



Geographical Profiles of COVID-19 Outbreak in Tokyo: An Analysis of the Primary Care Clinic-Based Point-of-Care Antibody Testing

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Abstract

Introduction: The primary care clinic plays a major role in triage for coronavirus disease 2019 (COVID-19), where seroprevalence in the setting of primary care clinic remains less clear. As a point-of-care immunodiagnostic test for the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the serosurvey represents an alternative to the polymerase chain reaction (PCR) test to measure the magnitude of COVID-19 outbreak in the communities lacking sufficient diagnostic capability for PCR testing. **Methods:** We assessed seropositivity for the SARS-CoV-2 IgG between April 21 and May 20, 2020, at 2 primary care clinics in Tokyo, Japan. **Results:** The overall positive percentage of SARS-CoV-2 IgG was 3.83% (95% confidence interval [CI]: 2.76-5.16) for the entire cohort (n = 1071). The 23 special wards of central Tokyo exhibited a significantly higher prevalence compared with the other areas of Tokyo after classification by residence ($P = .02$, 4.68% [3.08-6.79] vs 1.83 [0.68-3.95] in central and suburban Tokyo, respectively). In central Tokyo, the southern area showed the highest seroprevalence compared with the other areas (7.92% [3.48-15.01]), corresponding to the cumulative number of confirmed COVID-19 patients by PCR test reported by the Tokyo Metropolitan Government. **Conclusion:** The seroprevalence surveyed in this study was too low for herd immunity, suggesting the need for robust disease control and prevention. A regional-level approach, rather than state- or prefectural-level, could be of importance in ascertaining detailed profiles of the COVID-19 outbreak.

Keywords

COVID-19, antibody test, point-of-care testing, seroprevalence, community health, contagion

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Introduction

Primary care clinics perform a crucial role in the initial assessment of the coronavirus disease 2019 (COVID-19) and triage outpatients to determine those in need of intensive care in Japan.¹⁻⁴ However, a significant challenge for early identification of COVID-19 patients in the primary care setting is the fact that the patients show nonspecific or asymptomatic presentation.^{5,6} Understanding the magnitude of the first COVID-19 outbreak in the individual communities where we, as primary care physicians, are serving is of critical importance for public health purposes and improvement of diagnostic accuracy. The serosurvey is an alternative way to estimate the population of infected individuals during recent outbreak.^{7,8} Several reports on the antibody test are available. New York State announced that the seroprevalence for IgG of the severe acute respiratory syndrome

2 (SARS-CoV-2) in lower-income communities was higher than the overall population (27% versus 20% positive in New York City, respectively).⁹ In Los Angeles, California, the serosurvey revealed an antibody prevalence of approximately 5%.¹⁰ These surveillance efforts at the population level might help in the evaluation of herd immunity and the identification of risk factors as well. Of note, the World Health Organization cautioned that the presence of serum

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Table 1. Characteristics of Study Participants and Proportion Positive With SARS-CoV-2 IgG.

Characteristics	Sample size	Proportion of sample, % (95% CI)	No. positive	Proportion positive for SARS-CoV-2 IgG, % (95% CI)
Entire sample	1071	100	41	3.83 (2.76-5.16)
Sex				
Male	576	53.78 (50.74-56.80)	22	3.82 (2.41-5.73)
Female	495	46.22 (43.20-49.26)	19	3.84 (2.33-5.93)
Age, years				
≤17	13	1.21 (0.65-2.07)	0	0
18-34	134	12.51 (10.59-14.64)	11	8.21 (4.17-14.21)
35-54	653	60.97 (57.98-63.91)	19	2.91 (1.76-4.51)
≥55	271	25.30 (22.72-28.02)	11	4.06 (2.04-7.15)
Episodes of fever after December 2019	332	31.00 (28.24-33.87)	19	5.72 (3.48-8.79)
History of prior PCR testing for SARS-CoV-2	45	4.20 (3.08-5.58)	7	15.56 (6.49-29.46)
PCR positive	5	0.47 (0.15-1.09)	5	100
PCR negative	40	3.73 (2.68-5.05)	2	5.00 (0.61-16.92)
Cohabitant diagnosed with COVID-19	9	0.84 (0.38-1.59)	4	44.44 (13.70-78.80)
Health care worker	175	16.34 (14.17-18.69)	7	4.00 (1.62-8.07)

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; IgG, immunoglobulin G; PCR, polymerase chain reaction.

