

Short Communication

Comparison of anti-SARS-CoV-2 IgG seropositivity among vaccinated, unvaccinated, and COVID-19 survivor individuals: A cross-sectional study in Palembang, Indonesia

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Abstract

Measurement of anti-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) immunoglobulin G (IgG) antibody levels provides evidence of prior infection or vaccination. Persistent vaccine hesitancy underscores the importance of robust, evidence-based data to inform policy decisions. The aim of this study was to compare anti-SARS-CoV-2 IgG seropositivity among vaccinated individuals, unvaccinated individuals, and coronavirus disease 2019 (COVID-19) survivors in the community during the pandemic. In this cross-sectional study, 517 participants were enrolled, including 167 vaccinated individuals, 97 COVID-19 survivors, and 253 unvaccinated individuals, selected through multistage cluster sampling of 40 clusters. Anti-SARS-CoV-2 IgG seropositivity was defined as ≥ 50 AU/mL. Multivariable logistic regression was performed to evaluate associations between group type and seropositivity, adjusting for demographic factors, COVID-19 symptoms, hypertension, and body mass index (BMI). Vaccinated individuals demonstrated significantly higher odds of seropositivity compared with unvaccinated participants (odds ratio (OR)=5.60; 95% confidence interval (CI): 2.36–13.27). Covariates independently associated with seropositivity ($p < 0.05$) included the presence of COVID-19 symptoms, hypertension, and BMI. Vaccination was strongly associated with increased anti-SARS-CoV-2 IgG seropositivity in the community, independent of clinical and demographic factors. These findings support ongoing vaccination campaigns and highlight the relevance of comorbidities and symptomatic history in shaping humoral immune responses.

Keywords: COVID-19, IgG antibody, vaccinated, COVID-19 survivor, Indonesia

Introduction

In 2020, coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was identified as a global pandemic [1,2]. As of January 2023, more than 600 million people worldwide had confirmed SARS-CoV-2, with approximately 1% death [3]. Indonesia reported approximately 4.2 million confirmed cases of COVID-19 by the end of 2021 [4]. The coverage of the second dose of COVID-19 vaccination in Indonesia had only reached 32.73% in 2021 [5], partly because many people (63.9%) were still hesitant to receive vaccine against COVID-19 [6].

The introduction of SARS-CoV-2 into the body, either naturally or after administration of the COVID-19 vaccine, produces immunoglobulin G (IgG) antibodies as part of the immune



response. The level of IgG antibodies in the blood can be a parameter to determine whether a person has been infected with COVID-19 and to determine the effectiveness of vaccination [7]. An earlier study indicated that the specificity and sensitivity values of IgG detection using chemiluminescence immunoassay (CLIA) were 96.04% and 97.06%, respectively [8]. Studies assessing the levels of IgG antibody against SARS-CoV-2 in the vaccine group have been carried out in Turkey, the United States (US), Italy, the United Kingdom (UK), and Indonesia [9-14]. These studies showed that antibody production following vaccination was influenced by age, interval since the second vaccine dose, smoking status, body mass index (BMI), ethnicity, and hypertension [9-14].

Studies on unvaccinated individuals have been conducted, showing 44.5% positivity for anti-SARS-CoV-2 IgG antibodies in Indonesia [15], 6.3% in Pakistan [16], and 23.2% in India [17]. However, most previous studies [7-18] were conducted in a single group or population, limiting the understanding of how COVID-19 relates to specific environmental, social, or demographic conditions. Previous reports demonstrated that anti-SARS-CoV-2 antibody responses were associated with various factors, including circulating SARS-CoV-2 variants, ethnicity, poverty levels, income level, insurance coverage, unemployment level, access to health services, socioeconomic status, residential density, and race [13,19-22]. Further comparisons of antibody levels among vaccinated individuals, COVID-19 survivors, and unvaccinated groups are needed to provide evidence-based guidance for policymakers. Therefore, the aim of this study was to address the evidence gap by comparing seropositivity of anti-SARS-CoV-2 IgG antibodies among vaccinated individuals, unvaccinated individuals, and COVID-19 survivors, while controlling for sociodemographic variables, history of COVID-19 symptoms, nutritional status, and hypertension comorbidities.

