Original Article

Clinical Profile of COVID-19 Patients from March 2020 to March 2021 in Abepura Regional General Hospital (RSUD Abepura), Papua

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Abstract

Background: SARS-COV-2 infection has widely spread and caused high morbidity and mortality rates. Despite more than one year of the COVID-19 pandemic in Indonesia, there is no scientific report regarding COVID-19 from Papua. This study aims to assess the clinical profile of COVID-19 patients in Abepura Regional General Hospital (RSUD Abepura), Papua.

Methods: We retrospectively recorded patients' age, sex, race, comorbidities, admitting and principal diagnoses, length of stay (LOS), and outcome (deceased/discharged) from the medical records from March 2020 to March 2021. Categorical data were described in frequencies and percentage, while numerical data were described in mean±SD or median and IQR. We analyzed the association between independent variables (age, sex, race, comorbidities, and diagnoses) with LOS and mortality rate.

Results: We included 461 patients (58.6% female) with a median age of 36.90 (26.35-49.35) years who were hospitalized for 17 (12-25) days, in which 5.4% mortality occurred. Overall COVID-19 patients were dominated by non-Papuan race (75%). The most frequent comorbidities were hypertension (19.1%), electrolyte imbalance (10.2%), and diabetes (10.0%). Increased mortality rates were significantly associated with older age (≥65 years), cerebrovascular conditions, hypertension, coronary heart disease, liver disease, diabetes, and electrolyte imbalance (P<0.05). Moreover, several comorbidities, such as hypertension, coronary heart disease, diabetes and electrolyte imbalance, and a principal diagnosis of critical COVID-19, were associated with a significantly shorter period of LOS (P<0.05).

Conclusion: Mortality and LOS due to COVID-19 in RSUD Abepura, Papua, are influenced by older age and several comorbidities.

Keywords: comorbidity, coronavirus, COVID-19, length of stay, mortality, SARS-COV-2

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INTRODUCTION

The formerly named "2019 novel coronavirus" (2019-nCoV), which was initially identified in Wuhan, China, in December 2019, spread rapidly worldwide and became a pandemic by January 2020 when the World Health Organization (WHO) declared a global health emergency towards it.[1,2] On February 11, 2020, WHO issued the official name of the 2019-nCoV as Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-COV-2), which manifested as COVID-19. The clinical manifestations of COVID-19 range from a mild flu-like illness to severe acute respiratory distress syndrome (ARDS) and multi-organ failure.[2–4]

As of March 5, 2021, there were 115,289,961 confirmed cases of COVID-19 in 222 countries, which were responsible for 2,564,560 deaths (case fatality rate/CFR of 2.2%) globally. Indonesia was responsible for 1,368,069 confirmed COVID-19 cases with 37,026 deaths (CFR 2.7%). Moreover, at the beginning of July 2021, new cases surged to 2,313,829 cases, and 61,140 deaths were reported.[5] However, the scarcity of tracking and tracing in Indonesia's COVID-19 management system resulted in an enormous underreporting of COVID-19 cases.

Besides affecting people's health, COVID-19 has severely affected Indonesia's economic stability. An analysis involving more than 12,000 representative households across all 34 provinces in Indonesia held by UNICEF in May 2021 revealed that 74.3% of the participants experienced decreased earnings due to the unprecedented pandemic. The study also concluded that one in ten people in Indonesia lives below the national poverty line.[6] This

problem is even more evident in Papua, the country's most underdeveloped and impoverished area.[7]

In order to solve the burden of COVID-19, treating this highly contagious infection requires proper medical management, medication, and diagnostic equipment. However, these facilities are not always accessible in rural areas such as Papua. Limited diagnostic centers and capacity, challenging geographical conditions, and transportation costs hinder adequate COVID-19 management in Papua. The limitation of decent health facilities and low resources in Papua also contributes to undetected chronic comorbidities and worsens COVID-19 outcomes.[8]

In addition to those limitations, the COVID-19 pandemic has increased the healthcare system burden as Papua has long struggled with controlling various infectious diseases. According to the Health Ministry Annual Report, Papua has 86,022 active cases of malaria (2021), approximately 842,000 cases of tuberculosis (2017), and 3,753 cases of HIV (2019).[9–11] Additionally, non-infectious diseases (cardiovascular disease, chronic pulmonary disease, diabetes, and others) accounted for 73% of mortality.[12] Related to the COVID-19 pandemic, there is no current scientific report on COVID-19 research in Papua. Thus, this study aims to report the demographics, clinical manifestations, and comorbidities of COVID-19 patients from March 2020 to March 2021 in Abepura Regional General Hospital, Papua.

METHODS

In this retrospective cohort study, we observed and analyzed COVID-19 patients admitted to Abepura Regional General Hospital (RSUD Abepura), Papua, Indonesia, between March 2020 and March 2021. We conducted a descriptive and analytical study focusing on the association of clinical profile (demographic, comorbidities, and diagnoses) with mortality and length of stay (LOS). The diagnoses of COVID-19 complied with Indonesia's national COVID-19 guidelines during the study period.[13] We included all patients who were hospitalized due to COVID-19 with the following criteria: 1) asymptomatic or symptomatic patients who tested positive for SARS-COV-2 reverse transcription polymerase chain reaction (RT-PCR) (first RT-PCR and/or second RT-PCR), or 2) symptomatic patients (presenting with upper respiratory or pneumonia manifestations) who tested positive for SARS-COV-2 rapid antigen. However, we excluded suspected/probable COVID-19 patients who tested negative in two consecutive RT-PCR.

