DOI: 10.17816/KMJ2021-843

Concomitant diseases in COVID-19 and their impact on the risks of adverse outcomes

N.V. Ivanova[1]*, V.S. Belov[1], A.I. Samarkin[1], Z.N. Tretyakevich[1], V.M. Mikushev[2], Yu.V. Bruttan[1]

[1]Pskov State University, Pskov, Russia;
[2]Saint-Petersburg State University, Saint-Petersburg, Russia

Abstract

Aim. To analyze COVID-19 comorbidities and their impact on disease course and the risk for unfavorable outcomes.
Methods. This study examined a group of 110 patients aged 32 to 97 who were admitted to the intensive care unit of the Pskov Regional Infectious Diseases Hospital in the period from October 7, 2020 to March 23, 2021. The mean age of patients was 65 years, 51% (56 people) were male. The study recorded age, comorbidities on a binary scale (yes — no), course of the disease, the degree of lung injury, hospital length of stay, treatment outcome. The impact of comorbidities on the disease severity and outcomes was assessed by using logistic regression analysis.
Results. It was shown that a regional sample of patients showed an increased hospital mortality rate compared with the data of the ACTIV registry (33.5 versus 7.6%). Chronic respiratory diseases in patients with COVID-19 regional cohorts affected the fatal outcome 2.7 times less than those registered in the Russian register. The presence of endocrine and thrombotic circulatory system diseases was generally close to the register. Concomitant cardiovascular diseases in patients of the regional cohort affected the mortality of COVID-19 outcomes two times less (in patients of the region, the risk of mortality increased by 2.066 times) than in the registry. The reliability of the conclusions is confirmed by testing statistical hypotheses and reliability coefficients below 5%.
Conclusion. The study shows the statistically significant effect of comorbidities on the COVID-19 outcomes; the specificity of the results related to the sampling characteristics and the regional component.
Keywords: COVID-19, comorbid diseases, disease severity, statistical analysis.

For citation: Ivanova N.V., Belov V.S., Samarkin A.I., Tretyakevich Z.N., Mikushev V.M., Bruttan Yu.V. Concomitant diseases in COVID-19 and their impact on the risks of adverse outcomes. *Kazan Medical Journal.* 2021; 102 (6): 843–854. DOI: 10.17816/KMJ2021-843.

Background. Over the previous 2 years, acute respiratory disease caused by the Severe Acute Respiratory Syndrome CoronaVirus 2 (SARS-CoV-2) or COronaVIrus Disease 2019 (COVID-19), accompanied by respiratory tract damage with manifestations from asymptomatic to clinically severe pneumonia with the development of acute respiratory failure or acute respiratory distress syndrome, is rapidly spreading worldwide [1, 2].

COVID-19 is much more severe with concomitant pathology [3]. The presence of comorbidity in patients with COVID-19 leads to an increased negative impact of the virus; thus, chronic types of the pathology are activated and consequently, complications occur [4].

Therefore, according to the Russian registry ACTIV [5], which registered 4,751 hospitalised patients with COVID-19, the level of lethal outcomes in patients with a history of comorbid or polymorbid chronic diseases increased by 9.5 times compared with patients without COVID-19 while the mortality rate increased in all age groups [6]. In this case, nosocomial mortality amounted to 7.6%.

Moreover, [7] the mortality rate was significantly higher in patients of older age groups. Thus, according to data from China, the mortality rate in hospitalised patients with COVID-19 was up to 0.4% for patients under 50 years of age; 1.3% for 50–60 years old; 3.6% for 60–69 years old and 14.3% for the older generation (80 years and over) [8, 9]. In Italy, a higher mortality rate from COVID-19 was also recorded in patients of older age groups [10, 11], thus 31% of the deceased were 70–79 years old and 58% of the deceased were over 80 years old.

The risk of a severe and extremely severe course of coronavirus disease and unfavourable outcomes

For correspondence: zdravuniver@inbox.ru Received 14.09.2021; accepted 09.11.2021; published 15.12.2021.

in patients of older age groups is associated with decreased functions of the immune system and physiological reserves in the older generation [7], as well as with polymorbidity and comorbidity in such patients [5]. Despite the tropism for the respiratory tract epithelium, the virus attacks various systems of the human body, leading to the development of various disorders [12]. Thus, the presence of comorbidities in patients with COVID-19 significantly increases the risk of poor outcomes, especially in elderly patients.

This fact is confirmed by the findings of several clinical studies [13–18], which indicate numerous facts of a strong relationship and interaction between coronavirus infection and comorbid diseases. Therefore, the issues of assessing the level of nosocomial survival of patients with coronavirus infection and chronic comorbid or polymorbid diseases are relevant and are required to obtain an adequate and significant presentation of COVID-19.

This study aimed to analyse the comorbid COVID-19 diseases and the degree of their influence on the disease course and the risk of its unfavourable outcome.

Materials and methods. A group of 110 patients aged 32–97 years old, with an average age of 65 years, who were admitted to the intensive care unit of the Pskov Regional Infectious Diseases Hospital from 7 October 2020, to March 23, 2021, was subjected to a statistical study. Of the patients, 51% (56 patients) were males.

This retrospective study selected the patients according to the criterion of the presence of at least one chronic non-infectious concomitant disease using the method of continuous selection from anonymised case histories. The study period was determined by the request of the health authorities of the Pskov region (6 months) to obtain contemporaneous data on hospitalisation and referral of patients with COVID-19.

For the study, the age and concomitant diseases were recorded on a binary scale (yes, no), as well as the nature of the disease course (moderate or severe), the degree of lung damage in percent, the hospital stay duration, the treatment outcomes and the main and concomitant diagnoses according to the International Classification of Diseases, 10th Edition. A dataset was formed based on the primary data, which was examined using specialised software, including the Python programming language.

The research material is also based on the provided information in the Russian- and English-language scientific articles that focused on the analysis of the peculiarities of the coronavirus infection course caused by SARS-CoV-2 in patients with chronic concomitant, comorbid and polymorbid diseases. The focus was on systematic reviews and meta-analyses. All-Russian registry ACTIV SARS-CoV-2 [5] and similar national registries of the USA [19], China [20], Spain [21] and Italy [22] were used as a source of clinical data, as well as publications that describe the specificity of exacerbation of concomitant, comorbid and polymorbid diseases in patients with COVID-19.

