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Original Article

The Impact of Vaccination to Clinical Severity and Mortality of COVID-19 Patients

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Abstract

Background: SARS-CoV-2 was discovered in December 2019 and later become global pandemic. Preliminary studies stated that broad vaccine coverage will suppress mortality and incidence of COVID-19. Therefore, we conduct a cross-sectional study to assess the efficacy of COVID-19 vaccination. **Materials and Methods:** We collected secondary data from electronic medical records of 343 COVID-19 positive patients confirmed via reverse transcription polymerase chain reaction from July 2021 to December 2021. We analyzed epidemiologic data, vaccination history, baseline symptoms, comorbidity, baseline vital signs, and outcome using hypothesis testing χ^2 and logistic regression. **Results:** Sex had an χ^2 of 9.34 ($P < 0.001$) while type of vaccine had an χ^2 of 1.49 ($P = 0.22$) to clinical severity. Age, pulse rate, respiration rate, body temperature, and Glasgow coma scale were found to be significant risk factors to clinical severity. Number of vaccines previously received was found to be a protective factor to clinical severity (odds ratio (OR) = 0.49, 95% CI = 0.32–0.74, $P < 0.001$). We also found that sex ($\chi^2 = 10.42$, $P < 0.001$) was a predictor to discharge condition. Moreover, age was also found to be a significant predictor (OR = 1.03, 95% CI = 1.03–1.05, $P < 0.001$), as well as number of symptoms (OR = 0.66, $P < 0.001$), comorbidities (OR = 1.64, $P < 0.001$), pulse rate (OR = 1.04, $P < 0.001$), respiration rate (OR = 1.17, $P < 0.001$), and Glasgow coma scale (OR = 0.72, $P = 0.03$). **Conclusion:** Age, sex, number of vaccines received, number of symptoms, number of comorbidities, pulse rate, and respiration rate were significant predictors of clinical severity and outcome in COVID-19 patients. In addition, body temperature was also a predictor for clinical severity, while Glasgow coma scale was a predictor for outcome.

Keywords: Clinical severity, COVID-19, mortality, prediction model, vaccination

Introduction

In December 2019, world was made aware of the emerging mysterious pneumonia cases in Wuhan.[1] As of January 3, 2020, a total of 44 patients were reported, with 11 of them being identified as "severe" while the remaining 33 patients being stable.[1] Epidemiological tracing soon found out that majority of these patients had some form of contact with Huanan Market, a large wet market located in Wuhan which is known for circulating exotic animals to market's demands.[1] This was soon backed by phylogenetical tracing which found that SARS-CoV-2 shares 88% of two bat-derived SARS-like coronaviruses and distances from SARS-CoV (around 79%) and MERS-CoV (around 50%).[2] Bats were a part of the market before it was shut down by local authorities.

After a while, researchers discovered that COVID-19 could be transmitted via droplets and aerosols.[3,4] Mask mandates and physical distancing measures were soon enacted by governments all over the world. It was then proven that enaction of the said had protocols, if followed by strict enforcement, created a surge in number of cases.[5]

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Though a definite cure has not been found yet, the race toward vaccine development soon bore its fruit. COVID-19 vaccines were fully developed approximately only one year since the first sighting of SARS-CoV-2. These vaccines were of different platforms, with different methods of production, storage, logistic requirements, and administration schedule.[6-8] Those leading the race were Russia with its Sputnik V vaccine, the United States with its BNT162b2 and mRNA-1273 vaccine, China with its CoronaVac vaccine, and Great Britain with its ChAdOx1 vaccine. The Sputnik V and ChAdOx1 were both of adenoviral-based, a platform which involves planting a spike of the ancestral SARS-CoV-2 to an emasculated adenovirus. BNT162b2 and mRNA-1273 were mRNA-based vaccine, a platform which aims to inject an antigen-encoding messenger RNA which acts as a blueprint to build protein normally produced by SARS-CoV-2. This protein induces adaptive immune response specific to SARS-CoV-2's RNA. The CoronaVac vaccine works on the whole virus platform, specifically inactivated.

