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Risk factors of infection with SARS-CoV-2 Omicron BA.1 in Indonesia

Windi Nurdiana Utami, Chandrayani Simanjorang, Adzkia Avisena Maghfiroh, Bunga Andriana, Mugi Rahayu Lestari
Department of Public Health, Faculty of Health Sciences, Universitas Pembangunan Nasional Veteran Jakarta, Jakarta, Indonesia

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ABSTRACT

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) continues to mutate in Indonesia. The Omicron variant tends to have more cases but research related to this topic is still difficult to find. This study aimed to determine the risk factors for exposure to the Omicron variant of the SARS-CoV-2 virus. This study used a cross-sectional study design from SARS-CoV-2 surveillance data of the DKI Jakarta Health Office with a research sample of 3,480. Data analysis using Chi-square test followed by logistic regression test. The results found that men had a 1.82 higher risk of contracting the Omicron variant of SARS-CoV-2 than women. Elderly and adults had a 16.99 higher risk and 4.71 higher risk of developing the SARS-CoV-2 Omicron variant compared to children (p-value <0.05). People with a history of hypertension, diabetes mellitus, and cardiovascular had a 3.06, 3.05, and 4.56 higher risk of being infected with the Omicron variant of SARS-CoV-2 than those without a history of these comorbidities. It was concluded that the variable age is the riskiest factor. Vaccination does not reduce the risk of possible exposure to the Omicron variant, especially for those who are elderly, have a history of concomitant diseases, and are male.

Corresponding Author:

Chandrayani Simanjorang
Department of Public Health, Faculty of Health Sciences,
Universitas Pembangunan Nasional "Veteran" Jakarta
Limo Raya Street No.8, Limo, Limo District, Depok City, West Java 16514, Indonesia
Email: chandrayanis@upnvj.ac.id

1. INTRODUCTION

The illness brought on by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) virus is known as Coronavirus illness 2019 according to the World Health Organization (WHO). On December 31, 2019, influenza was identified as the first SARS-CoV-2 case in Wuhan, China [1]. The virus is still capable of producing new variants with traits distinct from those of earlier ones. Some variants can spread more rapidly and easily than others, which may increase SARS-CoV-2 cases. According to the Centers for Disease Control and Prevention (CDC), if the virus has a lower severity level but the capacity to spread more quickly, this will also result in a higher overall number of SARS-CoV-2 cases due to an increase in hospitalizations and a need for more medical personnel to provide patient care [2].

The B.1.1.529 variant of the SARS-CoV-2 virus, which was subsequently given the name omicron, was the new virus that appeared as a result of the mutation. On November 26, 2021, the WHO classified this variant as a variant of concern (VOC), replacing the earlier variants, Alpha, Beta, Gamma, and Delta. On November 24, 2021, WHO got the first report from South Africa regarding the Omicron variant. The number of cases occurring in South Africa is sharply rising, and they are dispersing to different regions. Samples

collected on November 11, 2021, revealed the presence of this Omicron variety in Botswana as well. Up until November 28, 2021, numerous instances were discovered abroad. The International Children's Emergency Fund (UNICEF) of the United Nations stated that the risk is significantly greater than that of the prior variants, and that an increase in viral mutations may happen if this variant spreads extensively and results in numerous infections [3]. The Omicron variant of SARS-CoV-2, which has been found in 188 nations as of March 31, 2022, is the predominant strain worldwide. Omicron variants make up nearly 99.7% of the sequences that were gathered between February 23 and March 24, 2022 [4].

On 16 December 2021, Indonesia reported the first case of COVID-19 Omicron variant from a sample collected on 8th December 2021. There are 6,025 COVID-19 Omicron variant reported to the global initiative on sharing all influenza data (GISAID) on 14th February 2022. COVID-19 Omicron variant has increased the number of bed occupancy rate (BOR) at national level from 25% to 30% as well as BOR in intensive care units (ICU) from 14% to 20% [5]. Because SARS-CoV-2 increases transmission and weakens the body's ability to fight off antibodies, it causes a very massive spread of the Omicron variant, which will have an effect on increasing the number of cases of illness in both mild, moderate, and severe categories [4]. The incubation period and treatment duration are quicker for those with the omicron variant than for those with the delta variant [6]. Additionally, as a result of prior infections and vaccinations, the number of severe SARS-CoV-2 cases has also decreased. When compared to the delta version, the omicron variant has less virulence, which lowers the risk of hospitalization and death [7]. However, the Omicron variant is known to be more transmissible, so it is better for people to receive any vaccinations to protect them from the sickness. The Omicron variant also had the highest number of mutations and that's why this variant can escape the immune system and has greater infectivity than any other variant of concerns (VOCs) of COVID-19 [8].

