RESEARCH

EVALUATION OF HOSPITALIZED YOUNGEST-OLD, MIDDLE-OLD AND OLDEST-OLD COVID-19 PATIENTS IN TERMS OF MORTALITY AND RISK FACTORS

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Abstract

Introduction: In the coronavirus disease 2019 (COVID-19) pandemic, severe disease is predominantly seen in advanced-aged patients. In our study, we evaluated hospitalized youngest-old (65–74 years), middle-old (75–84 years) and oldest-old (≥85 years) COVID-19 patients in terms of mortality and risk factors.

Materials and Methods: This retrospective study included hospitalized COVID-19 patients aged 65 years and older. Demographic characteristics, such as age, gender and comorbid conditions, baseline blood oxygen saturation levels, the necessity of oxygen treatments (nasal cannula,oxygen mask/reservoir oxygen mask), condition of the patients(mild, moderate, severe), baseline laboratory findings as C-reactive protein , white blood cell counts, thrombocyte counts, lymphocyte counts, D-dimer, alanine aminotransferase, aspartate aminotransferase and ferritin levels, pulmonary involvement on computerized tomography, the increase in oxygen requirements, the status of going to the intensive care unit and the status of receiving corticosteroids were recorded. Factors associated with mortality were analyzed.

Results: A total of 399 geriatric COVID-19 patients were included in this study: 214(53.6%) were female and 185 (46.4%) were male. The mean age of the patients was 75±7.87(min:65–max:96). In our study, the mortality rate was found to be higher in the middle-old and oldest-old groups than in the youngest-old group (p=0.01). Other factors associated with mortality were as follows: lower baseline oxygen saturation levels (p=0.03), necessity of higher oxygen treatment (p<0.01), higher pulmonary involvement on computerized tomography (p<0.01), corticosteroid use (p<0.01) and having Alzheimer's disease (p=0.03).

Conclusion: Our findings emphasize that older patients are more vulnerable to COVID-19 infection and require special attention.

Keywords: Geriatrics; SARS-CoV-2; Mortality.

INTRODUCTION

Today, people are living longer, especially in developed countries. Overall birth rates are decreasing and the elderly population has been rising. With the increase in life expectancy, the geriatric patient population accessing health services is also rising. Infectious diseases are the most common causes of hospitalization, morbidity and mortality among elderly individuals (1,2).

In the coronavirus disease 2019 (COVID-19) pandemic, which has been affecting the world since 2020, severe disease is predominantly seen in advanced-aged patients and/or in patients with underlying comorbidities (3). Physiological changes occurring with aging, such as the weakening of cellular and humoral immunity, have made elderly people more fragile throughout the pandemic. In some studies, it has been reported that the rates of hospitalization with the diagnosis of COVID-19 increase with age: 1% for those aged 20 to 29 years, 4% for those aged 50 to 59 years, and 18% for those over 80 years (4). A study in the United States showed that 80% of COVID-19-related deaths are over the age of 65 (5).

The geriatric population can be divided into three groups: ages 65–74 years, 75–84 years and≥85 years are named as youngest-old, middle-old and oldest-old, respectively (6).It should be noted that these elderly groups may vary and their responses to infections may be different. In our study, we evaluated hospitalized youngest-old, middle-old and oldest-old COVID-19 patients in terms of mortality and risk factors.

MATERIALS AND METHODS

This retrospective study included hospitalized COVID-19 patients aged 65 years and older between November 2021 and January 2022. The hospitalization rate of geriatric COVID-19 patients admitted to our hospital was 5.2%. Demographic characteristics, such as age, gender and comorbid conditions, were recorded. Ethical approval was obtained from the Izmir Bozyaka Training and Research Hospital Ethics Committee.

The patients' conditions were classified as having mild, moderate and severe during hospitalization (7). Mild cases were described as patients who had signs of COVID-19 but did not have dyspnea or abnormal chest imaging. Moderate cases were individuals who had pneumonia and whose blood oxygen saturation levels were over 94%. Severe cases had an oxygen saturation of ≤93%, respiratory frequency of ≥30 and/or lung infiltrates of more than 50%. Mild patients were hospitalized due to inadequate oral intake, need for isolation, lack of care and/or trauma.

