High Effectiveness of CoronaVac Vaccine Against Severe COVID-19 in Adult and Elderly Population in Indonesia

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Abstract. CoronaVac was the first COVID-19 vaccine used in Indonesia. Phase three clinical trial studies showed that the efficacy of CoronaVac in preventing SARS-CoV-2 infection ranged from 50.7-84.4%. The effectiveness of the COVID-19 vaccine in the adult group relatively was better than the elderly group, this study aimed to assess the real-world effectiveness of CoronaVac in adult and elderly age groups in Indonesia.This study was a single-center cohort retrospective study involving COVID-19 patients aged ≥18 years who were admitted to a secondary teaching hospital from June 1 to August 31, 2021. We analyzed two age group models based on WHO, adult (18-59 years) and elderly (≥60 years) models. We used binary logistic regression models to assess the effect of CoronaVac vaccination on severe COVID-19 with sex and comorbidity confounding models. A total of 706 patients were included in this study with 35.4% and 16.5% of patients vaccinated in the adult and elderly groups, respectively. The CoronaVac vaccine has high efficacy in preventing severe COVID-19 in the adult and elderly populations, 93.2% (95% CI: 47.4-99.1%) and 94.8% (95% CI: 55.4-99.4%), respectively. CoronaVac vaccine has a relatively high ef-

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fectiveness in protecting against severe COVID-19 in both adult and elderly populations.

Keywords: Effectiveness, CoronaVac, Severe, Adult, Elderly

1 INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a respiratory disease syndrome caused by severe acute respiratory syndrome 2 (SARS-CoV-2) which has widely caused the death of 6.9 million people worldwide since the first case until May 2023[1]. Most of the deaths occurred in the severe patient group. Risk factors for developing severe COVID-19 were male, older age, fever, cough, fatigue, delayed diagnosis, hypertension, diabetes, and chronic kidney disease[2]. The immune response induced by the COVID-19 vaccine was expected to effectively prevent SARS-CoV-2 infection, progressive severe infection, and death[3].

The development of the COVID-19 vaccine was a success in modern human science[4]. According to different targets and technologies, COVID-19 vaccines can be divided into inactivated vaccines, recombined spike protein vaccines, viral vector vaccines, RNA vaccines, live attenuated vaccines, and virus-like particle vaccines[5]. Less than two years after the COVID-19 pandemic, various vaccine types and manufacturers have been distributed to the general public in various countries, including Indonesia. CoronaVac was an inactive type vaccine developed by Sinovac® Life Sciences Company in China and CoronaVac became the first vaccine used in Indonesia and was approved and used in 55 other countries[6-7]. Clinical trial-phase three studies in Indonesia showed that the efficacy of CoronaVac in n preventing symptomatic confirmed cases of COVID-19 occurring at least 14 days after the second dose of vaccine using an incidence rate was 65.30%[8].

Vaccines were initially administered to adult and elderly subjects. FDA strongly believes the potential benefits of COVID-19 vaccination outweigh the potential risks of COVID-19 infection[9]. Elderly with frailty and disability are vulnerable groups with a high need for the COVID-19 vaccine, but they were also more susceptible to the development of vaccine-related side effects[10]. The effectiveness of the COVID-19 vaccine in the adult group was better than the elderly group, but the safety was worse than in the elderly[11].

A study of the effectiveness of CoronaVac against COVID-19 infection, hospitalization, and COVID-19-related death in the Indonesian population has previously been conducted in Bali using a test-negative design but did not assess the effectiveness of CoronaVac in the prevention of severe COVID-19[12]. Our previous research found that COVID-19 vaccination has a moderate preventive impact on hospitalization but a high preventive impact on severe COVID-19, ICU admission, and death[13]. The real-world studies on the effectiveness of the CoronaVac vaccine in Indonesia are still limited. Therefore, this study aims to assess the effectiveness of the CoronaVac vac-

cine against severe COVID-19 in adults and the elderly after full doses with a real-world model at a secondary COVID-19 referral hospital in West Sumatera.

2 METHODS

2.1 Study setting and participants

This study was a retrospective cohort study conducted at the Universitas Andalas Teaching Hospital. The subjects of the study were patients who came to the hospital with positive real-time polymerase chain reaction (RT-PCR) results and who were more than 18 years in June-August 2021. We excluded patients who were referred to tertiary hospitals due to clinical consequences and patients who received COVID-19 vaccines outside CoronaVac. The potential of redundant publication in this study can occur because we also used the same sample and method in our another research, Rohadi et al, 2023[13].