Male sex, elderly, history of smoking, obesity, hypertension, diabetes, malignancy, coronary heart disease, hypertension, chronic obstructive pulmonary disease (COPD), chronic kidney disease, and chronic liver disease are all associated with a higher risk of SARS-CoV-2 events [9]. According to a different study, there are a number of risk factors for the severity of SARS-CoV-2 that patients encounter, including age, lactate dehydrogenase (LDH) levels, and high levels of d-dim. Meanwhile, advanced age, leukocytosis, and elevated LDH levels are risk factors for dying from SARS-CoV-2. Because it is linked to diabetes and corticosteroid therapy, hyperglycemia is also linked to the mortality rate of SARS-CoV-2 cases [10].

In comparison to the Delta variant, the Omicron variant of SARS-CoV-2 caused a significant reduction in protection from vaccine-induced immunity or infection against SARS-CoV-2 [11]. This implies that immunization rates may have an impact on the prevalence of SARS-CoV-2 Omicron variants. Additionally, research by Accorsi *et al.* [12] revealed that individuals who received 3 doses of the SARS-CoV-2 vaccine developed a protective factor, with adjusted OR values of 0.35 (BNT162b2) and 0.28 (mRNA-1273) for the Omicron variant in comparison to individuals who did not receive any vaccination. In contrast to Omicron, vaccination is generally more effective at defending the organism against the delta variant.

Studies that explicitly address the risk factors for SARS-CoV-2 on the Omicron variant have not yet been published. Meanwhile, the SARS-CoV-2 variant known as Omicron is the one that causes the majority of SARS-CoV-2 cases in Indonesia and possibly the entire globe, according to the Ministry of Health of the Republic of Indonesia. The risk of the emergence of Omicron variants in Low Middle-Income Countries, including Indonesia, is covered in research done in 2023. However, it does not go into detail about the dangers of the SARS-CoV-2 Omicron variety [13]. Following that, a study done in 2023 by Wang and Lan addresses the transmissibility of the COVID-19 Delta and Omicron Variant and how it relates to control measures. It did not, however, address the COVID-19 Omicron Variant Risk Factor [14]. In addition, studies by Masrika *et al.* [6] and Accorsi *et al*. [12] addressed the connection between the vaccine and the SARS-CoV-2 Omicron variant, but they didn't go into detail about the variant's risk factors. It is very helpful to have knowledge of the risk factors for the Omicron variant as a foundation for developing strategies. For the public health sector to reduce the incidence of SARS-CoV-2 and lessen the severity that may be brought on by uncontrolled risk factors, an evidence-based strategy is essential [15]. Further study is required because, in addition, the widespread immunization program may have caused a change in the community's risk factors for SARS-CoV-2.

2. RESEARCH METHOD

This study used a cross-sectional study design from SARS-CoV-2 surveillance data from the DKI Jakarta Health Office. The study was conducted in April-June 2021. The population in the study was all Indonesians who had a history of exposure to SARS-CoV-2. The research sample is an individual who has been exposed to SARS-CoV-2 which is included in the surveillance data of the DKI Jakarta Health Office, and meets the inclusion and exclusion criteria as a sample. The initial data obtained was 7,498 cases, then through the cleaning process, the data obtained a research sample of 3,480 cases. Omicron case data collection is taken by the whole genome sequencing method, which is a comprehensive technique used in the

process of sequencing deoxyribonucleic acid (DNA) sequences into a whole genome picture by being identified in a geographical area or a limited period of time using next generation sequencing (NGS) technology [16], [17]. The dependent variable of the study is the case of the Omicron variant of SARS-CoV-2 in Indonesia. The independent variables of the study were age, gender, history of hypertension, history of diabetes mellitus, cardiovascular history, and vaccination status. The data analysis used in this study was multiple logistic regression analysis using SPSS software version 25. The first step was to perform bivariate analysis (Chi-square) to select independent variables as candidates. Then the second step is to enter variables with a value of $p \leq 0.25$ into the first model of multivariate analysis. The crude prevalence odds ratio (POR) and adjusted POR values were obtained with a degree of confidence of 95% (95% CI) and $\alpha=0.05$. The third stage is obtaining the risk factor model and determining which variable has the greatest impact on the Omicron variant of SARS-CoV-2. The final step is to conduct an interaction test to assess whether there is a modification of the effect between the risk factor variables. This research was approved by the UPN Veteran Jakarta Health Research Ethics Commission in June 2022 with letter number 341/VI/2022/KEPK.

