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Chapter

Frequency of Hyperglycemia in Patients with Covid-19 Infection and Pneumonia

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Abstract

Diabetes mellitus can increase the risk of death in COVID-19 by 12 times, according to the portal of the us Centers for disease control and prevention. Coronavirus-infected diabetics are six times more likely to need inpatient treatment, and diabetes is the second most severe complication in COVID-19 after cardiovascular diseases. The state of carbohydrate metabolism in patients with COVID-19 has not been sufficiently studied in clinical studies. Isolated studies indicate that viral infection may be accompanied by an increase in the concentration of glycated hemoglobin in patients with viral pneumonia. To assess the frequency of hyperglycemia and diagnosis of newly diagnosed diabetes mellitus in patients with COVID-19 and acute lung damage aged 41–80 years, who were hospitalized in a repurposed infectious diseases hospital in Moscow with a diagnosis of pneumonia. In the observational study analyzed laboratory and clinical diagnostic data of 278 patients who had, according to the anamnesis and the medical conclusions of impaired glucose tolerance and manifested forms of diabetes, including 163 men and 115 women, aged 41–80 years, admitted to the hospital for diagnosis and treatment in the period from 12.04.2020 on 10.11.2020 of diagnoses according to ICD-10: U07.1 Coronavirus infection. In the selected groups of patients, the initial and subsequent fasting blood glucose levels were analyzed after 8 hours without food intake on a stationary automatic analyzer and using portable glucose, meters using diagnostic test strips. The concentration of glucose and ketones in the urine was determined by a semi-quantitative method. We evaluated the dynamics of indicators when detecting pathological values of glucose concentration. Glucose levels above 6.4 mmol/l were taken as pathological. In patients aged 41–80 years who were hospitalized with covid-19 infection and pneumonia, fasting hyperglycemia was diagnosed in 31–47%, glucosuria in 1.9–6.1%, ketonuria – 20.4-46.2% of cases, in different age groups. In 16.6–31.3% of cases in patients with covid-19,after treatment and regression of changes in the lungs, normalization of glucose levels was observed, but in 14.8–16.7% of the changes persisted, and in 9–13% of them, after an additional study, newly diagnosed diabetes mellitus was diagnosed. Hyperglycemia was significantly more often detected in patients with arterial hypertension of 2–3 degrees of severity and with a tendency to reliability, in patients with obesity of 2–3 degrees. Lipid metabolism disorders (hypertriglyceridemia and hypercholesterolemia), which are characteristic of changes in carbohydrate metabolism in patients with impaired glucose tolerance and diabetes, were significantly more

often diagnosed in patients with covid-19 than in the group of patients with acute and chronic lung pathology without proven infection with this virus, but only in the group of patients aged 41–60 years. Covid-19 infection complicated by pneumonia occurs in individuals aged 41–80 years with a high incidence of hyperglycemia and ketonuria. The incidence of newly diagnosed diabetes mellitus in such patients is 9–13%.

Keywords: Covid-19 infection, pneumonia, hyperglycemia, diabetes mellitus

1. Introduction

The available data so far indicate that in SARS-CoV-2, the nature of the pathology goes beyond acute respiratory infection [1–4]. Researchers identify 2 more disease periods associated with SARS-coronavirus-2 infection, including a rare hyperinflammatory syndrome after an acute period and late inflammatory andvirological complications [1, 2]. These 3 disease periods not only determine the time course of SARS-CoV-2 infection at the population level, but also reflect the possible multiple organ involvement [1, 2, 5]. Patients may have pronounced cardiovascular and gastrointestinal lesions, and dermatological and cutaneous-mucous manifestations, such as giperosmolarna with Kawasaki disease [1, 2]. Laboratory studies can reveal elevated inflammatory markers (e.g., levels of C-reactive protein and ferritin), a coagulopathy (e.g. D-dimer) and elevated cardiac markers (troponin level), [6, 7]. According to the available data and according to some experts, the COVID-19 developing trebovatelna process or COVID-19-associated coagulopathy [5, 8, 9].

To the development of the disease most often predispose:

- cardiovascular diseases, especially arterial hypertension;
- diabetes mellitus;
- chronic lung disease;
- cancer (in particular, hematological malignancies, lung cancer, and metastasis);
- chronic kidney disease;
- obesity;
- smoking;
- immunodeficiency states;
- chronic liver diseases [10, 11].

According to sources from the Chinese center for disease control and prevention (February 2020) and who information materials [12, 13], the death rate from COVID-19 largely depends on the age of patients and the presence of chronic diseases, including diabetes mellitus (**Figure 1**). Based on the study of 72,314 cases of COVID-19, the researchers obtained the following statistics: patients suffering from cardiovascular diseases had a mortality rate of 13.2%, with verified diabetes mellitus 9.2%, with arterial hypertension 8.4%, with chronic forms of diseases respiratory tract 8%, with oncological pathology 7.6% [12, 13].