At hospitalization, blood oxygen saturation levels and the necessity of oxygen treatments (nasal cannula, oxygen mask/reservoir oxygen mask) were recorded. Also, the increase in oxygen requirements, the status of going to the intensive care unit and the status of receiving corticosteroids (none, 0,5-1 mg/kg i.v. methylprednisolone for up to 10 days or pulse steroid, ≥ 250 mg i.v.) were recorded.

Before hospitalization, patients who had received three doses of Sinovac (0-1-4. months), two doses of BioNTech (0-1. months) and one dose of BioNTech three months after two doses of Sinovac were considered fully vaccinated (8). Those who could not complete one of these vaccination schedules were considered incompletely vaccinated, and those without any vaccination were considered unvaccinated.

All patients underwent radiological imaging before hospitalization. According to a semi-quantitative scoring system, patients who had pulmonary involvement in computerized chest tomography (CT) were classified as follows: <5%, 5–25%, 26–49%, 50–75% and>75% (9).

At hospitalization, laboratory findings such as C-reactive protein (CRP), white blood cell counts, thrombocyte counts, lymphocyte counts,

D-dimer, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and ferritin levels were analyzed. The total length of hospital stay and mortality were also recorded.

Statistical Analysis

Descriptive statistics are given as numbers and percentages for categorical variables. Normal distribution was examined with visual (histogram and probability graphics) and statistical methods (Kolmogorov–Smirnov/Shapiro–Wilk tests). Non-normally distributed continuous variables were compared with the Mann–Whitney U test. Categorical variables were compared using the Pearsonchi-square test or Fisher's exact test. We used univariate Cox proportional hazard regression models to identify the factors associated with in-hospital mortality. Additionally, we produced Kaplan-Meier survival curves to compare median or mean ± SE (standard error) survival times between groups. Double-sided p-values of less than 0.05 were considered significant. Visualizations and statistical analyses were performed with R version 4.1.2 (https://www.r-project.org/).

RESULTS

A total of 399 geriatric COVID-19 patients were included in this study: 214(53.6%) were female and 185 (46.4%) were male. The mean age of the patients was 75±7.87(min:65–max:96). Of these patients, 348 (87.2%) had at least one comorbid condition. Among the patients, the most common comorbid condition was hypertension (n:226, 56.6%). The ratio according to the geriatric classification of the patients was as follows: 184(46.1%) of them were in the youngest-old (65–74 years), 146 (36.6%) were in the middle-old (75–84 years) and 69 (17.3%) were in the oldest-old (≥85 years) groups. Sociodemographic features, vaccination status, baseline clinical spectrum and oxygen requirement status of the patients are given in Table 1. Comorbid conditions according to geriatric age classification are given in Table 2.

Table 1. Sociodemographic features, vaccination status, baseline clinical spectrum and oxygen requirement status

	All n=399
Gender	
Female	214 (53.6)
Male	185 (46.4)
Geriatric age classification	
Youngest-old (65-74 years)	184 (46.1)
Middle-old (75-84 years)	146 (36.6)
Oldest-old (≥85 years)	69 (17.3)
Comorbid conditions	348 (87.2)
Hypertension	226 (56.6)
Diabetes mellitus	161 (40.4)
Chronic heart disease	120 (30.1)
End-stage renal disease	44 (11.0)
Chronic obstructive pulmonary disease	41 (10.3)
Cerebrovascular disease	38 (9.5)
Alzheimer's disease	35 (8.8)
Solid cancer	16 (4.1)
Hematological cancer	12 (3.0)
Organ transplantation	9 (2.3)
Asthma	7 (1.8)
Rheumatological disease	5 (1.3)
Trauma	2 (0.5)
Acute kidney failure	1 (0.3)
Vaccination status, n=398	
Unvaccinated	83 (20.9)
Incompletely vaccinated	123 (30.9)
Fully vaccinated	192 (48.2)
COVID-19 clinical spectrum	
Mild	22 (5.51)
Moderate	119 (29.8)
Severe	258 (64.7)
Oxygen requirement	
None	84 (21.1)
Nasal cannula	100 (25.1)
Oxygen mask	70 (17.5)
Reservoir oxygen mask	145 (36.3)