3. RESULTS AND DISCUSSION

The total number of SARS-CoV-2 cases in this study was 3,480 cases, of which 2,034 (58.4%) were the Omicron variant of SARS-CoV-2. SARS-CoV-2 patients were dominated by the adult age group (79.7%). The number of respondents was almost equal between men (48.8%) and women (51.2%) with 15.5% being health workers. Most of the respondents had received a complete SARS-CoV-2 vaccination (49.3%), most of whom had no history of hypertension, history of diabetes mellitus, or cardiovascular history. Further details can be seen in Table 1.

Table 1. Distribution of SARS-CoV-2 cases by type of variant, demographic characteristics, vaccination status, and comorbid history

Variable	n (=3,480)	Percentage (%)
Variant types of SARS-CoV-2		
Non-Omicron	1,446	41.6
Omicron	2,034	58.4
Age		
Elderly (≥60 years)	490	14.1
Adult (18-59 years)	2,775	79.7
Children (0-17 years)	215	6.2
Gender		
Man	1,698	48.
Woman	1,782	51.2
Profession		
Health workers	541	15.5
Not health workers	232	6.7
No/not yet working	337	9.7
Missing	2,370	68.1
Vaccination status		
Complete vaccine (2^{nd}/3^{rd} Dose)	1,717	49.3
1^{st} Dose of vaccine	120	3.4
Not yet vaccine	1,643	47.2
Hypertension history		
Yes	279	8.0
No	3,201	92.0
Diabetes mellitus history		
Yes	155	4.5
No	3,325	95.5
Cardiac history		
Yes	96	2.8
No	3,384	97.2

Based on bivariate analysis, there was a significant relationship between the variables age, gender, history of hypertension, history of diabetes mellitus, and history of heart disease with the Omicron variant of SARS-CoV-2. Even though the vaccination status variable had a p-value <0.25, this variable was not included in the multivariate analysis because the POR value was not significant, namely 1.18 as shown in Table 2. From the results of the multivariate analysis, the results of multiple logistic regression analysis as presented in Table 3 show that men had a 1.82 higher risk of contracting the Omicron variant of

SARS-CoV-2 than women (p-value 0.01; 95% CI 1.57-2.11). Elderly and adults had a 16.99 higher risk (95% CI 3.71-5.99) and 4.71 higher risk (95% CI 10.71-26.97) of getting the Omicron variant of SARS-CoV-2 than children (p-value <0.05). People with a history of hypertension, history of diabetes mellitus, and history of cardiovascular events had a 3.06 higher risk (95% CI 2.17-4.31), 3.05 higher risk (95% CI 1.87-4.97), and 4.56 higher risk (95% CI 2.1-9.92) to be infected with the Omicron variant of SARS-CoV-2 than people who do not have a history of these comorbidities.

Table 2. Relationship between types of SARS-CoV-2 variants and demographic characteristics, vaccination status, and comorbid history

Variable	Variant types of SARS-CoV 2				Total		p-value	Crude POR (95% CI)
	Non-Omicron		Omicron					
	N	%	N	%	N	%		
Age								
Elderly	385	78.6	105	21.4	490	100.0	0.01	1
Adult	1,033	37.2	1,742	62.8	2,775	100.0		0.04 (0.02-0.06)
Children	28	13.0	187	87.0	215	100.0		0.25 (0.16-0.37)
Gender								
Man	608	34.1	1,174	65.9	1,782	100.0	0.01	1
Woman	838	49.4	860	50.6	1,698	100.0		1.88 (1.64-2.15)
Vaccination status								
Complete vaccine	0	0.0	1,717	100.0	1,717	100.0	0.01	1
1st Dose	0	0.0	120	100.0	120	100.0		1.18 (0.01-10.00)
Not yet	1,446	88.0	197	12.0	1,643	100.0		1.18 (0.01-10.00)
Hypertension history								
Yes								
No	1,222	38.2	1,979	61.8	3,201	100.0	0.01	1
	224	80.3	55	19.7	279	100.0		6.59 (4.86-8.93)
Diabetes mellitus history								
Yes								
No	1,315	39.5	2,010	60.5	3,325	100.0	0.01	1
	131	84.5	24	15.5	155	100.0		8.34 (5.37-12.96)
Cardiac history								
Yes	1,358	40.1	2,026	59.9	3,384	100.0	0.01	1
No	88	91.7	8	8.3	96	100.0		16.41 (7.93-33.95)

Table 3. Multivariate analysis of regression factors associated with SARS-CoV-2 Omicron variant incidence

