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Predictor of death in elderly patients with Covid-19 : a retrospective cohort study at RSUP Prof Dr. I.G.N.G Ngoerah

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Background: COVID-19 in elderly has poor prognosis as well as patients with comorbidities. However, evidence that showed comorbidities in COVID-19 cause death, regardless of age, has not been obtained

Methods: A retrospective cohort study in patients aged 60 years and over with COVID-19 who were hospitalized in Prof. dr. I. G. N. G. Ngoerah Hospital was conducted by taking data from medical record

Results: The highest proportion of deaths were 130 men and 36 with hypertension comorbidities. Age was not significantly associated with death (p=0.60), male gender was significantly associated with death (p=0.005), smoking had significant effect on death (p=0.047). Based on the symptoms, there was no relationship between death and fever (p = 1.00), cough (p = 0.054), nausea and vomiting (p = 0.s35). However, there is significant relationship with shortness of breath (p = 0.00) and delirium (p = 0.00). Based on previous medical history, there was no significant association between death and diabetes (P=0.78), hypertension (p=0.26), COPD (p=1.0), ischemic stroke (p=0.11), heart disease (p=0.11), =0.057), congestive heart disease (p=0.65), kidney disease (0.81), and tumors (p=0.31). High D-dimer levels also were not associated with death (p=0.37). Treatment with antibiotics (p=0.04), anticoagulants (p=0.002) and corticosteroids (p=0.00) were significantly associated with death. The use of antiviral was not significantly associated with death (p=1.00).

Conclusion: Factors associated with the death of elderly patients with COVID-19 were male gender, smoking, treated with antibiotics, anticoagulants and corticosteroids.

Keywords: COVID-19, elderly, death predictors, hospitalized.

INTRODUCTION

The global pandemic triggered by the coronavirus (SARS-CoV-2) has placed the elderly population at a significantly higher risk. Statistics indicate that individuals over the age of 65 represent 30% of all COVID-19 cases, account for 45-50% of hospitalizations, and sadly, 80% of the fatalities attributed to the virus.[1] Following the World Health Organization's declaration of COVID-19 as a pandemic on March 12, 2020, the world has seen 241,886,635 confirmed cases and 4,919,755 deaths by October 21, 2021. Specifically, in Indonesia, the case count reached 4,237,834 with 143,120 deaths by the same date.[2] The elderly are particularly susceptible to COVID-19, largely due to immunosenescence, or the gradual decline of the immune system with age. According to the CDC, 31% of confirmed COVID-19 cases involved individuals aged 65 and above, and this age group constituted 45% of hospital admissions. Notably, individuals over 70 years old had a higher mortality rate than recovery rate, with those aged 60 and above experiencing the lowest recovery rate (9.4%) and the highest death rate (41%) across all age groups.[3]

The prognosis for COVID-19 is notably poorer in the elderly compared to younger individuals, with a significant number of hospitalizations involving older adults or those with chronic comorbid conditions.[3] The weakened immune system and altered immunoregulation in the elderly are key factors contributing to the high mortality rates from COVID-19 in this demographic.[4] A study conducted at Soewandi General Hospital revealed that elderly COVID-19 patients, particularly those with diabetes mellitus (DM) and hypertension (HT), showed significant differences in various health indicators, including hemoglobin, lymphocyte and hematocrit levels, mean platelet volume, neutrophil-lymphocyte ratio, and levels of

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SGPT, blood urea nitrogen, serum creatinine, and D-dimer, when compared to younger patients.[5]

Research at Cipto Mangunkusumo National Central General Hospital highlighted that the majority of elderly COVID-19 patients presented with fever, cough, and shortness of breath, and commonly had comorbidities such as diabetes mellitus, hypertension, and cancer. Only 14% of these patients had multiple comorbidities. The study also found a 23% mortality rate among hospitalized elderly COVID-19 patients, with 90% of the deceased being male.

MATERIAL AND METHODS

This research is a retrospective cohort study aimed at examining the general profile and characteristics of elderly patients (aged over 60 years) who were hospitalized with COVID-19. The study analyzed secondary data collected from Prof. Dr. I.G.N.G Ngoerah Hospital over the period from February 2022 to August 2022, encompassing a total of 390 patients who satisfied the inclusion criteria and none of the exclusion criteria. The ethical approval for this study was granted by the Ethical Committee of the Faculty of Medicine at Udayana University and Prof. Dr. I.G.N.G Ngoerah Hospital, with authorization from the hospital's Director. The research adhered to the principles outlined in the Declaration of Helsinki.

