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## SARS-CoV-2 Antibody Seroprevalence in Jakarta, Indonesia

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# SARS-CoV-2 Antibody Seroprevalence in Jakarta, Indonesia

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## Abstract

The SARS-CoV-2 transmission dynamics in low- and middle-income countries remain poorly understood. This study aimed to estimate the SARS-CoV-2 antibodies seroprevalence in Jakarta, Indonesia, and to increase knowledge of SARS-CoV-2 transmission in urban settings. A population-based serosurvey among individuals aged one year or older was conducted in Jakarta. Employing a multistage sampling design, samples were stratified by district, slum and non-slum residency, sex, and age group. Blood samples were tested for IgG against three different SARS-CoV-2 antigens. Seroprevalence was estimated after applying sample weights and adjusting for cluster characteristics. In March 2021, this study collected 4,919 respondents. The weighted estimate of seroprevalence was 44.5% (95% CI = 42.5-46.5). Seroprevalence was highest among adults aged 30-49 years, with higher seroprevalence in women and the overweight/obese group. Respondents residing in slum areas were 1.3-fold more likely to be seropositive than non-slum residents. It was estimated that 4,717,000 of Jakarta's 10.6 million residents had prior SARS-CoV-2 infection. This suggests that approximately 10 infections were undiagnosed/underreported for every reported case. About one year after the first COVID-19 case was confirmed, close to half of Jakarta's residents have been infected by SARS-CoV-2.

**Keywords:** antibodies, COVID-19, immunity, SARS-CoV-2, seroprevalence

## Introduction

Urban areas are home to just over half the world's population yet are estimated to account for 90% of SARS-CoV-2 infections.<sup>1,2</sup> Serosurvey data suggest striking urban-rural gradients across diverse geographic and economic contexts including New York, the United States (20% urban vs 3.4% rural),<sup>3</sup> Spain (14% vs 1.7%),<sup>4</sup> Kenya (9.3% vs 1.7%),<sup>5</sup> and India (33% vs 1%).<sup>6</sup> Specifically, cities in low- and middle-income countries (LMICs) are where the pandemic's effects are likely to be most severe.<sup>2</sup> Greater population size, density, and connectedness alongside poor hygiene and infrastructure increase the frequency of infectious contacts and high-risk exposures.<sup>2,7</sup> Recent urban expansion and growing inequalities amplify these vulnerabilities, with the billion people globally residing in slums at the greatest risk.<sup>7-9</sup> High poverty levels hinder the introduction of public health measures such as mobility restrictions,<sup>10,11</sup> which must be carefully weighed against their adverse

social and economic consequences.<sup>12,13</sup> Finally, inequities in access to basic health and laboratory services constrain the effectiveness of established control measures, including timely case detection and contact tracing.

In the Southeast Asia, 84% of the population resides in LMIC contexts, with nearly half in urban centers.<sup>14</sup> Prior to Delta variant-associated severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission in mid-2021, the region was lauded for its apparent success in controlling the coronavirus disease 2019 (COVID-19).<sup>15</sup> However, data to support these assertions have been limited. With levels of diagnostic testing among the region's LMICs 10- to 15- fold lower than in high-income countries, confirmed cases are likely to be under-reported.<sup>16</sup> Furthermore, the use of serosurveys to detect prior SARS-CoV-2 infection has been of poor quality.<sup>17-19</sup>

Indonesia is the largest LMIC in Southeast Asia and is home to the world's fourth-largest population.<sup>20</sup> Nearly 10% of inhabitants reside in and around the

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Special Capital Region of Jakarta. SARS-CoV-2 infections were first detected in early March 2020, with cases confirmed across all 34 provinces within just four weeks. Despite having the highest number of reported COVID-19 cases and deaths in Southeast Asia, SARS-CoV-2 transmission remains poorly understood in Indonesia.<sup>16</sup> Similar to other LMICs in the region, national per capita testing rates have been low at just 1/25 levels of the United States or Singapore, and 1/4 levels in India which has a comparable per capita health expenditure.<sup>16</sup> While testing levels in the Special Capital Region of Jakarta are 10-fold higher than the national average,<sup>21</sup> concerns remain regarding the extent of underdetection.