Data were presented as numbers and column percentages, n (%)

Table 2. Comorbid conditions according to geriatric age classification

	All n=399	Youngest-old n=184	Middle-old n=146	Oldest-old n=69	p
Comorbid conditions	348 (87.2)	154 (83.7)	128 (87.7)	66 (95.7)	0.04
Hypertension	226 (56.6)	105 (57.1)	80 (54.8)	41 (59.4)	0.81
Diabetes mellitus	161 (40.4)	90 (48.9)	56 (38.4)	15 (21.7)	<0.001
Chronic heart disease	120 (30.1)	50 (27.2)	45 (30.8)	25 (36.2)	0.36
End-stage renal disease	44 (11.0)	14 (7.61)	19 (13.0)	11 (15.9)	0.11
Chronic obstructive pulmonary disease	41 (10.3)	16 (8.70)	17 (11.6)	8 (11.6)	0.63
Cerebrovascular disease	38 (9.5)	16 (8.70)	13 (8.90)	9 (13.0)	0.55
Alzheimer's disease	35 (8.8)	3 (1.6)	15 (10.3)	17 (24.6)	<0.001
Solid cancer	16 (4.1)	8 (4.4)	6 (4.1)	2 (2.9)	0.95
Hematological cancer	12 (3.0)	7 (3.80)	3 (2.1)	2 (2.9)	0.69
Organ transplantation	9 (2.3)	7 (3.80)	2 (1.37)	0 (0.0)	0.18
Asthma	7 (1.8)	2 (1.09)	3 (2.05)	2 (2.9)	0.54
Rheumatological disease	5 (1.3)	3 (1.63)	2 (1.37)	0 (0.0)	0.85
Trauma	2 (0.5)	0 (0.0)	1 (0.7)	1 (1.5)	0.16
Acute kidney failure	1 (0.3)	0 (0.0)	1 (0.7)	0 (0.0)	0.54

Data were presented as numbers and column percentages, n (%)