To analyze the data, descriptive statistical methods were employed to outline the characteristics of the study participants in a tabulated format. Quantitative data were summarized using mean ± standard deviation, while qualitative data were displayed as frequency distributions. The normality of the data distribution was assessed using the Kolmogorov-Smirnov test. To explore the association between various independent variables and the mortality among the elderly COVID-19 patients, bivariable analysis was conducted. This involved creating 2x2 comparison tables for the variables, and if the data were not normally distributed, Fisher's test would be applied instead. The bivariable analysis yielded hazard ratios (HR), which illustrated the magnitude and direction of the associations, as well as the significance of the p-values. Statistical significance was determined by a two-tailed test with p-values less than 0.05, indicating a 95% confidence interval.

RESULTS

In this study, 390 patients were obtained as research subjects, with the majority of male patients are 263 peoples (67.44%) and 127 are female patients (32.56%). The mean age was 69.0 ± 7.5 years. The majority of patients are married (375 peoples). Based on educational status, the majority of patients had high school education of 130 peoples (33.33%), followed by 99 peoples (25.38%) did not school. Majority of patients have Hindu religion 317 peoples (81.28%), followed by Islam religion 34 peoples (8.72%). Based on occupation, most of the patients worked as non civil employees as 319 peoples (81.79%). Based on smoking status, only 60 peoples (15.38%) who smoke while the majority 330 peoples (84.62%) do not smoke.

The most common symptom experienced by patients when they came to the hospital was cough which was experienced by 280 peoples (71.79%), shortness of breath 277 peoples (71.03%), fever 256 peoples (62.4%), fatigue 129 peoples (33.08%), and nausea and vomiting 100 peoples (25.64%). The comorbidities experienced by the majority of patients were hypertension 181 peoples (46.41%), diabetes mellitus 121 peoples (31.03%), kidney disease 94 peoples (24.10%), congestive heart disease 52 peoples (13.33%), heart disease 45 peoples (11.54%), patients who underwent dialysis were 33 peoples (8.46%), ischemic stroke 27 peoples (6.92%), tumors 16 peoples (4.10%), asthma 7 peoples (1.79%) and liver disease, TB and COPD each 9 peoples (2.2%), bleeding stroke 6 peoples (1.54%), and autoimmune disease 1 people (0.26%). All patients were checked for COVID-19 antigen swab and was found 331 peoples (84.87%) positive for COVID-19.

Physical and laboratory examinations are shown in table 2 and the average blood pressure was 126.7 ± 22.2/ 75.5 ± 13.1 mmHg. The average of pulse rate was 91.1 ± 17.4 times per minute, respiratory rate was 23.8 ± 4.7 times per minute, temperature was 36.6 ± 0.75, and oxygen saturation was 89.9 ± 11.3%. In laboratory examinations, the average of hemoglobin was 12.7 ± 2.47 g/dl, HCT was 40.5 ± 26.76, leukocytes was 11.3 ± 7.22 g/dl, platelets was 239.1 ± 191.66, random blood sugar was 165.5 ± 111.37, and HbA1c was 7.2 ± 3.16. Based on blood gas analysis, the average of PH was 7.3 ± 0.4, PO2 was 100.9 ± 49.27, PCO2 was 38.7 ± 16.9, HCO3 was 22.3 ± 7.42, sodium levels was averaged 134.8 ± 12.7, potassium was 3.7 ± 0.84, SGOT was 66.09 ± 124.45, SGPT was 52.6 ± 100.63, IL-6 was 0.33 ± 1.41, CRP was 106.9 ± 186.09, and D-Dimer was 16.1 ± 127.92.

