CLINICAL STUDIES

CLINICAL-EPIEMIOLOGICAL AND EVOLUTIONARY ASPECTS IN THE FIRST 20 PATIENTS DIAGNOSED WITH COVID-19, HOSPITALIZED IN THE INFECTIOUS AND TROPICAL DISEASES CLINICAL HOSPITAL „DR. VICTOR BABES“

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ABSTRACT
In March 2020, the first patients diagnosed with COVID-19 were hospitalized in the Infectious and Tropical Diseases Clinical Hospital „Dr. Victor Babes“. Of the 20 patients, 11 were male and 9 were female. Patients were aged between 3 to 56 years. 8 patients traveled outside Romania during the incubation period of the disease. The most common symptom cluster encompassed the respiratory system: fever, cough and shortness of breath. 2 patients presented severe forms of disease that required transfer to the intensive care unit. Radiologically, 18 patients had interstitial lung damage. All patients had a favorable evolution.

Keywords: COVID-19, first patients, epidemiologic, clinical

INTRODUCTION
Coronaviruses belong to the family Coronaviridae, of the order Nidovirales, are viruses with a positive RNA genome, enveloped, and glycoprotein projections at this level suggest the appearance of halo or „crown“ visible on electron microscopy (1). There are 4 genera – alpha, beta, gamma, delta –, of which the first 2 affect mammals (2).

The virus is spread predominantly by air, through respiratory secretions, but also by fecal-oral route. Incubation varies between 3 and 14 days (3). The infection can be asymptomatic, mild, moderate or severe, even fatal. The main symptoms are fever, cough, dyspnea, headache, myalgia, anosmia, dysgeusia, diarrhea, vomiting (4). Severe forms may include respiratory failure, acute respiratory distress syndrome, septic shock, multiple organ failure/dysfunction (5).

Coronaviruses are a major public health problem because they can cross the species barrier. Thus, in the period 2002-2003 the first epidemic caused by SARS-CoV (Severe Acute Respiratory Syndrome – Coronavirus) broke out with a fatality rate of 10% (6,7), and in 2012, the epidemic caused by MERS (Middle East Respiratory Syndrome), broke out with a fatality rate in this case being 36% (8).
The novel coronavirus, later known as SARS-CoV-2, was identified in January 2020, after numerous cases of atypical pneumonia were reported in the Chinese city of Wuhan at the end of the previous year. The number of cases of infection caused by this virus has spread rapidly, across all continents, the World Health Organization declaring on March 11 the pandemic COVID-19.

In Europe, Italy was the first country to register a significant number of patients diagnosed with SARS-VOC2 infection. Of these, a significant percentage presented a severe form of the disease, requiring admission to the Intensive Care Units (9).

In Romania, the epidemic started on February 26, 2020 with the first case diagnosed in Gorj County, a patient contact with an Italian citizen.

The first cases were hospitalized in the Infectious and Tropical Diseases Clinical Hospital „Dr. Victor Babes” on March 9th, 3 members of the same family.

**OBJECTIVE**

To identify the socio-demographic, epidemiological and clinical-biological characteristics of patients.

**METHOD**

Retrospective, observational study on a group that includes the first 20 patients hospitalized and treated in the Infectious and Tropical Diseases Clinical Hospital „Dr. Victor Babes” from Bucharest.

The diagnosis of COVID-19 was established by PCR-type molecular tests of nasopharyngeal exudate.

Epidemiological data, clinical features and biological test results were obtained from patient observation sheets.

**RESULTS**

The group of studied patients consists of 11 men and 9 women aged between 3 years and 56 years. The average age is 34.45 years with a median of 35.5 years. 3 patients were under 18 years of age. From an epidemiological point of view, 8 patients were diagnosed with COVID-19 after returning to Romania - from Germany 2 patients, from London 2 patients, and 1 patient from Israel, Spain, Austria, Norway. The other 12 patients were healthcare workers at Gerota Hospital, where a patient recently returned from a trip to Israel was hospitalized with symptoms not characteristic of COVID-19, but which later progressed to severe pneumonia. He infected 50 members of medical staff.

All patients come from urban areas, most are non-smokers and deny excessive alcohol consumption.

In terms of severity, 18 patients had mild forms of disease, and 2 severe forms that required transfer to the intensive care unit. 14 patients had no associated conditions. One patient had an evolving pregnancy (S29) and minor left bundle branch block, and one patient with type 2 diabetes was being treated with oral antidiabetics, and another patient had sarcoidosis. Of the 2 patients with severe forms, one had grade 2 obesity, unbalanced type 2 diabetes, and the second had morbid obesity and obstructive sleep apnea syndrome, with the need for oxygen at home.

