UDC 616.988-022.6:616-071:615-074:355.72
https://doi.org/10.31612/2616-4868.4.2024.11

CLINICAL AND LABORATORY CHARACTERISTICS OF PATIENTS WITH CORONAVIRUS INFECTION COVID-19 AND ITS COMORBIDITY

Kateryna V. Yurko, Inna V. Andrusovych

Kharkiv National Medical University, Kharkiv, Ukraine

Summary

Introduction. The coronavirus disease has reached an alarming epidemic scale with extraordinary morbidity and mortality rates for the entire world population. The majority of patients with COVID-19 note damage to the respiratory tract and state a more severe course of the disease with the development of systemic damage. A more severe course of COVID-19 is associated with the presence of comorbid diseases.
Aim. To investigate and analyze clinical and laboratory manifestations and to determine the main comorbidities of patients with COVID-19 infection.
Materials and methods. The research was carried out in accordance with bioethical norms and rules. 179 patients with COVID-19 (the main group) and 42 people of the control group were examined. Diagnosis and treatment of the COVID-19 coronavirus infection was carried out taking into account the relevant national recommendations. The average value and standard deviation were statistically determined. The probability of differences was performed using the Mann-Whitney U-test and the Wilcoxon W-test of signed ranks. The threshold value of the level of statistical significance of all calculated features was taken as 0.05 (p=0.05).
Results. A high comorbidity with cardiovascular system pathology was found – 40.2 %, type 2 diabetes – 22.3 %, respiratory system diseases – 20.7 %. Disorders of the functional state of the cardiovascular system were determined: pulse values – 91.01±13.44, systolic (127.9±15.19) and diastolic (79.3±11.6) blood pressure. Changes in clinical blood analysis were noted: erythrocytes – 4.38±0.65 $x^{10}12$/l, hemoglobin – 127.6±21.2 g/l, hematocrit – 0.37±0.07, leukocytes – 10.7±7, 32 $x10^9$/l, segmented (65.4±14.8 %) and rod-nuclear (9.03±9.99 %) neutrophils, platelets – 226.1±90.6 x109/l, lymphocytes – 20.24±12.43 %, monocytes – 6.60±4.37 % and erythrocyte sedimentation rate (ESR) – 25.4±14.9 mm/h. Significant (almost fourfold) increases in IL-6 levels (24.56±22.9 pg/ml) and blood glucose concentrations (7.40±3.42 mmol/l) were determined.
Conclusions. A significant comorbidity of COVID-19 was determined and a significant prevalence of indicators of the functional state of the cardiovascular system and a decrease in the average levels of the quantitative composition of erythrocytes and indicators of hemoglobin and hematocrit were established. Significant leukocytosis, neutrophilia, lymphocytosis and monocytosis, significant excesses of ESR and IL-6 and blood serum glucose were determined, which confirmed the presence of a significant inflammatory reaction in response to infection with COVID-19.

Keywords: **COVID-19, comorbidity, clinical and laboratory characteristics**

INTRODUCTION

It is determined by many researchers that the coronavirus disease (COVID-19), the first manifestations of which were recorded at the end of 2019, in a relatively short period of time has acquired the threatening scale of an epidemic with extraordinary levels of morbidity and mortality (more than 10.0 % [1]) of the entire world population [2-4]. The World Health Organization defined this disease as severe acute respiratory syndrome (SARS), which was caused by the type 2 coronavirus (SARS-CoV-2) [5]. This disease was the third zoonotic coronavirus that triggered an epidemic in the last few years [6]. According to the definitions of scientists, bats

are considered the primary reservoir of this virus, as it was established that the viruses isolated from them are highly related to SARS-CoV-2 [7].

It was determined that this type of coronavirus primarily affects the epithelium of the respiratory tract [8] and enters the cells through interaction with the receptors of angiotensin 2-converting enzyme [9].

It should be noted that the majority of patients with COVID-19 have lesions of the respiratory tract and state a more severe course of the disease with the development of systemic lesions (resistant fever, acute lung injury, acute respiratory distress syndrome, shock, and multiple organ failure) [6, 10]. The development of multiple organ failure develops due to a combination of diffuse intravascular coagulation and the formation of large vessel thrombosis [3]. A more severe course of COVID-19 is associated with the presence of comorbid diseases. The risks of hospitalization in patients with COVID-19 and bronchial asthma are 1.5 times higher, with chronic kidney disease and diabetes – 4 and 3 times, respectively [11]. Scientists [10] determine that among the risk factors that affect the deterioration of the course of COVID-19, concomitant pathology is of primary importance.

High levels of population mortality due to COVID-19 are determined by the pathogenesis of the development of disorders, the main place of which is occupied by the inflammatory reaction and subsequent severe multiorgan damage [1]. Clinically, this manifests itself as SARS, which is characterized by diffuse damage to the alveoli at the level of hyaline membranes [12]. The immune response can be manifested by the development of a cytokine storm (a significant increase in the levels of interleukin (IL)-6, IL-17A and tumor necrosis factor-α) [1]. Stimulation of thrombus formation is significantly enhanced during the development of inflammation induced by endothelial dysfunction. This process is accompanied by the production of IL-6 by the endothelium, which strengthens its own immune response (up to the development of a state of hyperstimulation – a cytokine storm [4]).

In addition to an increase in the levels of IL-6 and IL-17A, these processes are accompanied by an increase in the levels of IL-1β, interferon-γ and macrophage inflammatory protein, which affects the link of hemostasis [1] through dysregulation of endothelial integrity and function and further intensification of von Willebrand factor production [9] and adhesion molecules (E-selectin, integrins and type 1 intercellular adhesion molecule [8]). These pro-inflammatory cytokines determine the excessive formation of blood clots and hyperactivation of platelets [1]. As a result, the endothelium performs a proinflammatory and procoagulant effect and strongly involves platelets and leukocytes in this process [8].

