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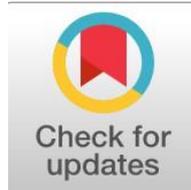
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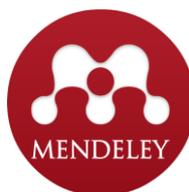# Article information

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Clinical and Laboratory Features of COVID-19 in Patients With Comorbid Conditions

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Abstract

General Background: Coronavirus disease 2019 (COVID-19) is a multisystem infectious disease with diverse clinical manifestations and outcomes, particularly among hospitalized patients. **Specific Background:** Individuals with chronic diseases frequently experience more complicated clinical courses during COVID-19 infection, requiring detailed clinical and laboratory assessment to understand disease progression. **Knowledge Gap:** Despite numerous investigations, uncertainty remains regarding which clinical and laboratory characteristics are associated with severe and critical forms of COVID-19 in patients with multiple underlying conditions. **Aims:** This study analyzed the clinical manifestations and laboratory characteristics of COVID-19 patients with comorbid conditions and identified indicators associated with severe disease progression. **Results:** A total of 182 hospitalized patients with moderate, severe, and critical COVID-19 were examined during 2021–2022 using comprehensive clinical, laboratory, and instrumental assessments. The majority presented with severe disease (80.8%). Coronary heart disease, hypertension, anemia, type 2 diabetes mellitus, and obesity were the most frequent accompanying conditions. Severe and critical cases were more common among elderly individuals and those with multiple concurrent disorders. Clinical manifestations included fever, cough, dyspnea, and weakness, frequently accompanied by bilateral or polysegmental pneumonia and respiratory failure. Laboratory findings showed leukocytosis, neutrophilia, lymphopenia, elevated erythrocyte sedimentation rate, increased C-reactive protein levels, hyperglycemia, and altered liver and renal function markers, particularly in critically ill patients. **Novelty:** The study provides integrated clinical and laboratory characterization of hospitalized COVID-19 patients with multiple concurrent diseases. **Implications:** Identification of these clinical and laboratory indicators supports early risk stratification, timely initiation of intensive treatment, and improved management of patients with severe COVID-19.

Highlights:

- Elderly Hospitalized Individuals Frequently Present Severe or Critical Disease Stages.
- Respiratory Failure and Bilateral Pneumonia Appear Commonly in Advanced Clinical Cases.
- Systemic Inflammation Markers and Metabolic Abnormalities Increase in Critically Ill Groups.

Keywords: COVID-19, Comorbidities, Laboratory Parameters, Pneumonia, Respiratory Failure.

Introduction

Worldwide, numerous studies are being conducted on the diagnosis, clinical course, and improvement of treatment and prevention methods for COVID-19 [1,2,3]. However, scientists around the world have not yet reached a definitive conclusion as to which patients are at risk of developing severe and critical forms of the disease. COVID-19 is a multisystem disease with a wide range of symptoms. The development of persistent symptomatic (subacute) and post-COVID syndromes does not depend on the severity of the disease. Patients who have recovered from acute COVID-19 may experience various symptoms, which can change over time [4,5].

The relevance of the problem is due to the fact that, according to the COVID-19 information resource, the number of patients who had recovered from coronavirus infection reached 6,161,835 from January to December 2020, of whom: moderate severity – 480,692; severe – 110,178; critical – 78,669; mild and other conditions – 5,492,296. Currently, according to the World Health Organization (WHO), complications after COVID-19 affect at least 10% of recovered individuals [6].

According to the data available to date, more than 86.6% of the adult population aged 30–79 years is susceptible to the disease. COVID-19 manifests with varying degrees of severity, ranging from mild to severe forms [3, 6, 13]. Children are less susceptible to infection, with statistics reporting 7–11% exposure and 1.7–2.2% incidence of illness [7,8]. Unlike adults, in 90% of cases, COVID-19 in children occurs in mild or moderate forms, or remains asymptomatic [9]. Nevertheless, children can act as latent carriers of the virus and pose a risk to individuals with comorbidities and the elderly (cardiovascular diseases, diabetes, hypertension, respiratory diseases), immunocompromised individuals (HIV infection, low CD4 count), and pregnant women, as these groups are at higher risk of infection [10,11].