2.2 Age, vaccination status, and outcome

This study was analyzed within two groups, namely the adult group and the elderly group. The adult group was defined as subjects aged 18-59 years, while the elderly group was defined as ≥60 aged subjects. Vaccination status was categorized into unvaccinated and vaccinated groups. Determination of the dose considers the seroconversion process in the formation of specific antibodies after active immunization. In the CoronaVac vaccine, a full doses antibody response was expected after 14 days after the second dose injection. Therefore, the vaccinated group was defined as having a positive RT-PCR result for at least 14 days after the second dose of vaccine injection. Unvaccinated patients were defined as not receiving any dose, receiving one dose, or receiving a second dose <14 days after the first dose). The definition of severe COVID-19 was a patient with clinical signs of pneumonia (fever, cough, shortness of breath, rapid breathing) plus one condition such as respiratory frequency >30 x/min, severe respiratory distress, or SpO2 <93% in room air at the first admission.

2.3 Statistical analysis

Univariate analyses were performed to examine the frequency of age, sex, comorbidities, initial symptom, the status of vaccination, and severity of COVID-19 in admission. The chi-square or Fisher exact test was used to analyze categorical variables. Meanwhile, T-test or Mann-Whitney test was used to compare the mean of numerical data. Multivariable logistic regression was used to determine the risk factor for severe COVID-19 in the adult and elderly groups. Confounding factors included in the analysis were sex and comorbidities. Variables with $p<0.05$ were considered statistically significant. Vaccine effectiveness (VE) was calculated as, VE = (1-aOR) X 100%. SPSS software (version 20.0: Inc, Chicago, IL, USA) was used for statistical analysis.

2.4 Ethical clearance and informed consent

The Ethics Commission of the Faculty of Medicine, Universitas Andalas was declared the ethical clearance of our study with approval number 798/UN.16.2/KEP-FK/2022. The need for informed consent was waived owing to the retrospective nature and the data was processed anonymously.

3 RESULTS

3.1 Subjects characteristics

Between 1 June-31 August, 706 patients consisting of 567 (80.3%) adult patients (18-59 years old) and 139 (19.7%) elderly patients (≥60 years old) were included as subjects in this study. Males were more dominant in the elderly group statistically, while the adult group was dominated by female. The adult group was dominated without comorbid diseases. Whereas hypertension, diabetes, liver disease, kidney disease, and cardiovascular disease were statistically more common in the elderly age group. Statistically. the initial symptoms such as fever, dyspnea, cough and hypoaugesia were common in elderly group, while flu, sore throat and hyposmia were common in adult group. In this stud, only 31.7% were found to have been vaccinated with the two doses of CoronaVac, 35.4% and 16.5% of adult and elderly subjects, respectively. Statistically, severe COVID-19 was also more common in elderly patients. Details can be seen in Table. 1.

Table. 1 Baseline characteristics and clinical outcomes according to the status of Covid-19 vaccination

Characteristic	Adult (n=567)		Elderly (n=139)		p-value*
Age, median (IQR)	33	(25)	66	(8)	
Male	231	(40.7)	72	(51.8)	**0.024**
Co-morbidities					
No co-morbidity	368	(64.9)	38	(28.1)	**<0.001**
Hypertension	45	(7.9)	62	(44.6)	**<0.001**
Diabetes	36	(6.3)	30	(21.6)	**<0.001**
Respiratory disease	36	(6.3)	15	(10.8)	0.103
Liver disease	21	(3.7)	15	(10.8)	**0.001**
Renal disease	6	(1.1)	8	(5.8)	**0.002**
Cardiovascular disease	5	(0.9)	13	(9.4)	**<0.001**
Initial symptoms					
Asymptomatic	40	(7.1)	5	(3.6)	0.193
Fever	247	(43.6)	85	(61.2)	**<0.001**
History of fever	104	(18.3)	19	(13.7)	0.239
Dispnea	96	(16.9)	74	(54)	**<0.001**