Some scientists [4] define the complex processes of inflammation, immune response, and procoagulation in COVID-19 as Virchow's triad (damage to blood vessels, impaired blood flow, and hypercoagulation). This triad explains and combines all the processes that precede thrombus formation in patients with COVID-19 [4]. Pathogenetically, dysregulation of the complement system is another mechanism for the development of increased coagulation (which enhances pro-inflammatory effects and prothrombotic effects: activation of platelets, endotheliocytes, tissue factors and expression of von Willebrand factor [9].

Thus, determining the clinical and laboratory manifestations of COVID-19 and the accompanying pathology of such patients is a very urgent task of modern medicine.

AIM

To investigate and analyze clinical and laboratory manifestations and to determine the main comorbidities of patients with COVID-19 infection.

MATERIALS AND METHODS

The study was conducted at the department of infectious and pediatric infectious diseases, parasitology, Phthisiology and pulmonology of the Kharkiv National Medical University and on the basis of the communal non-commercial enterprise (KNE) «Kharkiv Regional Infectious Hospital» of the Kharkiv City Council (KhCC) in the period 2020-2023 Laboratory methods of research were carried out on the basis of the KNE «Kharkiv Regional Infectious Disease Hospital» and on the basis of the laboratory complex of the Kharkiv Regional Center of Blood Service and Medical Laboratory «Analytika».

The conducted research was carried out in accordance with the existing international and domestic bioethical norms and rules (Nuremberg Code of Ethical Principles of Conducting Experiments on Humans, Declaration of Helsinki, International Guidelines on the Ethics of Biomedical Research, Council of Europe Convention on Human Rights and Biomedicine, and others). All subjects were informed about their voluntary participation in the study and the confidentiality of the information received and participated in the study entirely of their own free will (confirmed by personally signing the appropriate informed consent). Were examined 179 patients with coronavirus infection COVID-19 (according to ICD XI revision – code RA01.0 «Identified COVID-19») aged 20-88, who were treated at the KNE «Kharkiv Regional Infectious Disease Hospital» KhCC in the period 2020-2021 (main group) and 42 people of the control group (practically healthy people who are blood donors, randomized by age and sex).

Among all examined (n=221), the average age was 56.20±15.06 years; there were almost equal numbers of

men and women (50.23 % and 49.77 %, respectively); the majority were elderly and senile (50-59 years old – 23.08 %; 60-69 years old – 22.62 % and over 70 years old – 22.17 %) compared to those examined under 40 (16.29 %) and 40-49 (15.84 %) years old. In the main (n=179) group, the average age of patients was 58.75±13.82 years; the majority (53.63 %) were female compared to males (46.37 %) and belonged to the elderly and senile (50-59 years – 25.70 %; 60-69 years – 24.58 % and over 70 years old – 25.14 %) compared to persons under 40 (11.17 %) and 40-49 (13.41 %) years old. Among the individuals of the control group (n=42), the average age was 45.36±15.31 years; the majority were men (66.67 %) versus women (33.33 %) and persons under 40 (38.10 %) and 40-49 (26.19 %) as opposed to 50-59 (11.90 %), 60-69 (14.29 %) and 70 and older (9.52 %) years.

Diagnosis and treatment of the COVID-19 coronavirus infection was carried out taking into account the relevant national recommendations [13-16].

The statistical calculation of the obtained results was carried out using the appropriate package of statistical application programs: Microsoft Excel 365, Statsoft Statistica 10.0 and IBM SPSS 25.0 for Windows. The distribution of the obtained quantitative signs was assessed visually using the graphical method and using the Kolmogorov-Smirnov and Lilliefors and Shapiro-Wilk criteria. The evaluation of the obtained data determined significant differences from the normal nature of the distribution, therefore, in the future, the methods of non-parametric statistics were used for calculations.

To characterize the central tendency and variability of quantitative signs (continuous or interval), the average value (M) and standard square deviation (SD, σ) were determined. Results were presented as: M±SD.

The probability of differences in the obtained quantitative values of two unrelated groups was performed using the Mann-Whitney U-test, and in related groups, using the Wilcoxon W-test of signed ranks. The obtained qualitative (binomial, ordinal, nominal, etc.) indicators were presented in absolute and relative (percentage) values. The results were presented as: abs. (%). Comparison of groups by qualitative characteristics was performed by constructing four-field or arbitrary tables and calculating the Pearson's χ^2 conjugation criterion and providing the appropriate value of the χ^2 criterion.

The threshold value of the level of statistical significance of all calculated features was taken as 0.05 (p=0.05). When conducting multiple comparisons of the obtained values, Bonferroni correction was used to correct the confidence level.

The work is a fragment of research work. The Department of Infectious and Pediatric Infectious Diseases, Parasitology, Phthisiology and Pulmonology Kharkiv National Medical University «Aetiopathogenetic, clinical and immunological features of the course of current viral and bacterial infectious diseases and improvement of medical and diagnostic tactics» (state registration number 0120U002111), deadline: 2020-2024, project leader – Professor of the Department of Infectious and Pediatric Infectious Diseases, Parasitology, Phthisiology and Pulmonology Kharkiv National Medical University, Doctor of Medical Sciences, professor Vasily P. Malyi.

RESULTS

First of all, we determined the age characteristics of patients with the COVID-19 coronavirus infection and persons of the control group – table 1.

Table 1

Age and anamnestic characteristics of the examined patients of the main group and persons of the control group (M±SD)

Indicator	main group (n=179)	control group (n=42)	p
Age, years	58,7±13,9	45,4±15,5	<0,001
Pre-hospitalization duration, days	5,68±4,16	–	–
Duration of hospitalization, days	18,5±8,83	–	–

Notes: Probability of difference between main and control groups.

