ORIGINAL ARTICLE

Clinical characteristics, comorbidities and mortality in critically ill mechanically ventilated patients with Covid-19: a retrospective observational study

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ABSTRACT

Aim To analyse demographic data, clinical symptoms and signs, laboratory data and comorbidities in patients with COVID-19 pneumonia admitted to the intensive care unit (ICU), mechanically ventilated with fatal outcome.

Methods Medical records of 92 patients were retrospectively analysed. Demographic data, clinical symptoms and comorbidities were collected on the day of hospital admission. Clinical signs and laboratory data were collected on the day of hospital admission (T1), on the day of starting non-invasive ventilation (T2), and on the day of starting invasive ventilation (T3).

Results Average age of the patients was 60.05 years. Patients over 50 years of age, 71 (77.1%) (p=0.000), and males, 62 (67.4%; p=0.001) were predominant. The most common patient symptoms were exhaustion, myalgia, dyspnoea and cough. Hyperthermia was recorded on the day of hospital admission. Tachycardia, hyperglycaemia, hypoxemia were recorded at all observed study times. The most common comorbidity was hypertension arterialis with a very strong correlation with fatal outcome, followed by diabetes mellitus and chronic heart disease that were moderately correlated with fatal outcome.

Conclusion The treatment of COVID-19 patients in ICU with mechanical ventilation has a high failure rate. Demographic data, clinical symptoms and signs as well as accompanying comorbidities can be a significant component in making decisions about diagnostic-therapeutic procedures.

Key words: comorbidity, fatal outcome, intensive care unit, invasive ventilation

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INTRODUCTION

In December 2019, acute respiratory disease, now known as the new pneumonia COVID-19, occurred in Wuhan, Hubei Province, China and quickly spread to other parts of the world (1,2). This ongoing global pandemic is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). From the first case in December 2019 in China to the pandemic in March 2020 more than 120 million confirmed cases and more than 2.8 million deaths have made this pandemic one of the deadliest in history (3). The spectrum of clinical features of COVID-19 infection in the intensive care unit (ICU) varies from mild pneumonia to a critical condition with acute respiratory distress syndrome (ARDS). Previous studies have described epidemiological characteristics, clinical presentation, and outcomes of patients with COVID-19 pneumonia (4,5).

Approximately one in ten patients with SARS-CoV-2 becomes symptomatic (6). Symptoms of COVID-19 are highly variable, ranging from asymptomatic, mild, or severe pneumonia–like symptoms (7). A large number of COVID-19 pneumonia leads to ARDS and it is usually developed at day eight or nine after the symptom onset (8). Reportedly, in most studies from Europe and North America 10-20% of patients admitted to hospital were diagnosed with ARDS and were treated with different forms of mechanical ventilation support according to the level of respiratory failure, clinical condition and duration of illness (9,10). Mortality of patients with COVID19-pneumonia, especially those with the most severe form of ARDS when invasive mechanical ventilation (IMV) is required, is extremely high, and it is up to 40.5% (11).

A large number of patients hospitalized at the ICU with COVID19 pneumonia have comorbidities that negatively affect the prognosis of the disease (12). In Bosnia and Herzegovina there are no epidemiological data related to COVID-19 patients.

The aim of our study was to analyse demographic data, clinical symptoms and signs, laboratory data and comorbidities in patients with COVID-19 pneumonia admitted to the ICU and mechanically ventilated, with the fatal outcome.

PATIENTS AND METHODS

Patients and study design

This observational, retrospective, cross-sectional study was conducted between July 2020 and February 2021 in the Department of Anaesthesiology and Intensive Care Unit at the Cantonal Hospital Zenica, Bosnia and Herzegovina.

The study included 92 adult patients with positive SARS-CoV 2 polymerase chain reaction (PCR) of nasopharyngeal swabs. All observed patients were invasively mechanically ventilated due to Covid-19 ARDS. Patients with milder form of ARDS treated only with non-invasive ventilation (NIV) support measures were excluded from the study.

After admission at the ICU, the treatment of the patients followed internal institutional protocol made by the council consisting of an internist, an infectologist and an anaesthesiologist. The drug therapy included corticosteroids, anticoagulants, proton pump inhibitors, probiotics and vitamin supportive therapy. Efforts were made to avoid intubation where feasible using NIV support measures and including prone positioning. The patients were selected for IMV by attending anaesthesiologist according to the criteria (13). The IMV was initially managed with a lung protective ventilator strategy targeting tidal volume of 6 mL/kg of ideal body weight, moderate positive end expiratory pressure (10-12 cmH_2O) and plateau pressure <30 cmH_2O. In patients with compliant lungs, tidal volumes were liberalized to 7-8 mL/kg of ideal body weight as long as plateau pressure remained <30 cmH_2O. Alternatively, some patients were switched to pressure control ventilation (14).