Methods of information systematisation and aggregation, as well as technologies of retrospective cohort analysis, content analysis and structuring of clinical and scientific-analytical information, were used as analytical tools in the study.

Statistical analysis included the construction of logit regression models, in which coefficients are interpreted as increasing or decreasing the chances of lethal outcome or severe/moderate disease. The calculations were performed using the specialised open-source software in the R and Python languages. Adequacy was assessed for the models. The coefficients of the model were tested for significance by testing the null hypothesis about the equality of the corresponding coefficient at 0 as a confidence level of 95% and a critical *p*-value of 5%. Due to the limited volume of the article, statistical calculations are not presented in full.

Results. A cohort of patients with COVID-19, who were admitted to the intensive care unit of the Pskov Regional Infectious Diseases Hospital from 7 October 2020, to March 23, 2021, was formed to study the regional aspects of the impact of comorbidities on the course severity and outcomes of COVID-19. A total of 110 patients were included in the cohort with a history of indications for the presence of comorbidities. The correspondence of the distribution of patients in the sample to the age and gender composition of the Pskov region population was assessed. The hypothesis of significant gender differences was not accepted. The age composition of the cohort corresponds to the age composition of patients in the dominant group aged 40–60 years; therefore, the obtained data does not exclude the unfavourable prognostic value of the presence of comorbid diseases for all patients with COVID-19 in the region.

Hospital mortality was 33.55% (38 patients). The mean hospital stay for the cohort under consideration was 10.1 days, with a 95% confidence interval (CI) of 8.9–11.2, with the average duration of stay of surviving patients for 10.5 (95% CI: 10.2–12.8) versus 7.4 (95% CI: 5.2–9.5) among the deceased. Cardiovascular diseases (CVD) was observed in 94 (85%) patients, endocrine pathology in 39 (35%), chronic respiratory diseases in 20 (18%) and nervous system and the gastrointestinal tract

Table 1. Coefficients of the z variable of the hospital mortality logit regression model.

Diseases	Constant, B0	Endocrine pathology, B1	Chronic respiratory diseases, B2	Nervous system disorders, B3	Genitourinary system disorders, B4	Diseases of the circulatory system, B5
Value	−3.590	1.89308	1.282604	2.814009	−1.398384	1.688544

Table 2. Coefficients of the z variable of the logit regression model of disease severity

Diseases	Constant, B0	Endocrine pathology, B1	Chronic respiratory diseases, B2	Nervous system disorders, B3	Genitourinary system disorders, B4	Diseases of the circulatory system, B5
Value	−1.688	1.066561	0.34032	1.753548	−1.402984	0.5017507

Table 3. The risk of increased mortality rate in patients with concomitant pulmonary diseases.

Concomitant diseases	Increase in mortality rate	95% confidence interval	Source
Acute respiratory distress syndrome	36.667	27.668–48.556; $p < 0.01$	[5. 27, 28]
Chronic obstructive pulmonary disease	3.53	1.79–6.96; $p < 0.001$	[29]

in 17 (15%) and 13 (12%) patients, respectively. On average, each patient had two comorbidities.

The study sample included only patients who had a history of comorbidities, thus the degree of association between various chronic comorbidities and the aforementioned types of identified complications from COVID-19 was assessed. Regression models were obtained that characterise the disease severity and the outcome prognosis of such course, the model has the logit regression form in both cases, and the auxiliary variables z are equal (Tables 1 and 2).

Further, only the results assessing the mortality in the patient cohort are considered. If the patient had chronic respiratory diseases before hospitalisation, his risk of lethal outcome insignificantly increased, only by 1.302 times (odds ratio [OR]: 1.302; 95% CI: 0.438–3.872; $p < 0.01$). A patient's history of endocrine diseases (type 2 diabetes mellitus and obesity) increased the risk of an unfavourable outcome by 3.111 times (OR: 3.111; 95% CI: 1.263–4.665; $p < 0.01$). A history of a comorbid cluster of the cardiovascular system diseases (arterial hypertension, ischaemic heart disease and chronic heart failure) in a patient with COVID increased the mortality risk by 2.066 times (OR: 2.066; 95% CI: 0.422–10.121; $p < 0.01$).

Discussion. The comparison of data from registers of hospitalised patients with confirmed SARS-CoV-2 infection in Russia [5] and similar registries from other countries, such as the USA [19], China [20], Spain [21] and Italy [22], with research results, performed in this work, highlights the risk of increased mortality depending on the presence of concomitant diseases. The results are tabulated below. Only statistically significant coefficients of the logit regression models are presented throughout.

The uncomplicated course of COVID-19 can be represented in the form of three phases that correspond to the typical clinical stages of disease development and course, namely the stage of incubation stage, clinical manifestations and immunisation [23, 24]. In patients (primarily elderly people) with concomitant, comorbid and polymorbid diseases (chronic pulmonary disorders, arterial hypertension, ischaemic heart disease, coagulopathy, diabetes mellitus, chronic kidney and liver diseases), the immune system is not able to effectively respond to the virus replication in the acute phase and the viral disease becomes urgent [25].

COVID-19 and associated pulmonary diseases. The study of the pathogenesis of infection with the SARS-CoV-2 virus by the Consensus of experts of the Russian Society for Cardiosomatic Rehabilitation and Secondary Prevention, the Russian Society of Cardiology, the Russian Respiratory Society, the Union of Rehabilitation Therapists of Russia, the Russian Union of Nutritionists, Dietitians and Food Industry Specialists and the Russian Society for the Prevention of Noncontagious Diseases [12] showed that the main target of the virus is type II alveolocytes in the lungs. A viral infection that affects these cells acts as a trigger, which starts the process of releasing pro-inflammatory cytokines from activated macrophages, which is subsequently transformed into a cytokine storm during hyperactivation of the body's immune system and contributes to damage the lung tissue, as well as other organs of a patient with COVID-19 [26].

The risk of increased mortality rate in patients with concomitant pulmonary diseases is presented in Table 3.

COVID-19 and CVDs. The main adverse reactions in patients with COVID-19 and concomitant

Table 4. The risk of the increased mortality rate of patients from concomitant cardiovascular diseases.