A public health study conducted in the United States concluded that higher vaccination coverage is associated with lower rates of population level COVID-19 mortality and incidence.[9] This nationwide study also serves as a prove of the pre-existing preliminary studies published by scientists of vaccine developers. Analogous to these kinds of study, we performed a cross-sectional study while putting into measure other demographic, baseline symptoms, and comorbidities to assess the efficacy of COVID-19 vaccination in real-life setting.

Materials and Methods

This observational study analyzes secondary data from electronic medical records of 343 COVID-19 positive patients confirmed via reverse transcription polymerase chain reaction admitted to Udayana University Hospital during the second wave of COVID-19 cases within the country (July–December 2021). Data were gathered from medical record of patients admitted between January to March 2022 in Udayana University Hospital. Ethical approval was released by the ethical committee of Udayana University (registry number 2869. UN14.2.2.VII.14/LT/2021). Information about subjects is kept highly confidential and are only used in accordance with research ethical guidelines.

Our hospital operated at its maximum bed capacity during the very peak of the second wave and a triage system was adopted. Therefore, only patients showing moderate to critical symptoms according to the national guideline were admitted.[10] A COVID-19 case was said to be moderate if patients present pneumonia-like symptoms or pneumonia signs in their X-ray. This goes up to critical COVID-19 case, defined as those who had acute respiratory distress syndrome (ARDS), sepsis, or septic shock. Patients showing no to mild symptoms were given education and sent home for remote monitoring by their local primary healthcare facility, and therefore they were not included in analysis.

Variables included in our analysis are divided into epidemiologic data, vaccination history, baseline symptoms, comorbidity, baseline vital signs, and outcome. Epidemiologic data included patients' age and sex. We excluded patients below 18 years old from our study. Vaccination history included number of doses received and specific type of vaccine received. Baseline symptoms includes binomial yes–no answer to cough, flu, throat soreness, chest tightness, shivering, cephalgia, weakness, myalgia, nausea, and vomiting, abdominal pain, diarrhea, and anosmia. Comorbidity includes binomial yes–no answer to pregnancy, diabetes, heart diseases, hypertension, malignancy, immunologic diseases, chronic renal diseases, chronic liver diseases, chronic obstructive pulmonary diseases, and asthma. Baseline vital signs measured were pulse rate, respiration rate, body temperature, and Glasgow coma scale score during admission. Outcomes include binomial yes–no answer to manifestation of critical clinical symptoms and mortality. Critical symptoms were defined as ARDS, sepsis, and/or septic shock based on national guideline.[10]

We will first report separately all independent variables between the two groups. Hypothesis testing via χ^2 analysis will then be performed on nominal independent variables while logistic regression will be performed on numerical independent variables gathered to the dependent variables: clinical severity and mortality. Significant variables will then be further opted for multivariate logistic regression to find the impact and significance of each individual variables to critical clinical symptoms and mortality. All analyses were performed using IBM SPSS Statistics 25 (IBM SPSS Statistics for Windows, Version 25.0, IBM Corp. Released 2017, Armonk, NY).

Results

This study included a total of 343 subjects admitted to Udayana University Hospital between July to December 2021 when Indonesia was facing its second peak COVID-19 wave. Subjects ranged from 19 to 95 years old, with a mean of 52.38 ± 16.21 years old (Table 1). Male patients predominate females, constituting 52.8% patients admitted. Our patients are almost equally divided between vaccinated (53.6%) and unvaccinated (46.4%), with most of those vaccinated getting CoronaVac (75%). A complete descriptive analysis is shown in Table 1.