It was established that patients with a coronavirus infection probably (p<0.001) had higher age characteristics (58.7±13.9 years) compared to individuals of the control group (45.4±15.5 years). At the same time, among patients of the main group, the average length of time before their hospitalization in the clinic was 5.68±4.16 days, and the length of hospitalization itself was 18.5±8.83 days – table 1.

In turn, according to the clinical characteristics of the state of the cardiovascular system (CVS) and the respiratory system of the examined persons compared to the control group, a significant prevalence of indicators of the functional state of the CVS was probably established: respectively, pulse values – 91.01±13.44 and 71.1±6.52 beats/min (p<0.001), systolic blood pressure (SBP) – 127.9±15.19 and 119.9±8.37 mm Hg. Art. (p=0.001), diastolic blood pressure (DBP, unlikely) – 79.3±11.6 and 78.7±7.0 mm Hg. Art. (p=0.754), which determined the degree of response to infection with the COVID-19 infection – table 2.

Table 2

Clinical characteristics of patients in the main group and those in the control group (M±SD)

Indicator	main group (n=179)	control group (n=42)	p
Pulse, beats/min	91,01±13,44	71,1±6,52	<0,001
Temperature,^{0}C	37,67±0,85	36,7±0,22	<0,001
SBP, mm Hg Art.	127,9±15,19	119,9±8,37	0,001
DBP, mm Hg Art.	79,3±11,6	78,7±7,0	0,754
Saturation, %	76,0±11,6	97,9±1,52	<0,001

Notes: Probability of difference between main and control groups.

At the same time, among the patients of the main group, there was probably ($p<0.001$) a significant decrease in the average levels of saturation compared to the individuals of the control group (76.0±11.6 and 97.9±1.52 %, respectively) and an increase in body temperature to subfebrile values (respectively 37.67±0.85 and 36.7±0.22^{0}C), which also marked the degree of response to infection with the COVID-19 virus – table 2.

In addition, we determined the gender characteristics of the examined patients of the main group and persons of the control group, as well as medical and anamnestic characteristics of the course of the disease due to COVID-19. The study proved that the subjects of the main and control groups were probably of equal age-sex characteristics, which indicated the representativeness of the results obtained in our study in terms of all studied parameters and the ability of the formed sample to characterize the general population. Thus, it was established that probably ($p=0.018$; $\chi^2=5.606$) among the patients of the main group, the majority were women (53.6 %) compared to men (33.3 %), and among the control group – on the contrary, the majority there were men (66.7 %) in contrast to women (46.4 %) – table 3.

Table 3

Age-sex and clinical anamnestic characteristics of the examined patients of the main group and persons of the control group (abs. (%))

Indicator		main group (n=179)	control group (n=42)	p, χ^2
Sex	female	96 (53,6)	14 (33,3)	0,018 5,606
	male	83 (46,4)	28 (66,7)	
Age group	up to 40 years	20 (11,2)	16 (38,1)	<0,001 26,786
	40-49 years	24 (13,4)	11 (26,2)	
	50-59 years	46 (25,7)	5 (11,9)	
	60-69 years	44 (24,6)	6 (14,3)	
	70 and older years	45 (25,1)	4 (9,5)	
The difficulty of the course	non-available	–	42 (100,0)	–
	severe	93 (52,0)	–	
	medium severity	60 (33,5)	–	
	easy	26 (14,5)	–	
Lethality		35 (19,6)	–	–
accompanying pathology				
CVD		72 (40,2)	–	–
Hypertensive disease (HD)		1 (0,6)	–	–
Heart failure (HF)		–	–	–
Pathology of the respiratory system		37 (20,7)	–	–
Type 2 diabetes (T2DM)		40 (22,3)	–	–
Gastrointestinal tract (GT)		18 (10,1)	–	–
Thrombosis		1 (0,6)	–	–
Stroke		5 (2,8)	–	–
Infarct		8 (4,5)	–	–
Neurological pathology		5 (2,8)	–	–
Other diseases		34 (19,0)	–	–

Notes: Probability of difference between main and control groups.

At the same time, it is probable ($p<0.001$; $\chi^2=26.786$) that among patients with COVID-19, the majority were older people (50-59 years old – 25.7 %; 60-69 years old – 24.6 % and 70 years and older – 25.1 %) compared to younger patients (11.2 % under 40 years and 13.4 % between 40 and 49 years), and in the control group, the majority were younger (38.1 % under 40 years and 40-49 years old – 26.2 % of people), in contrast to older people

(50-59 years old – 11.9 %; 60-69 years old – 14.3 % and 70 years and older – 9.5 %) – table 3.

It should be noted that the examined patients of the main group were characterized mainly by a severe course of the disease due to COVID-19 (52.0 %) and had a moderately severe (33.5 %) course in contrast to a mild one (14.5 %). At the same time, significant levels of mortality (19.6 %) were determined among the examined patients of the main group. These features confirmed the need for hospitalization in severe and moderate course of this infection and indicated a significant prevalence of severe forms of the disease – table 3.

In addition, a large percentage of existing concomitant pathology was determined among the patients of the main group, which significantly aggravated the course of the main disease and characterized the presence of most severe and moderate forms of the disease and high levels of mortality among such persons. Thus, a high prevalence of CVD was established – 40.2 %, presence of T2DM – 22.3 %, diseases of the respiratory system – 20.7 %, and other diseases – 19.0 %. In addition, diseases of the GT were noted – 10.1 %, heart attacks – 4.5 %, neurological pathology – 2.8 %, strokes – 2.8 %, thrombosis – 0.6 % and HD – 0.6 % – table. 3.