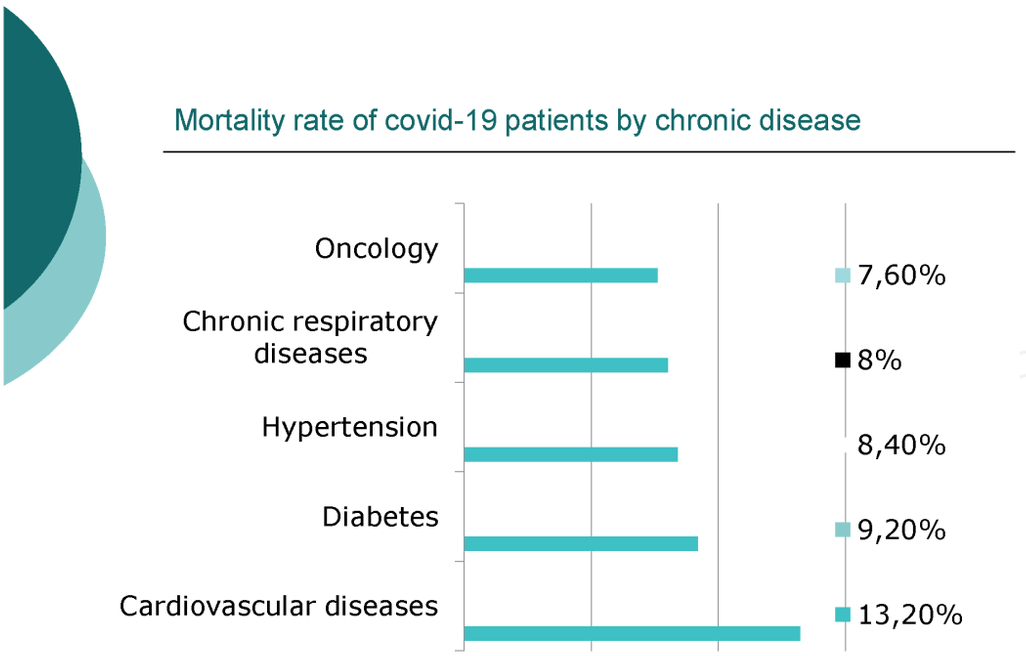


Figure 1.
Mortality rate of covid-19 patients by chronic disease (sources: WHO, Chinese authorities as of February 2020), [12, 13].

Diabetes can increase the risk of death in COVID-19 by 12 times, according to the portal of the US Centers for disease control and prevention [14]. Coronavirus-infected diabetics are six times more likely to need hospital admission and inpatient treatment, and diabetes is the second most severe complication in COVID-19 after cardiovascular disease [15].

The state of carbohydrate metabolism in patients with COVID-19 has not been sufficiently studied in clinical studies. Isolated studies indicate that viral infection may be accompanied by an increase in the concentration of glycated hemoglobin in patients with viral pneumonia [16–18].

2. Purpose and objectives of the study

To assess the frequency of fasting hyperglycemia and the frequency of diagnosis of newly diagnosed diabetes mellitus in patients with COVID-19 and acute lung damage aged 41–80 years, who were hospitalized in a repurposed infectious diseases hospital in Moscow with a diagnosis of pneumonia.

3. Material and methods

We have analyzed laboratory and clinical diagnostic data of 278 patients who had, according to the anamnesis and the medical conclusions of impaired glucose tolerance and manifested forms of diabetes, including 163 men and 115 women, aged 41–80 years, admitted to the hospital for diagnosis and treatment in the period from 12.04.2020 on 10.11.2020 of diagnoses according to international classification of diseases and causes of death revision 10 (ICD-10): U07.1 Coronavirus infection caused by a virus COVID-19, virus identified (confirmed by laboratory testing regardless of the severity of clinical signs or symptoms); J12.9 community acquired pneumonia. Patients 'data were archived in the city computer system of DZM KIS EMIAS (unified medical information and analytical system Department of health

of the city of Moscow). All patients were admitted to the hospital with fever symptoms, cough complaints, and shortness of breath. After inpatient treatment, all patients showed regression of inflammatory changes in the lungs and improvement of their condition. Patients were divided into groups depending on their age and the results of biochemical (PCR diagnostics and enzyme immunoassay for determining the concentration of M and G-immunoglobulins) and clinical-radiological studies

