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Research Article

FACTORS ASSOCIATED WITH MORTALITY OF ELDERLY PATIENTS WITH COVID-19 INFECTION AT M. DJAMIL HOSPITAL, PADANG, WEST SUMATRA, INDONESIA

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ABSTRACT

Background:
To analyze the factors influencing the mortality incidence of elderly patients with COVID-19 infection in Padang, West Sumatra, Indonesia.
Methods: This is a retrospective study at M. Djamil Hospital, Padang. Data was collected from the medical records of COVID-19 patients treated during July-September 2021.
Results: Of the 243 elderly patients who experienced COVID-19, the most deaths were male (58.6%) with an average age of 69.64 ± 7.74 years. Multivariate analysis showed that patients with critical-severe clinical symptoms (odds ratio (OR) 12.95; 95% confidence interval (CI) 6.66–25.19), heart disease (OR 6.94; 95% CI 1.63–29.60), respiratory rate ≥30 breaths per minute (OR 3.48; 95% CI 1.04–11.60), pulse ≥100 beats per minute (OR 2.88; 95% CI 1.03–8.04), using a ventilator or high-flow nasal cannula (OR 19.78; 95% CI 5.92–66.10), prothrombin time >13.16 second (OR 12.35; 95% CI 2.43–62.77), interleukin-6 >6 pg/mL (OR 15.19; 95%CI 2.53–91.26), and random blood glucose >199 mg/dL (OR 3.45; 95% CI 1.02–11.68) have a high risk of death.
Conclusion: Elderly patients with COVID-19 infection with critical-severe clinical symptoms accompanied by heart disease, using ventilator or high-flow nasal cannula, longer prothrombin time, high level of interleukin-6, and random blood glucose have higher risk of mortality.

Keywords: COVID-19, elderly, mortality, patient, infection, public health

INTRODUCTION

The Coronavirus Disease 2019 (COVID-19) pandemic has had a significant impact on the global health system, especially on vulnerable population groups such as the elderly. Since it was first identified in Wuhan, China, in December 2019, COVID-19 has caused millions of deaths worldwide, with higher mortality rates recorded in patients aged 60 years and older. In the United States, COVID-19 infections have struck 90 million and caused the deaths of more than 1 million people as of September 2022.[1]

Coronavirus Disease 2019 was first discovered in Indonesia in March 2020. As of April 1, 2022, around 6 million cases of COVID-19 have been obtained in Indonesia. M. Djamil Hospital in Padang, West Sumatra, is one of the COVID-19 referral centers in the Sumatra region and often receives severe cases. COVID-19 mortality in West Sumatra as of April 2022 found 2,322 out of 103,537 positive confirmed cases.[2]

The death rate due to COVID-19 is increasing with age. The highest mortality rate was obtained in the elderly group, about eighty percent of deaths occurred in patients aged 65 years and older.[1,3] The high mortality rate is thought to be influenced by age, cytokine storm conditions that occur when exposed to infection, COVID-19 virulence, and comorbid factors.

The elderly population is a vulnerable group in this pandemic. The occurrence of immunosenescence characterized by a dysregulation in immune function accompanied by an increased risk of age-related inflammation is the main cause of high mortality in the elderly with COVID-19 infection. Some studies show that the elderly population is more susceptible to COVID-19 and has a worse prognosis. Research showed that COVID-19 patients admitted to the intensive care unit (ICU) were older than patients in non-ICU.[4] Another study found that the average age of COVID-19 patients who died was 64.6 years.[5]

Various studies show that in addition to chronological age, a number of other factors also affect the mortality rate of elderly patients with COVID-19. These factors include clinical conditions upon hospital admission, nutritional status, use of breathing apparatus, and levels of certain inflammatory biomarkers. A deeper understanding of the factors that correlate with mortality in older adults is essential to support more informed clinical decision-making, efficient allocation of medical resources, and the development of health policies that are more adaptive to the needs of these vulnerable populations.