Objective of the study: to analyze the clinical and laboratory characteristics of patients with COVID-19 at the present stage and to identify laboratory predictors of progression to severe and fatal forms of the disease.

Materials and Methods

We present data from our own study on the clinical and immunological parameters of patients with COVID-19. Material collection was carried out during 2021–2022 at the Zangiata Specialized Multidisciplinary Infectious Diseases Hospital, Block B. A total of 182 patients aged 23 to 63 years were examined. All patients underwent a complete clinical evaluation, including laboratory and instrumental investigations. A control group of 20 individuals was also examined.

Of the 182 patients, 18 were diagnosed with COVID-19 of moderate severity, 147 with severe COVID-19, and 17 with critical COVID-19.

The diagnosis was established based on clinical and functional data in accordance with the provisional guidelines "Prevention, Diagnosis, and Treatment of the Novel Coronavirus Infection (COVID-19)."

The obtained data were subjected to statistical analysis using Excel 2016, applying Student's t-test for variation statistics.

Results and Discussion

The largest group of patients examined consisted of those with severe forms of the disease (147; 80.8%), followed by patients with moderate forms (18; 9.9%) and those with critical forms (17; 9.3%).

The mean age of patients with moderate COVID-19 was 56.56 ± 3.2 years, those with severe disease – 63.01 ± 1.2 years, and those with critical disease – 62.18 ± 3.4 years (Fig. 1).

Analysis of the disease frequency by sex depending on severity showed that among patients with moderate COVID-19, women predominated (66.7%), whereas among those with critical disease, men predominated (76.5%). In the severe group, the distribution between men and women was nearly equal (49.7% and 50.3%, respectively).

Fig. 1. Distribution of examined patients by age depending on disease severity, %.
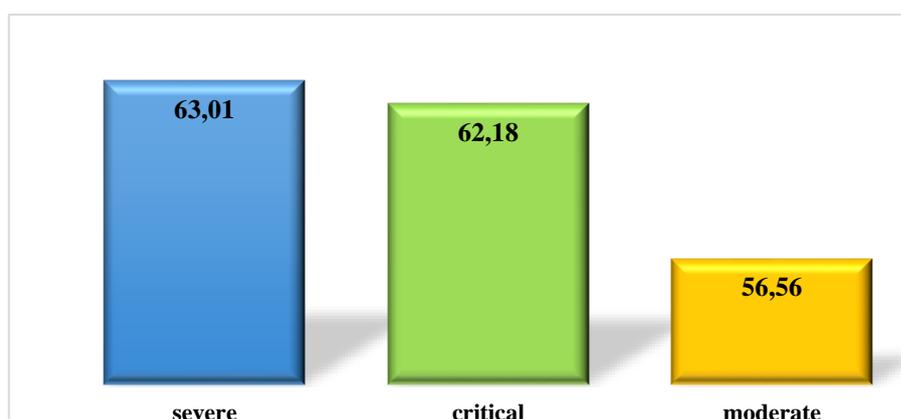
We analyzed the timing of hospital admission. The majority of patients were admitted between days 2 and 10 of the disease (108; 59.34%), with the highest numbers on day 3 (16; 8.9%), day 5 (16; 8.9%), day 7 (20; 11.0%), and day 10 (24; 13.2%). Patients with critical disease were mainly admitted on day 5 of illness (6; 35.3%).

Of the 182 patients, the majority were retirees (125; 68.7%) and unemployed individuals (38; 20.9%).

We analyzed the frequency of comorbid conditions among the patients. The analysis showed that 100.0% (182) of the patients had at least one comorbidity. The most common was coronary heart disease (CHD), identified in 110 patients (60.44%), and it was significantly more frequent in patients with critical (70.59%) and severe disease (62.59%). Hypertension (HT) was found in 93.4% of patients, with most cases being grade 3 hypertension, occurring similarly in patients with severe (65.31%) and critical (64.71%) disease. Another common comorbidity was anemia, observed in 120 patients (65.93%), mostly of grade 1 (44.9%) and grade 2 (20.4%) severity, predominantly among those with severe disease. Type 2 diabetes mellitus was diagnosed in 61 patients (33.5%), with 52 cases (28.6%) in patients with severe disease.