To better understand the dynamics of SARS-CoV-2 transmission in an urban LMIC context in the Southeast Asia, a serological assessment was conducted in the Special Capital Region of Jakarta, Indonesia. The objectives were to estimate the seroprevalence of SARS-CoV-2 antibodies in the population by age group, sex, area of residence (slum/non-slum), and COVID-19 characteristics to compare seroprevalence to reported caseloads and to assess whether levels of prior SARS-CoV-2 infection approaches herd immunity thresholds.

## Method

This population-based cross-sectional survey was conducted in March 2021 in the Special Capital Region of Jakarta, Indonesia, one year after the first COVID-19 cases were confirmed. Respondents included residents aged one year and older across six municipalities of the province. All samples were collected in advance of initiating COVID-19 vaccination programs for general population.

A multistage sampling design was employed. At the first stage, one hundred urban villages were selected by probability proportional to size (PPS) sampling, with urban village populations as size. The urban villages were selected independently in every subdistrict and stratified by slum and non-slum areas. Sample sizes of urban villages in each slum/non-slum stratum were allocated proportionally to the total number of urban villages in each stratum. Urban villages containing slums were based on Statistics Indonesia/*Badan Pusat Statistik* (BPS) data. At the second stage, within each selected urban village, one neighborhood was selected by PPS sampling. Finally, individuals within each neighborhood were stratified by sex and age group. The number of individuals in each stratum was derived from lists provided by the Civil Registry Office and cross-checked by local health care provider staff. Sample sizes were estimated assuming a 5% SARS-CoV-2 antibody prevalence (absolute precision  $\pm 1\%$ ), a design effect of 2, and an 80% response rate.<sup>22</sup>

Prior to the survey, written informed consent was obtained from individuals aged 18 years or older. For indi-

viduals aged 1-17 years, consent was obtained from caregivers. The serosurvey study was conducted by the Jakarta Provincial Health Office in collaboration with the US Centers for Disease Control and Prevention (US CDC), the Eijkman Institute for Molecular Biology (EIMB), and with academic support from the pandemic response team from the Faculty of Public Health, Universitas of Indonesia.

All eligible participants were invited to the survey venue at a specified time. Non-attendees were replaced with age-sex matched individuals from a civil registry list. Participants were interviewed for sociodemographic characteristics, records of having contact with a confirmed COVID-19 case or suspect in the past month, and ever been diagnosed with COVID-19. Given the one-year duration of exposure, non-specificity of symptoms, and potential for recall bias, the authors opted not to assess potential COVID-19 symptoms. The weight and height were also measured, and random blood glucose tests were conducted. Body mass index (BMI) was calculated as weight (kg)/height (m<sup>2</sup>) and classified for Asian populations.<sup>23</sup>

Finger-prick blood drop samples, approximately 50 microliters of blood per spot, were collected from participants using Whatman 903 protein saver cards. Dried blood spots were tested for SARS-CoV-2 antibodies using the Human IgG Tetracore® FlexImm Array Human IgG test. This multiplex test detected IgG antibodies against three different proteins of the SARS-CoV-2 virus (receptor binding domain (RBD) of SARS-CoV-2 spike protein, nucleocapsid protein, and a recombinant spike RBD and nucleocapsid hybrid protein). The assay utilized seven microspheres sets with three different SARS-CoV-2 antigen detection antibodies and four internal controls. The test performed in a 96-well microtiter plate can be used to test up to 90 samples in one batch. For quality control, a negative control serum, a positive control serum, and a calibrator were tested in duplicate on each plate. For the sample to be reported as seropositive, the sample should show reactivity to all three SARS-CoV-2 antigens above pre-determined cut-off thresholds. This multiplex assay was a research use-only test and has been evaluated in collaboration with the Malaria Branch, US CDC, Atlanta, GA. The sensitivity and specificity of the assay for control specimens from the US reached 100% for each,<sup>24</sup> with additional validation at the EIMB Research Laboratory with serum known to be positive for various endemic diseases, including malaria and other viral infection, showing no cross-reactivity.