Data such as age, sex, race, comorbidities, admitting and principal diagnoses (i.e., mild, moderate, severe, and critically ill), length of stay (LOS), and outcomes (discharged or deceased), were obtained from medical records and recorded using Microsoft Excel (Microsoft, USA) by the research team. Patient ID was recorded as initials to ensure anonymity; comorbidities were obtained from history taking, physical examination, laboratory, and radiology tests; admitting diagnoses were recorded at admission by doctors on duty; the attending pulmonologist established principal diagnoses; length of stay was calculated from the admission day until deceased/discharged. The ethical clearance for this study was exempted by the Medical and Ethics Committee of Abepura Regional General Hospital (RSUD Abepura), Papua, Indonesia.

Descriptive statistics included frequencies and percentages for each categorical data. We presented normally distributed numerical data in mean±SD, while median and interquartile range (IQR) to present skewed numerical data. The descriptive study was explained in tables and graphs. Analytical statistics included a normality test followed by a comparison/association test. When the Kolmogorov-Smirnov normality test showed a skewed distribution, we utilized Mann-Whitney or Kruskal-Wallis test (followed by a post hoc test with Bonferroni correction when necessary) to analyze the association between independent variables (age, sex, race, comorbidities, admitting and principal diagnoses) and LOS. We used the t-independent or ANOVA test when the data showed normal distribution. We used the Chi-square test to analyze the association between independent variables with mortality when the independent

variables consisted of two groups; otherwise, Fisher's exact test was used. Moreover, the significance value was set to $P<0.05$. All analyses were conducted in IBM SPSS.

RESULTS

A total of 461 patients comprising 270 females (58.6%) and 191 males (49.4%) with a median age of 36.90 years old (IQR 26.35-49.35) were included in this study (Figure 1). According to the age group (Figure 1), most of the included patients were between 19 and 44 years old (60.5%), followed by the age group of 45 to 64 years old (28.0%), 0 to 18 years old (6.5%) and ≥65 years old (5.0%). Regarding race, we recorded that overall COVID-19 patients were dominated by non-Papuan (75%) than Papuan (25%).

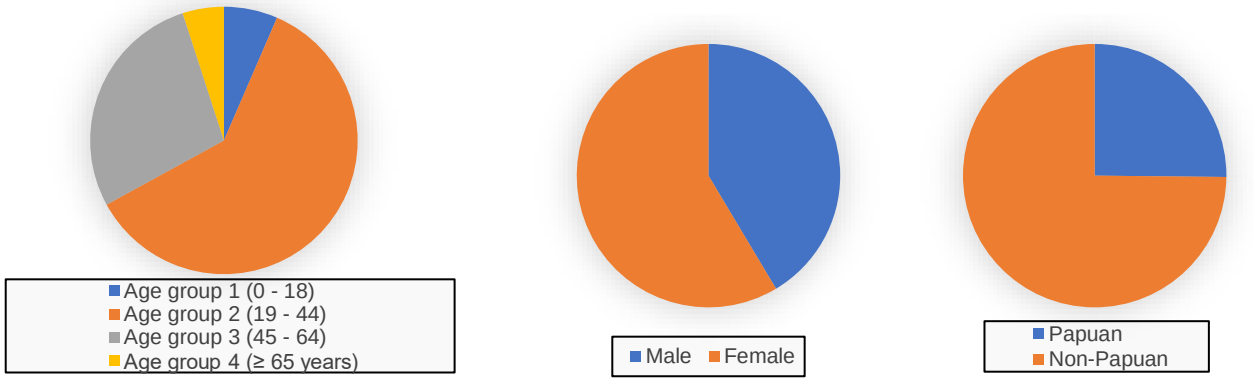

Figure 1. Proportion of COVID-19 patients based on age group (A), sex (B), and race/ethnicity (C)