Obesity of varying degrees was found in 25 patients (13.8%), with 23 cases (12.6%) among patients with severe disease. Of all patients with overweight or obesity, 82.6% were female.

Several isolated cases of other comorbidities were also recorded: chronic hepatitis C (8; 4.4%), concomitant HIV infection (2; 1.1%), bronchial asthma (2; 1.1%), chronic obstructive pulmonary disease (COPD) in 5 patients (2.7%), liver cirrhosis (5; 2.7%), cachexia (7; 3.84%), and chronic pyelonephritis (5; 2.7%).

Many patients had multiple comorbidities. Our results regarding the analysis of concomitant diseases were consistent with previously published data from Italy and China, where the authors reported that patients infected with SARS-CoV-2 most commonly had hypertension, diabetes mellitus, and cardiovascular diseases in their medical history [12,13,14].

Compared to patients under 65 years of age, the older group had a higher prevalence of chronic comorbidities, particularly hypertension, chronic obstructive pulmonary disease (COPD), diabetes mellitus, cardiovascular diseases, and malignancies (all $P < 0.05$).

Next, we conducted a comparative analysis of the clinical manifestations in the patients with coronavirus infection included in our study.

One of the initial manifestations of the disease in the patients we examined was fever (98; 53.8%). Careful collection of the medical history revealed that most patients initially experienced a temperature up to 38°C, which later increased above 38°C, indicating a possible development of a COVID-19 complication—pneumonia. Comparative analysis of body temperature depending on disease severity showed that temperatures between 37°C and 38°C were observed with similar frequency in patients with moderate COVID-19 (64.22 ± 2.14%), while temperatures between 38°C and 39°C were more frequently recorded in patients with critical disease (45.5 ± 2.03%). Temperatures above 39°C were noted in 2 patients with severe disease (2.50 ± 0.18%) and 2 patients with critical disease (4.08 ± 0.20%).

Weakness was observed in 172 patients (94.51%), being more pronounced in those with severe disease (97.3%). Among the 182 patients with COVID-19, cough affected 133 patients (73.08%), mostly dry, occasionally with minimal sputum. Cough was reported in 109 patients (74.15%) with severe disease, in 13 of 18 patients (72.2%) with moderate disease, and in 11 of 17 patients (64.7%) with critical disease. Dyspnea was present in 170 patients (93.4%), with this symptom occurring in 142 patients (96.6%) in the severe group, 16 patients (88.9%) in the moderate group, and 12 patients (70.6%) in the critical group. Muscle pain was also a frequent symptom. Myalgia was reported in 85 patients (46.7%), predominantly in those with severe disease (71 patients; 48.3%). Among patients with critical disease, myalgia was more characteristic (52.5%) compared to patients with moderate (38.9%) and severe (46.7%) disease ($P < 0.05$). Headaches were reported by 90 patients (49.45%), with prevalence of 49.7% in the severe group, 55.56% in the moderate group, and 41.2% in the critical group.

We conducted an analysis of the physical examination of patients. Based on measurements of blood pressure (BP), pulse rate, respiratory rate, and blood oxygen saturation, it was found that, as expected, an increase in body temperature was accompanied by a rise in pulse rate[15]. In patients with moderate COVID-19, the average pulse increased to 86.83 ± 3.42 beats per minute, in those with severe disease to 90.23 ± 1.42 bpm, and in patients with critical disease, the pulse rate rose to 101.2 ± 2.36 bpm.

It has been shown that SARS-CoV-2 infection triggers an excessive, uncontrolled innate immune response with the release of an unbalanced amount of pro-inflammatory cytokines ("cytokine storm"), which in turn causes tissue damage, primarily affecting the lungs and blood vessels (Pathological Anatomy of SARS-CoV-2 Infection: N. B. Paramonova, T. P. Nekrasova, E. V. Kurilina, A. D. Kukleva, D. V. Kalinin, G. A. Demyashkin, S. A. Demura, E. M. Gretsov, T. R. Bagdasaryan, D. D. Protsenko, Y. S. Berezovsky, E. A. Kogan, A. B. Ponomarev, S. G. Radenska-Lopovok, L. A. Semenova, A. S. Tertychniy). Among the patients we observed, 97 (53.30%) presented with bilateral viral pneumonia, 76 (41.76%) had polysegmental pneumonia, and in 9 patients (4.95%), the disease occurred without lung involvement[16,17,18].