SARS-CoV-2 IgG should not convey a risk-free status for the future possibility of infection with COVID-19.¹¹

We previously reported our interim analysis of point-of-care antibody testing for COVID-19, conducted in primary care clinics throughout Tokyo, Japan.¹² Here, we describe our extensive analysis, which revealed the unique geographical characteristics of participants identified as SARS-CoV-2 IgG positive.

Methods

The institutional review board of Navitas Clinic approved this study (Approval Number: NC2020-01). Written consent was obtained from all participants before testing.

Participant Recruitment

This study summarizes the results of the antibody testing performed between April 20 and May 20, 2020. Web postings on the homepage of our clinics helped recruit asymptomatic subjects. The two study sites were clinics (Navitas Clinic Shinjuku and Tachikawa in Tokyo, Japan) (Supplemental Appendix 1) located in large railway stations where upper respiratory tract infection is the most common cause for patient visits.^{13,14} Study participants paid the entire cost of the point-of-care testing since insurance and public funding was not yet available to defray costs.

Antibody Test

Detection of the SARS-CoV-2-specific IgG antibody in peripheral blood was assessed by point-of-care immunodiagnostic test based on immunochromatographic assay

(SARS-CoV-2 Antibody Testing Kit IgG RF-NC002, Kurabo Industries Ltd). The rapid test implemented in this study indicated 76.4%, 100%, and 94.2% positive, negative, and overall agreement rates, respectively, following the manufacturer's instructions.

Statistical Analysis

Descriptive statistics were used to summarize participant characteristics. The percentages of IgG positive were presented with 95% confidential interval (CI). The 95% CI was calculated with the Clopper-Pearson method using PASS 14 (NCSS, LLC). All other statistical analyses were performed with IBM Statistics 26 (IBM Corp). Statistical significance was considered when the 2-sided *P* value was <.05.

Results

Participant Characteristics and Seroprevalence

The overall positive percentage of SARS-CoV-2 IgG antibody was 3.83% (95% CI: 2.76-5.16) for the entire cohort (*n* = 1071; Table 1). No increase in the seroprevalence was observed during the study period (Supplemental Appendix 2). The prevalence of seropositivity was significantly higher among participants with a history of fever after December 2019 (*P* = .03; 5.72 [3.48-8.79]) versus those without an episode of fever (2.98 [1.87-4.47]). We saw a total of 45 participants who previously tested for SARS-CoV-2 by polymerase chain reaction (PCR), and 7 among them exhibited IgG positive (15.56% [6.49-29.46]). All PCR-positive participants showed positive results of IgG (*n* = 5), whereas IgG positive was also seen in 2 with the PCR negative. The

Table 2. Comparison of Participant Characteristics Between Central and Suburban Areas of Tokyo.^a

Characteristics	Central Metropolitan Tokyo (n = 565)	Suburban Tokyo (n = 317)	P
Sex			ns
Male	318 (56)	143 (45)	
Female	247 (44)	174 (55)	
Age, years			ns
≤17	9 (2)	1 (<1)	
18-34	74 (13)	35 (11)	
35-54	355 (63)	185 (58)	
≥55	127 (22)	96 (30)	
Episodes of fever after December 2019	160 (28)	114 (36)	.02
History of PCR test for SARS-CoV-2	28 (5)	10 (3)	ns
PCR positive/negative	4/24	0/10	
Cohabitant diagnosed with COVID-19	6 (1)	1 (<1)	ns
Health care worker	87 (15)	60 (19)	ns
Positive for SARS-CoV-2 IgG	27 (4.8)	5 (1.6)	.02

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; IgG, immunoglobulin G; PCR, polymerase chain reaction; ns, not significant.

^aThe number and percentage, n (%), are shown after the classification by residence. The P values were calculated with Fisher's exact test.

seroprevalence in health care workers, including physicians, nurses, pharmacists, and laboratory technicians (n = 175), was 4.00% (1.62-8.07), which did not differ significantly from seropositivity among the participants.