Namber. Disease, degree of respiratory failure	**Group 2 (41–60 years old) (n = 57)**	**Group 4 (61–80 years old) (n = 59)**	**The difference in percentages**
1. Segmental pneumonia of one lung	1 (1.7%)	0	1.7%
2. Focal pneumonia of one lung	2(3,5%)	0	3,5%
3. Lobar pneumonia of one lung	11(19,3%)	15(25,4%)	6,1%
4. Polysegmental pneumonia of 2 lungs	8(14%)	14(23,7%)	9,7%
5. Acute bronchitis	0	2(3,4%)	3,4%
6. Chronic bronchitis, exacerbation	4(7%)	5 (8.5%)	1.5%
7. Chronic obstructive bronchitis (COBD), exacerbation	6(10,5%)	9(15,2%)	4,7%
8. COBD out of exacerbation	9(15,8%)	4((6,8%)	9%
9. Bronchial asthma	9(15,8%)	4((6,8%)	9%
10. Bronchiectasis	0	2(3,4%)	3,4%
11. Benign formation of the bronchus	0	1(1,7%)	1,7%
12. Pneumosclerosis	3(5,3%)	9(15,2%)	9,9%
13. Emphysema of the lungs	1(1,7%)	4(6,8%)	5,1%
14. Bullous emphysema	0	2(3,4%)	3,4%
15. 1-sided hydrothorax	3(5,3%)	4(6,8%)	1,5%
16. 2-sided hydrothorax	8(15,8%)	5(8,5%)	7,3%
17. Exudative pleurisy	2(3,5%)	3(5,1%)	1,6%
18. Pneumothorax	0	2(3,4%)	3,4%
19. Atelectasis lungs	0	2(3,4%)	3,4%
20. Pulmonary embolism (PE) of the 1st lung	8(14%)	1(1.7%)	12.3%
21. PE of 2 lungs	1(1,7%)	0	1,7%
22. Stagnation in the pulmonary circulation (stagnation in the MCC)	2(3,5%)	2(3,4%)	0,1%
23. Acute respiratory viral infections	1(1,7%)	0	1,7%
24. Sleep apnea syndrome	1(1,7%)	0	1,7%
25. Respiratory failure 0	. 1(1,7%)	1(1,7%)	0
26. Respiratory failure 1 degree	. 2(3,4%)	4(6,8%)	3,4%
27. Respiratory failure 2 degree	2(3,4%)	0	3,4%

Table 1.
The nature of the respiratory system pathology and the frequency of respiratory failure in two groups of patients without clinical, radiological and biochemical signs of COVID-19.

MSCT (multispiral computed tomography of the chest and lung radiography) performed in all 278 patients. Diagnosis COVID-19 was verified from 162 patients, including 86 men and 76 women who were divided into two groups according to age: 1st - 86 patients at the age from 41 to 60 years, an average of 50.7 ± 1.8 years, men 50(58.1 per cent), women 36(41.9 percent) and 3-group, 76 patients aged 61 to 80 years, an average of 70.3 ± 2.6 years, men 36,women 40. The comparison group consisted of 116 patients, including 77 men and 39 women with pathology of respiratory system coming to the hospital on an emergency basis with referral physician diagnosis of SMP J12.9 community acquired pneumonia, in which the results of the study in the hospital signs of infection COVID-19 have been identified. By age, these patients were divided into two groups: group 2–57 patients aged 41–60 years, average 50.2 ± 2.4, men 36, women 21 and group 4–59 patients, including 41 men and 18 women, age from 61 to 80 years, average age 66.3 ± 1.5 years. The nature of the pathology of the lungs and respiratory system in patients without signs of covid-19 infection is shown in **Table 1**.

The nature of lung damage according to the chest MSCT method and the severity of respiratory failure in patients with COVID-19 and pneumonia are shown in **Table 2**.

In the selected groups of patients, theinitial and subsequent fasting blood glucose levels were analyzed after 8 hours without food intake on a stationary automatic analyzer and using portable glucose, meters using diagnostic test strips. The concentration of glucose and ketones in the urine was determined by a semi-quantitative method. We evaluated the dynamics of indicators when detecting pathological values of glucose concentration. Glucose levels above 6.4 mmol/l were taken as pathological.

Number Disease	**Group 1 (41–60 years old) (n = 86)**	**Group 3 (61–80 years old) (n = 76)**	**The difference in percentages**
1. Pneumonia of the 1st lung	6(7%)	5(6,6%)	0,4%
2. Pneumonia of 2 lungs	69(80,2%)	63(82,9%)	2,7%
3. No pneumonia	11(12,8%)	8(10,5%)	2,3%
4. MSCT scan 1(the degree of lung damage according to the results of multispiral computed tomography)	31(41,3%)	21(27,6%)	13,7%
5. MSCT scan 2	36(48%)	47(61,9%)	13,9%
6. MSCT scan 3	8(10,7%)	7(9,2%)	1,5%
7. MSCT scan 4	0	1(1,3%)	1,3%
8. Respiratory failure 0	4(4,6%)	3(3,9%)	0,7%
9. Respiratory failure 1 degree	4(4,6%)	2(2,6%)	2%
10. Respiratory failure 2 degree	0	3(3,9%)	3,9%

Note: MSCT scan 0 Lungs are clean, there are no lesions. CT1 Focal inflammatory processes filling no more than 25% of alveoli. CT2 Half of the lung tissue is affected. CT3 Up to 75% of lungs are involved in the pathological process. CT4 Bilateral interstitial pneumonia, complete filling of the lung tissue with exudate. The condition is designated by the term respiratory distress syndrome, requires connection to a ventilator. From the site: https://tyubik.net/lecheniye-preparatami/991-kt-1-2-3-4-chto-jeto-znachit-pri-koronaviruse .html.