Concomitant diseases	Increase in mortality	95% confidence interval	Source
Acute myocardial infarction	1.40	1.112–1.763; $p < 0.001$	[3]
Arterial hypertension	3.123	12.324–4.198; $p < 0.001$	[5]
Ischaemic heart disease	3.829	3.032–4.836; $p < 0.001$	[5]
Atrial fibrillation	4.239	3.17–5.669; $p < 0.001$	[5]
Heart rhythm disorder	2.75	1.43–5.25; $p < 0.001$	[35]
Chronic heart failure	6.72	3.34–13.52; $p < 0.001$	[35]
Deep vein thrombosis	2.305	0.668–7.953; $p = 0.17$	[5]*
Stroke	12.665	5.643–28.425; $p < 0.01$	[5]
Pulmonary artery thromboembolism	17.877	8.877–36.832; $p < 0.01$	[5]
Combination of arterial hypertension and chronic heart failure	3.963	3.022–5.197; $p < 0.01$	[5]
Combination of arterial hypertension, ischaemic heart disease and chronic heart failure	4.082	3.054–5.455; $p < 0.01$	[5]
Combination of arterial hypertension, ischaemic heart disease, chronic heart failure and obesity	3.869	2.578–5.806; $p < 0.01$	[5]

CVDs [30–39] include direct viral damage to cardiomyocytes, renin-angiotensin-aldosterone system dysregulation, pathological myocardial response to a cytokine storm, mutually potentiating immunological response, hypercoagulation due to endothelial dysfunction, increased platelet activity and von Willebrand factor. The response of the cardiovascular system to SARS-CoV-2 invasion into the human body cells ultimately causes impaired structural integrity of the myocardium, pericardium and the conducting system, accompanied by increased levels of troponin and the N-terminal propeptide of natriuretic hormone, which serve as laboratory markers of cardiac pathology [33, 34].

The risk of increased mortality rate in patients from concomitant CVDs is presented in Table 4.

COVID-19 and concomitant diseases of the endocrine system. Endocrine system disorders are detected on average in 30% of patients infected with SARS-CoV-2 [23, 40]. The publications [18, 41] noted that the increased risk of COVID-19 in patients with diabetes mellitus is due to impaired immunity due to hyperglycaemia and a sharp carbohydrate metabolism disorder. The immune system of patients with obesity is constantly active and thus copes worse with COVID-19, especially when a systemic inflammatory response is formed. This leads to a significantly increased severity of COVID-19 [42].

The risk of increased mortality rate in patients from concomitant CVDs is presented in Table 5.

COVID-19 and concomitant kidney diseases. The prevalence of renal dysfunction among the population is approximately 10%, which is due to the high prevalence of arterial hypertension and type 2 diabetes mellitus [18, 43]. The risk of increased mortality rate in patients from concomitant kidney disease is presented in Table 6.

COVID-19 and comorbid liver diseases. Studies [46, 47] revealed that many patients with COVID-19 (14%–53%) develop liver dysfunctions. Liver damage develops mainly in older males with an increased body mass index and a history of background liver diseases [48]. Hepatic dysfunction may be due [48] to the direct cytopathic effect of the virus, the uncontrolled immune response of the infected organism, sepsis, thrombovasculitis, ischaemia and drug damage to the liver in patients infected with SARS-CoV-2. The SARS-CoV-2 virus is capable of inducing apoptosis in liver cells [49].

Hypercytokinaemia triggers a chain of events that lead to multiple organ damage, including pathological liver reactions [50]. As noted [51], due

Table 5. The risk of the increased mortality rate of patients from concomitant cardiovascular diseases.

Concomitant diseases	Increase in mortality rate	95% confidence interval	Source
Diabetes mellitus	2.85	No data available	[40]
Type 1 diabetes mellitus	3.79	1.228–11.691; $p < 0.001$	[5]
Type 2 diabetes mellitus	2.659	2.089–3.386; $p < 0.001$	[5]
Diabetes mellitus + obesity + cardiovascular diseases	2.242	1.595–3.151; $p < 0.01$	[5]
Diabetes mellitus + arterial hypertension + ischaemic heart disease + chronic heart failure	4.215	2.784–6.382; $p < 0.01$	[5]

Table 6. The risk of increased mortality rate in patients from concomitant kidney diseases.

Concomitant diseases	Increase in mortality rate	95% confidence interval	Source
Chronic kidney disease	3.358	2.486–4.536; $p < 0.01$	[5, 44, 45]
Patient's age 60 years old or older	3.987	2.874–5.53; $p < 0.01$	[5]

Table 7. The risk of the increased mortality rate of patients from concomitant liver diseases.

Concomitant diseases	Increase in mortality rate	95% confidence interval	Source
Chronic liver diseases	2.8	1.9–4.0; $p < 0.001$	[52]
Hepatic cirrhosis	4.6	2.6–9.3; $p < 0.001$	[53]

Table 8. The risk of the increased mortality rate of patients from concomitant neuropsychiatric diseases.

Concomitant diseases	Increase in mortality rate	95% confidence interval	Source
Cerebral circulation disorders	5.02	3.592–7.015; $p < 0.01$	[5]
Stroke	3.1	1.07–8.94; $p < 0.01$	[57]

to the significant vulnerability of the liver to circulatory disorders and its high metabolic activity and intense blood supply, hypoxia caused by complications of COVID-19 can lead to liver ischaemia and reperfusion dysfunction.

The risk of the increased mortality rate of patients from concomitant liver diseases is presented in Table 7.

COVID-19 and concomitant neuropsychiatric diseases. Neurotic disorders are mainly detected in patients with severe COVID-19, namely in 75.7% of patients, who also have comorbid or polymorbid diseases, similar to the cluster of the type 'arterial hypertension + ischaemic heart disease + diabetes mellitus'.

The two main pathological mechanisms of the viral effect in COVID-19 on the nervous system include the direct invasion of SARS-CoV-2 into the nervous tissue and viral penetration through the ethmoid bone and olfactory bulbs [54, 55]. As indicated [56], neurological disorders are registered in approximately 36.4% of patients with COVID-19.

The risk of the increased mortality rate of patients from concomitant neuropsychiatric diseases is presented in Table 8.

Thus, the information can be summarised as follows.

1. The average age of patients with COVID-19 in different registries is quite similar and amounts to 63.4 years in Russia [5], 63 years in the USA [19], 64 years in China [20], 69 years old in Spain [21] and 63 years in Italy [22]. By gender, the spread is more significant and the ratio of female/male is 54%/46% in Russia [5], 40%/60% in the USA [19], 51%/49% in China [20], 43%/57% in Spain [21] and 18%/82% in Italy [22].