This study aims to analyze various factors related to mortality in elderly patients due to COVID-19 at M. Djamil Hospital Padang, West Sumatra, Indonesia, a regional referral hospital. Thus, it is expected to contribute to more effective efforts to overcome the impact of the pandemic, especially in the context of protecting the elderly population.

MATERIAL AND METHODS

This is a retrospective study comprising 243 elderly patients hospitalized at M. Djamil Hospital, Padang, from July to September 2021. Inclusion criteria were elderly patients aged 60 years and over who were diagnosed with COVID-19 based on positive polymerase chain reaction results. Patients with incomplete data were not included in the study. Characteristics data of patients such as age; sex; weight and height; vital signs when admitted (pulse, respiratory rate [RR], temperature, and blood pressure); oxygen saturation based on pulse oximetry;

and laboratory data such as hemoglobin, leukocytes, platelets, ratio neutrophil lymphocytes, blood glucose, electrolytes, kidney function (urea, creatinine), liver function (alanine aminotransferase [ALT], aspartate aminotransferase [AST], albumin), hemostasis factors (prothrombin time [PT], activated partial thromboplastin time [APTT], d-dimer), and interleukin-6 (IL-6) were collected from medical records and subsequently analyzed. Multivariate analysis is used to determine the factors affecting mortality.

RESULTS

Two hundred forty-three patients were included in the analysis: 111 subjects died, and 132 lived upon discharge from the hospital. Of the 243 elderly patients, 58.6% of those who died were male. No statistical relationship was found between age and mortality of elderly COVID-19 patients, likewise with gender, body mass index, and the symptoms of fever, cough, dyspnea, sore throat, runny nose, muscle aches, anosmia, diarrhea, nausea vomiting, and fatigue. The analysis showed a significant relationship between loss of consciousness, severity, and heart disease with mortality (Table 1).

Table 1. Characteristics of elderly COVID-19 patients

Variable	Died (n = 111)	Lived (n = 132)	P
Age (years)			
≥70	39 (35.1)	48 (36.4)	0.842
60–69	72 (64.9)	84 (63.6)	
Gender, n (%)			
Male	65 (58.6)	66 (50.0)	0.182
Female	46 (41.4)	66 (50.0)	
BMI (kg/m^2)			
≥23.0	73 (65.8)	77 (58.3)	0.235
<23.0	38 (34.2)	55 (41.7)	
Symptoms, n (%)			
Fever	53 (47.7)	65 (49.2)	0.816
Cough	106 (95.5)	124 (93.9)	0.591
Dyspnea	108 (97.3)	125 (94.7)	0.309
Loss of consciousness	19 (17.1)	10 (7.6)	0.022
Sore throat	8 (7.2)	8 (6.1)	0.720
Runny nose	2 (1.8)	3 (2.3)	0.797
Muscle aches	5 (4.5)	2 (1.5)	0.165
Anosmia	23 (20.7)	31 (23.5)	0.606
Diarrhea	4 (3.6)	9 (6.8)	0.267
Nausea or vomiting	13 (11.7)	16 (12.1)	0.922
Fatigue	3 (2.7)	4 (3.0)	0.879
Disease severity, n (%)			
Critical–severe	97 (87.4)	46 (34.8)	0.000
Moderate–mild	14 (12.6)	86 (65.2)	
Comorbid, n (%)			
Diabetes	40 (36.0)	38 (28.8)	0.228
Heart disease	23 (20.7)	10 (7.6)	0.003
Hypertension	55 (49.5)	69 (52.3)	0.672
COPD	1 (0.9)	3 (2.3)	0.402
Asthma	2 (1.8)	6 (4.5)	0.232
Stroke	5 (4.5)	3 (2.3)	0.331
CLD	2 (1.8)	1 (0.8)	0.463
CKD	10 (9.0)	6 (4.5)	0.162
Malignancy	5 (4.5)	4 (3.0)	0.544

BMI, body mass index; DM, diabetes mellitus; COPD, chronic obstructive pulmonary disease; CLD, chronic liver disease; CKD, chronic kidney disease

Table 2 shows that diastolic blood pressure <90 mmHg, respiratory rate ≥30 times per minute, oxygen saturation <95%, pulse ≥100 bpm, and oxygen requirements using ventilator or high-flow nasal cannula (HNFC) were clinical factors that played a role in the COVID-19 mortality in the elderly patients at M. Djamil Hospital Padang.