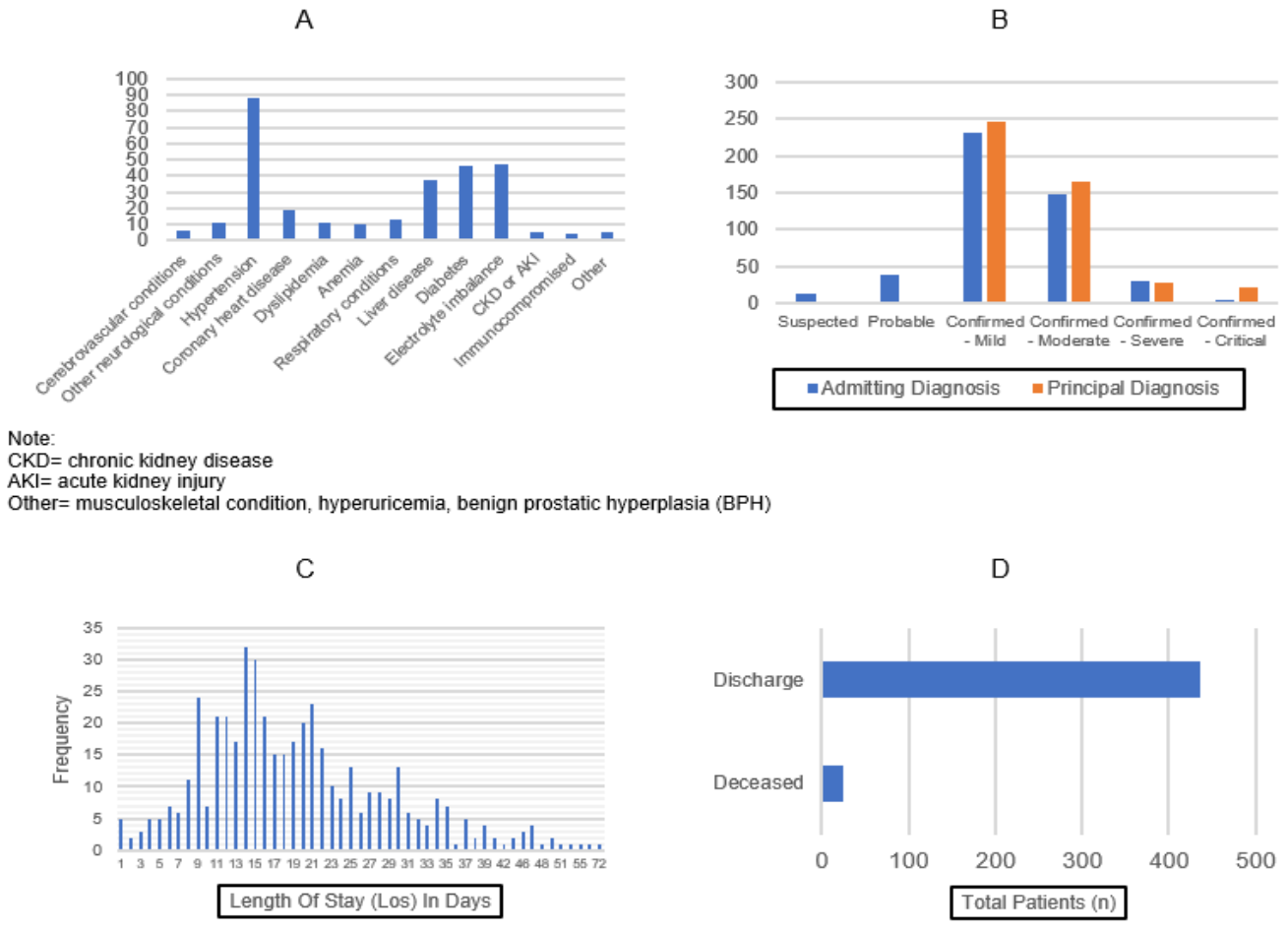

Figure 2. The proportion of pre-existing comorbidities (A), admitting and principal diagnoses (B), length of stay (C), and outcomes in COVID-19 patients.

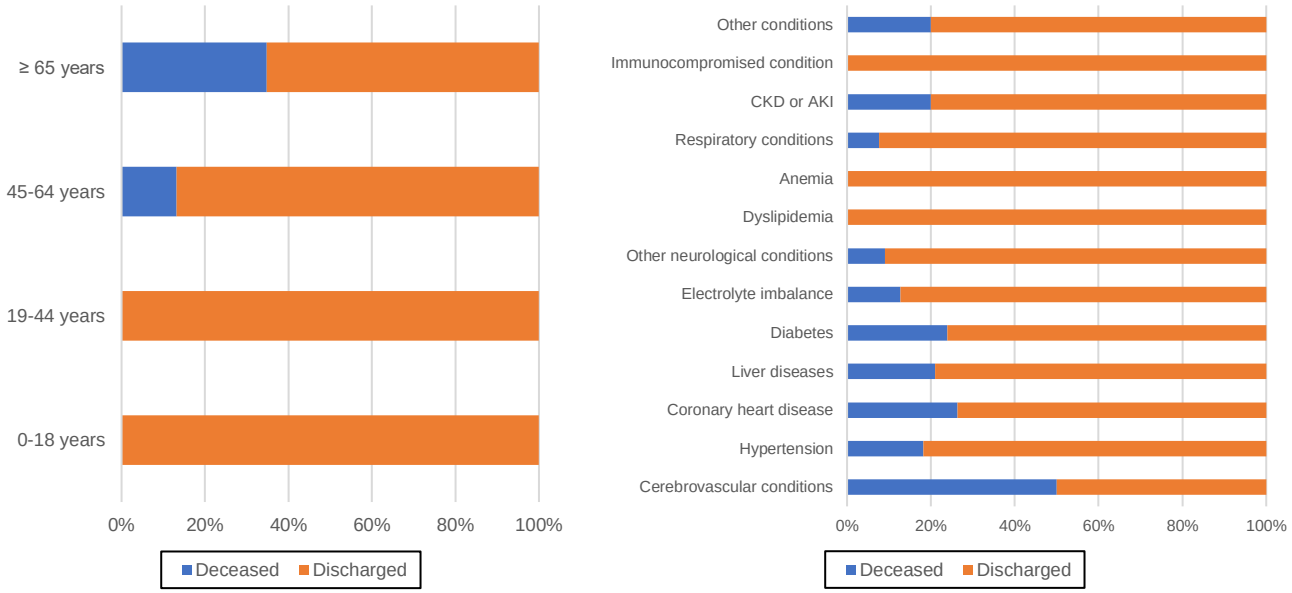

Fig. 3. The outcomes of hospitalized COVID-19 patients based on age groups (A) and comorbidities (B).