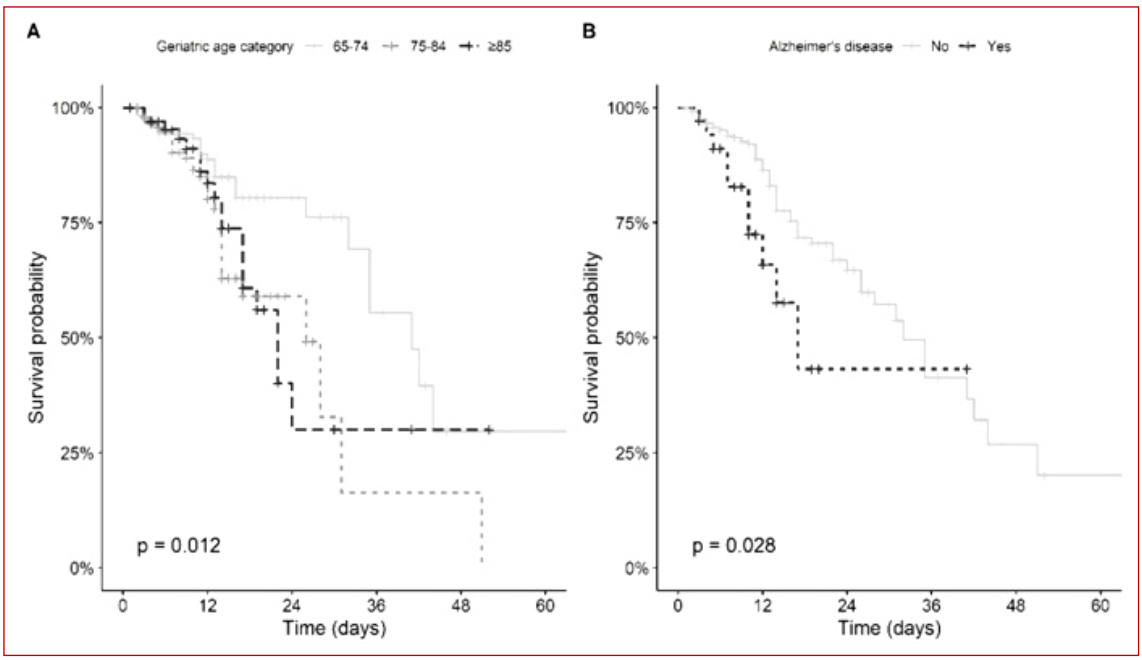

Figure 1. Kaplan–Meier survival curves

Figure 1 shows Kaplan Meier survival curves for in-hospital mortality in terms of age groups and Alzheimer's disease. There was a significant difference in the mean survival times between the youngest-old (mean±SE: 39.8± 3.53), middle-old (mean±SE: 25.3± 3.45) and the oldest-old (mean±SE: 30.7± 5.33) age groups (p=0.01). Also, patients with Alzheimer's disease had a lower mean survival time (mean±SE: 33.6± 7.56 vs 34.3± 2.57, p=0.03).

Table 3. Baseline radiological and laboratory findings

	All n=399
Pulmonary involvement on computerized chest tomography	
None	25 (6.3)
<5%	37 (9.3)
5–25%	155 (38.8)
25–50%	130 (32.6)
50–75%	49 (12.3)
75–100%	3 (0.8)
C-reactive protein (mg/L)	
<5	113 (28.3)
≥5	286 (71.7)
Lymphocyte count (103 /UL)	
≤0.8	122 (30.6)
>0.8	277 (69.4)
Thrombocyte count (103 /UL)	
<150	85 (21.3)
≥150	314 (78.7)
Aspartate aminotransferase (U/L),n=397	
<50	337 (84.9)
≥50	60 (15.1)
Alanine aminotransferase (U/L), n=397	
<50	368 (92.7)
≥50	29 (7.3)
D-Dimer (ng/mL), n=397	
<1000	313 (78.8)
≥1000	84 (21.2)
Ferritin (ug/L), n=393	
<500	236 (60.1)
≥500	157 (39.9)

Data were presented as numbers and column percentages, n (%)

Comorbid conditions were higher in the oldest-old group (n=66, 95.7%) compared to the youngest-old group (n=348, 87.2%), (p=0.04).The ratio of diabetes mellitus was higher in youngest-old group (p<0.001) while the ratio of Alzheimer's disease was higher in the oldest-old group (p<0.001).

Radiological and laboratory findings at hospitalization are given in Table 3.

A total of 111 (27.9%) patients had an increased oxygen requirement on the median day 2 (min:1–max:26) of hospitalization. A hundred and fourteen (28.6%) patients had gone to the intensive care unit on the median day 3 (min:1–max:26) of hospitalization. Of the patients, 323 (81%) were discharged from the hospital, whereas 76 (19%) died.

The factors affecting in-hospital mortality due to COVID-19 are given in Table 4.

Data were presented as numbers and row percentages n (%) or median with minimum-maximum

DISCUSSION

During the COVID-19 pandemic, elderly patients were the most vulnerable group in terms of morbidity and mortality. In our study, the mortality rate was found to be higher in the middle-old and oldest-old groups than in the youngest-old group. Other factors associated with mortality are as follows: lower baseline oxygen saturation levels, necessity of higher oxygen treatment, higher pulmonary involvement on CT, corticosteroid use and having Alzheimer's disease. Similarly to our work, another study evaluating clinical outcomes of geriatric patients found older age (85 years and older), abnormal chest CT findings and lower oxygen saturation levels to be significantly associated with mortality (10). Also, in two studies conducted in our country, low oxygen saturation levels on admission were found significantly associated with mortality among hospitalized geriatric COVID-19 patients (11,12).