Next, an analysis of the obtained laboratory-instrumental characteristics of the patients of the main group and the individuals of the control group was carried out.

First of all, we determined the peculiarities of the response of clinical blood analysis indicators to infection with COVID-19 at the time of admission to the clinic – table 4.

Table 4

Characteristics of the clinical blood analysis of the examined patients of the main group and persons of the control group at the time of admission to the clinic (M±SD)

Indicator	main group (n=179)	control group (n=42)	p
Erythrocytes, $x10^{12}$/l	4,38±0,65	4,94±0,52	<0,001
Hemoglobin, g/l	127,6±21,2	136,5±11,8	0,009
Hematocrit	0,37±0,07	0,43±0,03	<0,001
Leukocytes, $x10^{9}$/l	10,7±7,32	5,9±1,2	<0,001
Segmented nuclear (s/n) neutrophils, %	65,4±14,8	78,5±3,9	<0,001
Rod-nuclear (r/n) neutrophils %	9,03±9,99	7,23±2,87	0,252
Platelets, $x10^{9}$/l	226,1±90,6	270,9±26,5	<0,001
Lymphocytes, %	20,24±12,43	7,90±2,4	<0,001
Monocytes, %	6,60±4,37	5,14±1,9	0,036
Erythrocyte sedimentation rate (ESR), mm/h	25,4±14,9	2,50±1,44	<0,001

Notes: Probability of difference between main and control groups.

The results showed a decrease in the average levels of the quantitative composition of erythrocytes (the levels of which were still within the physiological norm), hemoglobin (lower limits of reference values were noted), hematocrit (lower limits of the norm), leukocytosis, significant neutrophilia and lymphocytosis and monocytosis, and significant excesses of ESR. These features confirm the presence of a significant inflammatory response in response to COVID-19 infection and indicate a likely high discrepancy with the control group, which was within the normal range (table 4).

Thus, the values of the clinical blood test among the main group and the control group were as follows: erythrocytes – 4.38±0.65 and 4.94±0.52 $x10^{12}$/l ($p<0.001$), hemoglobin – 127.6±21.2 and 136.5±11.8 g/l ($p=0.009$), respectively hematocrit – 0.37±0.07 and 0.43±0.03 ($p<0.001$), leukocytes – 10.7±7.32 and 5.9±1.2 $x10^{9}$/l ($p<0.001$), s/n – 65.4±14.8 and 78.5±3.9 % ($p<0, 001$) and r/n (not significant) – 9.03±9.99 and 7.23±2.87 % ($p=0.252$) neutrophils, platelets – 226.1±90.6 and 270.9±26.5 $x10^{9}$/l ($p<0.001$), lymphocytes – 20.24±12.43 and 7.90±2.4 % ($p<0.001$), monocytes – 6.60±4.37 and 5.14±1.9 % ($p=0.036$) and ESR – 25.4±14.9 and 2.50±1.44 mm/h ($p<0.001$) – table 4.

In turn, the levels of IL-6 in patients with COVID-19 were expected to be significantly (almost four times) higher than the reference values and at the time of admission to the clinic were recorded at the levels of 24.56±22.9 pg/ml – table 5.

Table 5

Characteristics of IL-6 concentration of examined patients of the main group and individuals of the control group at the time of admission to the clinic (M±SD)

Indicator	main group (n=179)	control group (n=42)	p
IL-6, pg/ml	24,56±22,9	–	–

Notes: Probability of difference between main and control groups.

These values are precisely characteristic of patients infected with COVID-19, as IL-6 is a marker of the cytokine response and at the same time a marker of sepsis and an indicator of the threat of a cytokine storm [6], which often develops in severe forms of infection, and is clinically marked by a significant increase in the concentration of IL-6 in the blood plasma of patients with COVID-19. In the case of a cytokine storm effect, IL-6 affects the blood clotting process, causing disseminated intravascular coagulation syndrome and cardiomyopathy and significant respiratory failure.

In turn, the concentration of glucose in the blood serum of patients with SARS-CoV-2 infection was significantly elevated (7.40±3.42 mmol/l) and significantly ($p<0.001$) almost one and a half times higher than the levels of the control group (4.78±0.65 mmol/l) – table 6.

Table 6

Characteristics of glucose concentration of examined patients of the main group and persons of the control group at the time of admission to the clinic (M±SD)

Indicator	main group (n=179)	control group (n=42)	p
Blood serum glucose, mmol/l	7,40±3,42	4,78±0,65	<0,001

Notes: Probability of difference between main and control groups.

It should be noted that high glucose levels are often associated with a significantly severe course of COVID-19 (ranging from lung damage to the development of thrombosis and multiple organ failure), and the significant excesses among patients in the main group explain their hospitalization, as its risks increase almost 3-fold in T2DM and increased glucose levels [11].

DISCUSSION

Our results regarding the significant comorbidity of patients with COVID-19 and significant disorders of clinical and laboratory parameters are fully confirmed by the results of other studies. Thus, in the presence of concomitant hypertension, the risk of mortality increases by at least 1.7-3.5 times [1], in the presence of grade I-II obesity – by 3 times [11]. According to the results of Pranata R. et al. [17], CVD and cerebrovascular disease were the leading comorbidity in patients with COVID-19. Another meta-analysis by Pranata R. et al. [18] showed the impact of concomitant hypertension on the course of COVID-19: hypertension was significantly associated with total negative outcomes of COVID-19: hazard ratio (HR)=2.11 [95.0 % confidence intervals (CI) 1.85-2.40], $p<0.001$. Analysis by COVID-19 outcome groups showed that HD was significantly ($p<0.001$) associated with increased mortality: HR=2.21 [95.0 % CI 1.74-2.81]; severe COVID-19: HR=2.04 [95.0 % CI 1.67-2.47], $p<0.001$; SARS development: HR=1.64 [95.0 % CI 1.11-2.43], $p<0.001$; need for transfer to the intensive care unit: HR=2.11 [95.0 % CI 1.34-3.33], $p<0.001$; and infection progression: HR=3.01 [95.0 % CI 1.51-5.99], $p<0.001$ [18].

