

## Covid-19: Course and prognosis in patients with severe clinical form

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### Abstract

Our aim is to identify factors of unfavorable prognostic significance in hospitalized patients with severe COVID-19, an analysis of clinical and demographic characteristics and routine laboratory tests was performed. For the following period: March - July 2023, 25 patients with severe COVID-19 needing intensive care and treatment were hospitalized in Military Medical Academy Sofia (Bulgaria). The diagnosis has been confirmed by RT-PCR analysis for SARS-CoV-2 detection. According to the prognosis, the target group of patients were divided into two groups - discharger and deceased. The average age of the analyzed cohort was 77.6 years. The most commonly reported clinical symptoms include fever, cough, shortness of breath, and neurological symptoms. We found that all patients with severe COVID-19 were comorbid and elderly. The average hospital stay in intensive care is 11.9 days. Nearly half of the cases had fatal outcome (12/25). Among the factors associated with the clinical severity of COVID-19 and mortality are advanced age, presence of chronic concomitant diseases, development of pneumonia and/or neurological complications, as well as deviations in some laboratory parameters.

**Keywords:** Severe COVID-19; Demographic Factors; Comorbid Conditions; Prognosis.

### 1. Introduction

At the end of 2019, an outbreak of atypical pneumonia with an unknown causative agent was reported for the first time in China. In a very short period of time, a newly emerging infectious disease called Coronavirus disease (COVID-19) has spread worldwide, becoming a pandemic. The identified etiological agent turned out to be a new  $\beta$  - coronavirus, which received the name Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Recorded unprecedented high rates of morbidity and mortality have made COVID-19 a serious threat to public health. This caused the introduction and implementation of strict quarantine measures and the mobilization of all health resources. COVID-19 has shown exceptional clinical variability, from asymptomatic and mild forms to severe disease with pneumonia and multiorgan dysfunction, and in some cases - death. Common symptoms include fever, cough, and shortness of breath. Observations show an increased incidence of affecting the central and peripheral nervous system, as well as skeletal muscle. The key role of systemic hyperinflammation (cytokine storm) and immunothrombosis in severe forms of COVID-19 described in both adults and children has been identified [1]. Hospitalized patients were predominantly with hypoxaemia – a result from viral induced inflammation of the pulmonary parenchyma accompanied by increased coagulation activity [2]. The data show that 20-40% of hospitalized patients with COVID-19 require admission to the intensive care unit [3], and in 35-50% of them the outcome is fatal [4]. A number of studies have highlighted that among those suffering from COVID-19 with the need for intensive care are mainly those patients who have underlying chronic diseases [5].

Our goal is to summarize the data of patients with severe COVID-19 in order to study the risk factors for disease progression.

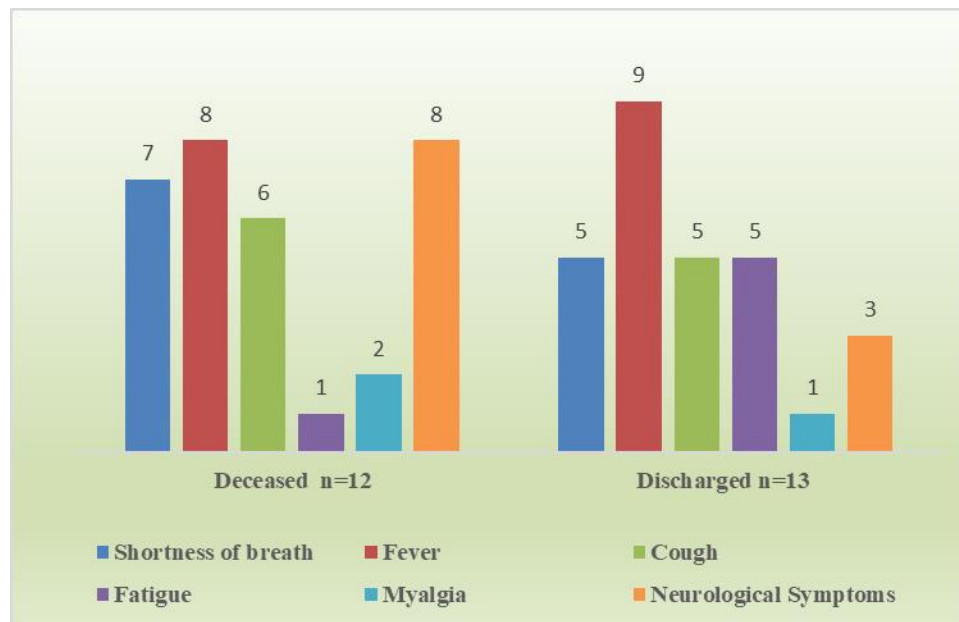
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## 2. Materials and methods