Methods

Study design

This study employed a cross-sectional design that included three groups: vaccinated individuals, unvaccinated individuals, and COVID-19 survivors. The study was conducted between November 2021 and March 2022 in Palembang, Indonesia. Data collection and blood specimen sampling were performed on 517 participants selected through multistage random sampling from designated clusters.

Sample criteria

Inclusion criteria for the vaccinated group were age ≥ 18 years, completion of two doses of the COVID-19 vaccine, a minimum interval of four months between the last vaccination and sample collection, and no history of confirmed COVID-19 infection. For the COVID-19 survivor group, participants were required to be ≥ 18 years old, have at least a four-month interval between COVID-19 diagnosis and sample collection, and not have received any COVID-19 vaccination. For the unvaccinated group, inclusion criteria were age ≥ 18 years and no known history of COVID-19 vaccination or confirmed COVID-19 infection, as assessed by interview.

Sample size and sampling method

The minimum sample size for the vaccinated group was calculated assuming a 10% prevalence of vaccinated individuals in the population, with 2% precision and a 95% confidence level. For the COVID-19 survivor group, the minimum sample size was similarly estimated using a 10% population prevalence, 2% precision, and a 95% confidence level. For the unvaccinated group, the minimum required sample was calculated using the formula by Lameshow [23], based on an estimated population variance of 15% and 2% precision.

Sampling was conducted using a multistage cluster design across 40 selected clusters. At the time the study commenced, full COVID-19 vaccination coverage in the city was 46.89% [24]. Cluster sampling was carried out in five stages: (1) 40 clusters were randomly selected with probability proportional to size using the Indonesian Ministry of Health application standard, C Survey application; (2) the population of each selected cluster was enumerated by neighborhood; (3) one neighborhood was randomly chosen within each cluster; (4) households were listed within

each selected neighborhood; and (5) households were randomly sampled according to the required sample size.

Study variables

The main independent variables consisted of vaccinated, unvaccinated, and COVID-19 survivor groups. Control variables included age group, sex, occupation, history of COVID-19 symptoms, hypertension status, supplement consumption, and BMI [25]. The respondents' characteristics and COVID-19 history were identified using a questionnaire. Hypertension status was determined through blood pressure measurement using a digital sphygmomanometer during the study and a history of hypertension diagnosed by a doctor. BMI status was calculated based on weight measurement using a digital scale and height measurement using a microtoise (Jiangsu Suhong Medical Instruments, Jiangsu, China).

The dependent variable was serostatus, defined as seropositive when anti-SARS-CoV-2 IgG antibody levels exceeded 50 AU/mL and seronegative when levels were below 50 AU/mL [26]. IgG examination was conducted using the SARS-CoV-2 IgG II Quant kit (Abbott, Illinois, USA) based on the chemiluminescent microparticle immunoassay (CMIA) method with the Architect™ i2000 analyzer (Abbott, Illinois, USA). This assay quantitatively measures IgG antibodies against the SARS-CoV-2 spike receptor binding domain (S-RBD). A total of 75 µL of serum sample was used, and anti-SARS-CoV-2 IgG antibody levels were measured in AU/mL units [23].

Statistical analysis

Seropositive anti-SARS-CoV-2 IgG antibodies were grouped into positive (≥ 50 AU/mL) and negative (< 50 AU/mL). Multivariate analysis was performed by multiple logistic regression analysis and data processing using SPSS software (IBM, New York, USA).

