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Clinical Features and Analysis of Survival in a Sample of Patients Infected with SARS-COV-2 in the Specialized Hospital for Geriatric and Palliative Medicine "November 13" – Skopje

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Abstract

BACKGROUND: New worldwide intensive studies of a new virus called severe acute respiratory syndrome coronavirus-2 (SARS-COV-2) have shown that in its clinical manifestations, the virus has an extremely different expression in different population groups, with age being found to be one of the most common and significant variables.

AIM: The objective of this study is to categorize the difference between clinical and laboratory parameters of a sample of patients infected with SARS-COV-2 in the Specialized Hospital for Geriatric and Palliative Medicine "November 13" – Skopje, between survived and deceased patients, impact on the number and severity of comorbidities on the severity of the clinical picture and the survival rate.

MATERIALS AND METHODS: In our study, we analyzed data from a sample of 113 patients hospitalized in our institution. The study is cross-sectional and observational, and in the methodology, we analyzed demographic data by gender and age groups, analysis of comorbidities, functional and nutritional status of patients, and risk factors for mortality and survival rate. For this purpose, we used several geriatric scores: Cumulative Illness Rating Scale scale–Geriatric (CIRS-G), degree of functional ability (Bartel), and the Geriatric Nutritional Index (GNRI) score.

RESULTS: The deceased patients had a significantly higher CIRS-G score, while no significant difference in functional (Bartel) and GNRI scores was found. Multivariate regression analysis showed that lymphocytopenia and low saturation were high-risk factors for death in the geriatric population.

CONCLUSION: Providing hospital-level care for the elderly with SARS-COV-2 contributes to a lower mortality rate.

Introduction

New studies in the world are intensively working on the new virus, severe acute respiratory syndrome coronavirus-2 (SARS-COV-2), it has been shown that in its clinical manifestations, this virus gives extreme expression in different population groups, where age is one of the most common and significant variables. As data on this virus continue to emerge in studies from different countries, a significant difference in the severity and fatality of the disease between different patients becomes apparent. The World Health Organization (WHO) attributed 90% of all SARS-COV-2 deaths to the elderly over the age of 60 years [1], [2], [3].

Establishing an accurate clinical picture of SARS-COV-2 can be difficult in a few people, and a clinical presentation is with atypical symptoms in the elderly [4], [5], [6].

The normal aging process is associated with profound changes in the immune system. First, there are significant changes in T and B lymphocytes, involution of the thymus gland. Aging leads to a decline in both humoral and cellular immune factors [7], [8]. Defective T cells suggest that CD4 cells become incapable of generating efficient memory and produce fewer cytokines and reduced proliferation and differentiation after antigenic stimulation [8]. They have also been verified in B cells, which are also recognized as age-induced changes in the immune system, the percentage has been found to change significantly with age, and the causes of antibodies are less functional compared to young individuals [7], [8], [9].

Identifying the factors that cause the deterioration of COV-2 in the elderly and their correlation with survival may help to predict the risk that occurred in the disease, to be detected and revised to develop strategies to protect and minimize

the death outcome from SARS-COV-2 infection in the elderly population [10], [11], [12].

For that purpose, we conducted this study, on a sample of risk with SARS-COV-2 deaths, at the age of over 65 years, placed in the Specialized Hospital for Medical Medicine "November 13", became infected with SARS-COV-2 during the hospital stay, to categorize the difference between the clinical and laboratory parameters of the changes in correlation with the disease, the influence of the number and the result of the quantity and the result of standard comorbidities, high functional and nutritional status, identify the factors who face the outcome of SARS infection-2 in the past and the duration of survival.

Materials and Methods

Study design

The study is designed as a cross-sectional, observational study, which was conducted on patients hospitalized in the Specialized Hospital for Geriatric and Palliative Medicine "November 13" – Skopje, with proven infection with SARS-COV-2 virus.