Table 2. The clinical picture of elderly COVID-19 patients

Variable	Died (n = 111)	Lived (n = 132)	P
Systolic blood pressure (mmHg)			
≥140	44 (39.6)	54 (40.9)	0.841
<140	67 (60.4)	78 (59.1)	
Diastolic blood pressure (mmHg)			
≥90	16 (14.4)	35 (26.5)	0.021
<90	95 (85.6)	97 (73.5)	
Respiratory rate (breaths/minute)			
≥30	36 (32.4)	10 (7.6)	0.000
<30	75 (67.6)	122 (92.4)	
Temperature (°C)			
≥37.5	37 (33.3)	44 (33.3)	1.000
<37.5	74 (66.7)	88 (66.7)	
Saturation (%)			
<95	61 (55.0)	37 (28.0)	0.000
≥95	50 (45.0)	95 (72.0)	
Pulse (beats/minute)			
≥100	43 (38.7)	30 (22.7)	0.007
<100	68 (61.3)	102 (77.3)	
O_2 requirements			
Ventilator or HFNC	94 (87.7)	36 (27.3)	0.000
NRM or nasal cannula	17 (15.3)	96 (72.7)	

HFNC, high-flow nasal cannula; NRM, nonrebreathing mask

Urea, creatinine, neutrophil–lymphocyte ratio, alanine aminotransferase (ALT), prothrombin time (PT), activated partial thromboplastin time (APTT), interleukin-6 (IL-6), ferritin, albumin, and random blood glucose (RBG) were factors that associated with mortality in elderly with COVID-19 (Table 3).

Table 3. Laboratory findings

Variable	Died (n = 111)	Lived (n = 132)	P
Hemoglobin (g/dL)			
<10.0	17 (15.3)	9 (6.8)	0.033
≥10.0	94 (84.7)	123 (93.2)	
Leucocyte (/mm^3)			
<10000	46 (41.4)	91 (68.9)	0.000
≥10000	65 (58.6)	41 (31.1)	
Platelets (/mm^3)			
<100000	9 (8.1)	4 (3.0)	0.080
≥100000	102 (91.9)	128 (97.0)	
NLR			
>3.3	98 (88.3)	88 (66.7)	0.000
≤3.3	13 (11.7)	44 (33.3)	
Urea (mg/dL)			
>50	58 (52.3)	28 (21.2)	0.000
0–50	53 (47.7)	104 (78.8)	
Creatinine (mg/dL)			
>1.3	40 (36.0)	21 (15.9)	0.000
0–1.3	71 (64.0)	111 (84.1)	
AST (U/L)			
>37	69 (62.2)	42 (31.8)	0.000
0–37	42 (37.8)	90 (68.2)	
ALT (U/L)			
>40	39 (35.1)	31 (23.5)	0.046
0–40	72 (64.9)	101 (76.5)	
Sodium (mmol/L)			
<130	22 (19.8)	27 (20.5)	0.902
≥130	89 (80.2)	105 (79.5)	
Potassium (mmol/L)			
<3.5	26 (23.4)	22 (16.7)	0.188
≥3.5	85 (76.6)	110 (83.3)	
D-dimer (ng/mL)			
≥500	104 (93.7)	114 (86.4)	0.061
<500	7 (6.3)	18 (13.6)	
PT (s)			
>13.16	23 (20.7)	6 (4.5)	0.000
≤13.16	88 (79.3)	126 (95.5)	
APTT (s)			
>30.11	36 (32.4)	21 (15.9)	0.002
≤30.11	75 (67.6)	111 (84.1)	
IL-6 (pg/ml)			
>6	107 (96.4)	95 (72.0)	0.000
≤6	4 (3.6)	37 (28.0)	
Ferritin (mcg/L)			
>434	99 (89.2)	96 (72.7)	0.001
≤434	12 (10.8)	36 (27.3)	
Albumin (g/dL)			
<3.0	50 (45.0)	30 (22.7)	0.000
≥3.0	61 (55.0)	102 (77.3)	

NLR, neutrophil–lymphocyte ratio; AST, aspartate aminotransferase; ALT, alanine aminotransferase; PT, prothrombin time; APTT, activated partial thromboplastin time; IL-6, Interleukin-6.