Results

Characteristics of respondents

A total of 517 participants were included in this study, comprising 167 vaccinated individuals, 97 COVID-19 survivors, and 253 unvaccinated individuals. The characteristics of the study population are presented in **Table 1**. The majority of respondents were aged 50–59 years (27.1%), female (76.8%), housewives (56.9%), had no history of COVID-19 symptoms (70.0%), were non-hypertensive (60.3%), reported supplement consumption (77.8%), and were classified as obese I (BMI: 25–29.9) (34.6%).

Table 1. Characteristics of total sample (n=517)

Variables	Total sample	
	Frequency	Percentage
Groups		
Unvaccinated	253	48.9
COVID-19 survivor	97	18.8
Vaccinated	167	32.3
Age (year)		
18–29	69	13.3
30–39	100	19.3
40–49	115	22.2
50–59	140	27.1
≥ 60	93	18.0
Sex		
Female	397	76.8
Male	120	23.2
Occupation		
Others	74	14.3
Housewife	294	56.9
Private employees	55	10.6
Trader/laborer	46	8.9
Civil servants	31	6.0
Healthcare workers	17	3.3
Experienced symptoms of COVID-19		
No	362	70.0

Variables	Total sample	
	Frequency	Percentage
Yes	155	30.0
Hypertension		
No	312	60.3
Yes	205	39.7
Supplement consumption		
No	115	22.2
Yes	402	77.8
Nutritional status (BMI)		
Underweight: <18.5	38	7.4
Normal: 18.5–22.9	124	24.0
Overweight: 23–24.9	92	17.8
Obese I: 25–29.9	179	34.6
Obese II: ≥30	84	16.2

Prevalence of anti-SARS-CoV-2 IgG seropositivity

The prevalence of anti-SARS-CoV-2 IgG seropositivity observed in this study is presented in **Table 2**. Seropositivity was detected in 95.2% of vaccinated individuals, 93.8% of COVID-19 survivors, and 83.0% of unvaccinated individuals. Among the control variables, the highest prevalence was observed in participants aged 18–29 years (92.8%), women (91.6%), health workers (94.1%), those with a history of COVID-19 symptoms (95.5%), individuals with hypertension (92.2%), participants not consuming supplements (89.6%), and those classified as obese class II (94.1%).

Table 2. Distribution of anti-SARS-CoV-2 IgG antibody seropositive

Variables	Total sample		Negative antibodies (<50 AU/mL)		Positive antibodies (≥50 AU/mL)	
	n	n	%	n	%	
Main independent variable						
Population Groups						
Unvaccinated	253	43	17.0	210	83.0	
COVID-19 survivors	97	6	6.2	91	93.8	
Vaccinated	167	8	4.8	159	95.2	
Control variables						
Age (years)						
18–29	69	5	7.2	64	92.8	
30–39	100	13	13.0	87	87.0	
40–49	115	14	12.2	101	87.8	
50–59	140	14	10.0	126	90	
≥60	93	11	11.8	82	88.2	
Sex						
Female	397	33	8.3	364	91.7	
Male	120	24	20.0	96	80.0	
Occupation						
Others	74	13	17.6	61	82.4	
Housewife	294	23	7.8	271	92.2	
Private employees	55	9	16.4	46	83.6	
Trader/laborer	46	6	13.0	40	87.0	
Civil servants	31	5	16.1	26	83.9	
Healthcare workers	17	1	5.9	16	94.1	
Experienced symptoms of COVID-19						
No	362	50	13.8	312	86.2	
Yes	155	7	4.5	148	95.5	
Hypertension						
No	312	41	13.1	271	86.9	
Yes	205	16	7.8	189	92.2	
Supplement consumption						
No	115	12	10.4	103	89.6	
Yes	402	45	11.2	357	88.8	
Nutritional status (BMI)						
Underweight: <18.5	38	8	21.1	30	78.9	
Normal: 18.5–22.9	124	20	16.1	104	83.9	
Overweight: 23–24.9	92	6	6.5	86	93.5	
Obese I: 25–29.9	179	18	10.1	161	89.9	
Obese II: ≥30	84	5	6.0	79	94.0	