Table 2.
The frequency of detection of pneumonia in one and two lungs, the severity of pneumonia according to the criteria of multispiral computed tomography of the lungs, and the severity of respiratory failure in two groups of patients of different ages with COVID-19 (number of cases, frequency in %).

To assess hyperglycemia and diabetes, the "criteria for newly diagnosed diabetes mellitus" were used [World Health Organization, WHO, 9 June 2012]:

- Diabetes symptoms + increased venous blood plasma glucose concentration of 11.1 mmol/l when measured randomly. A measurement is considered random at any time of the day, without taking into account the time since the last meal. The classic symptoms of diabetes are polyuria, polydipsia, and weight loss in the absence of obvious causes.

- Fasting glucose concentration in blood plasma is 7.0 mmol/l or in whole blood 6.1 mmol/l. Measurement of glucose concentration is considered to be performed on an empty stomach, if at least 8 hours have passed after a meal.

- The concentration of glucose in blood plasma is 11.1 mmol/l 2 hours after taking 75 g of glucose (glucose tolerance test).

If there are no symptoms of diabetes, a second test should be performed on a different day to confirm the diagnosis. If the diagnosis cannot be confirmed by the level of fasting glycemia or by random measurement, a glucose tolerance test is performed.

Note: The normal concentration of fasting plasma glucose is considered to be 6.1 mmol/l. Impaired glucose tolerance is diagnosed when the fasting plasma glucose concentration is 6.1–7.0 mmol/l. A preliminary diagnosis of diabetes mellitus is established at an fasting plasma glucose concentration of 7.0 mmol/l. The diagnosis of diabetes must be confirmed.

At values above 7.0 mmol/l, according to WHO recommendations, 2012, a glucose tolerance test was performed and the level of glycosylated hemoglobin in the patient's peripheral blood was determined. The level of triglycerides and cholesterol in the blood serum was determined using a Getpremier spectrophotometer (USA). The level of pathologically elevated triglyceride concentrations was considered to be values above 2.8 mmol/l, cholesterol concentrations above 5.2 mmol/l.

Exclusion criteria. The sample did not include patients with worsening of pneumonia, transfer to the intensive care unit, death due to complications of covid infection, cirrhosis of the liver, oncopathology and hemoblastosis, chronic kidney disease of stages 4 and 5, purulent lung lesions, heart failure above stage 2A, with previously diagnosed diabetes and glucose tolerance disorders.

Methods of statistical processing of the obtained data. All the results of the study were processed statistically using the Exsel and Statgraphics software packages (version 2.6). The student's "t-test" was used to compare continuous variables. The Chi – square test or Fisher's exact test were used to evaluate a feature that characterizes the frequency of the phenomenon. The values were compared with the non-Gaussian distribution using the Mann–Whitney U-test. The average intergroup differences of the same type of indicators were compared with the assessment of the reliability of the detected differences.Were considered to be reliable values at $p < 0,05$.

4. Results and discussion

The detection rate of hyperglycemia exceeded 30% in group 1 of patients aged 41–60 years with COVID-19 and pneumonia, hyperglycemia persisted during the hospital follow - up period – in 14%, and the frequency of newly diagnosed diabetes mellitus exceeded 9% (**Table 3**). For all these parameters, we did not find any

Number	Indicator	Group 1 (n = 86, men 50, women 36) Patients with COVID-19 and pneumonia	Group 2 (n = 57, men 36, women 21) Patients with lung pathology	Difference in %	The significance of differen-ces, p
1.	Increased blood glucose concentration	27(31,4%)	27(47,4%)	16%	>0,05
2.	Normal concentration of glucose in the blood	59(68,6%)	30(52,6%)	16%	>0,05
3.	The frequency achieved of normoglycemia at higher rate	17 of 27 (63%)	21 of 27 (77.8%)	14.8%	>0,1
4.	Frequency of preservation of hyperglycemia during the period of inpatient treatment	4 of 27 (14.8%)	4 of 27 (14.8%)	0	>0,5
5.	Frequency identified the glycosuria	4 of 65 (6.1%)	1 of 47 (2.1%)	4%	>0.3
6.	Average values of glucose concentration in urine (mmol/l)	17,6 ± 3,86 (2,8–56)	1,7	—	—
7.	Without glucosuria	61 of 65 (93.9%)	46 of 47(97,9%)	4%	>0,3
8.	Ketonuria rate	30 of 65 (46.2%)	6 of 47 (12,8%)	33,4%	<0,01
9.	The average values of the concentration of ketones in the urine (mmol/l)	1,99 ± 0,26 (0,1-7,8)	3,52 ± 0,56 (0,1–10)	43,4%	<0,001
10.	No detected ketonuria	35 of 65 (53.8%)	41 of 47(87,2%)	33,4%	<0,01
11.	Newly diagnosed diabetes (DM)	8 of 86 (9.3%)	5 of 57 (8,8%)	0,5%	> > 0,5

Table 3.
Frequency of diagnosis of hyperglycemia, glucosuria, ketonuria and newly diagnosed diabetes mellitus in groups of patients aged 41–60 years with COVID-19 and pneumonia (group 1) and in patients with respiratory system damage without COVID-19 infection (group 2).

significant differences from the average values in the 2nd comparison group.The frequency of diagnosis of ketonuria in urine was 3.6 times higher in group 1 (the difference was statistically significant, p).