Characteristics of study participants are presented as numbers and percentages. The overall prevalence of SARS-CoV-2 antibodies was estimated by using sampling design and poststratification weights derived from the sex and age distributions in the population. Estimates are

presented as percentages and confidence intervals. Analysis was performed using Stata 17 (StataCorp, 2021).

The potential levels of underdetection of the COVID-19 cases were estimated in two ways. First, the self-reported COVID-19 diagnoses were compared to those seropositive by laboratory assessment. Second, to calculate the infection-to-case ratio, the adjusted seroprevalence estimates from the sample to the population aged one year or older residing in the same geographic area was applied. These figures were compared to a database of standard case report forms for all confirmed PCR-positive cases presented to health facilities in the Special Capital Region of Jakarta for one year, from March 2020 to March 2021.

The data analysis consisted of descriptive statistics, and the frequency, percentage, mean, and standard deviation distribution were included. The bivariate analysis using a Chi-square test was also utilized to assess the relationship between healthcare workers' knowledge, attitudes, and sociodemographic characteristics of COVID-19 prevention practices. Multiple logistic regression with a significance level of 0.05 was carried out to identify the odds ratio and factors associated with the COVID-19 prevention practices.

## Results

### Seroprevalence of SARS-CoV-2 Antibodies

A flow chart of participant enrolment is presented in Figure 1, and the characteristics of 4,919 respondents are shown in Table 1. More than half of respondents (60.1%) resided in an area with a slum neighborhood, and a few respondents (6.4%) had elevated blood glucose. Half of the sample was overweight or obese. Only 4.1% of respondents had a prior COVID-19 diagnosis, and 7.8% had exposure to a known positive case in the past month.

Table 2 profiles SARS-CoV-2 seropositivity by respondent characteristics. A total of 44.5% (95% CI 42.5-46.5) of respondents were tested positive for the SARS-CoV-2 antibody. Seropositive status ranged from one-third among children under five to one-half of adults aged 40-49 years old. Women had a marginally-higher prevalence than men. Respondents residing in areas with slum neighborhoods had a 1.3-fold greater prevalence than non-slum residents. There were no differences between participants with abnormal blood glucose levels relative to those with glucose in the normal range. Respondents who were overweight and obese had a higher prevalence than those with normal BMI or below. Those who had previous contact with a confirmed case or who had confirmed COVID-19 themselves were more likely to test positive for SARS-CoV-2 antibodies.

Figure 2 profiles infection-to-case ratios for the sero-

survey sample alongside estimates for the Special Capital Region of Jakarta population. Of 2,185 respondents tested SARS-CoV-2 antibody positive, 92.2% (95% CI = 95.2-93.5) had not received a prior positive diagnosis by RT-PCR, resulting in an infection-to-case ratio of 10.4:1. Based on levels of seroprevalence detected in this study, it was estimated that 4,717,000 residents had a prior infection with SARS-CoV-2 by March 31, 2021. During this period, the Special Capital Region of Jakarta recorded 382,055 cumulative positive COVID-19 cases, suggesting 91.9% of the cases were undetected with an infection-to-case ratio of 11.3:1.

## Discussion

This study presented the results of a serological as-

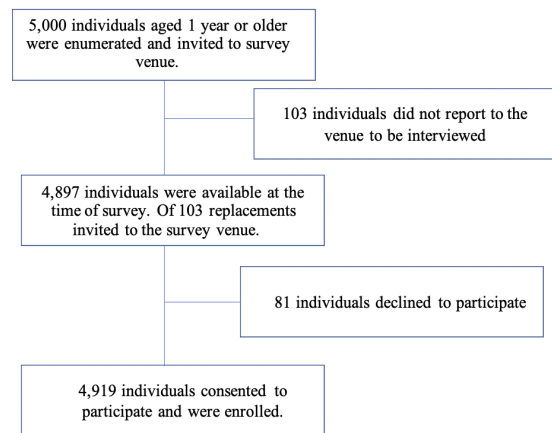


Figure 1. Participant Enrollment Diagram Flow

Table 1. Serosurvey Participant Characteristics (n = 4,919)