2. The hospital mortality rate by cohorts of registries of those infected with the SARS-CoV-2 virus is 7.6% in Russia [5], 21% in the USA [19], 3.2% in China [20], 2.9% in Spain [21] and 7.2% in Italy [22]. This spread in mortality data is since, in several countries in the Eurasian region, patients with a mild course of COVID-19 were often hospitalised, especially in 2020.

3. The most common complications leading to lethal outcomes in infection caused by SARS-CoV-2 were acute respiratory distress syndrome (55.59%), acute renal injury (43.5%), cytokine storm (35.97%), bacterial pneumonia (14.91%), pulmonary artery thromboembolism (5.59%), sepsis (4.04%) and stroke (3.73%).

4. Among concomitant diseases, the main factors that increase the risk of lethal outcome are chronic heart failure (increased risk of mortality by 6.72 times), impaired cerebral circulation (5.02 times), hepatic cirrhosis (4.6 times), atrial fibrillation (4.239 times), ischaemic heart disease (3.829 times), type 1 diabetes mellitus (3.79 times), chronic obstructive pulmonary disease (3.53 times), chronic kidney disease (by 3.358 times), arterial hypertension (3.123 times), chronic liver disease (2.8 times) and type 2 diabetes mellitus (2.659 times).

5. The presence of a history of comorbid diseases in patients, as a rule, results in a severe course of COVID-19 and an increase in the mortality rate, with a combination of 'arterial hypertension + ischaemic heart disease + chronic heart failure' by 4.082 times, 'arterial hypertension + chronic heart failure' by 3.963 times, 'arterial hypertension + ischaemic heart disease + chronic heart failure + obesity' by 3.869 times, 'diabetes mellitus + arterial hypertension + ischaemic heart disease + chronic heart failure' by 4.215 times, 'diabetes mellitus + obesity + CVD' by 2.242 times, 'diabetes mellitus + obesity + arterial hypertension' by 2.177 times.

A history of comorbidity in patients with COVID-19 is one of the most significant risk factors for lethal outcomes. Only 4.88% of the deceased had no concomitant diseases, whereas comorbidity was recorded in 52.03% of the deceased [5]. Additionally, [5] the presence of two or more concomitant diseases in patients over the age of 60 increases the risk of the lethal outcome by >4.5 times. The probable reasons for the negative prognostic significance of concomitant CVDs in COVID-19 are associated with a higher prevalence of CVD in older age groups and functional impairments of the immune system in CVD, as well as in diabetes mellitus.

6. The comparison of the regional aspects of the influence of concomitant diseases on mortality in infection caused by SARS-CoV-2, the data of the ACTIV registry [5] revealed that the average age of patients included in the regional cohort is 64.5 years, which is close to the average age (63.4 years) of patients included in the ACTIV registry. The gender distribution of patients with COVID is also close, as according to the regional data, the ratio of females to males is 49% to 51% and 54% to 46% according to the ACTIV registry. Hospital mortality was 33.55% according to the regional cohort data and 7.6% according to the ACTIV registry data. The excess mortality rate of patients with COVID-19 in the region by almost five times is due to the inclusion in the cohort of patients admitted to the Pskov Regional Infectious Diseases Hospital with severe and extremely severe forms of COVID-19 (Materials and Methods).

7. A history of concomitant diseases in regional patients with COVID-19 also increases the risk of an unfavourable outcome, as in patients registered in the ACTIV registry. However, their impact on mortality risk is different. Chronic respiratory diseases in patients with COVID-19 of the regional cohort affect the fatal outcome weaker by 2.7 times than in patients included in the ACTIV registry (an increase in the risk of mortality by 1.302 times at the regional level versus 3.53 times). The presence of endocrine diseases in the regional cohort patients increases the risk of the lethal outcome by 3.11 times, which is generally close to the ACTIV registry data presented above (type 1 diabetes mellitus increases the risk of mortality by 3.79 times, whereas type 2 diabetes mellitus increases it by 2.659 times). Concomitant CVDs in the regional cohort patients affect mortality in COVID-19 less (increase by 2.066 times) than in patients registered in the ACTIV registry (the risk of mortality increases from 3.869 to 4.082 times)

CONCLUSIONS

1. The comorbidity and polymorbidity in patients with infection caused by SARS-CoV-2 are significant risk factors for the lethal outcome of infectious disease and a predictor of a poor prognosis for COVID-19. Disease history, such as chronic heart failure, diabetes mellitus, stroke, hepatic cirrhosis and atrial fibrillation, before the infection with SARS-CoV-2, increases the risk of lethal outcome from a new coronavirus infection by four times or more.

2. The data for the Pskov region as a whole correlate with the data for the rest of the regions of Russia. This considers the area as a model region for further research, including the long-term consequences of the new COVID-19. Concurrently, there are certain peculiarities (several comorbid diseases have a lesser effect on the risk of mortality and the severity of the disease course than in the available all-Russian databases).

3. According to the ACTIV registry, the hospital mortality rate for patients with SARS-CoV-2 was 7.6%, whereas 33.55% according to the regional cohort.

Author contributions. N.V. I. was the work supervisor, performed systematisation of initial data; V.S.B. reviewed the ACTIV registry, performed statistical data processing; A.I.S. performed statistical analysis of data; Z.N.T. created the idea of the study, performed analysis and systematisation of the initial data; V.M.M. performed the statistical analysis, assessed significance of the results; Yu.V.B. processed the results using the Python language.

Funding. The study had no external funding.

Conflict of interest. The authors declare no conflict of interest.

Acknowledgments. The authors express their gratitude to the management and staff of the Pskov Regional Infectious Diseases Hospital, the Pskov Regional Clinical Hospital, the Pskov City Hospital, as well as the staff and personally the Chairperson of the Health Committee of the Pskov Region Marina Valerievna Garashchenko. Experimental data processing was performed at the Sofia Kovalevskaya Pskov State University.

REFERENCES

1. Brugliera L., Spina A., Castellazzi P., Cimino P., Tettamanti A., Houdayer E., Arcuri P., Alemanno F., Mortini P., Iannaccone S. Rehabilitation of COVID-19 patients. *J. Rehabil. Med*. 2020; 52 (4): jrm00046. DOI: 10.2340/16501977-2678.

