48)	1.50 (2.07)	1.33 (1.37)	2.58 (3.69)	4.44 (5.90)	3.29 (4.52)	.29
Median [Min, Max]	3.00 [0, 21.0]	0.500 [0, 5.00]	1.00 [0, 4.00]	1.00 [0, 14.0]	2.00 [0, 18.0]	1.00 [0, 21.0]	

(Continues)

TABLE 1 (Continued)

	Unvaccinated (*N* = 22)	Partially vaccinated (*N* = 6)	Fully vaccinated (Janssen) (*N* = 6)	Fully vaccinated (Moderna) (*N* = 26)	Fully vaccinated (Pfizer-BNT) (*N* = 9)	Overall (*N* = 69)	*p*-value
Frailty							
Mean (SD)	3.68 (2.82)	2.17 (2.04)	2.00 (1.26)	2.38 (1.36)	1.67 (1.58)	2.65 (2.10)	.17
Median [Min, Max]	3.00 [0, 10.0]	2.00 [0, 6.00]	1.50 [1.00, 4.00]	2.00 [0, 5.00]	1.00 [0, 5.00]	2.00 [0, 10.0]	
Positive social interaction							
Mean (SD)	2.21 (1.59)	1.89 (1.61)	3.61 (2.03)	2.74 (1.52)	1.78 (1.56)	2.45 (1.63)	.29
Median [Min, Max]	1.00 [1.00, 5.00]	1.00 [1.00, 5.00]	4.83 [1.00, 5.00]	3.00 [1.00, 5.00]	1.00 [1.00, 5.00]	1.00 [1.00, 5.00]	
PTSD score							
Mean (SD)	0.955 (1.68)	0.167 (0.408)	0 (0)	0.577 (1.36)	1.11 (1.76)	0.681 (1.43)	.539
Median [Min, Max]	0 [0, 5.00]	0 [0, 1.00]	0 [0, 0]	0 [0, 5.00]	0 [0, 4.00]	0 [0, 5.00]	

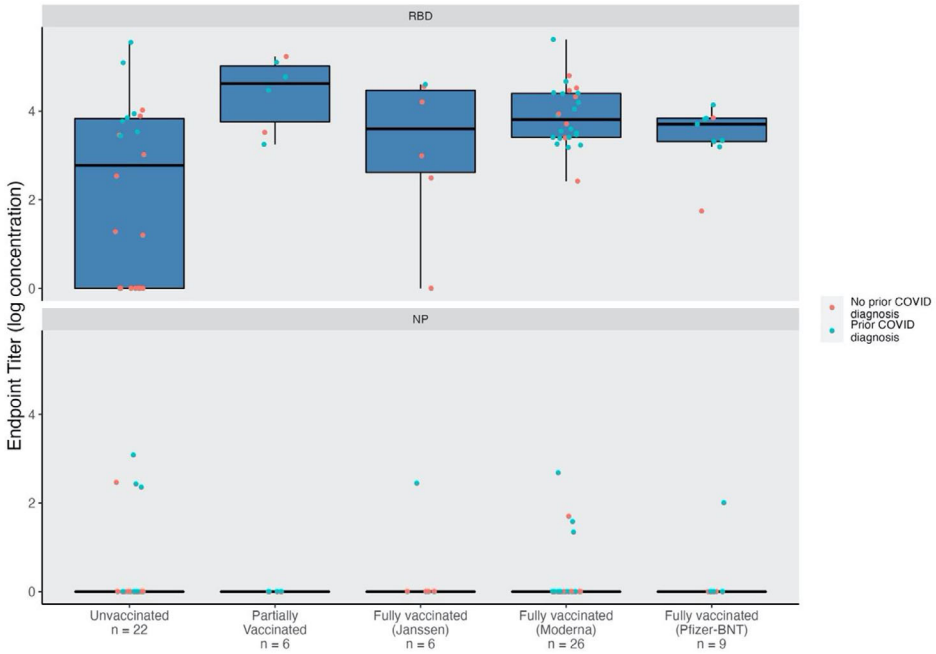

FIGURE 1 Anti-RBD and anti-NP IgG log titers by prior COVID-19 diagnosis and vaccination status [Color figure can be viewed at wileyonlinelibrary.com]

4.4 | Psychosocial characteristics

Social support was reported as moderate ($X = 41.9$), while depression and anxiety were considered mild ($X = 3.09$ and 3.29), respectively. PTSD was self-reported as low ($X = 0.681$). No statistically significant differences were observed across vaccination status categories.