In our study, we analyzed data from a sample of 113 patients, hospitalized in our institution, who became infected with SARS-COV-2 during their stay in our hospital. We diagnosed the disease with polymerase chain reaction testing from a nasopharyngeal swab, which was taken at the place where the patient was lying, then sent and examined in the Laboratory at the Macedonian Academy of Sciences and Arts. All other laboratory tests were performed in our laboratory in the Specialized Hospital for Geriatric and Palliative Medicine "November 13" – Skopje.

We determined the methodology with

1. Analysis of the demographic data of the patients, sex, and age, where we classified the age groups into three groups (from 65 to 75 years), (from 75 to 85 years), and (> from 85 years) including several patients under the age of 65 years and have chronic progressive diseases at an advanced stage due to which they stay in our institution for a long time, and are of interest in terms of the outcome of the study (fourth group <65 years)
2. Based on the recommendations of the WHO and other studies, based on clinical and laboratory parameters, we classified the disease as mild, moderate, severe, and critical – required mechanical ventilation due to respiratory failure or due to severe deterioration of organ failure. We analyzed the most common clinical symptoms and signs of the disease, laboratory parameters, lung complications, and the need for oxygen support. We referred the patients who were in critical condition to one of the COVID-19 centers in Skopje

3. The number and severity of comorbidities, we analyzed using: The Cumulative Illnes Rating Scale–Geriatric (CIRS - G) score. Patients with CIRS-G <10 (low risk), CIRS-G 10-20 (medium risk), and CIRS-G> 20 (high risk)
4. Veterans Health Administration COVID-19 (VACO) is a COVID-19 mortality index. It estimates a 30-day cause of death after COVID -19 infection, including demographic data (age and sex) and preexisting comorbidities in patients. We compared the obtained value according to this score with our real patient mortality rate (in%) and analyzed the reasons for that
5. Bartel index is a scale used to measure the functional status of the patient by measuring performance in the activities of daily living. According to the obtained result (from 0 to 100), we divide the patients into five groups (80–100) – these are patients who could live independently, (60–79) – patients who have little dependence on help, (40–59) – partially dependent patients from another person, and (20–39) – highly dependent patients and <20 completely dependent patients
6. Geriatric nutritional risk GNRI = (14.89. Serum albumin (g/dl) + 41.7 × BMI/22).

Statistical analysis

The statistical analysis of the data obtained from the research was done in the statistical program Skopje, Macedonia. Kolmogorov–Smirnov test was used to test the normality of data distribution.

Categorical (attributive) variables are represented by absolute and relative numbers. Numerical (quantitative) variables are represented by average, standard deviation, median value, and interquartile range.

Chi-square test, Mann–Whitney test, and Student's *t*-test were used to compare the qualitative variables between surviving and deceased patients. The two groups were used to compare the two groups in terms of continuous variables.

Statistical significance was defined at the level of $p < 0.05$.

Results

Patients were most often aged 75–85 years – 35.4% (40 patients). No statistically significant difference was found in the distribution of patients

aged: (<65 years), (65–75), (75–85), and (>85) years, depending on the outcome of the disease (p = 0.74). The outcome of the disease was not significantly associated with the sex of the patients (p = 0.098). Existing patients had significantly more frequent symptoms of fever and chills, confusion, present lung findings suspicious of pneumonia, and oxygen requirement compared with surviving patients. All patients had the symptom of malaise and exhaustion, and a small number of patients had diarrhea (Table 1). In our study, surviving and surviving patients with COVID-19 had similar platelet counts (p = 0.28), while all other laboratory parameters presented significantly different values depending on the outcome of the disease. Existing patients had significantly higher leukocytes (8.05 vs 5.1, p = 0.00001), neutrophil/lymphocytes ratio (4.98 vs. 2.15, p = 0.000019), D-dimers (1558.06 vs 819.9, p <0.0001), ferritin (460 vs. 3, = 0.012), C-reactive protein (19.4 vs. 4.8, p = 0.00008), and significantly higher lactate dehydrogenase (198 vs. 155, p = 0.00037) (Table 2).