A study by Covino et al. evaluated factors affecting mortality among COVID-19 patients aged ≥ 80 years and determined that worse clinical and radiological presentation, increasing age and dementia were significantly associated

Table 4. Factors affecting in-hospital mortality due to COVID-19

	Mortality		p	Hazard Ratio (95% CI)
	No, n=323	**Yes, n=76**		
Gender, n (%)			0.66	
Female	172 (80.4)	42 (19.6)		Ref.
Male	151 (81.6)	34 (18.4)		0.90 (0.57–1.42)
Geriatric age classification, n (%)			**0.01**	
Youngest-old (65–74 years)	157 (85.3)	27 (14.7)		Ref.
Middle-old (75–84 years)	115 (78.8)	31 (21.2)		2.12 (1.25–3.60)
Oldest-old (≥85 years)	51 (73.9)	18 (26.1)		1.89 (1.04–3.45)
Comorbid conditions, n (%)			0.17	
Not existing	44 (86.3)	7 (13.7)		Ref.
Existing	279 (80.2)	69 (19.8)		1.71 (0.78–3.72)
Hypertension, n (%)			0.87	
Not existing	139 (80.3)	34 (19.7)		Ref.
Existing	184 (81.4)	42 (18.6)		0.96 (0.61-1.52)
Diabetes mellitus, n (%)			0.29	
Not existing	196 (82.4)	42 (17.6)		Ref.
Existing	127 (78.9)	34 (21.1)		1.27 (0.81–2.00)
Chronic heart disease, n (%)			0.06	
Not existing	236 (84.6)	43 (15.4)		Ref.
Existing	87 (72.5)	33 (27.5)		1.55 (0.97–2.46)
End-stage renal disease, n (%)			0.66	
Not existing	286 (80.6)	69 (19.4)		Ref.
Existing	37 (84.1)	7 (15.9)		0.84 (0.39–1.84)
Chronic obstructive pulmonary disease, n (%)			0.10	
Not existing	295 (82.4)	63 (17.6)		Ref.
Existing	28 (68.3)	13 (31.7)		1.65 (0.90–3.03)
Cerebrovascular disease, n (%)			0.06	
Not existing	296 (82.0)	65 (18.0)		Ref.
Existing	27 (71.1)	11 (28.9)		1.84 (0.97–3.51)
Alzheimer's disease, n (%)			**0.03**	
Not existing	298 (81.9)	66 (18.1)		Ref.
Existing	25 (71.4)	10 (28.6)		2.09 (1.07–4.08)
Vaccination status, n (%)			0.12	
Unvaccinated	62 (74.7)	21 (25.3)		Ref.
Incompletely vaccinated	94 (76.4)	29 (23.6)		0.92 (0.52–1.62)
Fully vaccinated	166 (86.5)	26 (13.5)		0.58 (0.33–1.04)
COVID-19 Clinical spectrum, n (%)			0.20	
Mild	21 (95.5)	1 (4.5)		Ref.
Moderate	109 (91.6)	10 (8.4)		1.87 (0.24–14.6)
Severe	193 (74.8)	65 (25.2)		3.04 (0.42–22.0)

Table 4 continued.