Variable	Category	n	%
Sex	Male	2,262	46.0
	Female	2,657	54.0
Age (years)	1-4	187	3.8
	5-14	874	17.8
	15-29	827	16.8
	30-39	714	14.5
	40-49	1,016	20.7
	50-59	725	14.7
Area of residence	60+	578	11.8
	Non-slum	1,964	39.9
Body mass index	Slum	2,955	60.1
	Underweight (<18.5 kg/m <sup>2</sup> )	287	7.5
Blood glucose level	Normal weight (18.5-25.0 kg/m <sup>2</sup> )	1,625	42.4
	Overweight (25.1-27.0 kg/m <sup>2</sup> )	574	15.0
	Obesity (>27.0 kg/m <sup>2</sup> )	1,344	35.1
Contact with COVID-19 suspects or confirmed cases in the past month	<200 g/dL	3,451	93.6
	200 g/dL	236	6.4
Previous positive COVID-19 diagnosis	Yes	385	7.8
	No	4,408	89.6
	Do not know	126	2.6
COVID-19 diagnosis	Yes	201	4.1
	No	4,413	89.7
	Do not know	305	6.2

Table 2. Seroprevalence by Population Characteristics (n = 4,919)

Variable	Category	Participants Tested (n)	Unweighted Seroprevalence (%; 95% CI)	Sampling Design Weighted Seroprevalence (%; 95% CI)	Post-stratification Weighted by Sex and Age Distribution in Population (%; 95% CI)
Overall		4,919	45.0 (43.6–46.4)	44.7 (42.7–46.7)	44.5 (42.5–46.5)
Sex	Male	2,262	41.2 (39.2–43.3)	41.1 (38.5–43.7)	41.1 (38.4–43.8)
	Female	2,657	48.2 (46.3–50.1)	48.2 (45.8–50.5)	47.9 (45.6–50.3)
Age group, years	1-4	187	31.7 (25.4–38.8)	32.4 (25.9–39.6)	31.8 (25.4–39.0)
	5-14	874	40.4 (37.2–43.7)	40.1 (36.4–44.0)	40.1 (36.3–44.0)
	15-29	827	42.0 (38.6–45.4)	41.3 (37.6–45.1)	41.2 (37.4–45.0)
	30-39	714	47.8 (44.1–51.4)	49.4 (45.1–53.7)	49.2 (44.8–53.5)
	40-49	1,016	49.9 (46.8–52.9)	49.4 (46.0–52.7)	49.0 (45.7–52.4)
	50-59	723	48.7 (45.1–52.3)	47.8 (43.7–52.0)	47.8 (43.7–51.8)
	60+	578	43.9 (39.9–47.9)	42.5 (37.9–47.3)	43.1 (38.5–47.8)
Area of residence	Non-slum	1,964	38.0 (35.8–40.1)	37.5 (34.0–41.2)	37.5 (34.1–41.1)
	Slum	2,955	49.6 (47.8–51.4)	48.7 (46.4–51.1)	48.4 (45.9–50.8)
Body mass index	Underweight	287	37.3 (31.9–43.0)	35.1 (29.2–41.4)	33.8 (27.9–40.3)
	Normal	1,625	42.5 (40.1–44.9)	42.0 (39.5–44.6)	42.0 (39.5–44.6)
	Overweight	574	52.2 (48.1–56.3)	51.7 (47.2–56.3)	52.9 (48.3–57.4)
	Obesity	1,344	51.1 (48. –53.8)	51.6 (48.4–54.9)	51.6 (48.2–54.9)
Blood glucose level	<200 g/dL	3,431	46.2 (44.5–47.9)	46.0 (43.7–48.3)	45.9 (43.6–48.2)
	≥200 g/dL	236	53.0 (46.6–59.3)	52.3 (45.0–59.4)	53.0 (45.7–60.1)
Contact with COVID-19 suspects or confirmed cases in the past month	Yes	385	59.9 (54.9–64.7)	60.1 (54.3–65.6)	59.8 (53.9–65.5)
	No	4,408	43.6 (42.1–45.0)	43.2 (41.2–45.3)	43.1 (41.0–45.2)
	Do not know	126	49.2 (40.6–57.9)	47.7 (37.1–58.4)	46.6 (36.2–57.4)
Previously positive COVID-19 diagnosis	Yes	201	87.6 (82.2–91.5)	87.7 (81.9–91.8)	87.5 (81.4–91.8)
	No	4,413	42.6 (41.2–44.1)	42.3 (40.2–44.4)	42.0 (39.9–44.1)
	Do not know	256	51.2 (45.6–56.7)	48.5 (41.8–55.3)	49.5 (42.7–56.2)