In the study of lipid metabolism in groups of patients it was found that pukazatel the frequency of hypertriglyceridemia was 25% in the 1st group of patients and was significantly higher than the values of the comparison group - 2-group, in which cases the improvement in the levels of TG in peripheral blood have been identified (**Table 4**). The average values of the concentrations of this lipid was also significantly higher in patients with COVID-19 and pneumonia (group 1), by 43.4% ($p < 0,001$). The frequency of hypercholesterolemia was higher in the 1st group of patients – in 22.2% of patients and exceeded by 18.4% (significantly, p).

The frequency of hyperglycemia detection exceeded 45% in group 3 patients aged 61–80 years with COVID-19 and pneumonia, hyperglycemia persisted during the hospital follow - up period – in 16.7%, and the frequency of newly diagnosed diabetes mellitus exceeded 13% (**Table 5**). In these parameters, except for the frequency of hyperglycemia preservation, we did not detect significant differences from the average values in group 4 comparison.

This indicator was 20.4% higher in the 1st group of patients, the difference was significant ($p < 0.05$). The frequency of diagnosis of ketonuria in urine was 2.0 times higher in group 1 (the difference is statistically unreliable, $p > 0.2$), but the average concentration of ketone bodies was 47.9% lower (significantly, $p < 0,001$).

We did not detect any cases of pathological elevation of TG levels in peripheral blood in groups 3 and 4 of patients (**Table 6**). The Mean values of the concentration of this lipid also did not differ significantly and significantly in patients with COVID-19 and pneumonia (group 3), and in patients of the comparison group (group 4). The frequency of hypercholesterolemia was also higher in the 4th group of patients – in 23.6% of patients and exceeded by 14.7% (unreliable, $p > 0,05$).

To clarify the nature of the association of hyperglycemia with comorbidity and the nature of therapy in patients with COVID-19 and pneumonia, we compared the

Number	Indicator	Group 1 (n = 86) Patients with COVID-19 and pneumonia	Group 2 (n = 57) Patients with lung pathology	Difference in %	Significance of differen-ces, p
1.	Frequency of hypertriglyceridemia	25%	0	25%	<0.03
2.	Without hypertriglyceridemia	75%	100%	25%	<0,03
3.	The average values of triglycerides concentration in blood (mmol/l)	2,43 ± 0,49 (0,76-6,81)	1,39 ± 0,08 (1,14-1,80)	42,8%	<0,001
4.	Frequency of hypercholesterolemia	22,2%	4%	18,4%	<0,05
5.	Frequency of normocholesterolemia	77,8%	96%	18,4%	<0,05
6.	Average values of concentration of cholesterol in blood (mmol/l)	3,86 ± 1,07 (0,62-7,75)	3,95 ± 0,98 (1,83-5,31)	2,3%	>0,3

Table 4.
The nature of changes in the concentration of triglycerides and cholesterol in peripheral blood in patients aged 41–60 years with COVID-19 and pneumonia (group 1) and in patients with respiratory system damage without COVID-19 infection (group 2), M ± m, the frequency of the sign in % and the significance of differences.

Number	Indicator	Group 3 (n = 76, male 36, female 40) Patients with COVID-19 and pneumonia	Group 4 (n = 59, men 41, women18) Patients with lung pathology	Difference in %	The significance of differences
1.	Elevated blood glucose	36 of 76 (47.3%)	35 of 59 (59,3%)	12%	> > 0,1
2.	The normal concentration of glucose in blood	40 of 76(52.7%)	24 of 59(40.7%)	12%	>0,1
3.	Frequency achieved normoglycemia at higher rate	28 of 36 (77.8%)	20 of 35 (57.1%)	20.7%	<0,05
4.	Frequency of preservation of hyperglycemia during the period of inpatient treatment	6 of 36 (16,7%)	5 of 35 (14.3%)	2.4%	>0,3
5.	The identified frequency of glycosuria	1 of 54 (1.9%)	8 of 48 (16.7%)	14,8%	>0,1
6.	Average values of glucose concentration in urine (mmol/l)	5.5	2,35 ± 0,74 (0,1–5,6)	—	
7.	Without glucosuria	53 of 54 (98.1%)	40 of 48 (83,3%)	14,8%	>0,1
8.	Ketonuria rate	11 of 54 (20.4%)	5 of 48 (10,4%)	10%	>0,2
9.	The average values of the concentration of ketones in the urine (mmol/l)	1,27 ± 0,21 (0,1-6,0)	2,44 ± 0,37 (0,1–8)	47,9%	<0,001
10.	No detected ketonuria	43 of 54 (79.6%)	43 of 48 (89,6%)	10%	>0,2
11.	Newly diagnosed DM	10 of 76 (13.1%)	5 of 59(8,5%)	4,6%	>0,3