Table 4. Factors affecting in-hospital mortality due to COVID-19

Baseline oxygen saturation levels	92 (45–99)	89 (73–98)	**0.03**	0.96 (0.93–1.00)
The necessity of oxygen treatment, n (%)			**<0.001**	
None	79 (94.0)	5 (6.0)		Ref.
Nasal cannula	98 (98.0)	2 (2.0)		0.25 (0.05–1.30)
Oxygen mask	45 (64.3)	25 (35.7)		2.68 (1.02–7.09)
Reservoir oxygen mask	101 (69.7)	44 (30.3)		2.52 (0.99–6.42)
Pulmonary involvement on computerized chest tomography, n (%)			**<0.001**	
None	23 (92.0)	2 (8.00)		Ref.
<5%	29 (78.4)	8 (21.6)		3.24 (0.69–15.3)
5–25%	137 (88.4)	18 (11.6)		1.22 (0.28–5.29)
25–50%	101 (77.7)	29 (22.3)		1.92 (0.46–8.09)
50–75%	32 (65.3)	17 (34.7)		1.91 (0.44–8.36)
75–100%	1 (33.3)	2 (66.7)		54.8 (7.35–409)
C-reactive protein (mg/L), n (%)			0.98	
<5	93 (82.3)	20 (17.7)		Ref.
≥5	230 (80.4)	56 (19.6)		0.99 (0.60–1.66)
Lymphocyte count (103 /UL), n (%)			**0.02**	
≤0.8	88 (72.1)	34 (27.9)		Ref.
>0.8	235 (84.8)	42 (15.2)		0.58 (0.37–0.91)
Thrombocyte count, (103 /UL), n (%)			0.16	
<150	63 (74.1)	22 (25.9)		
≥150	260 (82.8)	54 (17.2)		
Aspartate aminotransferase, (U/L), n=397			0.35	
<50	278 (82.5)	59 (17.5)		Ref.
≥50	43 (71.7)	17 (28.3)		1.30 (0.75–2.25)
Alanine aminotransferase, (U/L), n=397			0.35	
<50	298 (81.0)	70 (19.0)		Ref.
≥50	23 (79.3)	6 (20.7)		0.67 (0.29–1.56)
D-dimer, ng/mL, n=397			0.80	
<1000	253 (80.8)	60 (19.2)		Ref.
≥1000	69 (82.1)	15 (17.9)		1.08 (0.61–1.91)
Ferritin, ug/L, n=393			0.41	
<500	194 (82.2)	42 (17.8)		Ref.
≥500	125 (79.6)	32 (20.4)		1.22 (0.77–1.94)
Corticosteroid use			**<0.001**	
None	89 (95.7)	4 (4.30)		Ref.
Methylprednisolone (0.5–1 mg/kg i.v.) up to 10 days	189 (87.9)	26 (12.1)		1.75 (0.61–5.04)
Pulse steroid (≥ 250 mg i.v)	45 (49.5)	46 (50.5)		4.53 (1.60–12.8)

Data were presented as numbers and row percentages n (%) or median with minimum-maximum

with mortality (13). Consistent with this, we found a higher mortality rate among patients with more radiological involvement, those who were older and those with Alzheimer's disease. We also found that older patients had a higher rate of Alzheimer's disease. In another study evaluating risk factors for death and severe disease among COVID-19 patients over 70 years and older, it was found that older age and cognitive decline were associated with in-hospital mortality (14). Also other studies show COVID-19 associated mortality are increased in Alzheimer's disease patients (15,16).

We did not find any significant association between vaccination status and mortality. Contrary to this, another study found that being unvaccinated and not being fully vaccinated were both significantly associated with increased risk of death among elderly patients in Hong Kong during the fifth COVID-19 wave in 2022 (17).

We found that receiving corticosteroid treatment was associated with mortality among elderly patients. In a work evaluating the relationship between in-hospital mortality and corticosteroid treatment among elderly COVID-19 patients, the factors associated with mortality were as follows: corticosteroid use, increasing age, oxygen saturation levels <90% and lowest lymphocyte counts(Odds Ratio = 0.49 [0.38–0.63]) (18).In our study, we showed that patients with lymphocyte counts higher than 0.8x103 /UL had (Hazard Ratio=0.58 [0.37-0.91]) decreased the risk of death. In a study by Gulec-Balbay E et al, predicting mortality risk in hospitalized geriatric patients with COVID-19 pneumonia, the need for corticosteroid and pulse corticosteroid therapy increased the mortality (19).

CONCLUSION

In conclusion, our findings demonstrated that patients in the oldest-old and middle-old groups have a higher mortality risk than those in the youngest-old group. Increasing age, lower baseline oxygen saturation levels, the necessity of higher oxygen, higher radiological involvement, use of corticosteroids and having Alzheimer's disease were found to be strong risk factors for in-hospital mortality.

Our findings emphasize that older patients are more vulnerable to COVID-19 infection and require special attention.

