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PRELIMINARY REPORT

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Seroprevalence of SARS-CoV-2 in Utsunomiya City, Greater Tokyo, after the first pandemic in 2020

Nobutoshi Nawa MD, PhD, MPH[1] | Jin Kuramochi MD, PhD[2] | Shiro Sonoda MD, PhD[2] | Yui Yamaoka MD, PhD[3] | Yoko Nukui MD, PhD[4] | Yasunari Miyazaki MD, PhD[5] | Takeo Fujiwara MD, PhD, MPH[3]

[1]Department of Medical Education Research and Development, Tokyo Medical and Dental University, Tokyo, Japan

[2]Kuramochi Clinic Interpark, Utsunomiya, Japan

[3]Department of Global Health Promotion, Tokyo Medical and Dental University, Tokyo, Japan

[4]Department of Infection Control and Prevention, Medical Hospital, Tokyo Medical and Dental University, Tokyo, Japan

[5]Department of Respiratory Medicine, Tokyo Medical and Dental University, Tokyo, Japan

Correspondence
Takeo Fujiwara, Department of Global Health Promotion, Tokyo Medical and Dental University (TMDU), 1-5-45 Yushima, Bunkyo-ku, Tokyo 113-8519, Japan.
Email: fujiwara.hlth@tmd.ac.jp

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Abstract

Background: A seroepidemiological study was conducted on a random sample of households in Utsunomiya City, Tochigi Prefecture, Greater Tokyo, Japan, to assess the seroprevalence of SARS-CoV-2.

Methods: The level of IgG antibodies in the blood of the recruited subjects was assessed using chemiluminescence immunoassay analysis. In addition, the population-based prevalence of SARS-CoV-2 was estimated.

Results: Three positive afebrile cases were confirmed. The estimated unweighted prevalence and weighted prevalence of SARS-CoV-2 infection were 0.40% and 1.23%, respectively.

Conclusions: This study suggests that the prevalence of SARS-CoV-2 may have been underestimated. Wider testing strategies may lead to revealing more SARS-CoV-2 cases.

KEYWORDS
communicable diseases, coronavirus infections, seroepidemiologic studies

1 | INTRODUCTION

The number of confirmed cases of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections in Japan is substantially lower compared with those reported in the United States and the UK,[1] potentially because of the under-implementation of reverse transcriptase polymerase chain reaction (RT-PCR) tests. Some studies have reported that more than half of the SARS-CoV-2 infections are asymptomatic,[2] confirming the importance of conducting seroepidemiological studies.[3] While seroepidemiological studies in Japan have been reported to have a prevalence of 0.10% in Tokyo, 0.17% in Osaka, and 0.03% in Miyagi,[4] sampling bias has not been considered. The objective of the study presented in this paper was to assess the seroprevalence of SARS-CoV-2 in a random sample of households in Utsunomiya City, Tochigi Prefecture, Greater Tokyo, Japan.

2 | METHODS

The Utsunomiya COVID-19 seROprevalence Neighborhood Association (U-CORONA) study was launched to assess the seroprevalence of SARS-CoV-2 in Utsunomiya City. The survey was

conducted between June 14, 2020, and July 5, 2020, that is, between the first and second waves of the pandemic.[5] Invitations enclosed with a questionnaire were sent to 2290 people in 1000 households randomly selected from Utsunomiya City's basic resident registry. Written informed consent was obtained from all the participants. The level of IgG antibodies in the blood of the participants was assessed using chemiluminescence immunoassay analysis (Shenzhen YHLO Biotech Co., Ltd., Shenzhen, China).[6] According to the manufacturer, the sensitivity and specificity of the assay with a cutoff value of 10 AU/ml were 97.3% and 96.3%, respectively. Confidence intervals for unweighted seroprevalence were calculated using the exact binomial distribution. Furthermore, multiple imputation was applied to estimate the population-based weighted prevalence using baseline data from the registry, including age, gender, distance to clinic, residential district, and the number of cohabitants of participants and nonparticipants, considering the difference between participants and nonparticipants. Confidence intervals for weighted seroprevalence were calculated 50 times using the logit-transformed standard error and then combined using Rubin's rules. The analysis was performed in Stata 14 (StataCorp LP, College Station, TX, USA) and R version 3.6.0 (R Core Team, 2019). The study was approved by the research ethics committee at Tokyo Medical and Dental University.