2. World Health Organization. *Coronavirus disease 2019 (COVID-19) Situation Report — 48*. https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200308-sitrep-48-covid-19.pdf?sfvrsn=16f7ccef_4 (access date: 27.08.2021).

3. Wang D., Hu B., Hu C., Zhu F., Liu X., Zhang J., Wang B., Xiang H., Cheng Z., Xiong Y., Zhao Y., Li Y., Wang X., Peng Z. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020; 323 (11): 1061–1069. DOI: 10.1001/jama.2020.1585.

4. Baumann T., Delgado J., Montserrat E. CLL and COVID-19 at the Hospital Clinic of Barcelona: an interim report. *Leukemia*. 2020; 34: 1–3.

5. Arutyunov G.P., Tarlovskaya E.I., Arutyunov A.G., Belenkov Y.N., Konradi A.O., Lopatin Y.M., Rebrov A.P., Tereshchenko S.N., Chesnikova A.I., Hayrapetyan H.G., Babin A.P., Bakulin I.G., Bakulina N.V., Balykova L.A., Blagonravova A.S., Boldina M.V., Vaisberg A.R., Galyavich A.S., Gomonova V.V., Grigorieva N.U., Gubareva I.V., Demko I.V., Evzerikhina A.V., Zharkov A.V., Kamilova U.K., Kim Z.F., Kuznetsova T.Yu., Lareva N.V., Makarova E.V., Malchikova S.V., Nedogoda S.V., Petrova M.M., Pochinka I.G., Protasov K.V., Protsenko D.N., Ruzanov D. Yu., Sayganov S.A., Sarybaev A.Sh., Selezneva N.M., Sugraliev A.B., Fomin I.V., Khlynova O.V., Chizhova O.Yu., Shaposhnik I.I., Schukarev D.A., Abdrahmanova A.K., Avetisian S.A., Avoyan H.G., Azarian K.K., Aimakhanova G.T., Ayipova D.A., Akunov A.Ch., Alieva M.K., Aparkina A.V., Aruslanova O.R., Ashina E.Yu., Badina O.Y., Barisheva O. Yu., Batchayeva A.S., Bitieva A.M., Bikhteyev I.U., Borodulina N.A., Bragin M.V., Budu A.M., Burygina L.A., Bykova G.A., Varlamova D.D., Vezikova N.N., Verbitskaya E.A., Vilkova O.E., Vinnikova E.A., Vustina V.V., Galova E.A., Genkel V.V., Gorshenina E.I., Gostishev R.V., Grigorieva E.V., Gubareva E.Yu., Dabylova G.M., Demchenko A.I., Dolgikh O.Yu., Duvanov I.A., Duyshobayev M.Y., Evdokimov D.S., Egorova K.E., Ermilova A.N., Zheldybayeva A.E., Zarechnova N.V., Ivanova S.Yu., Ivanchenko E.Yu., Ilina M.V., Kazakovtseva M.V., Kazymova E.V., Kalinina Yu.S., Kamardina N.A., Karachenova A.M., Karetnikov I.A., Karoli N.A., Karpov O.V., Karsiev M.Kh., Kaskaeva D.S., Kasymova K.F., Kerimbekova Zh.B., Kerimova A.Sh., Kim E.S., Kiseleva N.V., Klimenko D.A., Klimova A.V., Kovalishena O.V., Kolmakova E.V., Kolchinskaya T.P., Kolyadich M.I., Kondriakova O.V., Konoval M.P., Konstantinov D.Yu., Konstantinova E.A., Kordukova V.A., Koroleva E.V., Kraposhina A.Yu., Kriukova T.V., Kuznetsova A.S., Kuzmina T.Y., Kuzmichev K.V., Kulchoroeva Ch.K., Kuprina T.V., Kouranova I.M., Kurenkova L.V., Kurchugina N.Yu., Kushubakova N.A., Levankova V.I., Levin M.E., Lyubavina N.A., Magdeyeva N.A., Mazalov K.V., Majseenko V.I., Makarova A.S., Maripov A.M., Marusina A.A., Melnikov E.S., Moiseenko N.B., Muradova F.N., Muradyan R.G., Musaelian Sh.N., Nikitina N.M., Ogurlieva B.B., Odegova A.A., Omarova Yu.M., Omurzakova N.A., Ospanova Sh.O., Pahomova E.V., Petrov L.D., Plastinina S.S., Pogrebetskaya V.A., Polyakov D.S., Ponomarenko E.V., Popova L.L., Prokofeva N.A., Pudova I.A., Rakov N.A., Rakhimov A.N., Rozanova N.A., Serikbolkyzy S., Simonov A.A., Skachkova V.V., Smirnova L.A., Soloveva D.V., Soloveva I.A., Sokhova F.M., Subbotin A.K., Sukhomlinova I.M., Sushilova A.G., Tagayeva D.R., Titojkina Yu.V., Tikhonova E.P., Tokmin D.S., Torgunakova M.S., Trenogina K.V., Trostianetckaia N.A., Trofimov D.A., Tulichev A.A., Tupitsin D.I., Tursunova A.T., Ulanova N.D., Fatenkov O.V., Fedorishina O.V., Fil T.S., Fomina I.Yu., Fominova I.S., Frolova I.A., Tsvinger S.M., Tsoma V.V., Cholponbaeva M.B., Chudinovskikh T.I., Shakhgildyan L.D., Shevchenko O.A., Sheshina T.V., Shishkina E.A., Shishkov K.Yu., Sherbakov S.Y., Yausheva E.A. International register "Dynamics analysis of comorbidities in SARS-CoV-2 survivors" (AKTIV SARS-CoV-2): analysis of predictors of short-term adverse outcomes in COVID-19. *Russian Journal of Cardiology.* 2021; 26 (4): 4470. (In Russ.) DOI: 10.15829/1560-4071-2021-4470.

6. Ruan Q., Yang K., Wang W., Jiang L., Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. *Intensive Care Med*. 2020; 46 (5): 846–848. DOI: 10.1007/s00134-020-05991-x.