A detailed review of the electronic medical records of 25 patients (14 men and 11 women) in need of intensive care hospitalized in MMA-Sofia for March - July 2023 period was performed. The average age of the analyzed cohort was 77.6 years. Demographic data, clinical symptoms, premorbid history, laboratory abnormalities, vaccine status, and disease outcome were included. In all patients with severe COVID-19, the diagnosis was laboratory-confirmed with a positive real-time reverse-transcriptase–polymerase-chain-reaction (RT-PCR) analysis [6]. Samples from the upper respiratory tract (nasopharyngeal and oropharyngeal swabs) or from the lower respiratory tract (sputum or bronchoalveolar lavage) were examined. For the purposes of this study, the patients were divided into two groups – survivors (discharged) and deceased.

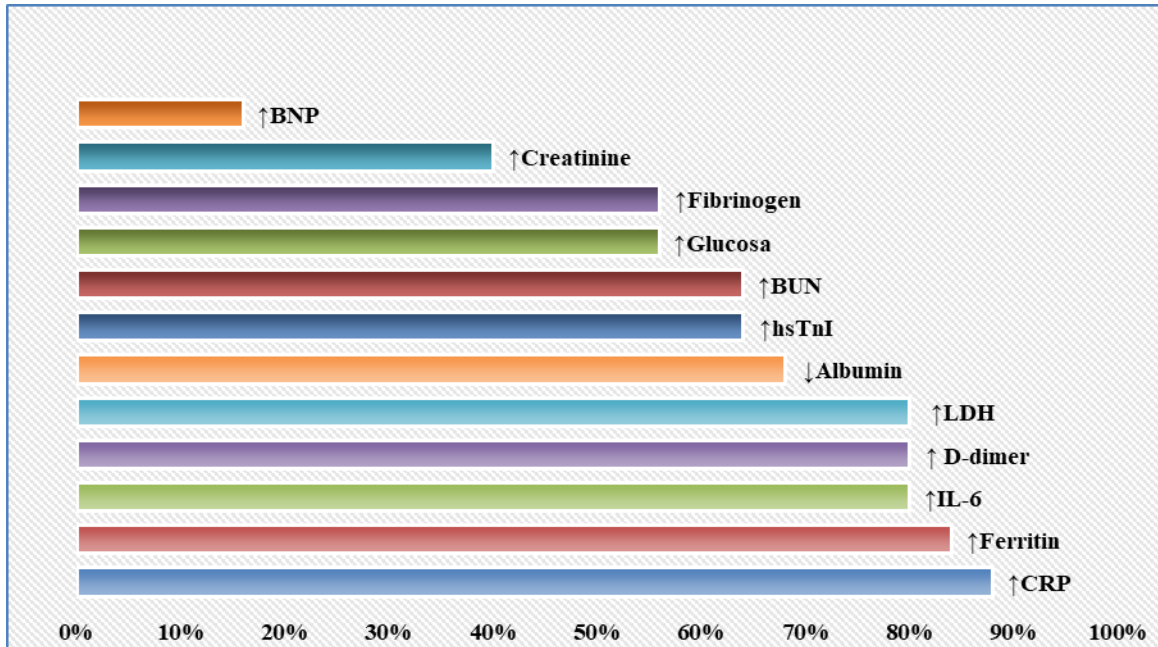
## 3. Results

The distribution of the 25 patients hospitalized with severe COVID-19 according to demographic indicators shows that the patients are in the age range of 60-91 years, 56% of them are men and 44% are women. The average age of women (78.5 years) is higher than that of men (76.9 years). The most commonly reported clinical symptoms include fever, shortness of breath, fatigue, cough, neurological manifestations, myalgia and sore throat (fig.1).