3 | RESULTS

Among 2,290 candidates, 753 returned the questionnaire and 742 received IgG tests (32.4% participation rate). Among the 742 participants, 86.8% were 18 years old or older, 52.6% were women, 71.1% resided within 10 km from the test clinic, and 89.2% lived with another person (Table 1). The age and gender distributions and distance to the clinic of participants were similar to those of nonparticipants, while the proportion of single-person households was higher among nonparticipants than participants (16.2% vs. 10.8%). The residential distribution of nonparticipants and participants across the districts was significantly different (south: 28.0% vs. 22.8%; center: 31.6% vs. 38.1%, respectively).

Three positive cases were confirmed through quantitative antibody testing. No positive cases were found among the people who lived in the same household with the people tested positive. All the cases were afebrile. The estimated unweighted prevalence

TABLE 1 Demographic characteristics of study participants

	Participants in unimputed dataset (n = 742 from 341 households)	Number and prevalence of positive test in unimputed dataset (n = 742)	Weighted prevalence in imputed dataset (n = 2,290)
Variable	**N or Mean (% or SD)**	**N (%, 95% CI)**	**% (95% CI)**
Whole sample	742 (100.0)	3 (0.40, 0.08-1.18)	1.23 (0.17-2.28)
Age (in years)			
<10	56 (7.6)	0 (0.00, 0.00-6.38)	NA
10-17	42 (5.7)	0 (0.00, 0.00-8.41)	NA
18-65	463 (62.4)	3 (0.65, 0.13-1.88)	1.29 (0.14-2.43)
≥65	181 (24.4)	0 (0.00, 0.00-2.02)	NA
Gender			
Male	352 (47.4)	3 (0.77, 0.16-2.23)	1.90 (0.05-3.76)
Female	390 (52.6)	0 (0.00, 0.00-1.04)	NA
Distance to clinic (km)			
<1	4 (0.5)	0 (0.00, 0.00-60.24)	NA
1-10	524 (70.6)	2 (0.38, 0.05-1.37)	1.04 (0.00-2.15)
≥10	214 (28.8)	1 (0.47, 0.01-2.58)	1.42 (0.00-4.07)
Residential district			
Center	283 (38.1)†	1 (0.35, 0.01-1.95)	1.11 (0.00-2.85)
East	290 (39.1)†	2 (0.69, 0.08-2.47)	1.55 (0.00-3.45)
South	169 (22.8)†	0 (0.00, 0.00-2.16)	NA
Number of cohabitants			
1	80 (10.8)†	0 (0.00, 0.00-4.51)	NA
2	211 (28.4)†	0 (0.00, 0.00-1.73)	NA
≥3	451 (60.8)†	3 (0.67, 0.14-1.93)	1.50 (0.02-2.98)

Abbreviation: NA, not available.

†$P < .05$ for comparison between those who participated and those who did not.

and weighted prevalence of SARS-CoV-2 infection were 0.40% (95% confidence interval: 0.08%–1.18%) and 1.23% (95% confidence interval: 0.17%–2.28%), respectively (Table 1).

4 | DISCUSSION

The unweighted seroprevalence and weighted seroprevalence of SARS-CoV-2 in Utsunomiya City of Japan were found to be 0.40% and 1.23%, respectively, much lower than that in Los Angeles, United States (4.31%).[7] These results suggest that the majority of the population in Utsunomiya City was not infected. However, the number of unweighted and weighted estimated cases was 2,074 and 6,378 among 518,610 individuals, respectively, about 90 and 277 times higher than the number of confirmed cases in Utsunomiya City as of June 14, 2020, respectively, with 23 cases being due to the first pandemic.[5]

The main limitation of the study is the low participation rate. Furthermore, the prevalence could have been underestimated due to healthy volunteer bias. To address this issue, multiple imputation was applied to estimate the true prevalence of SARS-CoV-2 in the target sample, including nonparticipants. However, because of the household-based design of the study, participants who do not usually participate in clinical studies may have been pressured to do so by other household members.

According to the study, the prevalence of SARS-CoV-2 may have been underestimated. Wider testing strategies, for example, using RT-PCR and antigen testing, may reveal more SARS-CoV-2 cases. Further prospective studies with the same cohort would enable monitoring SARS-CoV-2 antibody levels.

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CONFLICT OF INTEREST

Authors declare no conflict of interests for this article.

ORCID

Nobutoshi Nawa https://orcid.org/0000-0001-6785-7867

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