Baseline symptoms and comorbidities of subjects analyzed are shown in Table 2. Most of subjects analyzed had cough (95.9%), weakness (91.3%), chest tightness (61.2%), and nausea and/or vomiting (50.7%). A sizable portion developed throat soreness (39.1%), cephalgia (36.2%), flu

Table 1: Epidemiologic and vaccination profile of subjects analyzed (n = 343)

	n (%)
Age (years)	
18–20	5 (1.5)
21–30	36 (10.5)
31–40	51 (14.9)
41–50	48 (14.0)
51–60	96 (28.0)
61–70	61 (17.8)
71–80	30 (8.7)
≥ 81	16 (4.7)
Sex	
Male	181 (52.8)
Female	162 (47.2)
Number of vaccines received	
Unvaccinated	159 (46.4)
Vaccinated (1st dose)	48 (14.0)
Vaccinated (2nd dose)	136 (39.7)
Type of vaccine	
CoronaVac	138 (75.0)
ChAdOx1	46 (25.0)

Table 2: Baseline symptoms and comorbidities

	n (%)
Baseline symptoms	
Cough	329 (95.9)
Weakness	313 (91.3)
Chest tightness	210 (61.2)
Nausea and/or vomiting	174 (50.7)
Throat soreness	134 (39.1)
Cephalgia	124 (36.2)
Flu	107 (31.2)
Anosmia	98 (28.6)
Diarrhea	46 (13.4)
Myalgia	29 (8.5)
Abdominal pain	8 (2.3)
Shivers	4 (1.2)
Comorbidities	
Hypertension	73 (21.3)
Diabetes mellitus	68 (19.8)
Heart disease	53 (15.5)
Asthma	15 (4.4)
Pregnancy	10 (2.9)
Malignancy	6 (1.7)
Chronic obstructive pulmonary disease	6 (1.7)
Immunologic disease	5 (1.5)
Renal disease	5 (1.5)
Liver disease	1 (0.3)

(31.2%), and anosmia (28.6%). Subjects analyzed also had a sizable amount of hypertension (21.3%), diabetes mellitus (19.8%), and heart disease (15.5%). Table 3 shows that 20.4% of all subjects analyzed developed critical symptoms such as ARDS, sepsis, and/or septic shock. Mortality rate

Table 3: Distribution of clinical outcomes

	n (%)
Clinical severity	
Critical (ARDS, sepsis, and/or septic shock)	70 (20.4)
Non-critical	273 (79.6)
Discharge condition	
Non-survivors	60 (17.5)
Survivors	283 (82.5)

ARDS, acute respiratory distress syndrome

was around 17.5%, notably higher than those reported by other sources due to the fact that the hospital only admits people with moderate symptoms or worse.

χ^2 analysis was then performed on nominal variables, namely sex and type of vaccine. Sex had an χ^2 of 9.34 ($P < 0.001$) while type of vaccine had an χ^2 of 1.49 ($P = 0.22$) to clinical severity. Age, pulse rate, respiration rate, body temperature, and Glasgow coma scale were found to be significant risk factors to clinical severity (Table 4). Number of vaccines previously received was found to be a protective factor to clinical severity (odds ratio = 0.49, 95% CI = 0.32–0.74, $P < 0.001$).

Upon testing our hypothesis on discharge condition, we found that sex (χ^2 = 10.42, $P < 0.001$) was a predictor to discharge condition (Table 5). Moreover, age was also found to be a significant predictor (OR = 1.03, 95% CI = 1.03–1.05, $P < 0.001$), as well as number of symptoms (OR = 0.66, $P < 0.001$), comorbidities (OR = 1.64, $P < 0.001$), pulse rate (OR = 1.04, $P < 0.001$), respiration rate (OR = 1.17, $P < 0.001$), and Glasgow coma scale (OR = 0.72, $P = 0.03$).