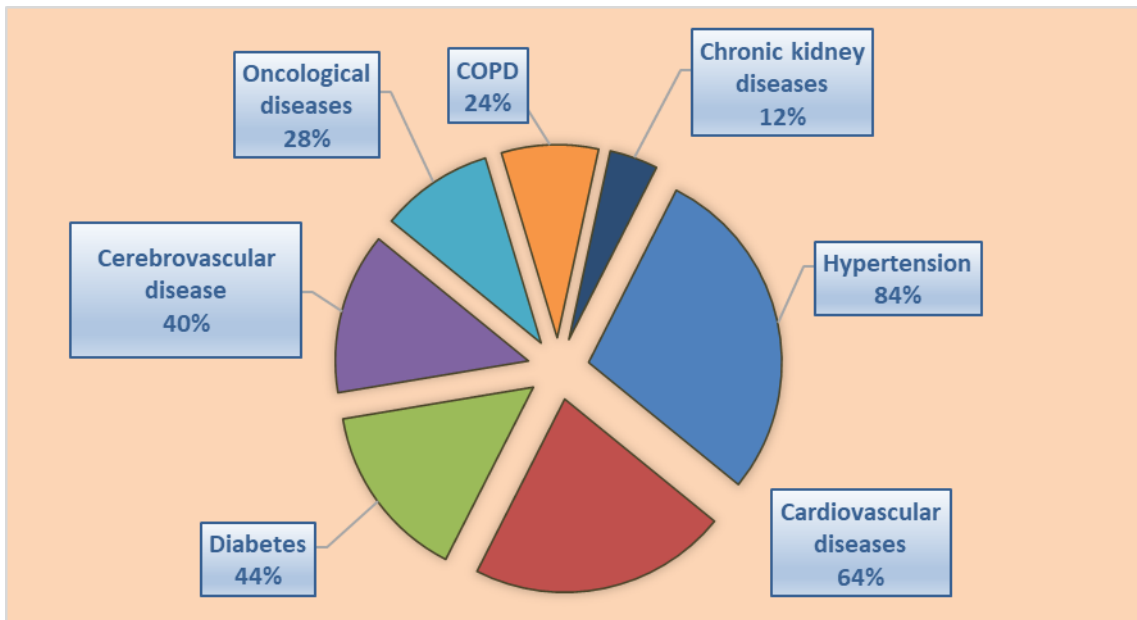
**Figure 1** Clinical symptoms in patients with severe COVID-19.

Radiological or computer tomography (CT) evidence of pneumonia are 76% of hospitalized patients with severe COVID-19 was reported, pleural effusion was found in 24% of them have and 16% have developed ischemic stroke. At the time of admission, most patients had a mean oxygen saturation of 86%. Among the commonly found abnormal laboratory findings are lymphopenia, increased values of C-reactive protein (CRP), Ferritin, Lactate Dehydrogenase (LDH), Interleukin 6 (IL-6), D-dimer, high-sensitivity Troponin I (hsTPI), blood urea nitrogen (BUN), glucose, fibrinogen, creatinine and decreased albumin (fig.2).



**Figure 2** Abnormalities in laboratory results.

All patients were comorbid, with a history of one or more co-existing chronic illnesses. The most frequently reported were hypertension, cardiovascular disease (CVD), diabetes, cerebrovascular disease, oncological disease, chronic obstructive pulmonary disease (COPD) and chronic kidney disease (fig.3).



**Figure 3** Frequency of comorbidities.

Average hospital stay in intensive care unit (ICU) was 11.9 days (3-25 days). In almost half of the cases, the outcome of the disease was fatal (12/25). The recorded deaths were in older patients (78.9 years) who were set up on mechanical ventilation. There was no difference in terms of sex (6 men and 6 women), but the average age of the deceased women (81.2 years) was higher than that of men (76.7 years). Discharged patients (8 men and 5 women) had an average age of 76.4 years. The number of unvaccinated patients (64%) over vaccinated patients (36%) predominates. A total of 9/12 deceased patients had negative vaccination status.

#### 4. Discussion

All hospitalized patients requiring intensive care received appropriate treatment, were on oxygen therapy or had to be switched on (put on / required) mechanical ventilation. Studies identify demographic characteristics and comorbidities as risk factors associated with severe forms of COVID-19 [7]. In our study the deceased were older (78.9 years) compared to survivors (mean age 76.4 years). We observed no gender differences in survival. The most commonly reported symptom was fever (68%). We defined as clinical markers of severity the development of pneumonia with respiratory failure and the presence of neurological symptomatology.