Zhou Y. et al. [10] showed that in patients with moderate to moderately severe COVID-19, comorbidities included obesity (42.0 % [95.0 % CI 34-49]), hypertension (40.0 % [95.0 % CI]), and T2DM (17.0 % [95.0 % CI 15-20]).

According to the results of Lu G. and Wang J. [19], in the first week after hospitalization significant decreases of leukocytes, neutrophils, lymphocytes, monocytes, eosinophils, erythrocytes, hemoglobin and the ratio of neutrophils, lymphocytes, platelets and platelet lymphocyte ratio.

According to Gordienko P. O. and Knyazkova I. I. [20], significant increases in IL-6 levels in COVID-19 were confirmed, which was associated with the severity of the disease.

Another study by Zizzo G. et al. [21] found that IL-6 levels in the blood circulation and bronchoalveolar lavage fluid in patients with COVID-19 progressively increase with increasing severity of the disease and reach maximum values in patients in critical condition. In mild COVID-19 disease, IL-6 is released by SARS-CoV-2-infected respiratory epithelial cells and by infiltration of CD14+CD16+ monocytes-macrophages and CD4+ T cells. In addition, the authors note that IL-6 significantly disrupts the regulation of the immune response in COVID-19, mainly acting in two ways: on the one hand, it can cause dysfunction of natural killer and cytotoxic CD8+ T cells, weakening antiviral protection; on the other hand, it can inhibit the differentiation of regulatory T cells and cause T helper 17 (TH17)-like polarization of γ/δ and α/β CD4+ T cells, which provokes the development of uncontrolled hyperinflammation. The authors determine that in the later stages, these mechanisms cause a condition similar to macrophage activation syndrome, which is accompanied by lymphocyte depletion and aberrant innate immune responses, vascular leakage, coagulopathy, and multiple organ failure, which was observed in our patients. In fact, in significantly severe COVID-19 disease, significantly increased levels of IL-6 are associated with higher viral load, lymphopenia, systemic inflammation, neutrophilia, hypoxemia, and a poor prognosis.

CONCLUSIONS

Thus, the study revealed a significant comorbidity of COVID-19 with the pathology of the CVS, T2DM,

respiratory system and other diseases. Significant predominance of indicators of the functional state of the CVS and a decrease in the average levels of the quantitative composition of red blood cells and hemoglobin and hematocrit were found. Significant leukocytosis, neutrophilia, lymphocytosis and monocytosis, significant elevations of ESR and IL-6 and serum glucose were detected, which confirmed the presence of a significant inflammatory response in response to COVID-19 infection.

Prospects for further research. For a more objective assessment of the results, further studies are needed due to a longer period.

FUNDING AND CONFLICT OF INTEREST

The study was conducted as a part of the complex research work of the Department of Infectious and Pediatric Infectious Diseases, Parasitology, Phthisiology and Pulmonology of Kharkiv National Medical University «Etiopathogenetic, clinical and immunological features of the course of current viral and bacterial infectious diseases and improvement of treatment and diagnostic tactics» (state registration number 0120U002111, term of execution 2020-2024). The authors declare the complete absence of any conflict of interest in the performance of this work.

COMPLIANCE WITH ETHICAL REQUIREMENTS

The ethical approval was obtained from Bioethics Committee of the Kharkiv National Medical University. All patients provided written consent to participate in research in accordance with the recommendations of the Ethics Committees for Biomedical Research, Ukrainian Health Legislation and the Declaration of Helsinki of 2000.

LITERATURE

1. Miesbach W., Makris M. COVID-19: Coagulopathy, Risk of Thrombosis, and the Rationale for Anticoagulation. Clin Appl Thromb Hemost. 2020. Vol. 26. P. 1-7. doi: https://doi.org/10.1177/1076029620938149.
2. Connors J. M., Levy J. H. COVID-19 and its implications for thrombosis and anticoagulation. Blood. 2020. Vol. 135 (23). P. 2033-2040. doi: https://doi.org/10.1182/blood.2020006000.
3. Ackermann M., Verleden S. E., Kuehnel M., Haverich A., Welte T., Laenger F., Vanstapel A., Werlein C., Stark H. et al. Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. N Engl J Med. 2020. Vol. 383 (2). P. 120-128. doi: https://doi.org/10.1056/NEJMoa2015432.
4. Ahmed S., Zimba O., Gasparyan A. Y. Thrombosis in Coronavirus disease 2019 (COVID-19) through the prism of Virchow's triad. Clin Rheumatol. 2020. Vol. 39 (9). P. 2529-2543. doi: https://doi.org/10.1007/s10067-020-05275-1.
5. Pons S., Fodil S., Azoulay E., Zafrani L. The vascular endothelium: the cornerstone of organ dysfunction in severe SARS–CoV-2 infection. Crit Care. 2020. Vol. 24 (1). P. 353. doi: https://doi.org/10.1186/s13054-020-03062-7.
6. Coomes E. A., Haghbayan H. Interleukin-6 in Covid-19: A systematic review and meta–analysis. Rev Med Virol. 2020. Vol. 30 (6). P. 1-9. doi: https://doi.org/10.1002/rmv.2141.
7. Андрейчин М. А., Ничик Н. А., Завіднюк Н. Г., Йосик Я. І., Іщук І. С., Івахів О. Л. COVID-19: епідеміологія, клініка, діагностика, лікування та профілактика. Інфекційні хвороби. 2020. Вип. 2. С. 41-55. doi: https://doi.org/10.11603/1681-2727.2020.2.11285.
8. McFadyen J. D., Stevens H., Peter K. The Emerging Threat of (Micro)Thrombosis in COVID-19 and Its Therapeutic Implications. Circ Res. 2020. Vol. 127 (4). P. 571-587. doi: https://doi.org/10.1161/CIRCRESAHA.120.317447.
9. Franchini M., Marano G., Cruciani M., Mengoli C., Pati I., Masiello F., Veropalumbo E., Pupella S., Vaglio S. et al. COVID-19-associated coagulopathy. Diagnosis (Berl). 2020. Vol. 7 (4). P. 357-363. doi: https://doi.org/10.1515/dx-2020-0078.
10. Zhou Y., Yang Q., Chi J., Dong B., Lv W., Shen L., Wang Y. Comorbidities and the risk of severe or fatal outcomes associated with coronavirus disease 2019: A systematic review and meta–analysis. Int J Infect Dis. 2020. Vol. 99. P. 47-56. doi: https://doi.org/10.1016/j.ijid.2020.07.029.
11. Середюк Н. М., Середюк В. Н., Скакун О. З., Ванджура Я. Л., Твердохліб І. З. Коронавірусна хвороба (COVID-19): особливості перебігу та лікування інфаркта міокарда і серцевої недостатності. Art of Medicine. 2020. Вип. 3 (15). С. 182-188. doi: https://doi.org/10.21802/artm.2020.3.15.182.
12. Magro C., Mulvey J. J., Berlin D., Nuovo G., Salvatore S., Harp J., Baxter-Stoltzfus A., Laurence J. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases. Transl Res. 2020. Vol. 220. P. 1-13. doi: https://doi.org/10.1016/j.trsl.2020.04.007.