The most common symptoms at admission were fever (17 patients), dry cough (10 patients), odynophagia (8 patients), chills (5 patients), shortness of breath (4 patients), myalgias, anosmia and dysgeusia (3 patients), one patient complained of digestive manifestations (watery stools).

Most often, patients associated fever and cough (9 patients), followed by fever, cough and difficulty breathing (4 patients).

From a biological point of view, 17 patients presented with moderate-mild inflammatory syndrome, with changes in CRP, ESR, fibrinogen. 5 patients associated with lymphocytopenia, and hepatocytolysis was present in 3 patients. From a radiological point of view, 12 patients had accentuated bilateral basal interstitial pattern (7 men, 4 women), 6 unilateral interstitial involvement, and 2 patients did not show any radiological changes.

In the case of patients with mild disease, the number of days of hospitalization varied between 10 and 25, with an average of 12.7 days, without a clear correlation with symptoms or age. Patients with severe forms needed 31 days of hospitalization. The discharge was not made according to the clinical criteria, but according to the epidemiological one (2 negative samples at 24-hour interval, PCR from the nasopharyngeal exudate).

Mild forms that associated radiological changes were treated with Azithromycin associated with Hydroxychloroquine, and forms with normal radiological imaging received only Hydroxychloroquine and symptomatic treatment.

Patients with a severe form of the disease additionally required oxygen therapy, hydroelectrolytic and
acid-base support, vitamin therapy, gastroprotection, low molecular weight heparin in prophylactic doses, corticosteroids, Lopinavir/Ritonavir, and broad-spectrum antibiotic therapy. Given that the initial therapeutic response was unfavorable, an IL-6 inhibitor was administered, which resulted in a clinically biologically and radiologically favorable slow evolution.

**DISCUSSION**

This study provides a summary of the picture of SARS-COV2 virus infection, at its onset in Romania. In the literature, the first studies on SARS-COV2 infection come from China, where the first cases were recorded. These suggest that advanced age, male gender and the presence of comorbidities are potential risk factors for a severe form of the disease. (10,11). In the present study, both patients with severe forms of the disease were male, 1 patient was suffering from grade 2 obesity, unbalanced type 2 diabetes, and the second from morbid obesity and obstructive sleep apnea syndrome, with the need for oxygen at home.

Another study by Tabata et al. (12) on a group of 104 patients confirmed with COVID-19 aboard the cruise ship Diamond Princess suggests that the presence of lymphocytopenia at the onset of the disease, advanced age and the presence of comorbidities were more common in patients with severe forms. (28 patients developed severe forms out of a total of 104 included in the study). Regarding the current group, patients who developed severe forms were not old, but both were associated with comorbidities, and lymphocytopenia was present from the time of hospital admission.

Regarding the radiological aspect, studies in China show that the most common lung damage is bilateral, in the lower lung fields, peripheral (13,14), characteristics found in the study group. In the 2 patients with severe form of the disease, the appearance of condensation foci with bilateral disposition, respectively of the alveolo-interstitial infiltrates was observed on the pulmonary radiograph, especially at the level of the lower lung fields, with an increase in intensity and projection area simultaneously with the evolution. unfavorable disease (decreased SaO2, dyspnea and polypnea). These types of lesions were also found in patients diagnosed with COVID-19, included in the study conducted by Shi et al. Although the paraclinical investigation performed in his study was the CT examination, in this case too a bilateral and peripheral arrangement of opacities in matte glass was observed, which, with the evolution of the disease, multiplied and were replaced by lung consolidation (15). Thus, the worsening of the radiological image may be a risk factor for the reserved prognosis of patients with COVID-19, along with other variables (advanced age, male sex, associated comorbidities).

**CONCLUSIONS**

Epidemiologically, all cases were connected with imported patients. In 8 cases, the infectious contact occurred outside of the country, and in 12 cases in the country, but starting from an import case, a clear pattern of disease associated with travel medicine, and the receptivity was general. The most common symptom cluster encompassed the respiratory system: fever, cough and shortness of breath. From a biological point of view, minimal changes were registered, and from a radiological point of view, changes were registered in 18 patients.

Most patients had mild forms of the disease, the number of days of hospitalization was on average 12.7 days in patients with mild forms, respectively 31 days in patients with severe forms. Obesity male sex, low lymphocyte count were determining risk factors for progression to a severe form of the disease.

Under treatment the evolution was favorable in all cases and no deaths were recorded.
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