Figure 2 shows that the most prevalent comorbidities were hypertension, electrolyte imbalance, and diabetes. Most patients (231/50.1%) were diagnosed with confirmed COVID-19 with mild manifestation at admission. However, after a complete examination, the study revealed that 53.6% of the patients were diagnosed with mild manifestation, 32.1% were moderate, 6.1% were severe, and 4.6% were critically ill (Table 1). These patients were hospitalized for a median of 17 days (IQR=12-25), ranging from 1 to 72 days (Figure 2), in which 25 deaths occurred (mortality rate 5.4%). Moreover, Figure 3 demonstrates that deceased cases were higher among the ≥65 years old group and patients with cerebrovascular conditions.

Table 1 presents the association between all independent variables (age, sex, race, comorbidities, admitting, and principal diagnoses) with mortality and LOS. Our analyses showed that all deceased patients were ≥45 years old, with patients ≥65 years old having a significantly higher risk of mortality compared to <65 years old (OR=13.21 [95% CI=4.93-35.39], *P*=0.0001). Moreover, a significant increase of mortality was found in patients presenting with cerebrovascular conditions (OR=19.68 [95% CI=3.76-103.17], *P*=0.003), hypertension (OR=8.99 [95% CI=3.82-21.13], *P*=0.0001), coronary heart disease (OR=7.54 [95% CI=2.47-22.99], *P*=0.002), liver disease OR=6.37 [95% CI=2.54-15.96], *P*=0.0001), diabetes (OR=9.00 [95% CI=3.80-21.32], *P*=0.0001), and electrolyte imbalance (OR=3.04 [95% CI=1.12-8.05], *P*=0.032). However, we could not analyze the association between admitting and principal diagnoses with mortality due to the small sample size for logistic regression.

As for the LOS, we found that Papuan patients have a significantly shorter LOS than non-Papuan (a median of 15 days vs. 18 days, *P*=0.007). Similarly, the patients with cerebrovascular conditions had a significantly shorter LOS than those without cerebrovascular conditions (a median of 9 days vs. 18 days, respectively, *P*=0.021). However, our further analyses demonstrated no significant LOS difference between deceased and discharged patients who presented with cerebrovascular conditions (Table 2).

In contrast, among COVID-19 patients with hypertension (a median of 3.50 days vs. 20.50 days), coronary heart disease (a mean of 8.40 days vs. 24.43 days), diabetes (a mean of 4.73 days vs. 21.94 days), and electrolyte imbalance (a median of 8 days vs. 19 days) exhibited significantly shorter LOS in deceased patients. Likewise, patients with a principal diagnosis of critical COVID-19 were hospitalized for a significantly shorter LOS than those with mild, moderate, and severe COVID-19 (*P*=0.0001, *P*=0.0001, *P*=0.024). Other independent variables showed no significant differences in terms of LOS.

Table 1. Characteristic of demographic, comorbidities, diagnoses, outcomes, and LOS in COVID-19 patients in RSUD Abepura.