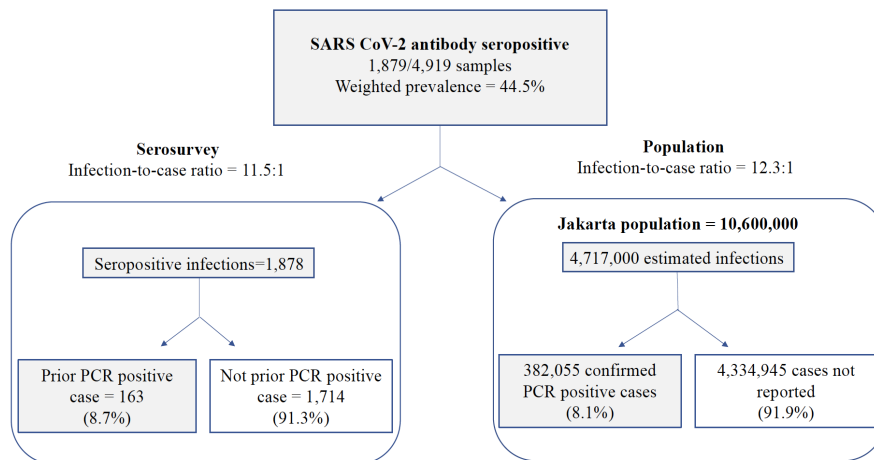


Figure 2. Infection-to-confirmed Case Ratios: Serosurvey and Population

assessment of SARS-CoV-2 antibody prevalence in the Special Capital Region of Jakarta, Indonesia. The findings suggested that within one year since the COVID-19 onset (March 2020 to March 2021), close to half (44.5%) of the population has been infected. By March 2021, there had been 4,717,000 prior infections in this urban center of 10 million people. Despite the Special Capital Region of Jakarta having the highest testing capacity in the country, levels of underdetection remain high. For each confirmed case, it was estimated that approximately ten infections were undiagnosed.

While seroprevalence peaked among working-age adults aged 30-49 years, children (5-14 years) were clearly susceptible, with nearly one-third tested positive for SARS-CoV-2 antibody. A higher seroprevalence was observed among women than men, which has been previously reported in urban centers in India,<sup>25</sup> and potentially linked to exposures resulting from women's household and social roles.<sup>26</sup> The higher seroprevalence among the overweight and obese relative to populations with normal or low BMI and those with COVID-19 diagnosis or contact was also observed. While obesity has been linked to

greater disease severity,<sup>27</sup> the link to the COVID-19 infection has not been previously described. Importantly, seroprevalence among residents in urban slums was 1.5-fold higher than non-slum residents, consistent with reports from LMICs elsewhere.<sup>25</sup>

This study's findings are in contrast with few previous serological assessments in the Southeast Asia, where lower levels of SARS CoV-2 exposure have been reported. These include assessments of hospital specimens in urban Malaysia (0.4%), health workers in Vietnam (0.6%), health workers in Thailand (5.7%), and the general population in Laos PDR (5.2%).<sup>17-19,28</sup> There is, however, strong concordance with population-based assessments from urban centers in South Asia including India and Bangladesh where seroprevalence levels of 54% (slums) and 63.1% respectively were observed.<sup>25,29</sup> Importantly, in all instances, these assessments were done in advance of widespread transmission of the highly contagious SARS-CoV-2 Delta variant in the South and Southeast Asia.