The Ethics Committee of the Cantonal Hospital Zenica approved this investigation.

Methods

All data were collected from the ICU electronic medical report and included: demographic data, comorbidities, clinical symptoms and signs, and laboratory data.

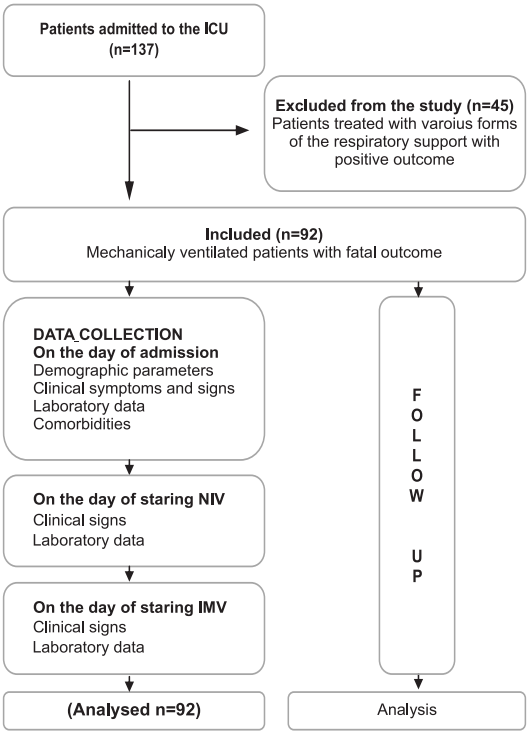
Demographic data involved age and gender.

Observed comorbidities were: diabetes mellitus, hypertension arterialis, chronic obstructive pulmonary disease (COPD), chronic heart disease, cerebrovascular disease (CVD) and malignant disease. Additionally, a correlation of the pre-

valence of individual comorbidities with fatal outcome was analysed.

Clinical symptoms were recorded on the day of admission at hospital: cough, dyspnoea, chest pain, exhaustion, abdominal pain, diarrhoea, nausea, vomiting, anorexia, headache, anosmia and myalgia. Clinical signs included temperature, heart rate, systolic and diastolic arterial pressure.

Laboratory data included blood glucose level, capillary oxygen pressure and capillary carbon dioxide pressure. Blood samples were taken on the day of hospital admission (T1), on the day of starting NIV support measure (T2) and on the day of endotracheal intubation and starting IMV (T3) (Figure 1).



ICU, intensive care unit; NIV, noninvasive ventilation; IMV, invasive mechanical ventilation;

Figure 1. Flow chart of the study protocol

Statistical analysis

A descriptive analysis of the baseline and clinical characteristics of the patients was performed. Categorical variables were presented as number and percentages and analysed using $\chi 2$ test. Continuous variables were presented as median and interquartile range and analysed using Wilcoxon rank test. A p value <0.05 was considered statistically significant. Pearson's correlation coefficient test was used to analyse the correlation of presented comorbidities with a fatal outcome. A positive correlation was considered as r>0.2: moderate 02.-0.5, very strong 0.5-0.8, excellent 0.8-1.

RESULTS

During eight months of the study period, 134 patients were admitted to the ICU due to Covid-19 ARDS and treated with various forms of respiratory support. The study sample consisted of 92 patients requiring IMV and with a fatal outcome.

The average age of the patients was 60.05 years (ranged between 26 and 75 years). Seventy one (77.1%) patients were over 50 and 21 (22.9%) were under 50 years of age (p<0.000). There were 30 (32.6%) female and 62 (67.4%) male patients (p<0.001).

The most common symptoms were exhaustion, in 83 (90.2%), myalgia in 76 (82.6%), dyspnoea in 69 (75%) and cough in 62 (67.4%) patients. A lower prevalence of headache, anosmia, vomiting, nausea, diarrhoea, and abdominal pain was noted (Table 1).