Table 4. Multivariate Analysis

Variable	Outcome		Bivariate		Multivariate	
	Died (n = 111)	Lived (n = 132)	p	OR (95% CI)	P	OR
Characteristics						
Disease severity, n (%)						
Critical–severe	97 (87.4)	46 (34.8)	0.000	12.953 (6.662–25.187)	0.008*	5.598 (1.582–19.808)
Moderate–mild	14 (12.6)	86 (65.2)				
Comorbid, n (%)						
Heart disease	23 (20.7)	10 (7.6)	0.003	3.189 (1.445–7.036)	0.009*	6.939 (1.627–29.597)
Clinical overview						
Diastolic blood pressure (mmHg)						
≥90	16 (14.4)	35 (26.5)	0.021	0.467 (0.242–0.899)	0.059	0.337 (0.109–1.040)
<90	95 (85.6)	97 (73.5)				
Respiratory rate (/minute)						
≥30	36 (32.4)	10 (7.6)	0.000	5.856 (2.476–12.488)	0.042*	3.480 (1.044–11.602)
<30	75 (67.6)	122 (92.4)				
Saturation (%)						
<95	61 (55.0)	37 (28.0)	0.000	3.132 (1.838–5.338)	0.991	0.994 (0.331–2.978)
≥95	50 (45.0)	95 (72.0)				
Pulse (beats/minute)						
≥100	43 (38.7)	30 (22.7)	0.007	2.150 (1.230–3.757)	0.043*	2.880 (1.032–8.038)
<100	68 (61.3)	102 (77.3)				
O_2 requirements						
Ventilator or HFNC	94 (87.7)	36 (27.3)	0.000	14.745 (7.751–28.050)	0.000*	19.777 (5.917–66.099)
NRM or nasal cannula	17 (15.3)	96 (72.7)				
APTT (second)						
>30.11	36 (32.4)	21 (15.9)	0.002	2.537 (1.375–4.682)	0.568	1.386 (0.451–4.260)
≤30.11	75 (67.6)	111 (84.1)				
IL-6 (pg/mL)						
>6	107 (96.4)	95 (72.0)	0.000	10.418 (3.581–30.312)	0.003*	15.188 (2.528–91.261)
≤6	4 (3.6)	37 (28.0)				
Ferritin (mcg/L)						
>434	99 (89.2)	96 (72.7)	0.001	3.094 (1.519–6.300)	0.279	0.457 (0.111–1.885)
≤434	12 (10.8)	36 (27.3)				
Albumin (g/dL)						
<3.0	50 (45.0)	30 (22.7)	0.000	2.787 (1.604–4.844)	0.794	1.140 (0.426–3.051)
≥3.0	61 (55.0)	102 (77.3)				
Random blood glucose (mg/dL)						
>199	47 (42.3)	23 (17.4)	0.000	3.480 (1.936–6.257)	0.046*	3.453 (1.020–11.682)
≤199	64 (57.7)	109 (82.6)				

NLR, neutrophil–lymphocyte ratio; AST, aspartate aminotransferase; ALT, alanine aminotransferase; PT, prothrombin time; APTT, activated partial thromboplastin time; IL-6, Interleukin-6.

Multivariate analysis showed that the condition of elderly patients with critical-severe clinical symptoms (odds ratio (OR) 12.95; 95% confidence interval (CI) 6.66–25.19), heart disease (OR 6.94; 95% CI 1.63–29.60), respiratory rate ≥30 breaths per

minute (OR 3.48; 95% CI 1.04–11.60), pulse ≥100 beats per minute (OR 2.88; 95% CI 1.03–8.04), using a ventilator or high-flow nasal cannula (HFNC) (OR 19.78; 95% CI 5.92–66.10), prothrombin time >13.16 second (OR 12.36; 95% CI 2.43–62.77), interleukin-6 >6 pg/mL (OR 15.19; 95% CI 2.53–91.26), and random blood glucose at admission >199 (OR 3.45; 95% CI 1.02–11.68) were significantly related to mortality (Table 4).