4.5 | Anti-RBD titers

Anti-RBD IgG titers were substantially elevated among vaccinated groups compared to unvaccinated participants (Figure 1). Among 15 unvaccinated participants with no prior COVID diagnosis, five (33.3%) had elevated anti-RBD IgG titers, suggesting that they had undiagnosed prior infection in the past. Among vaccinated participants, IgG titers differed across categories, but the differences did not reach statistical significance ($p = .069$). Participants vaccinated with Janssen had the lowest mean anti-RBD IgG titers, while partially vaccinated participants had the highest anti-RBD IgG titers. One participant vaccinated with Janssen 34 days prior to data collection had no detectable anti-RBD IgG titer.

Ten of 69 participants showed measurable anti-NP IgG titers, which is consistent among people with prior SARS-CoV-2 infection (Figure 1). Of these, one participant reported no history of COVID-19 diagnosis, and no symptoms consistent with COVID-19 in the past several months. These findings suggest the occurrence

TABLE 2 Correlates of anti-RBD IgG titers (log-transformed) among people experiencing homelessness in Los Angeles: Bivariate and multivariate models

	Bivariate			Multivariate		
Characteristic	Beta	SE[1]	*p*-value	Beta	SE[1]	*p*-value
Vaccination status						
Fully vaccinated (Moderna)	–	–		–	–	
Partially vaccinated	.50	.404	.225	.35	.395	.377
Fully vaccinated (Janssen)	−.75	.404	.070	−.86	.393	.034
Fully vaccinated (Pfizer-BNT)	−.45	.345	.195	−.41	.333	.222
Days since last dose	.00	.004	.347			
Prior COVID diagnosis						
No prior COVID diagnosis	–	–				
Prior COVID diagnosis	.37	.282	.199			
Age	.01	.011	.226			
Gender						
Male	–	–				
Female/Transgender	.32	.385	.417			
Social support	.00	.004	.283			
Depression	−.07	.033	.043	−.07	.032	.042
Anxiety	−.04	.035	.227			
Alcohol use	.25	.281	.370			
Frailty	−.08	.095	.418			
Homeless duration						
<6 months	–	–				
6 months—less than 2 years	−.36	.494	.467			
2–4 years	.13	.409	.757			
5 years or longer	.00	.418	.997			
Days in street	.01	.011	.558			
Heart disease	−.53	.95	.578			
High BP	.00	.388	.998			
Diabetes	−.37	.562	.513			
Osteoarthritis	.30	.683	.666			
COPD	−.23	.96	.810			
Number of comorbidities						
None	–	–				
1	.10	.355	.785			
2 or more	−.41	.572	.477			
Any comorbidity						
1	–	–				
0	.03	.317	.926			
Drug use disorder	.50	.381	.195			
Drug use category						
No disorder	–	–				
Mild/moderate	.23	.438	.604			
Severe	1.2	.669	.085			
Marijuana use	−.24	.278	.387			
Amphetamine use	.79	.942	.407			

(Continues)

TABLE 2 (Continued)

	Bivariate			Multivariate		
Characteristic	Beta	SE[1]	*p*-value	Beta	SE[1]	*p*-value
Methamphetamine use	−.26	.678	.708			
Heroin/Opiate use	.36	.559	.519			
Any drug use	.00	.277	.987			
Any drug or alcohol	.29	.412	.487			

[1]SE = standard error.

of undiagnosed and/or asymptomatic SARS-CoV-2 infections among PEH.

4.6 | Correlates of anti-RBD IgG titers—Bivariate model

In bivariate analyses of vaccinated participants (Table 2), anti-RBD IgG titers were negatively associated with depression ($b = -.07$, $p < .043$). Vaccination status and drug use category variables reached the $p < .1$ threshold in bivariate analysis for further evaluation for the multivariate model.