7. Tkacheva O.N., Kotovskaya Yu.V., Aleksanyan L.A., Milto A.S., Naumov A.V., Strazhesko I.D., Vorobyeva N.M., Dudinskaya E.N., Malaya I.P., Krylov K.Yu., Tyukhmenev E.A., Rozanov A.V., Ostapenko V.S., Manevich T.M., Shchedrina A.Yu., Semenov F.A., Mkhitaryan E.A., Khovasova N.O., Yerulanova E.A., Kotovskaya N.V., Sharashkina N.V. Novel coronavirus infection SARS-CoV-2 in elderly and senile patients: prevention, diagnosis and treatment. Expert Position Paper of the Russian Association of Gerontology and Geriatrics. *Kardiovaskulyarnaya terapiya i profilaktika*. 2020; 19 (3): 2601. (In Russ.) DOI: 10.15829/1728-8800-2020-2601.

8. *Chinese Center for Control and Prevention*. http://www.chinacdc.cn/en/COVID19/ (access date: 27.08.2021).

9. *Vital surveillances: The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) — China*. 2020. http://weekly.chinacdc.cn/en/article/id/e53946e2-c6c4-41e9-9a9b-fea8db1a8f51/ (access date: 28.08.2021).

10. Remuzzi A., Remuzzi G. COVID-19 and Italy: what next? *Lancet*. 2020; 395 (10231): 1225–1228. DOI: 10.1016/S0140-6736(20)30627-9.

11. Porcheddu R., Serra C., Kelvin D., Kelvin N., Rubino S. Similarity in Case Fatality Rates (CFR) of COVID-19/SARS-COV-2 in Italy and China. *J. Infect. Dev. Ctries.* 2020; 14 (2): 125–128. DOI: 10.3855/jidc.12600.

12. Bubnova M.G., Shlyakhto E.V., Aronov D.M., Belevsky A.S., Gerasimenko M.Yu., Glezer M.G., Gordeev M.N., Drapkina O.M., Ivanova G.E., Ioseliani D.G., Karamnova N.S., Kosmacheva E.D., Kuleshov A.V., Kukshina A.A., Lyadov K.V., Lyamina N.P., Makarova M.R., Meshcheryakova N.N., Nikityuk D.B., Pasechnik I.N., Persiyanova-Dubrova A.L., Pogonchenkova I.V., Svet A.V., Starodubova A.V., Tutelyan V.A. Coronavirus disease 2019: features of comprehensive cardiac and pulmonary rehabilitation. *Russian Journal of Cardiology*. 2021; 26 (5): 4487. (In Russ.) DOI: 10.15829/1560-4071-2021-4487.

13. Drapkina O.M., Karpov O.E., Lukyanov M.M., Martsevich S.Yu., Pulin A.A., Kutishenko N.P., Akimkin V.G., Andreenko E.Yu., Voronina V.P., Dindikova V.A., Dmitrieva N.A., Zagrebelny A.V., Lerman O.V., Makoveeva A.N., Okshina E.Yu., Kudryashov E.V., Klyashtorny V.G., Smirnov A.A., Fomina V.S. Prospective in-hospital registry of patients with suspected or documented COVID-19 infection and community-acquired pneumonia (TARGET-VIP): characteristics of patients and assessment of in-hospital outcomes. *Kardiovaskulyarnaya terapiya i profilaktika*. 2020; 19 (6): 2727. (In Russ.) DOI: 10.15829/1728-8800-2020-2727.

14. 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; 29 (8): 104949. DOI: 10.1016/j.jstrokecerebrovasdis.2020.104949.

15. Tanashyan M.M., Kuznetsova P.I., Raskurazhev A.A. Neurological aspects of COVID-19. *Annaly klinicheskoy i eksperimental'noy nevrologii*. 2020; 14 (2): 62–69. (In Russ.) DOI: 10.25692/ACEN.2020.2.8.

16. Lyalyukova E.A., Dolgalev I.V., Chernysheva E.N., Druk I.V., Konovalova G.M., Lyalyukov A.V. COVID-19 and liver dysfunction: current ideas and new therapeutic strategies. *Lechaschi Vrach*. 2021; (2): 20–25. (In Russ.) DOI: 10.26295/OS.2021.16.99.004.

17. Kuklina G.M., Makar'iants N.N. Description of COVID-19 infection course in a patient with multiple comorbidity: hairy cell leukemia, chronic generalized sarcoidosis and deep vein thrombosis in the lower extremities. Case report. *Consilium Medicum*. 2021; 23 (3): 292–295. (In Russ.) DOI: 10.26442/20751753.2021.3.200815.

18. Abdurakhmanov I.U., Umurzakov Sh.E., Zhamilova G.K., Satarova A.A., Aidarov Z.A. COVID-19 and comorbid pathology (literature review). *The Scientific Heritage*. 2021; (68): 56–64. (In Russ.)

19. National Institute for Health and Care Excellence, Royal College of General Practitioners, Healthcare Improvement Scotland SIGN. *COVID-19 rapid guideline: managing the longterm effects of COVID-19.* London: National Institute for Health and Care Excellence. 2020. https://www.nice.org.uk/guidance/ng188 (access date: 18.12.2020).

20. Glybochko P.V., Fomin V.V., Avdeev S.N., Moiseev S.V., Yavorovsky A.G., Brovko M.Yu., Umbetova K.T., Aliev V.A., Bulanova E.L., Bondarenko I.B., Volkova O.S., Gainitdinova V.V., Gneusheva T.Yu., Dubrovin K.V., Kapustina V.A., Kraeva V.V., Merzhoeva Z.M., Nuralieva G.S., Nail P.V., Panasyuk V.V., Politov M.E., Popov A.M., Popova E.N., Raspopina N.A., Royuk V.V., Sorokin Yu.D., Trushenko N.V., Khalikova E.Yu., Tsareva N.A., Chikina S.Yu., Chichkova N.V., Akulkina L.A., Bulanov N.M., Ermolova L.A., Zykova A.S., Kitbalyan A.A., Moiseev A.S., Potapov P.P., Tao E.A., Sholomova V.I., Shchepalina A.A., Yakovleva A.A. Clinical characteristics of 1007 intensive care unit patients with SARS-CoV-2 pneumonia. *Klinicheskaya farmakologiya i terapiya*. 2020; 29 (2): 21–29. (In Russ.) DOI: 10.32756/0869-5490-2020-2-21-29.

21. Zhang H., Penninger J.M., Li Y., Zhong N., Slutsky A.S. Angiotensin-converting enzyme 2 (ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. *Intensive Care Med*. 2020; 46 (4): 586–590. DOI: 10.1007/s00134-020-05985-9.