Parameter	Total N=461	Discharged (n=436)	Deceased (n=25)				LOS (days)	
			N	*P*	Effect size (Phi)	OR (95% CI)	Median (IQR)	*P*
LOS	17 (12-25)							
Age	36.90 (26.35-49.35)							
Age group								
0-18 years	30 (6.5%)	30 (6.5%)	0 (0,0%)	0.0001*[g]	0.297[g]	13.21 (4.93-35.39)[g]	15 (11-22)	0.193[a]
19-44 years	279 (60.5%)	279 (60.5%)	0 (0,0%)				18 (14-25)	
45-64 years	129 (28.0%)	112 (24.3%)	17 (3.7%)				18 (12-24.5)	
≥65 years	23 (5.0%)	15 (3.3%)	8 (1.7%)				13 (6-25)	
Sex								
Male	191 (41.4%)	177 (38.4%)	14 (3.0%)	0.128[b]	0.071	1.86 (0.83-4.20)	16 (12-24)	0.314
Female	270 (58.6%)	259 (56.2%)	11 (2.4%)				18 (13-26.25)	
Race								
Papuan	116 (25%)	106 (22.8%)	10 (2.2%)	0.079[b]	0.082	0.482 (0.210-1.104)	15 (12-21)	0.007†*
Non-Papuan	345 (75%)	330 (71.8%)	15 (3.2%)				18 (13-27)	
Comorbidity								
Cerebrovascular conditions (Ischemic stroke and hemorrhagic troke)								
Present	6 (1.4%)	3 (0.7%)	3 (0.7%)	0.003*	0.226	19.68 (3.76-103.17)	9 (1.75-16.75)	0.021*
Absent	455 (98.6%)	433 (93.9%)	22 (4.7%)				18 (13-25)	
Other neurological conditions (Tuberculoma, toxoplasmosis, cephalgia, and SOL)								
Present	11 (2.4%)	10 (2.2%)	1 (0.2%)	0.462	0.025	1.78 (0.22-14.44)	16 (9-24)	0.488
Absent	450 (97.6%)	426 (92.4%)	24 (5.2%)				17 (12-25)	
Hypertension								
Present	88 (19.1%)	72 (15.6%)	16 (3.5%)	0.0001*	0.274	8.99 (3.82-21.13)	20 (11.25-23)	0.949
Absent	373 (80.9%)	364 (79.0%)	9 (2.0%)				17 (12.5-25)	
Coronary heart disease								
Present	19 (4.1%)	14 (3.0%)	5 (1.1%)	0.002*	0.191	7.54 (2.47-22.99)	13 (8.25-22.50)	0.103
Absent	442 (95.9%)	422 (91.5%)	20 (4.3%)				18 (13-25)	
Diabetes								
Present	46 (10.0%)	35 (7.6%)	11 (2.4%)	0.0001*	0.272	9.00 (3.80-21.32)	17 (9-23.25)	0.298
Absent	415 (90.0%)	401 (87.0%)	14 (3.0%)				17 (13-25)	
Dyslipidemia								
Present	11 (2.4%)	11 (2.4%)	0 (0,0%)	1.000	0.037	1.06 (1.04-1.08)	21 (17-28)	0.278
Absent	450 (97.6%)	425 (92.2%)	25 (5.4%)				17 (12-25)	
Anemia								
Present	10 (2.2%)	10 (2.2%)	0 (0,0%)	1.000	0.036	1.06 (1.04-1.08)	15 (12.5-17)	0.149
Absent	451 (97.8%)	426 (92.4%)	25 (5.4%)				18 (12-25)	
Respiratory conditions (Pulmonary tuberculosis, asthma, and COPD)								
Present	13 (2.8%)	12 (2.6%)	1 (0.2%)	0.520	0.017	1.47 (0.18-11.80)	22 (13-34.5)	0.264
Absent	448 (97.2%)	424 (92.0%)	24 (5.2%)				17 (12-25)	
Liver disease (Hepatitis B or C, cirrhosis, and unexplained elevated liver enzyme)								
Present	38 (8.2%)	30 (6.5%)	8 (1.7%)	0.0001*	0.207	6.37 (2.54-15.96)	19 (13.5-25.25)	0.540
Absent	423 (91.8%)	406 (88.1%)	17 (3.7%)				17 (12-25)	
Electrolyte imbalance								
Present	47 (10.2%)	41 (8.9%)	6 (1.3%)	0.032*	0.109	3.04 (1.12-8.05)	18 (12-21)	0.555
Absent	414 (89.9%)	395 (85.7%)	19 (4.1%)				17 (12-25)	
CKD or AKI								
Present	5 (1.1%)	4 (0.9%)	1 (0.2%)	0.244	0.067	4.5 (0.48-41.83)	23 (10.5-25.5)	0.894
Absent	456 (98.9%)	432 (93.7%)	24 (5.2%)				17 (12-25)	
Immunocompromised condition (HIV/AIDS or cancer)								
Present	4 (0.9%)	4 (0.9%)	0 (0,0%)	1.000	0.022	1.06 (1.04-1.08)	21.5 (12-41.5)	0.532
Absent	457 (99.1%)	432 (93.7%)	25 (5.4%)				17 (12-25)	
Other (Musculoskeletal condition, hyperuricemia, benign prostatic hyperplasia)								
Present	5 (1.1%)	4 (0.9%)	1 (0.2%)	0.244	0.067	4.5 (0.48-41.83)	18 (11.5-26)	0.981
Absent	456 (98.9%)	432 (93.7%)	24 (5.2%)				17 (12-25)	

Parameter	Total N=461	Discharged (n=436)	Deceased (n=25)				LOS (days)	
			N	*P*	Effect size (Phi)	OR (95% CI)	Median (IQR)	*P*
Admitting Diagnosis								
Suspected	12 (2.6%)	12 (2.6%)	0 (0,0%)				13 (8.25-18.75)	
Probable	39 (8.5%)	29 (6.3%)	10 (2.2%)				15 (11-24)	
Confirmed Mild	231 (50.1%)	231 (50.1%)	0 (0,0%)		N/A[h]		17 (13-27)	0.004[a,f]
Confirmed Moderate	148 (32.1%)	147 (31.9%)	1 (0.2%)				19 (14-23.75)	
Confirmed Severe	30 (6.5%)	17 (3.7%)	13 (2.8%)				14 (6.75-21)	
Confirmed Critical	1 (0.2%)	0 (0,0%)	1 (0.2%)				-	
Principal Diagnosis								
Confirmed Mild	247 (53.6%)	247 (53.6%)	0 (0,0%)				17 (13-27)[c]	
Confirmed Moderate	165 (35.8%)	165 (35.8%)	0 (0,0%)		N/A[h]		19 (14-23.5)[d]	0.0001[a]*
Confirmed Severe	28 (6.1%)	22 (4.8%)	6 (1.3%)				15.5 (9.5-23)[e]	
Confirmed Critical	21 (4.6%)	2 (0.4%)	19 (4.1%)				5 (2.5-14.5)[c,d,e]	