13. Наказ МОЗ України від 28.03.2020 № 722 «Організація надання медичної допомоги хворим на коронавірусну хворобу (COVID-19)». URL: https://moz.gov.ua/article/ministry–mandates/nakaz–moz–ukraini–vid-28032020––722-organizacija–nadannja–medichnoi–dopomogi–hvorim–na–koronavirusnu–hvorobu–covid-19.
14. Наказ МОЗ України від 2.04.2020 № 762 «Про затвердження протоколу «Надання медичної допомоги для лікування коронавірусної хвороби (COVID-19)». URL: https://moz.gov.ua/article/ministry–mandates/nakaz–moz–ukraini–vid-2042020––762-pro–zatverdzhennja–protokolu–nadannja–medichnoi–dopomogi–dlja–likuvannja–koronavirusnoi–hvorobi–covid-19.
15. Протокол «Надання медичної допомоги для лікування коронавірусної хвороби (COVID-19)» від 01.04.2020 відповідно до Закону України від 30.03.2020 № 539IX «Про внесення змін до деяких законів України щодо забезпечення лікування коронавірусної хвороби (COVID-19)». URL: https://zakon.rada.gov.ua/laws/show/539-20#Text.
16. Зміни до Стандартів медичної допомоги «Коронавірусна хвороба (COVID-19)» (наказ МОЗ України від 20.05.2020 № 1227). URL: https://moz.gov.ua/article/ministry–mandates/nakaz–moz–ukraini–vid-20052020––1227-pro–zatverdzhennja–zmin–do–standartiv–medichnoi–dopomogi–koronavirusna–hvoroba–covid-19.
17. Pranata R., Huang I., Lim M. A., Wahjoepramono E. J., July J. Impact of cerebrovascular and cardiovascular diseases on mortality and severity of COVID-19-systematic review, meta-analysis, and meta-regression. J Stroke Cerebrovasc Dis. 2020. Vol. 29 (8). P. 104949. doi: https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104949.
18. Pranata R., Lim M. A., Huang I., Raharjo S. B., Lukito A. A. Hypertension is associated with increased mortality and severity of disease in COVID-19 pneumonia: A systematic review, meta-analysis and meta-regression. J Renin Angiotensin Aldosterone Syst. 2020. Vol. 21 (2). P. 1470320320926899. doi: https://doi.org/10.1177/1470320320926899.
19. Lu G., Wang J. Dynamic changes in routine blood parameters of a severe COVID-19 case. Clin Chim Acta. 2020. Vol. 508. P. 98-102. doi: https://doi.org/10.1016/j.cca.2020.04.034.
20. Гордієнко П. О., Князькова І. І. Особливості медикаментозного лікування артеріальної гіпертензії хворих на COVID-19. Збірник наукових праць ΛΌГОΣ. 2021. Вип. 3. С. 94-95. doi: https://doi.org/10.36074/logos-26.02.2021.v3.31.
21. Zizzo G., Tamburello A., Castelnovo L., Laria A., Mumoli N., Faggioli P. M., Stefani I., Mazzone A. Immunotherapy of COVID-19: Inside and Beyond IL-6 Signalling. Front Immunol. 2022. Vol. 13. P. 795315. doi: https://doi.org/10.3389/fimmu.2022.795315.