Table 1. Presentation of clinical symptoms in mechanically ventilated patients

Symptom	No (%) of patients with or without (YES/ NO) symptoms	p
Cough	62 (67.4) / 30 (32.6)	0.001
Dyspnoea	69 (75) / 23 (25)	0.000
Chest pain	46 (45.7) / 46(45.7)	0.404
Exhaustion	83 (90.2) / 9 (9.8)	0.000
Abdominal pain	9 (9.8) / 83 (90.2)	0.000
Diarrhoea	11 (11.96) / 81 (88.04)	0.000
Nausea	12 (13) / 80 (87)	0.000
Vomiting	15 (16.3) / 77 (83.7)	0.000
Anorexia	60 (67.4) / 32 (32.6)	0.004
Headache	27 (29.4) / 65 (70.6)	0.000
Anosmia	27 (29.4) / 65 (70.6)	0.000
Myalgia	76 (82.6) / 16 (17.4)	0.000

Mechanically ventilated patients with fatal outcome showed hyperthermia on the day of hospital admission, tachycardia, hyperglycaemia, and hypoxemia at all observed time periods, and hypocarbia on the day of hospital admission. In terms of systolic and diastolic blood pressure, the patients were normotensive at all observed study time periods (Table 2).

The most common comorbidity was hypertension, in 52 (56.5%) patients, followed by diabetes mellitus, in 34 (37.0%) patients, while the history of malignant disease was the rarest comorbidity, in three (3.3%) patients. All observed comorbidities showed a statistically significant positive correlation with fatal outcome except history of malignant disease: hypertensio arterialis (r=0.735), diabetes mellitus (r=0.493), chronic heart disease (r=0.284), COPD (r=0.261), and malignant disease (r=0.118) (Table 3).

Table 2. Clinical signs and laboratory findings in mechanically ventilated patients

Parameter	Time period	Median (IQR)	Reference range
Temperature (°C)	T1	37.3 (36.6-38.0)	<37
	T2	36.6 (36.3-36.8)	
	T3	36.5 (36.2-36.7)	
Heart rate (beat/minute)	T1	109 (90-120)	60-90
	T2	102 (83-115)	
	T3	85 (78-113)	
Systolic pressure (mmHg)	T1	130 (120-146)	<140
	T2	124 (120-135)	
	T3	120 (114-127)	
Diastolic pressure (mmHg)	T1	80 (70-90)	<85
	T2	76 (69-76)	
	T3	71 (63.7-81.5)	
Glucose (mmol/L)	T1	10.2 (8.6-12.4)	3.9-5.5
	T2	8.1 (6.5-8.6)	
	T3	7.6 (6.5-8.6)	
pO2 (mmHg)	T1	44.2 (36.2-51.6)	70-110
	T2	47.6 (40.5-54.1)	
	T3	45.2 (41.5-51.8)	
pCO2 (mmHg)	T1	33.9 (32.0-35.3)	32-42
	T2	35.1 (31.4-42.7)	
	T3	36.5 (32.5-50.4)	

IQR, interquartile range; T1, on the day of hospital admission; T2, on the day of starting noninvasive ventilation; T3, on the day of starting invasive mechanical ventilation; pO2, capillary oxygen pressure; pCO2, capillary carbon dioxide pressure;

Table 3. Prevalence of comorbidities and correlation with fatal outcome

Comorbidity	No (%) of patients with or without (YES/NO) comorbidity	p*	r	p†
Diabetes mellitus	34 (37.0) / 58 (63.0)	0.000	0.493	0.000
Hypertensio arterialis	52 (56.5) / 40 (43.5)	0.000	0.735	0.000
COPD	13 (14.1) / 79 (85.9)	0.012	0.261	0.012
Chronic heart disease	15 (16.3) / 77 (83.7)	0.006	0.284	0.006
Cerebrovascular disease	11 (12.0) / 81 (88.0)	0.023	0.238	0.023
Malignant disease	3 (3.3) / 89 (96.7)	0.256	0.118	0.261

*$\chi 2$ test; †Pearson's correlation coefficient test; r, correlation coefficient; COPD, chronic obstructive pulmonary disease;

Twenty four (26.1%) patients with one comorbidity and 24 (26.1%) with two comorbidities had statistically significant correlation with fatal outcome; thirteen patients (14.1%) had three comorbidities and only four (4.1%) had more than three comorbidities (Table 4).