Comparison of Seroprevalence Between Central Metropolitan Tokyo and Suburban Areas

The seroprevalence in the 23 special wards of central metropolitan Tokyo was significantly higher than in other areas of Tokyo after classification by residence ($P = .02$, 4.68% [3.08-6.79] versus 1.83 [0.68-3.95] in central and suburban Tokyo, respectively) (Table 2). We evaluated participant characteristics to determine whether the regional difference in seroprevalence was associated with their background. Consequently, statistical significance was only observed among of those with a history of fever. However, the proportion of those with a prior fever episode was lower in central Tokyo than in suburban areas (28% and 36%, respectively; $P = .02$). This was the opposite of our findings with seropositivity. We observed similar trends of seroprevalence in individual variables of participant characteristics after classification of residence, where the seropositivities in central Tokyo were higher than in suburban areas (Supplemental Appendix 3). Those aged 18 to 34 years in central Tokyo showed a notably large positive portion of 13.51% (6.68-23.45).

Geographical Trend of Seroprevalence in Central Tokyo

Additionally, we performed an exploratory analysis to determine the regional profile inside central Tokyo. The

highest prevalence occurred in the southern area (7.92% [3.48-15.01]) (Supplemental Appendix 4). We observed a similar regional trend in the cumulative number of COVID-19 patients per 100 000 people confirmed by PCR (Supplemental Appendix 5). Of note, the southern area has the largest number of physicians per unit population and the highest annual average income among the 4 areas of central Tokyo.

Discussion

The overall seroprevalence of SARS-CoV-2 in this study was less than 5%, suggesting that the majority of the community served by point-of-care clinics is immunologically naïve for SARS-CoV-2.^{15,16} We recognize the risks of a second wave of COVID-19 in our area and maintain vigilance to identify the patients at risk in primary care practice.

There were no significant differences in seroprevalence based on gender. Concerning age, younger participants <35 years old, but not those <18 years, exhibited the highest antibody-positive percentage in the comparison of age groups. However, the serosurvey in California did not detect any difference among age groups.^{10,17} The finding on age in this study indicates that we may miss the unknown bias in this study cohort and community. The locations of study clinics at major commuter stations and the study period during a national emergency to request staying at home may have biased measures of age distribution in seroprevalence. Also, while a history of fever contributed the seroprevalence in the analysis of the entire cohort, attention to patients without fever episodes is warranted since a history of fever did not influence seroprevalence after classification of residence. As

reported previously, the COVID-19 presents nonspecific symptoms.^{5,6} Therefore, primary care physicians should consider not only clinical presentations of patients but also the status of the outbreak in the community.

Naturally, prevalence is higher in a place of greater population density, such as central metropolitan Tokyo, where the primary transmission of SARS-CoV-2 by droplets is more effective. The regional trend of seroprevalence is similar to the cumulative number of COVID-19 patients per unit population. Of note, the greatest seroprevalence occurred in the southern part of central Tokyo, which represents the highest income area with the largest number of physicians per unit population. In contrast, the northern part of Tokyo exhibited both the lowest in seroprevalence and cumulative number of COVID-19 patients confirmed by PCR. These facts suggest that a community-based investigation of prevalence, rather than state- or prefecture-level, would be beneficial in exploring the cause of epidemic contagion.

The limitations of this study include selection bias, accuracy of the test kit and cohort size. The self-payment for the cost of the test and web-based participant recruitment likely fail to incorporate individuals at or near poverty as well as those unfamiliar with the internet. Limited sensitivity of the point-of-care test causes underestimation of seroprevalence. In contrast, overestimation may result if the proportion of participants with a history of fever in this study was higher than the general population.¹⁸ Notably, we observed 2 seropositive participants with negative prior PCR results, suggesting a limited ability of PCR testing in the first outbreak, and the potential of the antibody test to screen out infected people. However, our cohort is too small to make this conclusion definitely.^{7,19} Additionally, our cohort size is insufficient for subanalyses. For example, we estimate that over 4000 participants from central Tokyo would be required to detect a difference in the seroprevalence between those with and without fever episodes after classification of their residence (Supplemental Appendix 6).

In conclusion, our investigation of COVID-19 seroprevalence in the setting of primary care clinics in Tokyo, Japan, found a low antibody-positive proportion less than 5%. Primary care physicians should maintain their vigilance against future outbreaks. A robust emphasis on control and prevention of COVID-19 is crucial for the ongoing recovery phase of society.

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Supplemental Material

Supplemental material for this article is available online.

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