REFERENCES

1. Miesbach, W., Makris, M. (2020) COVID-19: Coagulopathy, Risk of Thrombosis, and the Rationale for Anticoagulation. Clin Appl Thromb Hemost, 26,1-7. doi: https://doi.org/10.1177/1076029620938149.
2. Connors, J. M., Levy, J. H. (2020.). COVID-19 and its implications for thrombosis and anticoagulation. Blood, 135(23),2033-2040. doi: https://doi.org/10.1182/blood.2020006000.
3. Ackermann, M., Verleden, S. E., Kuehnel, M., Haverich, A., Welte, T., Laenger, F., Vanstapel, A., Werlein, C., Stark, H., Tzankov, A., Li, W. W., Li, V. W., Mentzer, S. J., Jonigk, D. (2020). Pulmonary Vascular Endothelialitis, Thrombosis, and Angiogenesis in Covid-19. N Engl J Med, 383(2),120-128. doi: https://doi.org/10.1056/NEJMoa2015432.
4. Ahmed, S., Zimba, O., Gasparyan, A. Y. (2020). Thrombosis in Coronavirus disease 2019 (COVID-19) through the prism of Virchow's triad. Clin Rheumatol, 39(9),2529-2543. doi: https://doi.org/10.1007/s10067-020-05275-1.
5. Pons, S., Fodil, S., Azoulay, E., Zafrani, L. (2020). The vascular endothelium: the cornerstone of organ dysfunction in severe SARS–CoV-2 infection. Crit Care. 24(1),353. doi: https://doi.org/10.1186/s13054-020-03062-7.
6. Coomes E. A., Haghbayan H. (2020). Interleukin-6 in Covid-19: A systematic review and meta–analysis. Rev Med Virol, 30(6),1-9. doi: https://doi.org/10.1002/rmv.2141.
7. Andreichyn, M. A., Nychyk, N. A., Zavidniuk, N. H., Yosyk, Ya. I., Ishchuk, I. S., Ivakhiv, O. L. (2020). COVID-19: epidemiolohiia, klinika, diahnostyka, likuvannia ta profilaktyka [COVID-19: epidemiology, clinic, diagnosis, treatment and prevention]. Infektsiini khvoroby [Infectious diseases]. 2,41-55. doi: https://doi.org/10.11603/1681-2727.2020.2.11285. (In Ukrainian).
8. McFadyen, J. D., Stevens, H., Peter, K. (2020). The Emerging Threat of (Micro)Thrombosis in COVID-19 and Its Therapeutic Implications. Circ Res, 127(4),571-587. doi: https://doi.org/10.1161/CIRCRESAHA.120.317447.

9. Franchini, M., Marano, G., Cruciani, M., Mengoli, C., Pati I., Masiello, F., Veropalumbo, E., Pupella, S., Vaglio, S., Liumbruno, G. M. (2020). COVID-19-associated coagulopathy. Diagnosis (Berl), 7(4),357-363. doi: https://doi.org/10.1515/dx-2020-0078.
10. Zhou, Y., Yang, Q., Chi, J., Dong, B., Lv, W., Shen, L., Wang Y. (2020). Comorbidities and the risk of severe or fatal outcomes associated with coronavirus disease 2019: A systematic review and meta–analysis. Int J Infect Dis, 99,47-56. doi: https://doi.org/10.1016/j.ijid.2020.07.029.
11. Serediuk, N. M., Serediuk, V. N., Skakun, O. Z., Vandzhura, Ya. L., Tverdokhlib, I. Z. (2020). Koronavirusna khvoroba (COVID-19): osoblyvosti perebihu ta likuvannia infarkta miokarda i sertsevoi nedostatnosti [Corona virus disease (COVID-19): features of the course and treatment of myocardial infarction and heart failure]. Art of Medicine, 3(15),182-188. doi: https://doi.org/10.21802/artm.2020.3.15.182. (In Ukrainian).
12. Magro, C., Mulvey, J. J., Berlin, D., Nuovo, G., Salvatore, S., Harp, J., Baxter-Stoltzfus, A., Laurence, J. (2020). Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases. Transl Res, 220,1-13. doi: https://doi.org/10.1016/j.trsl.2020.04.007.
13. Nakaz MOZ Ukrainy vid 28.03.2020 № 722 «Orhanizatsiia nadannia medychnoi dopomohy khvorym na koronavirusnu khvorobu (COVID-19)» [Order of the Ministry of Health of Ukraine dated March 28, 2020 No. 722 «Organization of medical care for patients with the coronavirus disease (COVID-19)»]. Available from: https://moz.gov.ua/article/ministry–mandates/nakaz–moz–ukraini–vid-28032020––722-organizacija–nadannja–medichnoi–dopomogi–hvorim–na–koronavirusnu–hvorobu–covid-19. (In Ukrainian).
14. Nakaz MOZ Ukrainy vid 2.04.2020 № 762 «Pro zatverdzhennia protokolu «Nadannia medychnoi dopomohy dlia likuvannia koronavirusnoi khvoroby (COVID-19)» [Order of the Ministry of Health of Ukraine dated April 2, 2020 No. 762 «On approval of the protocol «Providing medical assistance for the treatment of coronavirus disease (COVID-19)»]. Available from: https://moz.gov.ua/article/ministry–mandates/nakaz–moz–ukraini–vid-2042020––762-pro–zatverdzhennja–protokolu–nadannja–medichnoi–dopomogi–dlja–likuvannja–koronavirusnoi–hvorobi–covid-19. (In Ukrainian).
15. Protokol «Nadannia medychnoi dopomohy dlia likuvannia koronavirusnoi khvoroby (COVID-19)» vid 01.04.2020 vidpovidno do Zakonu Ukrainy vid 30.03.2020 № 539IKh «Pro vnesennia zmin do deiakykh zakoniv Ukrainy shchodo zabezpechennia likuvannia koronavirusnoi khvoroby (COVID-19)» [Protocol «Provision of medical assistance for the treatment of coronavirus disease (COVID-19)» dated 04/01/2020 in accordance with the Law of Ukraine dated 03/30/2020 No. 539X «On Amendments to Certain Laws of Ukraine Regarding Provision of Treatment of Coronavirus Disease (COVID-19)»]. Available from: https://zakon.rada.gov.ua/laws/show/539-20#Text. (In Ukrainian).
16. Zminy do Standartiv medychnoi dopomohy «Koronavirusna khvoroba (COVID-19)» (nakaz MOZ Ukrainy vid 20.05.2020 № 1227) [Changes to the Medical Care Standards «Coronavirus Disease (COVID-19)» (Order of the Ministry of Health of Ukraine dated 05.20.2020 No. 1227)]. Available from: https://moz.gov.ua/article/ministry–mandates/nakaz–moz–ukraini–vid-20052020––1227-pro–zatverdzhennja–zmin–do–standartiv–medichnoi–dopomogi–koronavirusna–hvoroba–covid-19. (In Ukrainian).
17. Pranata, R., Huang, I., Lim, M. A., Wahjoepramono, E. J., July, J. (2020). Impact of cerebrovascular and cardiovascular diseases on mortality and severity of COVID-19-systematic review, meta-analysis, and meta-regression. J Stroke Cerebrovasc Dis, 29(8),104949. doi: https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104949.
18. Pranata, R., Lim, M. A., Huang, I., Raharjo, S. B., Lukito, A. A. (2020). Hypertension is associated with increased mortality and severity of disease in COVID-19 pneumonia: A systematic review, meta-analysis and meta-regression. J Renin Angiotensin Aldosterone Syst, 21(2),1470320320926899. doi: https://doi.org/10.1177/1470320320926899.
19. Lu, G., Wang, J. (2020). Dynamic changes in routine blood parameters of a severe COVID-19 case. Clin Chim Acta, 508:98-102. doi: https://doi.org/10.1016/j.cca.2020.04.034.
20. Hordiienko, P. O., Kniazkova, I. I. (2021). Osoblyvosti medykamentoznoho likuvannia arterialnoi hipertenzii khvorykh na COVID-19 [Peculiarities of medical treatment of arterial hypertension in patients with COVID-19.]. Zbirnyk naukovykh prats ΛΌΗΟΣ [Collection of scientific papers ΛΌΓΟΣ], 3,94-95. doi: https://doi.org/10.36074/logos-26.02.2021.v3.31. (In Ukrainian).
21. Zizzo, G., Tamburello, A., Castelnovo, L., Laria, A., Mumoli, N., Faggioli, P. M., Stefani, I., Mazzone, A. (2022). Immunotherapy of COVID-19: Inside and Beyond IL-6 Signalling. Front Immunol, 13,795315. doi: https://doi.org/10.3389/fimmu.2022.795315.