Note= *Statistically significant (*P*<0.05); [†]Analyzed with Mann-Whitney test; [an]Analyzed with Kruskal-Wallis test; [b]Analyzed with Chi-square; [c]Post hoc test showed a significant difference (*P*=0.0001); [d] Post hoc test showed a significant difference (*P*=0.0001); [e]Post hoc test showed a significant difference (*P*=0.024); [f] False-positive significance due to multiple comparison tests (post hoc test showed insignificant difference); [g]Comparison was between ≥65 years old and <65 years old; [h]Logistic regression test could not be performed due to the small sample size; N/A=data not available

Table 2. The association between the outcome in COVID-19 patients presenting with comorbidities with LOS

Comorbidities (n)	LOS (mean±SD or median (IQR))	*P*
Cerebrovascular conditions		
Deceased (3)	4.67±5.51	0.207[a]
Discharged (3)	16.67±12.66	
Hypertension		
Deceased (16)	3.50 (1.25-11)	<0.001*[b]
Discharged (72)	20.50 (16.25-24.75)	
Coronary heart disease		
Deceased (5)	8.40±10.14	0.021*[a]
Discharged (14)	24.43±12.58	
Liver diseases		
Deceased (8)	15 (6-24)	0.195[b]
Discharged (30)	19 (14-26.5)	
Diabetes		
Deceased (11)	4.73±3.58	<0.001*[a]
Discharged (35)	21.94±10.11	
Electrolyte imbalance		
Deceased (6)	8 (3.75-18.75)	0.029*[b]
Discharged (41)	19 (13-22)	
Other neurological conditions		
Deceased (1)	9.00	N/A[c]
Discharged (10)	18.90±10.87	
Dyslipidemia		
Deceased (0)	N/A[c]	N/A[c]
Discharged (11)	20.91±7.04	
Anemia		
Deceased (0)	N/A[c]	N/A[c]
Discharged (10)	14.60±3.20	
Respiratory conditions		
Deceased (1)	1.00	N/A[c]
Discharged (12)	25.75±14.25	
CKD or AKI		
Deceased (1)	12.00	N/A[c]
Discharged (4)	20.75±8.18	
Immunocompromised condition		
Deceased (0)	N/A[c]	N/A[c]
Discharged (4)	25.00±15.77	
Other		
Deceased (1)	11.00	N/A[c]
Discharged (4)	20.50±6.81	

Note: *Statistically significant (p<0.05); [an]Analyzed using a T-independent test; [b]Analyzed using Mann-Whitney;[c]Statistic test could not be performed due to the small sample size; N/A=data not available; CKD=chronic kidney disease; AKI=Acute kidney injury

DISCUSSION

Our study revealed that most confirmed COVID-19 cases in RSUD Abepura, Papua, from March 2020 to March 2021, were among young adults and the middle age group (19 to 44 years old) at about 61% of total cases. A previous epidemiological study in Jakarta also demonstrated that patients aged 20 to 49 dominated the COVID-19 cases with a proportion of 51.2%, followed by the 50 to 59 years old group (37.6%).[14]

Regarding patients' sex, we found more female patients than males in our study (59% vs. 41%, respectively). Several studies reported the COVID-19 incidence varied; some found the COVID-19 incidence was higher among males,[15,16,] while other studies found that females were counted higher.[17,18] However, there are similarities in multiple studies that show males are prone to progress into severe conditions.[16,19]

A study by Biswas et al showed that males were prone to SARS-COV-2 infection and associated with a significantly increased mortality risk than females because of the higher expression of angiotensin-converting enzyme 2 (ACE-2) in males.[20] In addition, Ciarambino et al found that males tend to have two times higher risk of mortality as androgen hormones (testosterone) were associated with immunosuppressive effects and reduced cellular immune activation.[21,22] On the contrary, estrogen plays a role in immune stimulation and responses, such as managing cytokines activity (IL-1, IL-10, and interferon-gamma).[21]

Moreover, our study also recorded two different races of COVID-19 patients in RSUD Abepura. The dominating race, non-Papuan patients, accounted for three-fold higher than Papuan (indigenous or mixed) patients. We assume that Papuan tend to settle in their homeland for living and working purposes rather than moving to other cities. Most non-Papuans travel for business from Papua to their residential city, particularly in the annual or "Hari Raya" exodus. Interestingly, the unequal distribution of COVID-19 testing in rural Indonesia occurs as moderate to low-income residents cannot afford it. Thus, it may be that many undiscovered cases of COVID-19 in Papua.