Among the group of 25 patients analyzed, 48% - had shortness of breath and 44% of them had cough. Hypoxemia < 92% of peripheral pulse oximetry is assumed to be an important prognostic indicator and is associated with worse clinical outcomes. In all patients on mechanical ventilation, the outcome of the disease was fatal. Severe forms of course of disease are usually accompanied by neurological complications. Analysis of the data showed that quantitative changes in patients' consciousness - from confusion to comatose state were documented in 48% of hospitalized ICU patients. Four patients were diagnosed with acute ischemic stroke, two of them (a woman of 81 and a man of 83) who were also multimorbid - have died. SARS-CoV-2 can generate a state of hypercoagulopathy and can trigger an autoimmune response. COVID-19 is assumed to stimulate the production of antiphospholipid antibodies (aPL) involved in the pathogenesis of ischemic stroke [8]. In SARS-CoV-2 infection, thromboinflammation and dysregulation of the renin-angiotensin-aldosterone (RAAS) system are predisposition to acute cerebrovascular events, especially in older patients with underlying diseases.

Another important factor is endothelial dysfunction, which negatively affects microcirculation. Also, hypoxia can worsen neurological damage, leading to a fatal vicious cycle. Studies show that more than 35% of patients with COVID-19 have neurological symptoms, and in some of them they may be the debut manifestation of the disease. Nervous system involvement is associated with longer hospital stays and higher mortality compared to patients without neurological involvement [9]. In our study, the average hospital stay of patients with neurological manifestations was 12 days, and in the four patients with ischemic stroke it was longer (15.7 days). Factors for prolonged hospital stay are sought among the reported indicators upon hospitalization. According to data from another study - the average length of hospitalization of patients treated in intensive care is 12 days - and it was found that they had various chronic diseases [10]. As the most common comorbidities among hospitalized patients with severe COVID-19, we found arterial hypertension (84%), cardiovascular disease (64%) and diabetes mellitus (44%). Other studies [11, 12] have also similar results. The vascular endothelium of people with diabetes, hypertension and CVD is primarily impaired - reason for more common complications. Patients with COVID-19 and oncological diseases [13] are a highly vulnerable group. To a large extent, the aggravated course of infection with SARS - CoV-2 in them is due to the systemic immunosuppressive state, determined by the main diagnosis and chemotherapy.

Bulgaria is among the countries with the highest mortality rate and the lowest COVID-19 vaccine coverage in Europe [14]. Negative attitude in terms of vaccines are confirmed by our data, which show that 64% of patients with severe COVID-19 have been unvaccinated. Comparative analysis showed higher hospital mortality rates among the group of unvaccinated patients (9/12) than those who were vaccinated (3/12). Of the group of discharged patients (n=13), six were vaccinated and seven unvaccinated.

We found that the most commonly recorded laboratory findings in patients with severe COVID-19 are lymphopenia, increased values of inflammatory biomarkers (CRP, Ferritin, IL-6), D-dimer and LDH. Lymphopenia early in the disease is a poor prognostic trait [15]. Observations have shown that increased levels of D-dimer, CRP, LDH, high-sensitivity cardiac troponin are associated with adverse outcomes [16].

Higher levels of IL-6 are strongly associated with shorter survival. Recorded abnormalities in indicators of cellular damage, especially elevated LDH values, suggest a greater burden of disease [17]. SARS infection - CoV-2 causes fairly permanent changes in some laboratory indicators, which often correlate with the severity of the disease.

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#### 5. Conclusions

A summary analysis of the data of hospitalized patients with severe COVID-19 is presented. Our study has some limitations, it is single-center and of limited sample size, however the results suggest that advanced age, aggravated premorbid status, clinical presentation (severe pulmonary and neurological involvement) and ICU admissions are among the risk factors for unfavorable prognosis.

Older and comorbid patients who have an impaired immune response are at increased risk of severe COVID-19. Knowledge of the characteristics related to the clinical severity of the disease is essential for the proper management of diagnostic and therapeutic activities in the most vulnerable population of patients with COVID-19.

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## Compliance with ethical standards

### *Disclosure of conflict of interest*

No conflict of interest to be disclosed.

### *Statement of informed consent*

Informed consent was obtained from all individual participants included in the study.

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