REFERENCES

1. Gavazzi G, Krause KH. Ageing and infection. Lancet Infect Dis 2002; 2:659–666. (doi: 10.1016/s1473-3099(02)00437-1)
2. Mouton CP, Bazaldua OV, Pierce B, Espino DV. Common infections in older adults. Am Fam Physician 2001; 63:257. (PMID: 11201692)
3. Zhou F, Yu T, Du R et al. Clinical course and risk factors for mortality of adult in patients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020;395:1054. (doi: 10.1016/S0140-6736(20)30566-3)
4. Verity R, Okell LC, Dorigatti I et al. Estimates of the severity of coronavirus disease 2019: a model-based analysis. Lancet Infect Dis 2020. (doi: 10.1016/S1473-3099(20)30243-7)
5. Fusco, MD,Shea, KM, Lin, J. et al. Health outcomes and economic burden of hospitalized COVID-19 patients in the United States. Journal of Medical Economics 2021;24(1), 308–317. (doi: 10.1080/13696998.2021.1886109)
6. Alterovitz SS, Mendelsohn GA. Relationship goals of middle-aged, young-old, and old-old Internet daters: an analysis of online personal ads. J Aging Stud 2013;27:159–65. (doi: 10.1016/j.jaging.2012.12.006)
7. National Institutes of Health. Clinical Spectrum of SARS-CoV-2 Infection. [Internet]. Available from: https://www.covid19treatmentguidelines.nih.gov/overview/clinical-spectrum/(Accessed on 14/12/2022)
8. Current Immunication Recommendations Against Covid-19. [Internet]. Available from: https://www.klimik.org.tr/2022/07/11/119309/ (Accessed on 14/12/2022)

9. Shi H, Han X, Jiang N et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. Lancet Infect Dis 2020;20:425. (doi: 10.1016/S1473-3099(20)30086-4)

10. Ulugerger Avci G, Bektan Kanat B, Suzan V et al. Clinical outcomes of geriatric patients with COVID-19: review of one-year data. Aging Clin Exp Res. 2022 Feb;34(2):465–474. (doi: 10.1007/s40520-021-02047-y)

11. Bağ Soytaş R, Ünal D, Arman P, et al. Factors affecting mortality in geriatric patients hospitalized with COVID-19. Turk J Med Sci. 2021 Apr 30;51(2):454-463. (doi: 10.3906/sag-2008-91)

12. Emektar E, Koc F, Goktas EF, Dagar S, Uzunosmanoglu H. Factors in Relation with in-Hospital Mortality in Geriatric Patients with COVID-19. Cyprus J Med Sci 2022;7(3):330-336. (doi: 10.4274/cjms.2022.2021-181)

13. Covino M, De Matteis G, Polla DAD et al. Predictors of in-hospital mortality AND death RISK STRATIFICATION among COVID-19 PATIENTS aged ≥ 80 YEARs OLD. Arch GerontolGeriatr. 2021 Jul–Aug;95:104383.(doi: 10.1016/j.archger.2021.104383)

14. De Smet R, Mellaerts B, Vandewinckele H et al. Frailty and mortality in hospitalized older adults with COVID-19: retrospective observational study. J Am Med Dir Assoc. 2020 Jul;21(7):928-932.e1.Epub 2020 Jun 9. (doi: 10.1016/j.jamda.2020.06.008)

15. Hardan L, Filtchev D, Kassem R, et al. COVID-19 and Alzheimer's Disease: A Literature Review. Medicina (Kaunas). 2021 Oct 25;57(11):1159. (doi: 10.3390/medicina57111159)

16. Zhang Q, Schultz JL, Aldridge GM, et al. COVID-19 Case Fatality and Alzheimer's Disease. J Alzheimers Dis. 2021;84(4):1447-1452. (doi: 10.3233/JAD-215161)

17. Smith DJ, Hakim AJ, Leung GM et al. COVID-19 mortality and vaccine coverage – Hong Kong Special Administrative Region, China, January 6, 2022–March 21, 2022. China CDC Wkly. 2022;4(14):288–292. (doi: 10.46234/ccdcw2022.071)

18. Lidou-Renault V, Baudouin E, Courtois-Amiot P et al. Corticosteroid therapy in COVID-19 associated with in-hospital mortality in geriatric patients: a propensity matched cohort study. The Journals of Gerontology. Series A, Biological Sciences and Medical Sciences. 2022 Jul;77(7):1352–1360. (doi: 10.1093/gerona/glac084)

19. Gulec-Balbay E, Altundal MMB, Kaypak MK, Cangur S, Kaya S. Clinical Characteristics Predicting Mortality Risk in Hospitalized Geriatric Patients with COVID-19 Pneumonia: a Retrospective Study. Clinical Laboratory. 2022 Aug;68(8). (doi: 10.7754/Clin.Lab.2021.211054)