Table 5.
Frequency of diagnosis of hyperglycemia, glucosuria, ketonuria and newly diagnosed diabetes mellitus in groups of patients aged 61–80 years with COVID-19 and pneumonia (group 3) and in patients with respiratory system damage without COVID-19 infection (group 4).

frequency of diseases recorded in medical records in 162 patients aged 41–80 years, including 63 with hyperglycemia and 99 with normoglycemia (**Table 7**). A statistically significant association with hyperglycemia was confirmed only for the diagnosis of grade 2–3 hypertension (arterial hypertension) – the difference between the groups was 22.8% ($p < 0,03$). The sign of grade 2–3 obesity was 16.8% more common in patients with hyperglycemia, the difference is on the verge of statistical significance ($p > 0.05$).

The study conducted in patients aged 41–80 years admitted to the hospital with suspected covid-19 infection revealed fasting hyperglycemia in 31–47% of different age groups, and newly diagnosed DM in 9–13% of patients. Comparison with groups of patients with acute and chronic lung pathology did not allow us to note significant and significant differences in these indicators. These data suggest that the development of covid infection with the addition of pneumonia is a significant factor in both the development of transient hyperglycemia and the manifestation of diabetes mellitus.

n/a number	Indicator	Group 3 (n = 76, male 36, female 40) Patients with COVID-19 and pneumonia	Group 4 (n = 59, men 41, women 18) Patients with lung pathology	Difference in %	Significance of differences
1.	Frequency of hypertriglyceridemia	0	0	0	—
2.	Without hypertriglyceridemia	100%	100%	0	0
.	The average values of triglycerides concentration in blood (mmol/l)	1,31 ± 0,08 (0,80-1,73)	1,45 ± 0,15 (0,62-2,25)	9,6%	>0,2
4.	Frequency of hypercholesterolemia	2,7%	> > 0,3	14,7%	>0,1
5.	Without hypercholesterolemia	91,1%	76,4%	14,7%	>0,1
6.	Average values of concentration of cholesterol in blood (mmol/l)	3,93 ± 0,83 (1,44-5,74)	4,04 ± 1,48 (3,19-7,43)	2,7%	>0,5

Table 6.
The nature of changes in the concentration of triglycerides (TG) and cholesterol (CH) in peripheral blood in patients aged 61–80 years with COVID-19 and pneumonia (group 3) and in patients with respiratory system damage without COVID-19 infection (group 4), M ± m, the frequency of the sign in % and the significance of differences.

Number	Indicator, type of pathology, treatment method	The frequency difference between	The accuracy of the indicator R
1.	Hypertension of 2–3 degrees of severity	22.8%	<0.03
2.	Grade 2–3 obesity	16.8%	>0.05
3.	Uterine fibroids (women)	11,1%	>0,2
4.	Paroxysmal and permanent-functional form of atrial fibrillation	10%	>0.2
5.	Chronic alcoholic disease	7.4%	>0.3
6.	Intracoronary transluminal angioplasty (TLAP) procedures, stenting	6.3%	>0.3
7.	Viral hepatitis B, C	6%	>0.3

Table 7.
The degree of difference in the frequency of certain forms of pathology and treatment measures in patients with COVID-19 and pneumonia aged 41–80 years, which prevailed in patients with hyperglycemia (n = 63), compared with patients with normal blood glucose concentration (n = 99).

Our data are confirmed by the results obtained in previous studies on the clinical assessment of the course of covid-19 in patients at a hospital in Wuhan (China). Thus, the authors reported that of 99 infected individuals, it was shown that 52% had elevated glucose levels, and in some patients with viral pneumonia, virus infection was accompanied by an increase in the concentration of glycated hemoglobin [19].

According to our data, in 16.6–31.3% of patients after treatment and regression of changes in the lungs, normalization of glucose levels was also observed, but in 14.8–16.7% the changes persisted, and in 9–13% of them, after an additional study, newly diagnosed diabetes mellitus was diagnosed. From these data, it can be assumed that the effect of covid-viral infection on carbohydrate metabolism in patients with pneumonia is observed mainly in the acute period of the disease, but in some patients, the disease in subsequent periods may manifest previously existing prerequisites for the development of chronic pathology (diabetes mellitus).