Factors associated with anti-SARS-CoV-2 IgG seropositivity

Factors associated with anti-SARS-CoV-2 IgG seropositivity are presented in **Table 3**. The percentage of seropositivity in the survivor group was not significantly different compared with the unvaccinated group. Control variables associated with anti-SARS-CoV-2 IgG antibody seropositivity were the presence of COVID-19 symptoms (odds ratio (OR): 5.38; 95% confidence interval (CI): 1.83–15.79), hypertension (OR: 2.27; 95%CI: 1.07–4.81), and BMI overweight (OR: 4.49; 95%CI: 1.26–15.95), obese II (OR: 3.95; 95%CI: 1.02–15.26).

Table 3. Comparison of anti-SARS-CoV-2 IgG antibody seropositivity of unvaccinated, COVID-19 survivors, and vaccinated groups

Variables	Total	Positive antibody (≥50 AU/mL)		Odds ratio	95% confidence interval	p-value
	n	n	%			
Main independent variable						
Population Groups						
Unvaccinated	253	210	83.0	Ref		
COVID-19 survivors	97	91	93.8	1.54	0.49–4.92	0.461
Vaccinated	167	159	95.2	5.60	2.36–13.27	<0.001*
Control variables						
Age						
				Ref		
18–29	69	64	92.8	0.43	0.13–1.46	0.177
30–39	100	87	87.0	0.33	0.09–1.15	0.081
40–49	115	101	87.8	0.39	0.12–1.33	0.132
50–59	140	126	90	0.40	0.11–1.43	0.157
≥60	93	82	88.2			
Sex						
				Ref		
Female	397	364	91.7	0.57	0.23–1.40	0.235
Male	120	96	80.0			
Occupation						
				Ref		
Others	74	61	82.4	0.43	0.04–4.80	0.489
Housewife	294	271	92.2	2.35	0.21–26.87	0.492
Private employees	55	46	83.6	0.81	0.77–8.50	0.860
Trader/laborer	46	40	87.0	1.96	0.22–17.61	0.548
Civil servants	31	26	83.9	0.78	0.08–8.20	0.839
Healthcare workers	17	16	94.1			
Experienced COVID-19 symptoms						
				Ref		
No	362	312	86.2	0.19	0.06–0.55	0.002*
Yes	155	148	95.5			
Hypertension						
				Ref		
No	312	271	86.9			
Yes	205	189	92.2	2.27	1.07–4.81	0.032*
Supplement consumption						
				Ref		
No	115	103	89.6			
Yes	402	357	88.8	0.60	0.28–1.31	0.202
Nutritional status (BMI)						
				Ref		
Underweight: <18.5	38	30	78.9			
Normal: 18.5–22.9	124	104	83.9	1.48	0.81–6.50	0.118
Overweight: 23–24.9	92	86	93.5	4.49	1.02–15.22	0.046*
Obese I: 25–29.9	179	161	89.9	2.29	0.49–4.92	0.461
Obese II: ≥30	84	79	94.0	3.95	2.36–13.27	0.000*

*Statistically significant at $p < 0.05$

Discussion

The results showed that the specificity of serum IgG antibodies against SARS-CoV-2 was 96.04%, while the sensitivity was 97.06% [8]. Previous studies on antibody levels among vaccinated groups conducted in several countries demonstrated that vaccines could induce the production of anti-SARS-CoV-2 IgG antibodies [9–14]. Increases in S-RBD SARS-CoV-2 antibodies after vaccination occur because viral particles in the vaccine trigger both humoral and cellular immune responses. Different types of vaccines are also associated with variations in antibody titers.