Cough	400	(70.5)	117	(84.2)	**0.002**
Flu	118	(20.8)	17	(12.2)	**0.029**
Sore throat	41	(7.2)	2	(1.4)	**0.018**
Hyposmia	182	(32.1)	29	(20.9)	**0.013**
Hypoaugesia	37	(6.5)	32	(23)	**<0.001**
Nause	33	(5.8)	6	(4.3)	0.625
Vomit	42	(7.4)	4	(2.9)	0.081
Loss of appatite	30	(5.3)	13	(9.4)	0.110
Headache	67	(11.8)	10	(7.2)	0.157
Outcome					
Severe COVID-19	30	(5.3)	47	(33.8)	**<0.001**
Status of vaccines					
Two doses	201	(35.4)	23	(16.5)	**<0.001**

*Chi-square test, except for age (Kruskall-Wallis test)

3.2 Risk factors for severe COVID-19 in adult and elderly subjects.

In the adult group (Table. 2), we found that male (p=0.024, aOR 2.678, 95% CI 1.141-6.285), at least one comorbid (p=0.009, aOR 4.547, 95% CI 1.455-14.205), diabetes (p=0.045, aOR 2.825, 95% CI 1.021-7.621) and renal disease (p=0.006, aOR 27.392, 95% CI 2.576-291.283) were factors that increased the risk of severe COVID-19. Meanwhile, in the elderly group (Table. 3), at least one comorbid (p=0.038, aOR 3.494, 95% CI 1.069-11.424), diabetes (p=0.002, aOR 5.540, 95% CI 1.902-16.141) and respiratory disease (p=0.019, aOR 6.291, 95% CI 1.345-29.415) were factors that increased the risk of severe COVID-19. Both groups, together, revealed that vaccination was a factor that reduced the risk of severe COVID-19.

Table 2. Risk factors for severe COVID-19 among adults patients (result of binary logistic regression test)

Variable	Adult (n=567)		Unadjustment			Adjustment			
			p-value	OR	(95% CI)[1]	p-value	aOR	(95% CI)[2]	aVE (95% CI)
Male	18	(3.2)	**0.031**	2.282	(1.077-4.833)	**0.024**	2.678	(1.141-6.285)	-
At least one comorbidities	25	(4.4)	**<0.001**	10.431	(3.926-27.711)	**0.009**	4.547	(1.455-14.205)	-
Hypertension	7	(1.2)	**0.003**	3.997	(1.612-9.910)	0.300			
Diabetes	10	(1.8)	**<0.001**	9.827	(4.178-23.113)	**0.045**	2.825	(1.021-7.621)	-
Respiratory disease	6	(1.1)	**0.004**	4.225	(1.606-11.117)	0.101			
Renal disease	4	(0.7)	**<0.001**	41.154	(7.206-235.035)	**0.006**	27.392	(2.576-291.283)	-
Cardiovascular disease	1	(0.2)	0.179						
Vaccinated	1	(0.2)	**0.005**	0.058	(0.008-0.430)	**0.010**	0.068	(0.009-0.526)	93.2 (47.4-99.1)

[1]Odd ratio (95% confidence interval)
[2]Adjusted odd ratio (95% confidence interval), calculatted by excluding variables with p-value≥0.1
[3]The variables were exluded in the adjusted model because the p-value of the Hosmer-Lemeshow test was <0.05 with inclusion of these variables

3.3 Vaccine effectiveness of CoronaVac against severe COVID-19 on adult vs elderly subjects.

After analyzing confounding factors such as sex and comorbidities, we found that the effectiveness of the CoronaVac vaccine in preventing severe COVID-19 was relative-

ly high in the adult and elderly age groups, 93.2% (95% CI: 47.4-99.1%) and 94.8% (95% CI: 55.4-99.4), respectively. (Table. 2 and Table. 3)

Table 3. Risk factors for severe COVID-19 among elderly patients (result of binary logistic regression test)

Variable	Elderly (n=139)		Unadjustment			Adjustment			
			p-value	OR	(95% CI)[1]	p-value	aOR	(95% CI)[3]	aVE (95% CI)
Male	25	(18)	0.814						
At least one comorbidities	43	(30.9)	**0.001**	6.601	(2.181-19.982)	**0.038**	3.494	(1.069-11.424)	-
Hypertension	24	(17.3)	0.275						
Diabetes	20	(14.4)	**<0.001**	6.074	(2.532-14.569)	**0.002**	5.540	(1.902-16.141)	-
Respiratory disease	12	(8.6)	**0.001**	10.171	(2.706-38.236)	**0.019**	6.291	(1.345-29.415)	-
Renal disease	6	(4.3)	**0.024**	6.585	(1.274-34.029)[3]				
Cardiovascular disease	6	(4.3)	0.328						
Vaccinated	1	(0.7)	**0.010**	0.069	(0.009-0.531)	**0.009**	0.052	(0.006-0.446)	94.8 (55.4-99.4)