DISCUSSION

In this current research, we assessed clinical and laboratory characteristics, comorbidities, and outcomes of elderly patients with COVID-19 infection in M. Djamil Hospital, Padang, West Sumatra, Indonesia. Based on a multivariate analysis of this research, we found that certain clinical conditions such as the severity of COVID-19 infection, heart disease, respiratory rate, pulse rate, and oxygen therapy support with ventilator or HFNC significantly influence the mortality of elderly patients in our center. This result is consistent with previous study which conducted on all age groups. The study reported that elderly patients had a higher mortality rate involving symptoms and comorbidities such as fever, pneumonia, acute respiratory distress syndrome, and type 2 diabetes mellitus.[6]

Elderly patients who have multimorbidity, frailty, and immunosenescence are more susceptible to severe COVID-19 infection.[7] Another multicenter research in the United States found more frequent atypical symptoms in the elderly including neurological symptoms such as confusion and changes in mental status, malaise, decreased functional status, immobility, and falls. Elderly patients can remain asymptomatic, or develop symptoms more slowly.[8] These patients also have a high risk of developing complications such as hypercoagulability, hypertension, memory impairment, respiratory failure, kidney disorders, mental disorders, heart rhythm disorders, fatigue, deep vein thrombosis, and pulmonary embolism.[9,10]

A meta-analysis by Dessie and Zewotir showed the presence of comorbidities of acute kidney injury, chronic obstructive pulmonary disease, diabetes, hypertension, cardiovascular diseases, cancer, increased d-dimer, male sex, old age, smokers, and obesity causing fatal COVID-19 infection.[3] According to the meta-analysis of Damayanthi et al., males with older age, dyspnea, and dementia have a greater risk of death. These factors are related to the mortality of the elderly (75 years and older) suffering from COVID-19.[11] The aging process in a person result in various changes, such as a decline in immunity, the presence of several chronic degenerative diseases, and poor nutritional status, which makes elderly person more prone to severe infection. Immunosenescence contributes to susceptibility to infection.[12]

Our study showed that heart disease is a predisposition to COVID-19 mortality in elderly patients. This result is consistent with research conducted by Gu et al. After adjusting for age, gender, and the early period of the pandemic in China, coronary heart disease (CHD) was the only comorbidity that yielded a significant mortality risk: patients who had COVID-19 with preexisting CHD had an estimated 2.9 times higher risk of death than those without CHD.[13] On the other hand, COVID-19 can lead to cardiovascular complications such as myocardial infarction, heart failure, myocarditis, and arrhythmias.[14] Harrison et al. found cardiovascular disease as a risk factor for COVID-19 mortality [OR 2.65

(1.86-3.78)]. Various risk factors for cardiovascular disease such as diabetes, smoking, and obesity play a role in COVID-19 through inflammatory pathways, immune function, and respiratory function.[15]

The current study found that a pulse rate ≥100 beats per minute affects COVID-19 patient mortality in the elderly. This result is similar to the study conducted by Gopalan et al. which found that, among the 746 hospitalized COVID-19 patients, 487 were "survivors" and 259 were "nonsurvivors" (deaths). The adjusted ORs of factors (OR (95% CI)) significant in the multivariable logistic regression were pulse rate ≥100 beats per minute: 2.02 (1.19–3.47) with hypertension and gender not retaining their significance.[16]