22. Zhou P., Yang X.L., Wang X.G., Hu B., Zhang L., Zhang W., Si H.R., Zhu Y., Li B., Huang C.L., Chen H.D., Chen J., Luo Y., Guo H., Jiang R.D., Liu M.Q., Chen Y., Shen X.R., Wang X., Zheng X.S., Zhao K., Chen Q.J., Deng F., Liu L.L., Yan B., Zhan F.X., Wang Y.Y., Xiao G.F., Shi Z.L. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020; 579 (7798): 270–273. DOI: 10.1038/s41586-020-2012-7.

23. Mitkovskaya N., Grigorenko E., Ruzanov D., Statkeych T. COVID-19 coronavirus infection and comorbidity. *Nauka i innovatsii*. 2020; (7): 50–60. (In Russ.) DOI: 10.29235/1818-9857-2020-7-50-60.

24. Ling L., Lianfeng L., Wei C., Taisheng L. Hypothesis for potential pathogenesis of SARS-CoV-2 infection — a review of immune changes in patients with viral pneumonia. *Emerg. Microbes Infect*. 2020; 9 (1): 727–732. DOI: 10.1080/22221751.2020.1746199.

25. Siddiqu H.K., Mehra M.R. COVID-19 illness in native and immunosuppressed states: A clinical-therapeutic staging proposal. *J. Heart Lung Transplant*. 2020; 39 (5): 405–407. DOI: 10.1016/j.healun.2020.03.012.

26. Samsonova M.V., Chernyaev A.L., Omarova Zh.R., Pershina E.A., Mishnev O.D., Zayratyants O.V., Mikhaleva L.M., Kalinin D.V., Varyasin V.V., Tishkevich O.A., Vinogradov S.A., Mikhaylichenko K.Yu., Chernyak A.V. Features of pathological anatomy of lungs at COVID-19. *Pul'monologiya*. 2020; 30 (5): 519–532. (In Russ.) DOI: 10.18093/0869-0189-2020-30-5-519-532.

27. Lippi G., Henry B.M. Chronic obstructive pulmonary disease is associated with severe coronavirus disease 2019 (COVID-19). *Respir. Med*. 2020; 167: 105941. DOI: 10.1016/j.rmed.2020.105941.

28. Wu C., Chen X., Cai Y., Xia J., Zhou X., Xu S., Huang H., Zhang L., Zhou X., Du C., Zhang Y., Song J., Wang S., Chao Y., Yang Z., Xu J., Zhou X., Chen D., Xiong W., Xu L., Zhou F., Jiang J., Bai C., Zheng J., Song Y. Risk factors associated with acute respiratory distress syndrome and death in patients with Coronavirus Disease 2019 pneumonia in Wuhan, China. *JAMA Intern. Med*. 2020; 180 (7): 934–943. DOI: 10.1001/jamainternmed.2020.0994.

29. Parohan M., Yaghoubi S., Seraji A., Javanbakht M.H., Sarraf P., Djalali M. Risk factors for mortality in patients with Coronavirus disease 2019 (COVID-19) infection: a systematic review and meta-analysis of observational studies. *Aging Male*. 2020; 23 (5): 1416–1424. DOI: 10.1080/13685538.2020.1774748.

30. Bunova S.S., Okhotnikova P.I., Skirdenko Yu.P., Nikolaev N.A., Osipova O.A., Zhernakova N.I. COVID-19 andcardiovascular comorbidity: novel approaches to reduce mortality. *Kardiovaskulyarnaya terapiya i profilaktika*. 2021; 20 (4): 2953. (In Russ.)] DOI: 10.15829/1728-8800-2021-2953.

31. Chung M., Zidar D., Bristow M., Cameron S., Chan T., Harding C.V. 3rd., Kwon D., Singh T., Tilton J., Tsai E., Tucker N., Barnard J., Loscalzo J. COVID-19 and cardiovascular disease. *Circ. Res*. 2021; 128 (8): 1214–1236. DOI: 10.1161/CIRCRESAHA.121.317997.

32. Bubnova M.G., Aronov D.M. COVID-19 and cardiovascular diseases: from epidemiology to rehabilitation. *Pul'monologiya*. 2020; 30 (5): 688–699. (In Russ.) DOI: 10.18093/0869-0189-2020-30-5-688-699.

33. Siripanthong B., Nazarian S., Muser D., Deo R., Santangeli P., Khanji M.Y., Cooper L.T.Jr., Chahal C.A.A. Recognizing COVID-19 — related myocarditis: The possible pathophysiology and proposed guideline for diagnosis and management. *Hear. Rhythm*. 2020; 17 (9): 1463–1471. DOI: 10.1016/j.hrthm.2020.05.001.

34. Guo T., Fan Y., Chen M., Wu X., Zhang L., He T., Wang H., Wan J., Wang X., Lu Z. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020; 5 (7): 811–818. DOI: 10.1001/jamacardio.2020.1017.

35. Hessami A., Shamshirian A., Heydari K., Pourali F., Alizadeh-Navaei R., Moosazadeh M., Abrotan S., Shojaie L., Sedighi S., Shamshirian D., Rezaei N. Cardiovascular diseases burden in COVID-19: Systematic review and meta-analysis. *Am. J. Emerg. Med*. 2021; 46: 382–391. DOI: 10.1016/j.ajem.2020.10.022.

36. Petrikov S.S., Ivannikov A.A., Vasilchenko M.K., Esaulenko A.N., Alidzhanova Kh.G. COVID-19 and cardiovascular system: Pathophysiology, pathomorphology, complications, long-term prognosis. *Zhurnal im. N.V. Sklifosovskogo. Neotlozhnaya medicinskaya pomoshch'*. 2021; 10 (1): 14–26. (In Russ.) DOI: 10.23934/2223-9022-2021-10-1-14-26.

37. Klok F.A., Kruip M.J.H.A., van der Meer N.J.M., Arbous M.S., Gommers D.A.M.P.J., Kant K.M., Kaptein F.H.J., van Paassen J., Stals M.A.M., Huisman M.V., Endeman H. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb. Res*. 2020; 191: 145–147. DOI: 10.1016/j.thromres.2020.04.013.

38. Poissy J., Goutay J., Caplan M., Parmentier E., Duburcq T., Lassalle F., Jeanpierre E., Rauch A., Labreuche J., Susen S. Lille ICU Haemostasis COVID-19 group. Pulmonary Embolism in COVID-19 patients: awareness of an increased prevalence. *Circulation*. 2020; 142: 184–186. DOI: 10.1161/CIRCULATIONAHA.120.047430.