Variable	B	p-value	Adjusted POR	95% CI	
				Lower	Upper
Gender					
Man		-	1	-	-
Woman	0.60	0.01	1.82	1.57	2.11
Age					
Children	-	-	1	-	-
Adult	1.55	0.01	4.71	3.71	5.99
Elderly	2.83	0.01	16.99	10.71	26.97
Hypertension history					
Yes	-	-	1	-	-
No	1.12	0.01	3.06	2.17	4.31
Diabetes mellitus history					
Yes	-	-	1	-	-
No	1.11	0.01	3.05	1.87	4.97
Cardiac history					
Yes	-	-	1	-	-
No	1.51	0.01	4.56	2.1	9.92

Meanwhile, all non-Omicron cases have not been vaccinated. This is due to the new vaccination policy period when the Omicron variant appeared. Thus, the risk factors can change as vaccination coverage increases. Previous research stated that vaccination can provide protection against Omicron quickly over time, especially with booster vaccinations which can offer a significant increase in protection [18]. Complete vaccination is a significant protective factor in all elderly age groups, with a vaccine effectiveness of 76% [19]. However, these vaccination kits do not show consistent efficacy in preventing SARS-CoV-2 infection [6]. Research in Hong Kong and China found that the case fatality rate (CFR) of people who were not vaccinated was higher, 3.04%, while the CFR who received two doses and three doses of vaccination was lower, only 0.17% and 0.04% [20].

Gender and the frequency of the Omicron variant of SARS-CoV-2 were found to be related based on the findings of the multivariate analysis. In comparison to women, males had a 1.82 higher risk of contracting the SARS-CoV-2 Omicron variant (95% CI: 1.64-2.15). The positivity rate of SARS-CoV-2 cases in Wuhan, China in January-February 2020 was higher in men than in females, according to research by Liu [21] with a p-value of 0.01 [21]. Additionally, males are more likely to die from SARS-CoV-2 cases [22], have more severe SARS-CoV-2 symptoms [23], and have higher rates of SARS-CoV-2 infection and hospitalization than women [24]. According to a different theory, males with infections are more likely than females to require intensive care and die [25]. This is because males have an advantaged immune system called the innate adaptive immune system, as well as a different amount of X chromosomes. The elevated risk in men may also be brought on by aging-related declines in B cells, which impair the production of antibodies and weaken an individual's defenses against the SARS-CoV-2 virus [26].

The age of the patient and the prevalence of the SARS-CoV-2 Omicron strain are correlated. According to the findings of the multivariate analysis, adults had a 4.71 higher risk of contracting the Omicron variant of SARS-CoV-2 than younger age groups, and the elderly had a 16.99 higher risk (95% CI: 10.71-26.97). A recent meta-analysis of 33 trials involving 3,027 COVID-19 patients revealed that adults over the age of 65 were five times as likely to become critically ill or die [27]. SARS-CoV-2 can infect people of all ages, and if a person is over 60 and has comorbid conditions, their chance of developing a severe illness from the virus that can be fatal increases [28]. According to a study done by Alharbi *et al.* [24] in 2022, people over 60 are more likely to contract SARS-CoV-2 and are more likely to be found in hospitals, both ICU and non-ICU [25]. Additionally, elderly people are at risk for contracting SARS-CoV-2 with severe symptoms and a p-value of 0.001 [24].

According to the findings of the multivariate analysis, there is a link between a history of hypertension and instances of the Omicron variant of SARS-CoV-2. A person who has a history of hypertension had a 3.06 higher risk of becoming infected with the Omicron variant of SARS-CoV-2 compared to people who have no history of hypertension (95% CI: 2.17-4.31). Hypertension is the most common comorbidity among SARS-CoV-2 patients [29]. Previous research suggests hypertension affects about 49% (95% CI: 46-52) of 1,043 SARS-CoV-2 patients [30], [31]. Research in Iran found 23.8% of hypertensive patients developed into severe SARS-CoV-2 [29]. Additionally, a historical analysis of 25,207 cases at Fangcang Hospital in Shanghai, China, revealed that pre-existing comorbid conditions, such as risk factors for the Omicron variant of SARS-CoV-2, that can increase the severity to death [32].

The results of the multiple logistic regression multivariate analysis of this study indicate that diabetes mellitus is associated with cases of the Omicron variant of SARS-CoV-2. Patients with a history of diabetes mellitus had a 3.05 higher risk of being infected with the Omicron variant of SARS-CoV-2 than patients without a history of diabetes mellitus (95% CI: 1.87-4.97). Diabetes is one of the comorbidities that are most frequently present in SARS-CoV-2 patients with a prevalence of 7 to 30%. Those with diabetes who contract SARS-CoV-2 have a higher risk of hospitalization, severe pneumonia, and mortality compared to those without diabetes [33]. Another study found that diabetes was significantly associated with SARS-CoV-2 mortality and morbidity with a combined OR of 2.16 (95% CI: 1.74-2.68; p-value <0.01) [34].