Patients were given treatment of antibiotics, corticosteroids, antivirals, anticoagulants, vitamin D, IVIG and Anti IL-6 as shown in table 3. Patients were given antibiotics such as azithromycin was 106 patients (28.5%), levofloxacine was 111 patients (28.5%), ceftriaxone was 48 patients (12.3%), ciprofloxacine was 11 patients (2.8%), cefoperazone was 9 patients (2.3%), and cefepime was 3 patients (0.8%). Patients were not given antibiotics were 102 patients (26.2). Patients who were given corticosteroids were 303 patients with the majority was being given dexamethasone as 268 peoples (68.7%), followed by methylprednisolone as 21 peoples (5.4%). Heparin was the most choosen anticoagulant, was given to 134 peoples (34.4%), Enoxaparine was given to 114 peoples,

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Table 1. Characteristics of Subjects

Characteristics	Total (N= 390)	Percentage(%)
Gender		
Male	263	67.44
Female	127	32.56
Age		
Average	69.0 ± 7.5 years	
Marital status		
Married	375	96.15
Unmarried	15	3.85
Smoking Status		
Yes	60	15.38
No	330	84.62
Education		
Did not school	99	25.38
Elementary school	62	15.90
Junior high school	18	4.62
Senior high school	130	33.33
Diploma	6	1.54
Bachelor	75	19.23
Religion		
Buddhist	7	1.79
Hindu religion	317	81.28
Islam religion	34	8.72
Catholic	11	2.82
Christian	21	5.38
Work		
civil employee	71	18.21
Non civil employee	319	81.79
Symptom		
Fever	242	62.05
Shivering	46	11.79
Cold	30	7.69
Cough	280	71.79
Shortness of breath	277	71.03
Sore throat	42	10.77
Smelling loss	35	8.97
Nausea and vomiting	100	25.64
Diarrhea	23	5.90
Stomach pain	17	4.36
Muscle pain	14	3.59
Joint pain	19	4.87
Weakness	129	33.08
Headache	25	6.41
Delirium	54	13.85

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Characteristics	Total (N= 390)	Percentage(%)
Comorbid diseases		
Diabetes	121	31.03
Hypertension	181	46.41
Asthma	7	1.79
COPD	7	1.79
TB	7	1.79
Hemorrhagic stroke	6	1.54
Non hemorrhagic stroke	27	6.92
Heart disease	45	11.54
Congestive heart disease	52	13.33
Kidney disease	94	24.10
CKD with dialysis	33	8.46
Leukaemia	6	1.54
Tumors	16	4.10
Autoimmune	1	0.26
Liver disease	9	2.31

Table 2. Characteristics of physical and laboratory examination

Examination	Average	Standard Deviation
Physical examination		
Systolic blood pressure	126.7	22.2
Diastolic blood pressure	75.5	13.1
Pulse	91.1	17.4
Respiration	23.8	4.7
Temperature	36.6	0.75
Saturation	89.9	11.3
Laboratory examination		
Hemoglobin	12.7	2.47
HCT	40.5	26.76
Leukocytes	11.3	7.22
Platelets	239.1	191.66
Basophils	0.07	0.41
Eosinophils	0.06	0.31
Lymphocytes	1.59	5.21
Monocytes	1.09	4.85
When blood sugar	165.5	111.37
HbA1c	7.2	3.16
PH	7.3	0.4
PO2	100.9	49.27
PCO2	38.7	16.9
HCO3	22.3	7.42
Sodium	134.8	12.7
Potasium	3.7	0.84
Chloride	95.1	19.89
Ureum	31.3	27.76

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Examination	Average	Standard Deviation
Creatinin	2.5	4.92
SGOT	66.09	124.45
SGPT	52.6	100.63
CT	1.8	6.74
IL6	0.33	1.41
CRP	106.9	186.09
D-dimer	16.1	127.92

Table 3. Treatment given to the patient

Type of Drugs	Amount the patient	Percentage
Antibiotics		
Azithromycin	106	27.2
Ceftriaxone	48	12.3
Levofloxacine	111	28.5
Cefepime	3	0.8
Ciprofloxacine	11	2.8
Cefoperazone	9	2.3
No Antibiotics	102	26.2
Corticosteroids		
Dexamethasone	268	68.7
Methyl-prednisolone	21	5.4
No Corticosteroids	101	25.9
Anticoagulants		
Enoxaparine	114	29.2
heparins	134	34.4
warfarin	38	9.7
No Anticoagulants	99	25.4
Antivirals		
Favipiravir	32	8.2
Remdesivir	205	52.6
No Antivirals	105	26.9
Ivermectin	1	0.26
Vitamin D	33	8.46
Anti-IL-6	2	0.51
IVIG	1	0.26

warfarin was given to 38 peoples (9.7%), and patients without anticoagulants were 99 people (25.4%). For the antiviral administration, some patients were given remdesivir as 205 peoples (52.6%), without antiviral was 105 peoples (26.9%), favipirapir was given to 32 peoples (8.2%). Ivermectin was given to 1 person (0.26%), vitamin D was given to 33 patients (8.46%), anti-IL6 was given to 2 peoples (0.51%) and IVIG was given to 1 person (0.26%).