The present study revealed that seropositivity for anti-SARS-CoV-2 IgG antibodies in the unvaccinated group was 83.0%. This indicates that many people in the Palembang City community experienced asymptomatic COVID-19 infections. A total of 54.16% of individuals who

tested positive for SARS-CoV-2 antibodies did not exhibit clinical symptoms of COVID-19, indicating a high proportion of asymptomatic infections within the population. The seroprevalence of anti-SARS-CoV-2 antibodies in the community was substantially higher than the case numbers reported through the national surveillance system, highlighting potential underdetection and limitations in the surveillance system's capacity to capture the true burden of infection accurately [27]. This prevalence was also higher than the national figure of Indonesia.

These findings are consistent with a systematic review and meta-analysis conducted on the general population from January 2020 to April 2022 in multiple countries, which showed that nearly two-thirds of the global population were positive for SARS-CoV-2 [22]. Previous studies have also shown that the existing health infrastructure in Indonesia remains inadequate to handle the sudden and simultaneous increase in COVID-19 cases. This includes the limited capacity of health infrastructure to manage medical waste, which may serve as a transmission source [15]. People must also play an active role in promotive and preventive efforts to avoid contracting COVID-19. In Indonesia, 44.32% of study respondents do not comply with the recommended COVID-19 prevention behavior [28]. Several variables are significantly related to the prevention behavior of COVID-19 transmission in Indonesia, namely work, sex, knowledge, individual attitudes, and education [28,29].

These findings underscore the importance of both individual prevention behaviors and population-level immunity in reducing the burden of COVID-19. The present study revealed that vaccination was significantly associated with anti-SARS-CoV-2 IgG seropositivity, even after controlling for age, history of COVID-19 symptoms, hypertension, and BMI. Vaccinated individuals were 5.4 times more likely to be seropositive compared with unvaccinated individuals after adjustment for these variables. In contrast, antibody levels in the COVID-19 survivor group were not significantly different from those in the unvaccinated group, suggesting that prior infection alone may not confer sufficient or sustained humoral immunity.

Our results also showed that a history of COVID-19 symptoms was significantly related to the anti-SARS-CoV-2 IgG antibody seropositive. Previous research has demonstrated that IgG antibody levels remain detectable in most individuals for up to six months after symptom onset [30], with antibody titer positively correlated with post-infection period [16]. While an immune response can be generated even after mild infection, asymptomatic cases tend to have lower levels of antibodies [31]. Furthermore, this study identified hypertension as a factor significantly associated with the anti-SARS-CoV-2 IgG antibodies, consistent with earlier findings showing a correlation between hypertension and antibody levels [14].

The results show a meaningful association between seropositivity and nutritional status (BMI). This is in line with other studies reporting that anti-SARS-CoV-2 IgG antibody titers are lower in individuals with obesity compared to those with normal BMI [32,33]. These findings can serve as a basis for policymakers in formulating policy. However, this study has several limitations, including the absence of independent variables such as socioeconomic status and education. Previous reports have stated that economic status and education are related to COVID-19 prevention behavior [28,29].

Conclusion

This study demonstrated that the highest proportion of anti-SARS-CoV-2 IgG seropositivity was observed in the vaccinated group, after adjustment for demographic and health-related covariates. Seropositivity was independently associated with the presence of COVID-19 symptoms, hypertension, and BMI. Limitations include the cross-sectional design, reliance on a single blood sample, self-reported infection history, lack of access to national COVID-19 database, and the absence of information on vaccine dosing intervals. Despite these constraints, this study is the first to directly compare seropositivity across vaccinated, unvaccinated, and COVID-19 survivor groups in the community, providing important evidence to support vaccination policy.

Ethics approval

All respondents have read, fully approved, and signed the informed consent. Ethical approval was received from the Ethics Committee at Sriwijaya University. Ethical clearance from Sriwijaya University is Number 186/2021.

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Competing interests

The author declares that there is no conflict of interest in the writing of this study, and the content has no relationship with the study funder.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

We hereby confirm that no artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

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