Based on the results of multiple logistic regression multivariate analysis, cardiovascular disease is statistically associated with cases of the Omicron variant of SARS-CoV-2. Patients with a cardiovascular history had a 4.56 higher risk to be infected with the Omicron variant of SARS-CoV-2 than patients without a cardiovascular history (95% CI: 2.1-9.92). Apart from the lungs, SARS-CoV-2 can have a severe impact on the cardiovascular system [35]. Therefore, the cardiovascular implications result in a poorer prognosis in patients with SARS-CoV-2 [36]. Luo *et al.* research [37] stated that SARS-CoV-2 patients with a cardiovascular history had a 3 higher risk of experiencing a high level of severity than patients without a cardiovascular history (95% CI: 2.70-5.52). In addition, SARS-CoV-2 patients with a cardiovascular history had 2.65 higher risk to die than patients without a cardiovascular history (95% CI: 1.80-2.42).

In the case of SARS-CoV-2 variants other than Omicron (Alpha, Delta), the vaccination coverage is still not as large as today. Meanwhile, in the case of the Omicron variant of SARS-CoV-2, many have started to get vaccinated, both with two doses or three doses. SARS-CoV-2 vaccination can reduce hospitalization rates in instances of SARS-CoV-2 alpha, delta, and Omicron variants. However, vaccination protection against the Omicron variant of SARS-CoV-2 tends to be lower than protection against the alpha and delta variants. In addition, protection against infection from 2 doses of vaccination tends to decrease over time. However, the effectiveness of vaccination against infection decreased less over time after getting 3 doses compared to 2 doses. The third dose of SARS-CoV-2 vaccination contributes to protection against hospitalization due to SARS-CoV-2 infection in the Omicron variant [18]. There are several similarities in the risk factors for the Omicron variant of SARS-CoV-2 in this study with risk factor studies in the early days of the emergence of SARS-CoV-2. Namely age, gender, and history of diabetes [22], [38]. This by earlier study, which found that the age group over 70 years has a 69% greater vulnerability to SARS-CoV-2 than the

younger age group, which is around 21% [39]. Another early risk factor for the formation of SARS-CoV-2 is male gender; according to a Chinese study, 60% of COVID-19 patients in China were male. [40]. Pre-existing comorbidities, such as hypertension (16.9%), diabetes (8.2%), cardiovascular disease (3.7%), and chronic kidney disease (1.3%), are among the other risk factors for SARS-CoV-2 [41].

4. CONCLUSION

The results of the study found that the risk factors for the Omicron variant of SARS-CoV-2 in DKI Jakarta include age, heart history, hypertension history, DM history, and gender. Based on the results of multivariate analysis, it was found that the age variable was the riskiest factor. There is neither confounding nor modifying effects among the risk factors. Although most cases of the Omicron variant of SARS-CoV-2 have been vaccinated, the risk factors for infection remain high, especially in residents with elderly, comorbid history, and male gender.

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BIOGRAPHIES OF AUTHORS

Windi Nurdiana Utami has bachelor's degree in public health with majority in epidemiology. She also has experience of implementing health promotion, community environment, and health data analysis. She has qualitative and quantitave skills as well as project planning and management organization. She can be contacted at email: windinurdianau@upnvj.ac.id.

Chandrayani Simanjorang is a lecturer at Public Health Study Program, Universitas Pembangunan Nasional Veteran Jakarta. She has PhD degree in Epidemiogy and interested in epidemiology of communicable diseases. She is experienced in quantitative and qualitative studies and has published several research articles in national and international journals. She can be contacted at email: chandrayanis@upnvj.ac.id.

Adzkia Avisena Maghfiroh is a public health student concentrating in epidemiology. She is interested in some topics in public health, mainly epidemiology of communicable and non-communicable diseases and global health. She can be contacted at email: 2010713054@mahasiswa.upnvj.ac.id.

Bunga Andriana is a public health student concentrating in epidemiology. She has experience in implementing health promotion, problem-solving solutions, and health data analysis. She can be contacted at email: 2010713069@mahasiswa.upnvj.ac.id.

Mugi Rahayu Lestari is a public health student concentrating in epidemiology. She has experience analyzing health data, identifying and solving public health problems, and health promotion. Apart from being interested in epidemiology, she is also interested in community nutrition issues. She can be contacted at email: 2010713126@mahasiswa.upnvj.ac.id.