Table 1: Baseline characteristics of older patients with COVID-19 categorized by mortality outcome

Variable	Outcome of the patient with COVID-19			p
	n (%)	Surviving, n (%)	Deceased, n (%)	
Age groups				
<65	19 (16.82)	15 (17.65)	4 (14.29)	0.74 (NS)
65–75	31 (27.43)	25 (29.41)	6 (21.43)	
75–85	40 (35.39)	28 (32.94)	12 (42.86)	
>85	23 (20.35)	17 (20)	6 (21.43)	
Sex				
Men	38 (33.63)	25 (29.41)	13 (46.43)	0.098 (NS)
Women	75 (66,37)	60 (70.59)	15 (53.57)	
Fever	78 (69.03)	52 (61.18)	26 (92.86)	0.0017** (significant)
Diarrhea	12 (10.62)	7 (8.24)	5 (17.86)	0.15 (NS)
Cough	27 (23.89)	16 (18.82)	11 (39.29)	0.029* (significant)
Confusion	37 (32.74)	17 (20)	20 (71.43)	0.00000*** (significant)
Malaise	113 (100)	85 (100)	28 (100)	
Pneumonia	78 (69.03)	73 (85.88)	5 (17.86)	0.00000*** (significant)
With oxygen therapy	29 (25.66)	7 (8.24)	22 (78.57)	0.00000*** (significant)

Chi-square test; *p<0.05, **p<0.01, ***p<0.0001. NS: Not significant.

Patients with COVID-19 who survived and those who survived differed significantly in the CIRS-G score (p = 0.013). No statistically significant difference was found between the deaths and survivors of COVID-19 in relation to the Bartel index (p = 0.34) and the GNRI index (p = 0.25). Regarding the VACO index, our results for 30 days of survival, calculated with all the parameters for this index, show about 85%–90% coincidence with the predicted time of death.

The median survival time of patients who died was 22 days and that of patients with advanced malignancy was 17 days. The mean follow-up period of 2 months, after 21 days from the onset of the disease, patients were considered non-communicable, many of them were followed longer due to chronic complications (Table 3 and Figure 1).

This analysis indicated that low lymphocytes and low saturation, on admission and subsequently, are the highest risk factors for death in the study group.

Table 2: Differences in the most common laboratory parameters between alive versus death patients

Variable	Descriptive statistics (laboratory parameters)		p
	Mean ± SD	Median (IQR)/ minimum–maximum	
Leukocytes			
Surviving	5.53 ± 3.1	5.1 (4.1–6.5)	Z = 4.4
Deceases	8.68 ± 3.9	8.05 (6.3–11.3)	p = 0.00001*** (significant)
Lymphocytes			
Surviving	28.88 ± 10.9	27.7 (21.4–35.9)	Z = 4.59
Deceases	17.59 ± 9.6	16.15 (9.1–22.4)	p = 0.00000*** (significant)
Platelets			
Surviving	216.25 ± 74.6	206 (162–247)	Z = 1.08
Deceases	263.36 ± 159.6	218 (170–319)	p = 0.28 (NS)
Lymphocytes/ neutrophil ratio			
Surviving	2.61 ± 2.1	2.15 (1.36–3.18)	Z = 4.28
Deceases	6.31 ± 4.8	4.98 (2.48–9.23)	p = 0.000019*** (significant)
D-dimers			
Surviving	1413.01 ± 1422.3	819.9 (550–1670)	Z = 5.63
Deceases	4209.31 ± 2545.8	4525 (1558.06–6115)	p = 0.000000*** (significant)
Ferritin			
Surviving	681.67 ± 662.0	450 (340–736.4)	Z = 2.52
Deceases	857.62 ± 564.1	670 (460–1090)	p = 0.012* (significant)
CRP			
Surviving	23.76 ± 31.6	10.1 (4.8–28.3)	Z = 3.94
Deceases	53.55 ± 42.9	42.3 (19.4–70.9)	p = 0.00008*** (significant)
LDH			
Surviving	231.34 ± 164.8	184 (155–247)	Z = 3.56
Deceases	371.93 ± 361.2	296.5 (198–380)	p = 0.00037*** (significant)
Oxygen saturation			
Surviving	92.86 ± 3.3	80–98	t = 9.7
Deceases	83.82 ± 6.5	60–93	p = 0.000000*** (significant)