Of the total number of patients (n = 182), respiratory failure of varying severity was observed in 179 patients (98.35%): type 1 respiratory failure in 21 patients (11.53%), type 2 in 80 patients (43.95%), and type 3 in 78 patients (42.86%). In 3 patients (1.64%), no signs of respiratory failure were detected.

We conducted an analysis of the distribution of acute respiratory failure (ARF) according to disease severity and sex of the

patients. The results showed that type 1 ARF was predominantly observed in female patients, whereas type 2 and 3 ARF were mainly observed in male patients (Table 3.6).

The severity of pneumonia was determined by CT scan according to the accepted grading based on the extent of lung tissue involvement and was distributed as follows: CT-1 – 32.5%, CT-2 – 45%, CT-3 – 19.1%, and CT-4 – 3.3% of patients (Fig. 2).

Fig. 2. Lung condition in patients with COVID-19 according to CT data (%).
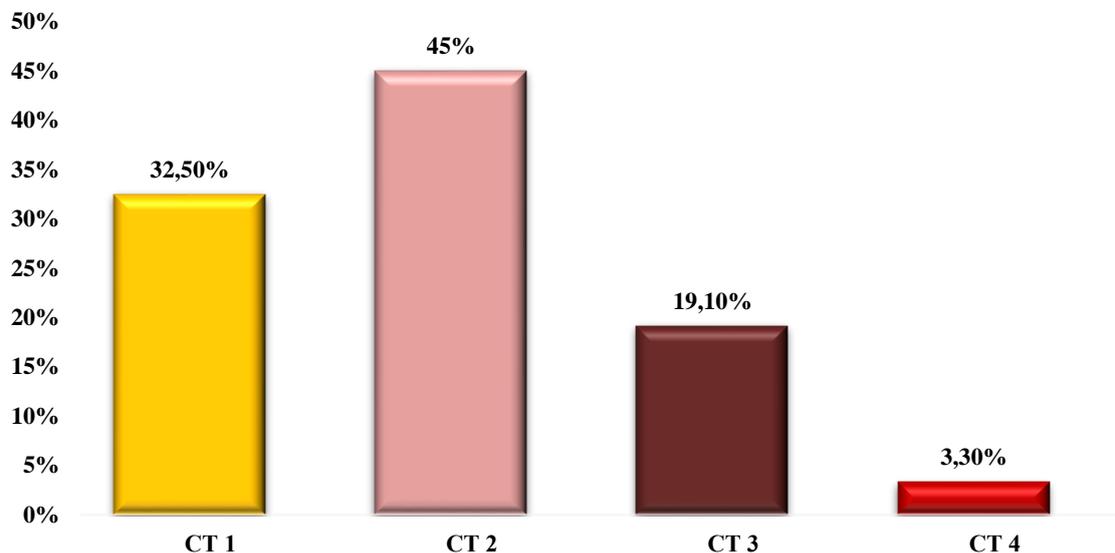
Compared to patients under 65 years of age, a higher proportion of elderly patients who underwent computed tomography upon admission showed bilateral lung involvement, combined pleural effusion, and higher rates of follow-up abnormalities on CT (P < 0.05).

We analyzed the prevalence of diabetes mellitus among the patients examined. According to the medical history, out of 182

patients, 61 (33.5%) were found to have type 2 diabetes mellitus, including 52 cases (28.6%) among patients with severe disease. Additionally, diabetes was newly diagnosed in 43 patients (23.63%) during the course of COVID-19.

The results of our observations of patients with COVID-19 showed that acute cardiovascular failure developed in 8 patients (4.40%) during the course of the disease, including 6 cases (4.0%) in patients with severe disease. Encephalopathy was observed in 12 patients (6.6% of the total group), of which 8 cases (5.44%) occurred in patients with severe disease.

Thus, the results of our analysis of the patients examined showed the development of complications characteristic of COVID-19 (bilateral or polysegmental pneumonia, acute cardiovascular and respiratory failure, diabetes mellitus), which were more pronounced in male patients over 60 years of age. In patients with severe and critical forms of the disease, all complications developed against the background of two or more concomitant conditions (CHD, hypertension, anemia, etc.).