Ventilators and high-flow nasal cannula requirements were the risks of mortality in the elderly patients in the present study. Research from Lee et al. also found that patients aged ≥80 years had a high risk of requiring mechanical ventilation/HFNC, and mortality among those severe patients was very high. Respiratory rate ≥30 breaths per minute had a high risk of COVID-19 patient mortality in the elderly.[17] This study is in line with research conducted by AbuRuz et al. which found that respiratory rate was one of the risk factors for mortality among COVID-19 hospitalized patients in United Arab Emirates ($p = 0.035$).[18] Another study found mortality of up to 55% in patients who used mechanical ventilation. The patients who died were older and had more comorbidities. The use of ventilators and HFNCs indicates severe respiratory distress. Aging in the respiratory system and immunity of the elderly may contribute to this condition.[19]

In old age, there is an increase in the level of cytokines and proinflammatory markers in circulation. High levels of IL-6 and IL-1, tumor necrosis factor-alpha, and C-reactive proteins in the elderly were associated with increased morbidity and mortality.[20] The presence of low-degree chronic inflammation (inflammaging) increases the risk of the occurrence of dangerous severe inflammatory conditions. Subjects who died in this study were generally admitted with severe infection severity and required high volumes of oxygen. The current study stated that IL-6 affects the mortality of COVID-19 patients in the elderly, similar to the study conducted by Avila-Nava et al.[21] which stated that the level of IL-6 is an indicator of mortality among hospitalized COVID-19 patients in Mexico. Research by Hafez et al. found that increased levels of IL-6 were related to intensive care unit treatment, disease severity, and mortality.[22] Two meta-analyses showed IL-6 as a strong predictor of the severity of COVID-19.[23,24] Interleukin-6 is one of the cytokines that can cause epithelial and endothelial cell death and increase vascular permeability which contributes to the occurrence of acute respiratory disesase syndrome (ARDS), multiple organ dysfunction, and death.[22] IL-6 released by macrophages and T cells is an inflammatory biomarker, high levels of IL-6 inhibit the cytotoxicity of natural killer cells.[25]

This study found that random blood glucose affects the mortality of COVID-19 patients in the elderly, in line with research conducted by Permana et al. which stated that RBG >140 mg/dL is significantly associated with mortality.[26] A retrospective study of 456 COVID-19 patients found glucose dysregulation affected mortality and length of stay.[27] Hyperglycemia can cause an increase in inflammatory cytokines that may play a role in the occurrence of cytokine storms and multiorgan failure.[28] Hyperglycemia may be associated with an

increased bond between SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) to tissues through glycosylation of the angiotensin-converting enzyme-2 receptor, which is the entry point to the virus into cells resulting in inflammation and an overactive immune response.[27,29] High glucose levels can also be a source of viral energy.[30]

In our study, we found that prothrombin time predicts the risk of mortality of COVID-19 patients, following the research conducted by Long which stated that d-dimer and prothrombin time could be used as significant indicators in predicting the mortality of COVID-19. Long said that 18 of the 23 COVID-19 patients who died had extended prothrombin time. Prothrombin and activated partial thromboplastin time are coagulation factors that can be used for early diagnosis of disseminated intravascular coagulation (DIC). Coagulation disorders are common in severe and critical patients.[31]

The aging process has caused various changes in a person's body. Immune system dysregulation known as immunosenescens makes the elderly susceptible to getting sick if infected with viruses or other germs. When sick, the elderly tend to experience more severe symptoms. Low-degree inflammation or known as inflammaging is found in the elderly, and the presence of inflammation due to COVID-19 makes the condition of the elderly more worrying. Nutritional deficient, comorbidities, and frailty status will aggravate the situation that increases the risk of mortality. Given the high complications and mortality of elderly COVID patients, preventive measures are needed. Things that can be done include the use of masks, maintaining distance, washing hands, avoiding crowds, and efficient air filtration7.

CONCLUSION

Factors associated with mortality of elderly patients with COVID-19 at M. Djamil Hospital are severe to critical symptoms, heart disease, RR ≥30 breaths per minute, pulse ≥100 beats per minute, using a ventilator or HFNC, PT >13.16 second, IL-6 >6 pg/mL, and RBG at admission >199 mg/dL.

Conflict of interest statement

The authors declare no conflict of interest.