*p<0.05, ***p<0.0001. Z: Mann–Whitney U-test, t: Student's t-test. IQR: Interquartile range, SD: Standard deviation.

Discussion

Elderly patients are more susceptible to more severe SARS-COV-2 infection due to a generally weaker immune response and the presence of comorbidities [13]. As a result, the treatment of these patients requires much greater caution and experience. In general, the clinical presentation in older adults with SARS-COV-2 is different from that in younger adults. Elderly patients show more atypical presentations of SARS-COV-2, such as confusion, extreme weakness, and fever, with fever, while cough, loss of smell and taste, and gastrointestinal manifestations are less common. It is well known that age can make the diagnosis more complicated, as older adults often have atypical manifestations, often accompanied by an exacerbation of their underlying disease[7], [14].

Pulmonary complications

Conditions such as chronic bronchitis and emphysema, which are common in the elderly, as well as muscle atrophy can lead to impaired lung function. Impaired lung function combined with reduced vital and reserve capacity of the lungs, as well as the impaired immune system in the elderly population, make them more susceptible to severe SARS-COV-2 infection and respiratory failure [7]. "Silent hypoxemia" - the phenomenon
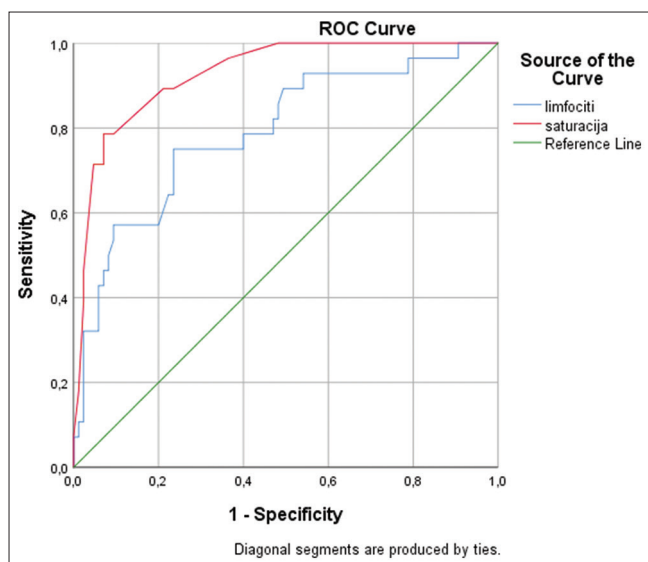
Figure 1: ROC death prediction curve in geriatric patients with COVID with lymphocytes and saturation

by which patients develop hypoxemia and respiratory failure without dyspnea is an atypical presentation of COVID-19 that appears to be particularly prevalent in the elderly population [14]. Cardiovascular complications — ACE number-2 cardiac myocardial receptors individuals are large, which may be associated with heart disease in patients with SARS-COV-2. Furthermore, myocardial cell injury may be secondary to impaired respiratory function and hypoxia, along with cardiotoxicity associated with antiviral therapies. They can cause conditions such as painful sinus syndrome or prolongation of the Q-T interval or lead to severe ventricular arrhythmias [15]. In our patients, diabetes was present in 75% of patients. Almost all of the patients examined in diabetes had a moderate-to-severe clinical picture, given the stress and inflammatory response induced by SARS-COV-2, which may increase the secretion of endogenous corticosteroid hormones, which may cause blood sugar fluctuations. In these patients, and in particular, the use of intravenously administered corticosteroids for therapeutic purposes, made hyperglycemia episodes even more common in our patients. The mortality rate was higher in patients with diabetes (85% of patients with diabetes as one of the comorbidities also had diabetes) [14]. Evolved clinical