In some instances, observed disparities in seroprevalence are likely explained by the earlier timing studies in the pandemic's trajectory, rural-urban gradients with lower population density in some settings, methodological differences in the sampling strategy, and the quality of antibody assays utilized.<sup>30</sup> The effective introduction of non-pharmaceutical interventions may also contribute to lower observed prevalence. However, most LMICs in the region face similar trade-offs as Indonesia regarding enforcing non-pharmaceutical interventions in the context of high poverty levels. With low testing levels and limited high-quality population-based serosurvey data, statements on the relative success of the Southeast Asia's COVID-19 control efforts should be interpreted cautiously.

This study has several limitations. First, the seroprevalence estimates are likely to be conservative. The multiplex antibody assay requires threshold levels of detection for three separate antibodies for a positive result to be reported. This may lead to false negatives, resulting in an underestimate of seroprevalence. Issues of antibody decay over time may further compound these issues, particularly given that this study took place one year after the first confirmed cases were identified in Indonesia.<sup>16</sup> Second, the assessments regarding the level of underdetection are not likely to be generalizable outside the Special Capital Region of Jakarta, Indonesia. National levels of testing outside the capital are 10-fold lower with correspondingly higher levels of underdetection. Third, while mobility restrictions were mandated in the Special Capital Region of Jakarta and Indonesia during the pandemic, these were loosely enforced. As a result, mobility in and around Jakarta area is likely to contribute to its high prevalence in the capital. Finally, the assessment oc-

curred before accelerated Delta variant transmission between June and August 2021, after which seroprevalence is likely to have increased even further.

## Conclusion

In conclusion, the findings of SARS-CoV-2 antibodies in nearly half of the Jakarta population adds to a growing body of evidence, suggesting urban centers in the LMICs remain the places in the world most highly affected by the COVID-19. Despite the high observed prevalence, substantial portions of the population remain vulnerable to infection. Given the rapid transmissibility of the Delta variant, even with vaccination rates in the Special Capital Region of Jakarta approaching 50% as of August 2021, it is unlikely that herd immunity has been achieved. While gradients in transmission between rural and urban settings have been reported worldwide, growing inequalities within urban centers and the concentration of vulnerabilities observed in slums are particularly worrisome. A comprehensive approach to the COVID-19 control in these contexts must combine proven public health interventions with broader approaches that address social determinants, including strategies to guarantee food and livelihood security, well-tailored community awareness efforts, special attention to the needs of homeless populations, and strategies to ensure safe urban mobility.

## Abbreviations

SARS CoV-2: Severe Acute Respiratory Syndrome Coronavirus-2; COVID-19: Coronavirus Disease 2019; IgG: Immunoglobulin G; CI: Confidence Interval; LMICs: Low- and Middle-Income Countries; PPS: Probability Proportional to Size; BPS: *Badan Pusat Statistik*; BMI: Body Mass Index; RBD: Receptor Binding Domain; US CDC: US Centers for Disease Control and Prevention; EIMB: The Eijkman Institute for Molecular Biology; RT-PCR: Reverse-Transcriptase Polymerase Chain Reaction.

## Ethics Approval and Consent to Participate

The study protocol was approved by the Ethics Committee of the University of Atmajaya (No. 1245A/III/LPPM.PM.10.05/11/2020). Prior to the survey, written informed consent was obtained from individuals aged 18 years or older. For individuals between 1 and 17 years, consent was obtained from caregivers.

## Competing Interest

The author declares that there are no significant competing financial, professional, or personal interests that might have affected the performance or presentation of the work described in this manuscript.

## Availability of Data and Materials

Data were available upon request.

## Authors' Contribution

HJ and PMP led the drafting of the manuscript. IA, HJ, MNF, PR, and

WW designed the survey with substantial inputs from PMP, SGM, RN, and WAH. IA, MNF, HJ, PR, SGM, RN, and WW performed the data analysis and interpretation. LT and NF led the training in sampling procedures, sample handling and management, laboratory assay, data analysis, and interpretation. W, DOTLH, ESW, RD, and RH led the training in data collection procedures and closely monitored the overall data collection process. KSAM, FAY, VU, JM, NV, and KV provided scientific inputs on the manuscript writing. All authors approved the final version for publication.

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