39. Inciardi R.M., Adamo M., Lupi L., Cani D.S., Di Pasquale M., Tomasoni D., Italia L., Zaccone G., Tedino C., Fabbricatore D., Curnis A., Faggiano P., Gorga E., Lombardi C.M., Milesi G., Vizzardi E., Volpini M., Nodari S., Specchia C., Maroldi R., Bezzi M., Metra M. Characteristics and outcomes of patients hospitalized for COVID-19 and cardiac disease in Northern Italy. *Eur. Heart J*. 2020; 41: 1821–1829. DOI: 10.1093/eurheartj/ehaa388.

40. Andreeva A.V., Markova T.N., Antsiferov M.B. Management of patients with diabetes mellitus and COVID-19. *Doctor.Ru*. 2021; 20 (2): 11–20. (In Russ.) DOI: 10.31550/1727-2378-2021-20-2-11-20.

41. Mokrysheva N.G., Galstyan G.R., Kirzhakov M.A., Eremkina A.K., Pigarova E.A., Melnichenko G.A. COVID-19 Pandemic and endocrinopathies. *Problemy Endocrinologii*. 2020; 66 (1): 7–13 (In Russ.) DOI: 10.14341/probl12376.

42. Finer N., Garnett S.P., Bruun J.M. COVID-19 and obesity. *Clin. Obes*. 2020; 10 (3); 12365. DOI: 10.1111/cob.12365.

43. Imanov B.Zh., Murkamilov I.T., Sabirov I.S., Sarybaev A.Sh. Effect of renal dysfunction on the cardiac-vascular system. The possibilities of early diagnosis of the renal dysfunction. *The Russian Archives of Internal Medicine*. 2018; 8 (4): 260–265. (In Russ.) DOI: 10.20514/2226-6704-2018-8-4-260-265.

44. Vykhrystsenka L.R., Schastlivenko A.I., Bondareva L.I., Sidarenko A.V., Muzyka O.G. Kidney damage in COVID-19 infection. *Vestnik Vitebskogo gosudarstvennogo meditsinskogo universiteta*. 2021; 20 (1): 7–23. (In Russ.) DOI: 10.22263/2312-4156.2021.1.7.

45. Su H., Yang M., Wan C., Yi L.X., Tang F., Zhu H.Y., Yi F., Yang H.C., Fogo A.B., Nie X., Zhang C. Renal histopathological analysis of 26 postmortem findings of patients with COVID-19 in China. *Kidney Int*. 2020; 98 (1): 219–227. DOI: 10.1016/j.kint.2020.04.003.

46. Ali N., Hossain K. Liver injury in severe COVID-19 infection: current insights and challenges. *Expert. Rev. Gastroenterol. Hepatol*. 2020; 14 (10): 879–884. DOI: 10.1080/17474124.2020.1794812.

47. Cai Q., Huang D., Yu H., Zhu Z., Xia Z., Su Y., Li Z., Zhou G., Gou J., Qu J., Sun Y., Liu Y., He Q., Chen J., Liu L., Xu L. COVID-19: Abnormal liver function tests. *J. Hepatol. PMC. PubMed*. 2020; 73: 566–574. DOI: 10.1016/j.jhep.2020.04.006.

48. Olry A., Meunier L., Delire B., Larrey D., Horsmans Y., Le Louet H. Drug induced liver injury and COVID-19 infection: The rules remain the same drug safety. 2020; 43: 615–617. DOI: 10.1007/s40264-020-00954-z.

49. Mehta P., McAuley D.F., Brown M., Sanchez E., Tattersall R.S., Manson J.J.; HLH Across Speciality Collaboration, UK. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020; 395: 1033–1034. DOI: 10.1016/s0140-6736(20)30628-0.

50. Feng G., Zheng K.I., Yan Q.Q., Rios R.S., Targher G., Byrne C.D., Poucke S.V., Liu W.Y., Zheng M.H. COVID-19 and liver dysfunction: current insights and emergent therapeutic strategies. *J. Clin. Transl. Hepatol*. 2020; 8 (1): 18–24. DOI: 10.14218/JCTH.2020.00018.

51. Singh S., Khan A. Clinical characteristics and outcomes of COVID-19 among patients with pre-existing liver disease in United States: a multi-center research network study. *Gastroenterology*. 2020; 159 (2): 768–771. DOI: 10.1053/j.gastro.2020.04.064.

52. Petrov V.I., Ponomareva A.V., Ivakhnenko I.V., Razvalyaeva O.V., Meshrqi B.A., Statsenko V.I. Etiopathogenetic aspects of liver injury in patients with COVID-19. *Vestnik Volgogradskogo gosudarstvennogo meditsinskogo universiteta*. 2020; (4): 9–15. (In Russ.) DOI: 10.19163/1994-9480-2020-4(76)-9-15.

53. Novikova L.B., Akopian A.P., Sharapova K.M., Latypova R.F. Neurological and mental disorders associated with COVID-19. *Arterial Hypertension*. 2020; 26 (3): 317–326. (In Russ.) DOI: 10.18705/1607-419X-2020-26-3-317-326.

54. Shepeleva I.I., Chernysheva A.A., Kiryanova E.M., Salnikova L.I., Gurina O.I. The nervous system damages and psychological and psychiatric complications on the COVID-19 pandemic. *Sotsial'naya i klinicheskaya psikhiatri*. 2020; 30 (4): 76–82. (In Russ.)

55. Li Y.C., Bai W.Z., Hashikawa T. The neuroinvasive potential of SARSCoV-2 may play a role in the respiratory failure of COVID-19 patients. *J. Med. Virol*. 2020; 92 (7): 703–704. DOI: 10.1002/jmv.25728.

56. Belopasov V.V., Yachou Y., Samoilova E.M., Baklaushev V.P. The Nervous System Damage in COVID-19. *Klinicheskaya praktika*. 2020; 11 (2): 60–80. (In Russ.) DOI: 10.17816/clinpract34851.

57. Trejo-Gabriel-Galán J.M. Stroke as a complication and prognostic factor of COVID-19. *Neurologia*. 2020; 35 (5): 318–322. DOI: 10.1016/j.nrl.2020.04.015.