Table 3: Differences between scores examined and indices between alive versus death patients

Variable	Patients with COVID-19			p
	n	Surviving, n (%)	Egsitus, n (%)	
CIRS-G				
High	6	2 (2.35)	4 (14.29)	0.013* (significant)
Medium	91	68 (80)	23 (82.14)	
Low	16	15 (17.65)	1 (3.57)	
Bartel index				
1	6	5 (5.88)	1 (3.57)	0.34 (NS)
2	9	6 (7.06)	3 (10.71)	
3	24	21 (24.71)	3 (10.71)	
4	29	23 (27.06)	6 (21.43)	
5	45	30 (35.29)	15 (53.57)	
GNRI index				
High	18	11 (12.94)	7 (25)	0.25 (NS)
Medium	65	52 (61.18)	13 (46.43)	
Low	30	22 (25.88)	8 (28.57)	

CIRS-G: Cumulative multimorbidity scale–geriatric, GNRI: Geriatric nutritional risk, NS: Not significant.

experience from other centers suggests that patients with cancer and SARS-COV-2 have more serious complications, which have been confirmed in our patients, such as severe pneumonia or sepsis, multiorgan failure, and higher mortality. Of the patients with palliative malignancy, most (about 80%) died within the first 2 weeks of infection, but there were some who contracted the infection [15].

From the beginning we concluded that of all patients infected with SARS-COV-2, despite advanced age and high comorbidity, most had a mild clinical picture – 54, moderate clinical picture – 30 patients, while severe clinical picture – 29 patients (respiratory rate ≥30 per min, dyspnea present, blood oxygen saturation ≤ 93%), only two critically ill patients were referred to a special COVID center.

In their paper, working at a geriatric center in France, Godaet Lidviene and coworkers state that laboratory tests often show thrombocytopenia and lymphocytopenia in adult patients with COVID-19 [16], [17]. In our series, lymphocytopenia was more common than thrombocytopenia or leukopenia. In our study, excised and surviving patients with COVID-19 had similar platelet counts (p = 0.28), while all other laboratory parameters presented significantly different values depending on the outcome of the disease. The most common complication in our patients, who developed a severe clinical picture, was the development of respiratory failure or sudden death as a result of multi-organ failure or possible vascular thromboembolism [16], [18], [19].

Timely testing and diagnosis of the disease, as well as timely intensive treatment with rehydration, multivitamin, anticoagulant, and antibiotic therapy, regular monitoring of clinical and laboratory parameters, and increased care, were crucial. Evaluation of secondary bacterial infections, delay and prevention of patient intubation, opportunities for early rehabilitation, and prevention of delirium were particularly important. We did not use antiviral drugs in the treatment [20].

Mortality rate

In our study group of 113 patients, 28 patients died (24.8%).

Compared to other studies, the authors note that the number of deaths was enormous, due to the routine unavailability of tests for COVID-19 diagnostics, as well as the insufficient number of medical staff employed in geriatric centers (mortality rate ranging between 60% and 70%) [20], [21].

Conclusions

The results of our study show that 75.2% of patients with SARS-COV-2 survived, indicating that

providing hospital care for elderly patients in these conditions of severe infection is not in vain. Although older age is highly associated with in-hospital mortality and reduced likelihood of cure in geriatric patients, timely inclusion of treatment protocols, assessment of disease severity, and comorbidities, multidimensional care, and rehabilitation improve survival rates [20].

This analysis indicated that low lymphocytes and low saturation, on admission and subsequently, are the highest risk factors for death in the study group.

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