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Author Contributions

Roza Mulyana: Conceptualization, Methodology, Investigation, Validation, Writing- Original draft preparation. Dwitya Elvira: Data curation, Validation, Writing-Reviewing and Editing. Rose Dinda Martini: Investigation, Validation, Writing-Reviewing and Editing

REFERENCES

1. Akbar MI, Nurmaladewi N, Aspian P, Pagala I, Rustam M. Assessing the service quality at health service facilities during the COVID-19 pandemic in North Buton District, Indonesia. Public Health of Indonesia. 2022 Dec 13;8(4):116-22.
2. West Sumatra Province. Data pantauan COVID-19 Provinsi Sumatera Barat 2022 [2022 West Sumatra Province COVID-19 monitoring data]. 2022; https://corona.sumbarprov.go.id.
3. Dessie ZG, Zewotir T. Mortality-related risk factors of COVID-19: A systematic review and meta-analysis of 42 studies and 423,117 patients. BMC Infectious

Diseases 2021; 21(1):855. https://doi.org/10.1186/s12879-021-06536-3.

4. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel Coronavirus–infected pneumonia in Wuhan, China. JAMA 2020;323(11):1061-9. https://doi.org/10.1001/jama.2020.1585.
5. Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. The Lancet Respiratory Medicine 2020;8(5):475-81. https://doi.org/10.1016/S2213-2600(20)30079-5.
6. Iftimie S, López-Azcona AF, Vicente-Miralles M, et al. Risk factors associated with mortality in hospitalized patients with SARS-CoV-2 infection: A prospective, longitudinal, unicenter study in Reus, Spain. PloS One 2020;15(9):e0234452. https://doi.org/10.1371/journal.pone.0234452.
7. Abul Y, Leeder C, Gravenstein S. Epidemiology and clinical presentation of COVID-19 in older adults. Infect Dis Clin N Am 2023;37:1–26.
8. Goldberg EM, Southerland LT, Meltzer AC, et al. Age-related differences in symptoms in older emergency department patients with COVID-19: Prevalence and outcomes in a multicenter cohort. J Am Geriatr Soc 2022;70(7):1918–30.
9. Cohen K, Ren S, Heath K, et al. Risk of persistent and new clinical sequelae among adults aged 65 years and older during the post-acute phase of SARS-CoV-2 infection: retrospective cohort study. BMJ 2022;376:e068414.
10. Katsoularis I, Fonseca-Rodrı´guez O, Farrington P, et al. Risks of deep vein thrombosis, pulmonary embolism, and bleeding after covid-19: nationwide self-controlled cases series and matched cohort study. BMJ 2022;377:e069590.
11. Damayanthi HD, Prabani KI, Weerasekara I. Factors associated with mortality of older people with COVID-19: A systematic review and meta-analysis. Gerontology and Geriatric Medicine 2021;7. https://doi.org/10.1177/23337214211057392.
12. Shaw AC, Bandaranayake T. Immunology of aging. In Halter JB, Ouslander JG, Studenski S, et al, (Eds.). Hazzard's geriatric medicine and gerontology 7th ed. New York: McGraw-Hill Education 2017, pp. 33-49.
13. Gu T, Chu Q, Yu Z, et al. History of coronary heart disease increased the mortality rate of patients with COVID-19: A nested case–control study. BMJ Open 2020;10(9), e038976. https://doi.org/10.1136/bmjopen-2020-038976.
14. Krishna BA, Metaxaki M, Sithole N, et al. Cardiovascular disease and COVID-19: a systematic review. IJC Heart & Vasculature 2024;54(101482). https://doi.org/10.1016/j.ijcha.2024.101482.
15. Harrison SL, Buckley BJ, Rivera-Caravaca JM, et al. Cardiovascular risk factors, cardiovascular disease, and COVID-19: an umbrella review of systematic review. European Heart Journal – Quality of Care and Clinical Outcomes 2021;7:330-9. https://doi:10.1093/ehjqcco/qcab029.
16. Gopalan N, Senthil S, Prabakar NL, et al. Predictors of mortality among

hospitalized COVID-19 patients and risk score formulation for prioritizing tertiary care—an experience from South India. PloS One 2022; 17(2): e0263471. https://doi.org/10.1371/journal.pone.0263471.