Prevalence of Death of COVID-19 Patients in the Elderly

Based on the ward, the majority of patients were treated in the isolation ward as 253 patients (64.9%), and in HCU-ICU ward was 137 peoples (35.1%). Patient outcomes are listed in Table 4. 173 patients (44.4%) died during admission, 106 patients recovered with negative PCR test result after admission (24.6%), 80 patients (18.5%) recovered with positive PCR test result after admission, and 50 patients (12.6%) recovered without PCR evaluation after admission.

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Table 4. Factors associated with the death of COVID-19 patients

factors	Proportions (N=390)	Percentage (%)	HR	P Value	95% CI
Man	130	33.33	1.84	0.005	1.2-2.8
Smoke	34	8.72	1.9	0.047	1.2-2.9
Fever	108	27.69	1.0	1,000	0.8-3.1
Cough	133	34.10	1.5	0.054	0.9-2.2
Congested	153	39.23	5.2	0.00	3.0-8.7
Nauseous vomit	41	10.51	0.78	0.35	0.5-1.2
Delirium	38	9.74	3.5	0.00	2.0-6.8
Diabetes	62	15.90	1.4	0.78	0.4-1.6
Hypertension	86	22.05	1.26	0.26	0.6-1.9
COPD	3	0.77	1,029	1.00	0.1-8.5
Blockage Stroke	16	4.10	1.9	0.113	0.8-4.2
Heart disease	26	6.67	1.89	0.057	0.4-2.7
Congestive Heart	25	6.41	1.18	0.65	0.6-2.1
Kidney illness	43	11.03	1.07	0.81	0.3-1.4
Tumor	5	1.28	0.5	0.31	0.1-1.6
D-Dimer	123	31.54	1.2	0.37	0.72-1.9
Antibiotics	139	35.64	0.019	0.04	1.0-2.61
Anticoagulants	142	36.41	2.1	0.002	1.3-3.5
Corticosteroids	148	37.95	2.8	0.000	1.6-4.4
With Antivirals	129	33.08	0.9	1,000	0.6-1.5
No Antivirals	44	11.28	1.01	1,000	0.64-1.5

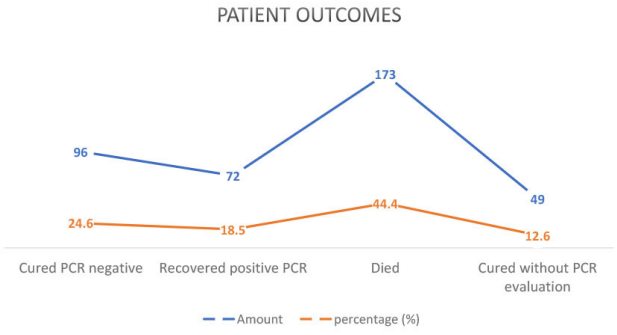

Figure 1. Patient Outcomes.

Factors associated with the death of COVID-19 patients in the elderly

The Chi-Square test was carried out to assess the Hazard Ratio (HR) of factors associated with death in elderly patients with COVID-19 at RSUP Prof. Dr. IGNG Ngoerah. The highest proportion of deaths were 130 males, and 36 comorbidities with hypertension. Age was not significantly associated with death (p=0.60), male gender was significantly associated with death (p=0.005), smoking had a significant effect on death (p=0.047).Based on the symptoms experienced by the patients, there was no relationship between death and fever (p = 1.00), cough (p = 0.054), nausea and vomiting (p = 0.35). However, there is a significant relationship with shortness of breath (p = 0.00) and delirium (p = 0.00). Based on the patient's previous medical history, there was no significant relationship between death and diabetes (P=0.78), hypertension (p=0.26), COPD (p=1.0), ischemic stroke (p=0.11), heart disease (p =0.057), congestive heart disease (p=0.65), kidney disease (0.81), and tumors (p=0.31). High D-dimer levels were also not associated with death in this study (p=0.37). Treatment with antibiotics (p=0.04), anticoagulants (p=0.002) and corticosteroids (p=0.00) were significantly associated with death.