We recorded the overall mortality rate of 5.4% and compared it between the age group of ≥65 years old and <65 years old, which showed that the age group of ≥65 was associated with a higher mortality rate (Table 1). A research article by Hazeldine and Lord explained that the physiological aging of the immune system, occurring as rising C-reactive protein (CRP) levels and some pro-inflammatory cytokines (e.g., TNF-α, IL-6, and IL-8), is associated with a chronically increased basal inflammation in healthy elderly that contributes to increased lung inflammation susceptibility.[21,23] The downregulation of the innate immune system in the elderly, such as phagocytosis, antigen-presenting process, and bactericidal activity, leads to extensive inflammation and tissue injury in severe SARS-COV-2 infection.[23,24]

The deceased case in our study was reported to be higher in non-Papuan patients, but it showed no difference between those two races regarding mortality. There was limited research on Indonesia's race and ethnicity towards COVID-19. However, some studies elucidated several factors that associated race and ethnicity with mortality, such as culture, behaviors, and socioeconomic status.[25] Another systematic review in the USA found that worse outcome of race and ethnicity-related COVID-19 was associated with lower socioeconomic status and poverty, which increased difficulty in accessing medical care (diagnostic testing and treatment); hence those factors contributed to higher mortality rates.[26]

Our study showed that cerebrovascular conditions (cerebral infarction or hemorrhagic stroke) constituted the most prominent comorbidity associated with mortality. The mortality risk in patients with cerebrovascular conditions was around 19 times higher than in COVID-19 patients without this comorbidity. Hypoxia in the central nervous system due to impairment of the alveolar gas exchange leads to cerebral insufficiency. As a result of hypoxia, anaerobic metabolism activation will produce acid metabolites. Then, the accumulation of

acid metabolites impacts cerebral adverse events, such as cells and interstitial edema, as well as blood flow impairment, worsened by cytokine cascades and coagulopathy during SARS-COV-2 infection triggering the acute cerebrovascular disease.[27] Through this mechanism, COVID-19 patients with cerebrovascular comorbidity, may exacerbate cerebral infarction or intracranial bleeding.[28] Thus, the incidence of severe infection and mortality is higher in this population.

Furthermore, hypertension remained the most significant proportion of comorbidities and was related to mortality in SARS-CoV-2 infection. The prevalence of hypertension was higher among older age with diabetes and kidney disease.[29] Rozaliyani et al reported that hypertension is the most frequent comorbidity of lethal outcomes among patients. They reported diabetes and heart disease as the second most common pre-existing condition among COVID-19 patients.[14]

Likewise, our study recorded hypertension (19.1%) as the most significant proportion of comorbidities among COVID-19 patients, followed by electrolyte imbalance (10.2%), diabetes (10%), liver disease (8.2%) and coronary heart disease (4.1%). Patients with hypertension were significantly associated with mortality, showing a nine-time higher mortality risk. Likewise, a previous study by Pranata et al demonstrated that hypertension comorbidity resulted in lethal outcomes.[30]

Previous studies also explained that hypertensive patients would be more severely affected by COVID-19 because of ACE-2.[30–32.] The virus is capable of binding the ACE-2 receptor on the lung epithelial cell. Hence, this binding negatively impacts the activity of ACE-2 to neutralize the inflammatory effect of angiotensin II and induce antioxidant roles of angiotensin 1-7.[30] The downregulation of ACE-2 simultaneously occurs with angiotensin II activation through type 1 receptors (ATR1) which caused dysregulation of the renin-angiotensin-aldosterone system (RAAS). Furthermore, it may induce vascular permeability, alveolar damage, pulmonary edema, and ARDS.[32–34]

The pre-existing cardiovascular condition we recorded in our study was coronary heart disease (CHD), demonstrating a strong association with mortality at around seven times more than patients without CHD. Kang et al found that COVID-19 patients with cardiovascular comorbidity had a higher tendency to have a cardiac injury than patients without cardiovascular comorbidity. The ACE-2 expression in human myocardial cells explains SARS-COV-2 infection-induced myocardial damage by several events, such as a hyperinflammation state that progresses to vascular inflammation, myocardial injury, unstable plaque, and hyper-coagulability.[35] In addition, heart damage worsened because of the imbalance between the demand and supply of oxygen to myocardial cells due to systemic consequences of COVID-19.[36]

Type 2 diabetes (T2D) was another pre-existing condition related to mortality (Table 1). In a previous study, diabetes was one of the cardiovascular risk factors that related to the severity and poor outcome in COVID-19 patients.[37] This finding is expected because diabetic patients have higher pro-inflammatory states, RAAS activity, vascular dysfunction, and prothrombotic condition prior to SARS-COV-2 infection. Besides, the immune imbalance in T2D patients, including elevated inflammatory markers (e.g., neutrophil, IL-6, and CRP) and delayed response and recruitment of CD4+ T cells, influence several detrimental outcomes.[38]

Furthermore, SARS-COV-2 infection in the T2D population induces direct beta cell destruction in pancreatic islets that impairs insulin production; therefore, the destruction of beta cells contributes to an over-inflammation state by releasing IL-1β and TNF-α that worsen systemic insulin resistance. Hence, type 2 diabetes patients, particularly among uncontrolled blood glucose T2D, tend to develop severe manifestations, complications (e.g., ARDS, septic shock, and disseminated intravascular coagulation/DIC) as well as higher mortality risk due to COVID-19.[38,39]

The mortality risk was also associated with the liver disease among hospitalized patients, including viral hepatitis and increased liver enzymes. A study

by Sharma et al supported our findings that patients with elevated AST and ALT were 3-fold and 2-fold at risk of adverse outcomes. Elevated AST and ALT levels indicate liver damage due to direct hepatotoxic injury caused by SARS-COV-2 infection in the biliary epithelium, which also expresses the ACE-2 receptor.[40]