17. Lee JY, Kim HA, Huh K, et al. Risk factors for mortality and respiratory support in elderly patients hospitalized with COVID-19 in Korea. J. Korean Med. Sci. 2020;35(23):e223. https://doi.org/10.3346/jkms.2020.35.e223.
18. AbuRuz S, Al-Azayzih A, ZainAlAbdin S, et al. Clinical characteristics and risk factors for mortality among COVID-19 hospitalized patients in UAE: Does ethnic origin have an impact? PloS One 2022;17(3): e0264547. https://doi.org/10.1371/journal.pone.0264547.
19. De Terwangne C, Sorgente A, Tortora R, et al. Mortality rate and predictors among patients with COVID-19 related acute respiratory failure requiring mechanical ventilation: a retrospective single centre study. J Crit Care Med (Targu Mures) 2021;7(1);21-7. https://doi: 10.2478/jccm-2020-0043.
20. Rao AV, Cohen HJ. Oncology and aging: general principles. In Halter JB, Ouslander JG, Studenski S, et al. (Eds.). Hazzard's geriatric medicine and gerontology,7th ed. New York: McGraw-Hill Education 2017, pp. 1423-40.
21. Avila-Nava A, Cortes-Telles A, Torres-Erazo D, et al. Serum IL-6: A potential biomarker of mortality among SARS-CoV-2 infected patients in Mexico. Cytokine 2021;143: 155543. https://doi.org/10.1016/j.cyto.2021.155543.
22. Hafez W, Nasa P, Khairy A, et al. Interleukin-6 and the determinants of severe COVID-19: a retrospective cohort study. Medicine 2023;102(45):p e36037. https://DOI: 10.1097/MD.0000000000036037.
23. Liu X, Wang H, Shi S, et al. Association between IL-6 and severe disease and mortality in COVID-19 disease: A systematic review and meta-analysis. Postgraduate Medical Journal 2022; 98(1165):871-9. https://doi.org/10.1136/postgradmedj-2021-139939.
24. Akbari H, Tabrizi R, Lankarani KB, et al. The role of cytokine profile and lymphocyte subsets in the severity of coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. Life Sci. 2020;258:118167. https://doi: 10.1016/j.lfs.2020.118167.
25. Cifaldi L, Prencipe G, Caiello I, et al. Inhibition of natural killer cell cytotoxicity by interleukin-6: implications for the pathogenesis of macrophage activation syndrome. Arthritis & Rheumatology 2015; 67(11): 3037-46. https://doi.org/10.1002/art.39295.
26. Permana H, Huang I, Susandi E, et al. The association of admission random blood glucose concentration and body-mass index with mortality in COVID-19 patients. Eur. Rev. Med. Pharmacol. Sci. 2021;25(22): 7144-50. https://doi.org/10.26355/eurrev_202111_27268.
27. Mirabella S, Gomez-Paz S, Lam E, et al. Glucose dysregulation and its association wirh COVID-19 mortality and hospital length of stay. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2022;102439. https://DOI: 10.1016/j.dsx.2022.102439.

28. Gianchandani R, Esfandiari NH, Ang L, et al. Managing hyperglycemia in the COVID-19 inflammatory storm. Diabetes 2020; 69(10):2048-53. https://doi.org/10.2337/dbi20-0022.
29. Brufsky A. Hyperglycemia, hydroxychloroquine, and the COVID-19 pandemic. J. Med. Virol. 2020; 92(7): 770-5. https://doi.org/10.1002/jmv.25887.
30. Kohio HP, Adamson AL. Glycolytic control of vacuolar-type ATPase activity: A mechanism to regulate influenza viral infection. Virology 2013;444(1-2):301-9. https://doi.org/10.1016/j.virol.2013.06.026.
31. Long H, Nie L, Xiang X, et al. D-Dimer and prothrombin time are the significant indicators of severe COVID-19 and poor prognosis. BioMed Res. Int. 2020;6159720. https://doi.org/10.1155/2020/6159720.