In patients with COVID-19, key laboratory parameters were analyzed upon hospital admission. Low hemoglobin levels were observed in patients with severe and critical disease (106.7 ± 2.0 g/L and 105.6 ± 8.3 g/L, respectively), whereas in patients with moderate disease, hemoglobin levels were 118.8 ± 6.1 g/L. An elevated leukocyte count was detected in patients with COVID-19. Analysis of complete blood count (CBC) parameters showed leukocytosis in patients with severe and critical disease (12.7 ± 0.69 and 15.7 ± 2.5 × 10^3/mm³, respectively). Elevated erythrocyte sedimentation rate (ESR) also indicated the presence of an inflammatory process, with values of 24.0 ± 1.2 mm/h in severe cases, 19.9 ± 3.1 mm/h in moderate cases, and 23.0 ± 3.5 mm/h in critical cases.

Comparison of biochemical blood test results revealed a significant increase in C-reactive protein (CRP; normal range 0−5 mg/L), with an average level of 37.5 ± 2.5 mg/L. The highest CRP levels were observed in patients with critical disease (63.2 ± 9.3 mg/L).

A significant increase in blood glucose levels was observed, most pronounced in patients with severe and critical disease (8.3 ± 0.38 and 8.2 ± 0.96 mmol/L, respectively). Additionally, patients with critical disease showed a slight elevation in liver enzyme levels, total and direct bilirubin, and blood urea (Table 1).

Table 1 . Biochemical blood test parameters of COVID-19 patients before treatment

Parameters	Moderate (n=18)	Severe (n=147)	Critical (n=17)	Total (n=182)
Glucose (3.3–6.5 mmol/L)	7,5±0,90	8,3±0,38	8,2±0,96	8,2±0,33
ALT ≤ 40 U/L	26,2±3,6	36,9±2,9	43,1±10,3*	36,4±2,5

AST ≤ 40 U/L	28,6±4,3*	43,6±4,4	63,5±23,0•	44,0±4,1
Total protein (64–85 g/L)	69,7±1,5	66,2±0,51	65,3±1,6	66,4±0,45
Albumin (35–50 g/L)	34,9±1,8	33,7±0,41	32,7±0,99	33,7±0,32
Cholesterol ≤ 5.17 mmol/L	3,3±0,0	4,0±0,28	3,5±0,17	3,9±0,11
Urea (2.5–8.3 mmol/L)	5,6±0,50*	9,9±0,72	9,1±0,99•	9,4±0,58
Creatinine (62–115 mmol/L)	81,6±6,0*	107,4±7,2	109,0±1,30•	104,8±5,8
Total bilirubin ≤ 21.0 mmol/L	7,9±0,58*	14,9±1,6	26,8±10,1*•	15,8±1,5
Direct bilirubin 0–5.1 mmol/L	2,6±0,44*	7,0±1,3	7,9±2,4•	6,9±0,79
C-reactive protein (CRP)	34,0±19,2	34,1±3,3	63,2±9,3	37,5±2,5
Potassium (K+)	4,6±0,17	4,2±0,19	4,5±0,25	4,3±0,07
Sodium (Na+)	144,8±6,2	149,1±1,8	152,3±2,0	149,4±0,65
Calcium (2.02–2.6 mmol/L)	1,9±0,09	2,0±0,20	1,80±0,0	2,0±0,06

Note: * – $P > 0.05$, the difference is significant compared with patients with severe disease;• – $P > 0.05$, the difference is significant compared with patients with moderate disease.

It should be noted that during the course of the disease, elevated blood urea levels persisted in patients with critical and severe disease (10.4 ± 1.6 mmol/L), and a slight increase in creatinine levels was observed, up to 127.9 ± 15.9 μmol/L ($P > 0.05$).

Conclusion

Thus, patients with severe and critical COVID-19 develop an immunodeficient state with lymphopenia and show elevated laboratory indicators of systemic inflammation (including leukocyte, platelet, and lymphocyte counts; levels of CRP, D-dimer, ferritin, ALT, AST, total and direct bilirubin, creatinine, and blood urea) compared with healthy individuals and patients with moderate disease. These results are considered prognostic markers, the assessment of which is essential for predicting severe disease progression and fatal outcomes, as well as for timely initiation of intensive interventions and adjustment of treatment strategies.

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