Table 4. Number of present comorbidities and correlation with fatal outcome

Number of comorbidities	No (%) of patients	p*	r	p†
1	24 (26.1)	0.000	0.383	0.000
2	24 (26.1)	0.000	0.383	0.000
3	13 (14.1)	0.012	0.261	0.012
>3	4 (4.3)	0.188	0.137	0.191

*$\chi 2$ test; †Pearson's correlation coefficient test; r, correlation coefficient;

DISCUSSION

In this observational, cross-sectional study, the demographic data, clinical symptoms and signs, laboratory data and comorbidities were retrospectively analysed among 92 patients with COVID-19 pneumonia admitted to the ICU, mechanically ventilated and with fatal outcome. The average age of 60 years was strongly associated with poor prognosis. On the other hand, results found in the United States showed that the median age of 47 years was associated with deterioration of respiratory status of the patients (15). The number of males in our study was significantly higher than females. In the elderly population, COVID-19 pneumonia predominates in females according to Guo et al. (16), as well as other studies (although without statistical significance) (17,18).

Huan et al. first reported clinical features of the patients with COVID-19 infection in the city of Wuhan and found clinical manifestations (fever, cough, dyspnoea, myalgia, and fatigue) were connected to the younger age (19). In our study, the highest prevalence of exhaustion, myalgia, dyspnoea, cough, anorexia and chest pain was recorded in the elderly; up to 90% of patients have more than one symptom, as it was previously reported (20).

In our study, regarding clinical signs, hyperthermia was observed only on the day of hospital admission, indicating the following of the protocol related to antipyretic and anti-inflammatory drugs during hospital treatment.

Hemodynamic instability in the form of tachycardia persisted at all observed time periods in our study as a compensatory response to the ongoing inflammatory process, hyperthermia, hypoxemia and consequent hypoperfusion in patients with COVID-19 pneumonia. Hemodynamic instability is supported by comorbidities of the observed patients and the damage of the heart muscle due to COVID-19 infection (21).

Despite therapeutic administration of insulin, hyperglycaemia was also maintained throughout all three observed time periods in our mechanically ventilated patients with fatal outcome. This could be a sign of poorly regulated disease in patients with previously reported diabetes mellitus (22). In patients without diabetes mellitus, hyperglycaemia can be classified as a result of a strong stress response to the inflammatory process, new-onset diabetes, unrecognized pre-diabetes or direct effect of the corona virus on the pancreas (23).

We found a low level of capillary oxygen pressure at all three time periods, regardless of different types of respiratory support administered. Severe

hypoxemia, despite the application of mechanical ventilation, indicates a serious damage to the respiratory membrane due to COVID-19 infection, consequent ARDS, and poor outcome (24,25).

Studies have shown a higher mortality rate in COVID-19 patients with pre-existing conditions compared to patients without comorbidities. The most common comorbidities are hypertension, diabetes mellitus, cardiovascular diseases, arthritis, stroke and cancerous conditions (26,27). The presented study confirmed a very strong correlation of hypertension with a poor clinical outcome, and it was found in 56.5% patients, either as a single or in combination with other comorbidities. According to Du et al., hypertension was independently associated with increased risk of mortality in 37% COVID-19 patients (28).

In our study, diabetes mellitus was recorded in 37.0% patients resulting in a moderate correlation with fatal outcome similarly with 39.6% in Seiglie et al. study (29).

History of COPD was revealed in 14.1% patients in our research resulting in moderate correlation with fatal outcome. In contrast, Leung et al. has found 33% of COPD patients (30). Patients with COPD already have a disrupted anatomical-physiological component of the lung and increased vulnerability to severe forms of COVID-19 infection (31).

Chronic heart disease was noted in 16.3% patients in our study and the correlation with fatal outcome was moderate. Similarly, Phelps et al. found that heart disease was presented in 22.1% patients (32).

History of CVD was recorded in 12% patients in our study with moderate correlation with fatal outcome, which is in concordance with 11.9% from Kummer et al. study (33).

In conclusion, the presented observational, cross-sectional study showed that patients with COVID-19 pneumonia admitted to the ICU, mechanically ventilated and with fatal outcome were on average 60 years old, predominantly males. On admission to the hospital, clinical presentation included exhaustion, myalgia, dyspnoea, cough, anorexia, chest pain, and hyperthermia, whereas tachycardia, hyperglycaemia, and hypoxemia existed until IMV administration. Concomitant diseases strongly contributed to the fatal outcome primarily in patients with previous hypertensio arterialis, diabetes mellitus, or chronic heart disease. Close monitoring, prompt diagnostic and therapeutic procedures are necessary in these patients from hospital admission to improve the clinical outcome.

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TRANSPARENCY DECLARATIONS

Competing interest: None to declare.

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