According to Weber et al, patients with a high level of AST and ALT during hospital admission were strongly associated with ICU admission and mechanical ventilator utilization.[41] Moreover, the poor outcome in patients with liver disease is a consequence of direct hepatocytes or cholangiocytes damage through ACE-2 receptor expression, followed by immune-mediated damage associated with liver injury, which may be resulted in a cytokine storm.[40,42] A study in China reported that some severe COVID-19 cases were also associated with hepatitis B infection.[43]

Electrolyte imbalance was described as increased, or decreased levels of sodium, potassium, and chloride recorded prior to COVID-19 or at patient admission to our hospital. Gastrointestinal symptoms in COVID-19 patients, such as diarrhea and nausea, resulted in electrolyte imbalance.[44] The kidney involvement of fluid and electrolyte imbalance also plays a vital role during SARS-COV-2 infection through several processes, such as decreased kidney perfusion, ischemic tubular damage, and RAAS activation that regulate electrolyte homeostasis.[45]

Again, inappropriate RAAS activation via ACE-2 expression is more likely to induce excessive excretion of electrolytes by the kidneys, contributing to higher mortality in COVID-19 patients with electrolyte imbalance.[44,45] Lippi et al recorded that sodium and potassium levels in severe COVID-19 were significantly lower than in non-severe COVID-19, particularly hypokalemia, which may worsen ARDS and cardiac injury.[46]

Our descriptive study showed that the overall median (IQR) LOS was 17 days (12-25 days). Most cases in our study manifested as mild-moderate clinical symptoms on both the admitting and principal diagnoses. Several factors influenced the prolonged hospitalization in this clinical manifestation group, such as 1) limited diagnostic tools in performing PCR tests, which nasopharyngeal/oropharyngeal swab samples should be examined in Jakarta in the first month of the pandemic, and 2) more extended time to acquire two consecutive negative PCR results, even though patients showed clinical improvement. Severe-critical manifestations exhibited less than 10% of overall positive cases and a shorter period of LOS. Rees et al found a shorter period of LOS among deceased (4-21 days) than discharged cases (4-53 days).[47]

This supports our finding that all deceased patients were hospitalized with severe-critically ill manifestations (median 15 days and five days, respectively. We assumed severe-critical conditions contributed to a shorter period of hospitalization due to late hospital arrival. Mortality-related shorter hospitalization period in this group was associated with the COVID-19 timeline that most severe-critical ill patients who arrived in the hospital were in the pulmonary phase/inflammatory phase, which exhibited dyspnea onset, bilateral pulmonary infiltrates, and ARDS progression. In this regard, patients showed life-threatening conditions, such as multi-organ failure and ARDS, resulting from immune system dysregulation and hypercoagulable condition during the pulmonary phase.[48]

Regarding race, our study found that Papuan patients (15 days) had shorter LOS than non-Papuan patients (18 days). Further observation is essential to discover whether the shorter LOS is associated with poor outcomes or not based on the association of race with other parameters (e.g., demographics, comorbidities, and diagnoses). Regarding comorbidity, patients with cerebrovascular conditions showed a shorter period of hospitalization than those without this comorbidity. We further analyzed the association of COVID-19 outcomes with LOS among patients with comorbidities. Our analyses demonstrated no significant LOS difference between deceased and discharged cerebrovascular-conditions-presenting patients (Table 2).

In contrast, other comorbidities, such as hypertension, coronary heart disease, type 2

diabetes, and electrolyte imbalance, significantly differed in a shorter period of LOS between deceased and fully recovered patients presenting with those comorbidities. In our study, a shorter period of LOS was predicted to be associated with severe illness progression and mortality. Zaenab et al also found that some comorbidities, such as hypertension, diabetes, and cardiovascular disease, were prone to worse outcomes (e.g., respiratory failure and mortality).[49]

LIMITATION

The retrospective cohort study in RSUD Abepura can be the closest reflection of COVID-19 incidence on behalf of the pandemic phenomenon in Papua, Indonesia. However, independent variables should be followed up continually, particularly with small samples and the association of race with other variables, to observe the correlation with COVID-19 outcomes. It is essential to add clinical symptoms to make the diagnoses more precisely analyzed in association with outcomes, which we only summarized as mild, moderate, severe, and critical ill manifestations. Hopefully, this research will proceed to the second year of the COVID-19 pandemic, guided by the national guideline following the pandemic period. Thus, we can observe the COVID-19 pandemic progression in Papua, Indonesia.

CONCLUSION

COVID-19 patients from March 2020 to March 2021 in RSUD Abepura, Jayapura, Papua, are predominantly aged 19 to 44. The higher incidence of mortality was influenced by older age (≥65 years old) and comorbidities. Cerebrovascular conditions, hypertension, diabetes, and cardiovascular disease were the main concerns related to higher mortality associated with SARS-COV-2 infection. In terms of LOS, severe to critical manifestation and deceased cases showed a shorter period of hospitalization. In addition, a shorter period of LOS was also shown among deceased or discharged patients presenting with hypertension, coronary heart disease, type 2 diabetes, and electrolyte imbalance, as those conditions were strongly associated with mortality. Delays in medical treatment and hospitalization may contribute to higher mortality in Jayapura. Accordingly, stakeholders' involvement is crucial to repeatedly promote public awareness of the disease.

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CONFLICT OF INTEREST

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