Discussion

We found that more male patients fall into critical condition than female patients. This finding is in line with other studies which found that more male patients admitted to the intensive unit care than female patients.[11,12] Females have some specific immune characteristic such as more durable CD8+ T cell cytotoxic, have more CD4+ T cells, and specialized immunoglobulin that increase the production of B cells that affect immune resistance.[12] Female immune system also associated to X-chromosomes which increases the immunity up to two times compared to male.[13] On the other hand, males also have factors that aggravate COVID-19 infection which are higher ACE2 receptor activity as entrance gate of SARS-CoV-2 and testosterone hormone that suppress immunomodulatory response.[12]

Socioeconomic factors such as inequalities in working hours and smoking behavior also contributed to the poor clinical output of male patients.[12,14] Therefore, these socioeconomic trends and habits also influence the high rate of comorbidities in COVID-19 patients which also affects clinical severity. We also found comorbidities per

Table 4: Chi square and regression analysis for observed variables to predict clinical severity

Variable	Critical	Non-critical	PR/OR (95% CI)	χ^2	*P*-value
Age in years; Mean (±SD)	57.7 (±14.8)	51.4 (±16.3)	1.03 (1.01–1.04)	–	0.01*
Sex; *n* (%)				9.34	<0.001†
Male	40 (71.4)	140 (49.1)	2.24 (1.30–3.84)	–	
Female	16 (28.6)	145 (50.9)			
Number of vaccines received; *n* (%)			0.49 (0.32–0.74)	–	<0.001*
Unvaccinated	47 (83.9)	164 (57.5)		–	
Vaccinated (1st dose)	2 (3.6)	29 (10.9)			
Vaccinated (2nd dose)	7 (12.5)	92 (32.3)			
Type of vaccine				1.49	0.22†
CoronaVac	8 (88.9)	84 (69.7)	3.25 (0.42–25.10)		
ChAdOx1	1 (11.1)	37 (30.3)			
Number of symptoms; Mean (±SD)	4.3 (±1.0)	4.7 (±1.3)	0.76 (0.59–0.97)	–	0.03*
Number of comorbidities; Mean (±SD)	1.1 (±0.8)	0.6 (±0.8)	1.87 (1.34–2.61)	–	<0.001*
Baseline vital signs; Mean (±SD)				–	
Pulse rate per minute	97.8 (±17.6)	87.0 (±16.5)	1.05 (1.02–1.07)		<0.001*
Respiration rate per minute	27.5 (±4.5)	22.5 (±5.1)	1.21 (1.13–1.30)		<0.001*
Body temperature (°C)	38.5 (±1.1)	37.8 (±1.2)	1.71 (1.28–2.29)		<0.001*
Glasgow coma scale score	14.7 (±1.4)	14.9 (±0.9)	0.86 (0.69–1.08)		0.20*

*Regression analysis; *Chi-square test

Table 5: Chi square and regression analysis for observed variables to predict discharge condition

Variable	Deceased	Alive	PR/OR (95% CI)	χ^2	*P*-value
Age in years; Mean (±SD)	58.8 (±16.0)	51.0 (±16.0)	1.03 (1.03–1.05)		<0.001*
Sex; *n* (%)				10.42	<0.001*
Male	43 (71.7)	138 (48.8)	2.26 (1.35–3.81)		
Female	17 (28.3)	145 (51.2)			
Number of vaccines received; *n* (%)			0.48 (0.32–0.72)		<0.001*
Unvaccinated	50 (83.3)	162 (57.2)			
Vaccinated (1st dose)	3 (5.0)	28 (9.9)			
Vaccinated (2nd dose)	7 (11.7)	93 (32.9)			
Type of vaccine				0.40	0.53†
CoronaVac	8 (80.0)	84 (70.6)	1.61 (0.36–7.22)		
ChAdOx1	2 (20.0)	35 (29.4)			
Number of symptoms; Mean (±SD)	4.1 (±1.1)	4.7 (±1.2)	0.66 (0.51–0.85)		<0.001*
Number of comorbidities; Mean (±SD)	1.0 (±0.8)	0.6 (±0.8)	1.64 (1.20–2.27)		<0.001*
Baseline vital signs; Mean (±SD)					
Pulse rate per minute	96.4 (±20.0)	87.2 (±16.0)	1.04 (1.02–1.06)		<0.001*
Respiration rate per minute	26.8 (±5.8)	22.6 (±4.9)	1.17 (1.10–1.25)		<0.001*
Body temperature (°C)	38.1 (±1.4)	37.9 (±1.2)	1.21 (0.94–1.54)		0.14*
Glasgow coma scale score	14.6 (±2.0)	15.0 (±0.5)	0.72 (0.53–0.97)		0.03*