Резюме

КЛІНІКО-ЛАБОРАТОРНІ ХАРАКТЕРИСТИКИ ХВОРИХ ІЗ КОРОНАВІРУСНОЮ ІНФЕКЦІЄЮ COVID-19 ТА ЇЇ КОМОРБІДНІСТЬ

Катерина В. Юрко, Інна В. Андрусович

Харківський національний медичний університет, м. Харків, Україна

Вступ. Коронавірусна хвороба має загрозливі масштаби епідемії з надзвичайними рівнями захворюваності та смертності усього світового населення. Більшість хворих із COVID-19 відзначає ураження респіраторного тракту та констатує більш важкий перебіг захворювання із розвитком системного ураження. Більш важкий перебіг COVID-19 асоційований із наявністю коморбідних захворювань.
Мета. Дослідити та проаналізувати клініко-лабораторні прояви та визначити основні супутні захворювання у пацієнтів з інфекцією COVID-19.
Матеріали та методи. Дослідження виконано згідно з біоетичними нормами та правилами. Обстежено 179 пацієнтів із COVID-19 (основна група) та 42 особи контрольної групи. Діагностування та лікування коронавірусної інфекції COVID-19 проводилося з урахуванням відповідних вітчизняних рекомендацій. Статистично визначали середнє значення та стандартне квадратичне відхилення. Вірогідність відмінностей проводили з використанням U-тесту Мана-Уітні та W-критерію знакових рангів Вілкоксона. Порогова величина рівня статистичної значущості усіх розрахованих ознак була прийнята за 0,05 (p = 0,05).
Результати. Констатовано високу коморбідність із патологією серцево-судинної системи (ССС) – 40,2 %, цукровим діабетом 2-го типу – 22,3 %, захворюваннями дихальної системи – 20,7 %. Визначено розлади функціонального стану ССС: пульсові значення – 91,01 ± 13,44, систолічний (127,9 ± 15,19) та діастолічний (79,3 ± 11,6) артеріальний тиск. Констатовано зміни клінічного аналізу крові: еритроцити – 4,38 ± 0,65 х1012/л, гемоглобін – 127,6 ± 21,2 г/л, гематокрит – 0,37 ± 0,07, лейкоцити – 10,7 ± 7,32 х109/л, сегментоядерні (65,4 ± 14,8 %) й палочкоядерні (9,03 ± 9,99 %) нейтрофіли, тромбоцити – 226,1 ± 90,6 х109/л, лімфоцити – 20,24 ± 12,43 %, моноцити – 6,60 ± 4,37 % та швидкість осідання еритроцитів (ШОЕ) – 25,4 ± 14,9 мм/год. Визначено значні (практично в чотири рази) збільшення рівнів IL-6 (24,56 ± 22,9 пг/мл) та концентрації глюкози крові (7,40 ± 3,42 ммоль/л).
Висновки. Визначено значну коморбідність COVID-19 та встановлено значні переважання показників функціонального стану ССС та зниження середніх рівнів кількісного складу еритроцитів і показників гемоглобіну й гематокриту. Визначено значний лейкоцитоз, нейтрофільоз, лімфоцитоз і моноцитоз, значні перевищення показників ШОЕ та IL-6 й глюкози сироватки крові, що підтверджувало наявність значної запальної реакції у відповідь на інфікування COVID-19.

Ключові слова: **COVID-19, коморбідність, клініко-лабораторні характеристики**