DISCUSSION

The study by Yang et al, which aligns with the findings of this research, reported that among 1,099 patients diagnosed with a new coronavirus-induced pneumonia, 15.1% were aged 60 years and above, with 27.0% of these older patients experiencing severe symptoms.[6] Similarly, a study by Azwar at the Indonesian National Hospital found that 66% of elderly COVID-19 patients were male, a figure that closely matches this study's finding of 67.44% male patients.[5]

Regarding symptoms, previous research[7] indicated that the most common symptoms among elderly COVID-19 patients were fever (66.7%), cough (64.8%), and fatigue (33.3%), along with other symptoms such as dyspnea, diarrhea,

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anorexia, headache, myalgia, and vomiting. This study's findings are consistent, with cough (71.79%), shortness of breath (71.03%), and fever (62.4%) being the most frequently reported symptoms upon hospital admission, followed by fatigue and nausea/vomiting.

Azwar's research also highlighted that the most prevalent chronic conditions in hospitalized elderly COVID-19 patients were diabetes mellitus, hypertension, and cancer.[4] This study observed similar trends, with hypertension, diabetes, and kidney disease being the most common comorbidities, alongside other conditions such as congestive heart disease, chronic kidney disease requiring dialysis, ischemic stroke, tumors, asthma, liver disease, TB, COPD, hemorrhagic stroke, and autoimmune diseases.

The severity of COVID-19 in the elderly, including a higher likelihood of ICU admission and increased mortality rates, was evident. Elderly patients had a significantly higher mortality rate (5.3%) compared to younger patients (1.4%).[8] In this study, 44.4% of the patients passed away during treatment. A multivariate regression analysis by Li et al. identified five significant factors associated with mortality in elderly COVID-19 patients: male gender, age, breathlessness, cerebrovascular disease, and COPD. Notably, the majority of deaths in this study were among males and those with hypertension.

This study found no significant correlation between patient age and mortality, possibly due to the predominantly elderly study population. Smoking was significantly associated with increased mortality, echoing meta-analysis findings that linked smoking history to a higher risk of severe COVID-19 outcomes. Other variables related to in-hospital mortality included cardiovascular diseases other than hypertension, dyspnea upon admission, elevated Brixia and CALL scores, high gamma-glutamyl transferase levels, high blood sodium levels, low lymphocyte counts, elevated D-dimer and serum interleukin-6 levels, high C-reactive protein levels, and corticosteroid therapy.[9] However, high D-dimer levels were not linked to mortality in this study.

No significant relationship was found between mortality and previous medical conditions such as diabetes, hypertension, COPD, obstructive stroke, heart disease, congestive heart disease, kidney disease, and tumors. Given these findings, it is crucial to adopt a careful approach to managing COVID-19 in the elderly, considering their distinct symptoms and prognosis. The vulnerability of elderly patients to adverse outcomes underscores the importance of preventive measures, early detection, and prompt treatment to mitigate the risks of severe complications.

CONCLUSIONS

In hospitals, the majority of elderly COVID-19 patients are male (67.44%), in a marital union (95.15%), with a background of high school education (33.33%), practicing Hinduism (81.28%), not engaged in white-collar employment (81.79%), and predominantly non-smokers (84.62%), averaging 69.0 ± 7.5 years in age. Coughing (71.79%) emerges as the most frequent symptom, while hypertension (46.41%) stands out as the leading coexisting condition. The mortality rate among these patients reaches 44%. Interestingly, there's no significant link between the patients' age and their mortality risk (p=0.60). However, being male significantly elevates the risk of death (p=0.005), as does smoking. Mortality does not significantly correlate with certain comorbidities such as diabetes (p=0.78), hypertension (p=0.26), COPD (p=1.0), ischemic stroke (p=0.11), heart disease (p=0.057), congestive heart failure (p=0.65), kidney disease (p=0.81), and tumors (p=0.31). Notably, treatments involving antibiotics (p=0.04), anticoagulants (p=0.002), and corticosteroids (p<0.001) have shown a significant association with mortality. Conversely, the use or non-use of antiviral medications did not significantly impact mortality rates (p=1.00). Symptoms like shortness of breath and delirium significantly increase the risk of death (both p<0.001), whereas high D-dimer levels do not significantly affect mortality outcomes in these patients (p=0.37).

AUTHORS' CONTRIBUTION

All authors contributed equally in the drafting, conducting and finalization of the article.

CONFLICT OF INTEREST

No conflict of interest was to declare

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