A feature of carbohydrate metabolism disorders in patients with COVID-19 and pneumonia in our study was a high frequency of ketonuria – more than 45% of patients aged 41–60 years studied in group 1. In the 3rd group of older patients, this pattern was less pronounced, the frequency of ketonuria exceeded 20%. We tried to link this feature of changes in the metabolism of ketone bodies with the vastness of the lung lesion and impaired gas exchange. However, a comparison of the rates of respiratory failure of varying severity in groups 1–3 of patients with COVID-19, as well as indicators of the severity of lung damage according to the diagnostic criteria of the chest MSCT method (multispiral computed tomography of the chest), did not reveal significant and significant differences between the groups. Based on the obtained data, we suggested that viral antigens can change the parameters of tissue membrane permeability for glucose in patients, with an increase in under-oxidized ketone bodies in the bloodstream and an increase in their urinary excretion. The rate of elimination of ketone bodies in the urine was apparently, higher in patients with COVID-19 in group 1 aged 41–60 years than in group 3, 61–80 years, which can be explained by a more preserved filtration function of the kidneys in the younger part of patients with this infection.

To date, apparently, only a few studies have estimated the prevalence of acidosis and ketoacidosis in a large number (n = 658) hospitalized patients with confirmed COVID-19 [20]. Of this sample, 42 (6.4%) patients had positive urine or serum ketones, with only three of 42 (7%) meeting the American Diabetes Association criteria for decompensated ketoacidosis (DKA). People with ketosis were about twice as likely to develop diabetes in this study, and three people who developed DKA were diagnosed with diabetes [20]. In a review and analytical article by employees from the Italian University and the Nephrological Center of Naples (Campania University, "Luigi Vanvitelli", and Nefrocenter Research & Nyx Start-UP, Naples, Italy), the nature of keto-acidotic conditions in patients with COVID-19 is analyzed The authors believe that at the onset of diabetes such conditions may include the so-called pre-diabetic state (impaired fasting glucose and impaired glucose tolerance), which occur with persistently normal levels of glycated hemoglobin, in addition, with a temporary hyperglycemic effect, usually observed in any acute or severe inflammatory disease, or symptoms and signs of ketoacidosis in patients, causes decompensated diabetes [21]. In actual clinical practice, clinicians may classify any event that occurs in people with high blood sugar levels as decompensated ketoacidosis (DKA), regardless of whether it was a real case of DKA or the accumulation of ketones was a consequence of respiratory acidosis potentiated by malnutrition (ion-controlled ketosis). A factor of keto-acidosis can also be a high concentration of inflammatory markers in the blood of patients with COVID-19, which is also typical for DKA, regardless of the concomitant disease [22, 23].

This assumption is confirmed by the results of studies in groups of patients with COVID-19 indicators of lipid metabolism. Since the natural type of lipid changes in diabetes mellitus, according to the literature, hypercholesterolemia are the most common types of lipid changes in diabetes mellitus, we analyzed these lipid parameters. The frequency of both hypertriglyceridemia and hypercholesterolemia in the

group of patients aged 41–60 years with COVID-19 and pneumonia exceeded 22% and was significantly higher than in the comparison group of patients of similar age without this viral infection. However, we did not find such differences in the groups of older patients. These data allowed us to assume that COVID-19 infection to a greater extent can affect glucose-dependent mechanisms of lipid exchange of triglycerides and cholesterol in patients with pneumonia at the age of 61 years than in older patients in whom lipid changes often cause not acute, and chronic factors associated with age-related changes of liver function and central hemodynamics. To clarify this issue, we analyzed the frequency of diagnosis of various forms of pathology, including cardiovascular, in patients with COVID-19 and pneumonia with hyperglycemia and normoglycemia in the general group of patients aged 41–80 years. The comparison allowed us to establish that hyperglycemia was significantly more often detected in patients with arterial hypertension of 2–3 degrees of severity and-with a tendency to reliability-more often in patients with obesity of 2–3 degrees. Neither coronary atherosclerosis (confirmed by coronary angiography and coronary stenosis plastic surgery), nor the frequency of previously developed cardiosclerosis with damage to the cardiac conduction system and the development of atrial fibrillation, nor liver damage in viral hepatitis and chronic alcoholism in the groups of patients with COVID-19 and pneumonia had a significant direct relationship with the frequency of detected cases of hyperglycemia.

5. Conclusions

1. In patients aged 41–80 years who were hospitalized with covid-19 infection and pneumonia, fasting hyperglycemia was diagnosed in 31–47%, glucosuria in 1.9–6.1%, ketonuria – 20.4-46.2% of cases, in different age groups.

2. In 16.6–31.3% of cases in patients with covid-19, after treatment and regression of changes in the lungs, normalization of glucose levels was observed, but in 14.8–16.7% of the changes persisted, and in 9–13% of them, after an additional study, newly diagnosed diabetes mellitus was diagnosed.

3. Hyperglycemia was significantly more often detected in patients with arterial hypertension of 2–3 degrees of severity and with a tendency to reliability, in patients with obesity of 2–3 degrees. Lipid metabolism disorders (hypertriglyceridemia and hypercholesterolemia), which are characteristic of changes in carbohydrate metabolism in patients with impaired glucose tolerance and diabetes, were significantly more often diagnosed in patients with covid-19 than in the group of patients with acute and chronic lung pathology without proven inyion with this virus, but only in the group of patients aged 41–60 years.