[1]Odd ratio (95% confidence interval)
[2]Adjusted odd ratio (95% confidence interval), calculatted by excluding variables with p-value≥0.1
[3]The variables were exluded in the adjusted model because the p-value of the Hosmer-Lemeshow test was <0.05 with inclusion of these variables

4 DISCUSSION

The Indonesian government started the COVID-19 vaccination program in January 2021. CoronaVac was the first vaccine to be granted emergency use authorization by the Indonesian Food and Drug Administration. A phase three clinical trial study conducted in Brazil showed that CoronaVac has 100% effectiveness in preventing severe COVID-19.(14) An Phase 3 clinical trial research in Indonesia and Turkey shows that CoronaVac has an effectiveness of 65.3% and 83.5% respectively in preventing symptomatic COVID-19 infection[14]. The results of our study indicate that CoronaVac provides relatively high protection against severe COVID-19 in adult (18-59 years) and elderly (≥60 years) age groups. These findings are consistent with a descriptive observational study in Colombia with 7849 people older than 18 years who found that two doses of CoronaVac have an effectiveness of 99.9% to prevent severe COVID-19[15]. A negative case-control study on vaccine efficacy against symptoms in the elderly in Brazil found it to be highest in the youngest age group (70-74 years) with vaccine efficacy of 59.0% and was observed to decline with increasing age[16]. A meta-analysis study involving 24 studies revealed that inactivated vaccines are effective in preventing infections, hospitalizations, ICU admissions, and deaths accompanied by a lower financial burden from the perspective of society in China[17].

Administering COVID-19 vaccines in the elderly was a challenge due to the immunosenescence process in both the innate and adaptive immune systems. Features of immunosenescence include an increase in the number of memory T cells, loss of ability to respond to antigens, and a long-lasting low-level inflammation called "aging inflammation"[18]. In the other side, the elderly could be the group with the greatest benefits of COVID-19 vaccination, especially in preventing severe COVID-19. In this study, it was found that the effectiveness of CoronaVac in preventing severe COVID-19 was slightly higher in the elderly group compared to the adult group. However, these results need to be interpreted carefully because the smaller sample size in the elderly group may be the cause bias.

Spike proteins play a role in viral host range and infectivity, they were important targets for inducing antibodies, especially neutralizing antibodies (NAbs) specific to SARS-CoV-2[19]. Significant increases in the levels of anti-RBD-specific IgG, anti-nucleocapsid IgG, and anti-spike trimeric IgG after the second dose and CoronaVac booster were noted in the adult and elderly groups. In adults, anti-nucleocapsid IgG and anti-spike trimeric IgG levels decreased significantly 7 months after the second dose. Higher antibody titers were associated with protection against severe COVID-19[10].

4.1 Strength and limitations

The strength of this study used a sample of COVID-19 patients confirmed through RT-PCR at a secondary referral hospital, therefore the demographic and clinical distribution obtained was evenly distributed and can represent the COVID-19 pandemic. This study has several limitations, first, the sample used in this study used a period when the Delta variant dominated. Some studies reveal that the effectiveness of factors was also influenced by the SARS-CoV-2 variant. Second, we did not analyze using other confounding factors beyond gender and comorbidities that may be associated with severe COVID-19 risk. Third, we assessed the clinical condition only at the time of admission.

4.2 Conclusions

In conclusion, the CoronaVac vaccine has a relatively high effectiveness in protecting against severe COVID-19 after adjusting for sex and comorbidities in adult and elderly populations. Therefore, efforts are needed to increase vaccination coverage in both adult and elderly groups, especially in developing countries such as Indonesia.

5 CONFLICT OF INTERESTS

The authors have declared that no competing interests exist.

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7 AUTHOR CONTRIBUTIONS

Conceptualization: DAR, EY, SPP
Data authorization: EY
Data curation: DAR
Methodology: DAR, CI
Analysis data: DAR, CI

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