4.7 | Correlates of anti-RBD IgG titers—Multivariable model

The final multivariable linear regression model predicting levels of anti-RBD IgG titers included vaccination history and depression (Table 2). Drug use category was evaluated for inclusion in the final model, but did not reach significance in the presence of vaccination history and depression and, thus, was removed from the model. Anti-RBD IgG titers were negatively associated with being vaccinated with Janssen compared to vaccination with Moderna when controlling for depression ($b = -.86$; $p = .034$). Depression was also independently associated with anti-RBD IgG after adjusting for vaccination status ($b = -.07$; $p = .042$).

5 | DISCUSSION

People experiencing homelessness (PEH) are at high risk for SARS-CoV-2 due to crowded shelter environments, and susceptible physical and mental health conditions (Baggett et al., 2018; Self et al., 2021). Yet, correlates of SARS-CoV-2 seropositivity among this most vulnerable population is not known.

Among the 69 PEH assessed in this study during the height of the COVID-19 pandemic in Skid Row, findings revealed one-third of PEH who were unvaccinated and did not have a history of prior diagnosis of COVID-19, had high levels of anti-RBD IgG, suggesting undetected SARS-CoV-2 infection in this group.

The low number of participants reporting prior COVID-19 diagnosis with elevated anti-NP IgG titers was unanticipated. However, this may be explained by recent findings demonstrating that antibodies against NP tend to decay rapidly initially after infection (Terpos et al., 2021); possibly rendering antibodies against NP an unreliable marker of previous exposure after 3 months. Additional research is needed to confirm the poor immune response to vaccinations among some PEH in this population.

In multivariable analysis, we found an independent negative association between SARS-CoV-2 antibody titers with vaccination with the Janssen vaccine (vs. Moderna) and depression. In a recent review of the literature on psychiatric adverse reactions to COVID-19 vaccines, Balasubramanian et al. (2022) contend that while a small minority of persons vaccinated do experience major adverse psychiatric reactions, a causal link cannot be made between any vaccine and the reaction due to the uncontrolled nature of the observations. Due to the reported increase in depressive symptoms among PEH during the COVID-19 pandemic (Riley et al., 2021; Scarlett et al., 2021), the modulation of this adverse outcome by COVID-19 vaccination is significant. Our findings suggest that integrated care for COVID-19 and depression may be warranted for PEH. This may include ensuring PEH with Janssen vaccination access to booster doses to generate robust immune protection, as well as referral for mental health symptoms.

This is important as depression has been shown to be associated with increased inflammation and reduced immune function (Sweetland et al., 2017). Social isolation and worry regarding isolation have been positively linked to depression (Scarlett et al., 2021) and/or anxiety (Riley et al., 2021) during the COVID-19 pandemic. Providing mental health services and social support to PEH with COVID-19 may moderate PEH concerns regarding isolation and manage depression and anxiety (Riley et al., 2021). In addition, providing treatment and primary prevention of COVID-19 to PEH may lead to significant physical and psychological benefits. Moreover, providing high-quality care to reduce depression among PEH could contribute to COVID-19 prevention.

Our finding of lack of association between anti-SARS-CoV-2 antibodies with sex and age was contrary to findings of Lo Sasso et al. (2021) who found that females had the highest levels of antibodies while the elderly had the lowest. In another study, Müller et al. (2021) reported similar findings to Lo Sasso et al. (2021), relative to the impact of age on antibody levels.

While the study has limitations related to sample size and representation of women, to our knowledge, this is the first study to date in which relationships between determinants of health and SARS-CoV-2 antibody response are highlighted. Future studies would benefit from studies composed of larger samples of PEH residing both in shelters and on the streets, as well as broader representation of gender and ethnicities. Further research is also needed with larger sample sizes to understand the low anti-RBD IgG titers among some PEH vaccinated with Janssen.

ACKNOWLEDGMENTS

We thank the dedicated and committed community-based organizations, providers, participants, and research team who helped us to successfully complete this study. This work was supported by the UCI Office of Research Craft-COVID.

CONFLICT OF INTEREST

None.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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How to cite this article: Nyamathi, A., Shin, S. S., Doratt, B. M., Jones-Patten, A., Salem, B., Gelberg, L., Lee, D., Garfin, D., Yadav, K., Chang, A. H., White, K., Arce, N., & Messaoudi, I. (2023). Correlates of SARS-CoV-2 anti-RBD IgG antibody titers among persons experiencing homelessness in Los Angeles. *Public Health Nursing*, 1–11. https://doi.org/10.1111/phn.13170