*Regression analysis; *Chi-square test

person at the critical group are higher than non-critical group whereby in line with previous statement.

Aside from gender, vaccination status also become a major key to predict clinical output. We notice that more patients admitted to hospital were vaccinated with CoronaVac than ChAdOx1. This finding happened due to the fact that Indonesians were hit by Delta variant (B.1.617.2) in the second wave of COVID-19 (July–December 2021) which altered vaccine effectiveness (VE) against COVID-19 infection especially CoronaVac as inactivated vaccine.[15,16] Nonetheless there were no significant difference between ChAdOx1 and CoronaVac as protective factor to clinical severity of COVID-19 infection.

Number of vaccines received were more significant to determine clinical severity. Previous research discovered that VE against Delta variant to prevent severe clinical output of ChAdOx1 is 91% and CoronaVac 75.3% after second dose, while ChAdOx1 had VE 44% and CoronaVac 13% after first dose.[16,17] Therefore, in addition to the type of vaccine used by the government and health care

Table 6: Multivariate logistic regression to clinical severity and discharge condition

Variable	Clinical Severity OR (95% CI)	Discharge Condition OR (95% CI)
Age	1.03 (1.00-1.05)	1.03 (1.01-1.06)
Sex	1.78 (0.86-3.70)	1.80 (0.90-3.61)
Number of Vaccines Received	0.51 (0.31-0.83)	0.51 (0.32-0.82)
Number of Symptoms	0.77 (0.55-1.08)	0.73 (0.53-1.01)
Number of Comorbidities	1.46 (0.97-2.21)	1.15 (0.77-1.73)
Pulse Rate per Minute	1.04 (1.01-1.07)	1.04 (1.01-1.06)
Respiration Rate per Minute	1.14 (1.06-1.23)	1.12 (1.05-1.19)
Body Temperature (°C)	1.62 (1.14-2.31)	-
Glasgow Coma Scale Score	-	0.60 (0.90-3.61)

facilities, it is necessary to pay attention to the number of doses that have been given to the community.

We acknowledged the possibility of bias in this data due to the triage system we applied during admission, where conditions in the field forced us to sort and filter patients based on clinical severity and their prognosis during the brief checkup in our hospital. Our hospital only admitted patients showing moderate to critical COVID-19 symptoms (ARDS, sepsis, and/or septic shock). Due to the fact that most vaccinated people developed only light symptoms, in patients were only given education and sent home for remote monitoring by their local primary healthcare facility. This may skew some numbers, causing high mortality rate and frequent manifesting of critical COVID-19 symptoms. Number of vaccines observed were mainly only CoronaVac and ChAdOx1, which in any way did not help broaden the vision towards other types of vaccines. We recommend to researchers attempting to replicate our study to patch weaknesses stated in this limitation, such as reaching out to more patients to add sample size, choose medical facilities which may eliminate the data skewing bias, and observe wider spectrum of vaccine types.

Conclusion

Age, sex, number of vaccines received, number of symptoms, number of comorbidities, pulse rate, and respiration rate were significant predictors of clinical severity and outcome in COVID-19 patients. In addition, body temperature was also a predictor for clinical severity, while Glasgow coma scale was a predictor for outcome.

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Conflicts of interest

There are no conflicts of interest.

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