Conflict of interest

Didn't show up.

Authors' contribution

Vechorko V. I.-the idea of research. Writing sections "research Results", "discussion of results", "Conclusions". Doroshenko D. A.-description of research methods.

Evsikov E. M.-a set of materials, statistical processing, design of the article text. Baykova O. A.-writing the section "Introduction", design of the article text. Teplova N.V. - writing the chapter "Discussion of results".

Annotation

History of the issue

Already in the initial period of studying the prognostic significance and danger to human health and life of the state of infection with the COVID-19 virus in January–April 2020, mainly thanks to research from Chinese medical centers, it was clarified that factors contributing to lung damage are highly likely the course of the disease in severe form, include: advanced age [6]; diabetes [6, 7, 24]; obesity [25]; chronic lung diseases [14], including asthma [12]; heart disease [12, 16]; hypertension [14]; chronic kidney disease [14].

In one of the first clinical observations of 41 COVID-19-infected people in Wuhan, China, it was shown that in 32% of cases, COVID-19 was combined with other diseases, including diabetes (20%), hypertension (15%) and cardio-vascular diseases (15%), [16]. Another report of patients who were discharged or died at clinics in Wuhan between January 1, 2020 and March 8, 2020 reported that patients with COVID-19 with diabetes had worse outcomes compared to patients of the same sex and age without diabetes. Advanced age and concomitant arterial hypertension independently contributed to the hospital death of patients with diabetes [6]. The results obtained at the Wuhan Jin Yin Tang Hospital showed that in intensive care units, 17% of patients suffered from chronic diseases, including diabetes (17%), cerebrovascular diseases (13.5%), chronic heart disease (10%) and T. D. During treatment in 35% of critically ill patients, hyperglycemia was a concomitant pathology, and mortality among patients with diabetes was 77.7% [16, 26].

In a retrospective study of 138 patients with COVID-19, from a clinic in this city in China, published on February 7, 2020, it was shown that 46.4% of patients had one or more comorbidities, of which 10% had diabetes, while in wards Intensive care (ICU) 22.2% of patients had diabetes, that is, 2 times more often [26]. The study of the relationship between diabetes and mortality and severity of COVID-19, as well as in determining the prevalence of diabetes in patients with COVID-19, has also been conducted in several meta-analyzes. Employees from the Institute of Gastroenterology, Delhi, India (Institute of Liver, Gastroenterology, & Pancreatico-Biliary Sciences, Sir Ganga Ram Hospital, New Delhi, India). searched PubMed for case–control studies in English published between January 1 and April 22, 2020 that had data on diabetes in patients with COVID-19. The incidence of diabetes was compared between patients with and without a combined mortality or severity endpoint. Included 33 studies (16,003 patients). The authors found that diabetes was significantly associated with mortality from COVID-19 with a pooled odds ratio of 1.90 [24]. Another meta-analysis conducted by researchers at the Faculty of Medicine, Universitas Pelita Harapan, Tangerang, Indonesia analyzed data from 6452 patients from 30 studies. A meta-analysis showed that diabetes was associated with an incidence of combined adverse outcomes (relative risk, RR 2.38) and its subgroup, which included mortality (RR 2.12), severe COVID-19 (RR 2.45), acute respiratory distress syndrome (ARDS) (RR 4.64) and disease progression (RR 3.31). It was concluded that diabetes was associated with mortality, severe COVID-19, ARDS and disease progression in patients with COVID-19 [7].

From the statistics of the 2020 epidemic in the North American continent, it follows that diabetes mellitus can increase the risk of death from COVID-19 by 12 times, according to the portal of the US Centers for Disease Control and Prevention. Patients infected with coronavirus with diabetes are six times more likely to need hospitalization for inpatient treatment, and diabetes is in second place in terms of severity of complications in COVID-19 after cardiovascular disease [10]. According to the China Cardiometabolic and Cancer Cohort (4C) nationwide study, compared with patients with normal glucose tolerance, people with impaired glucose tolerance or diabetes had a high risk of lung infection with a multifactorial adjusted odds ratio (OR; 95% CI) 1.56 (1.02–2.37) and 1.63 (1.01–2.61), respectively [27]. Epidemiological evidence from the United States suggests that diabetes is associated with a high risk of infectious disease. People with diabetes are at increased risk of bacteremic pneumococcal infection and are reported to have a high risk of nosocomial bacteremia with mortality rates up to 50% [28]. At the same time, the state of carbohydrate metabolism in patients with COVID-19 who have not previously suffered from diabetes has not been sufficiently studied in clinical studies. Hyperglycemia, even in people with no previous diabetes, has often been observed in complicated coronavirus disease 2019 (COVID-19), [17, 18]. Hyperglycemia in COVID - 19 is a strong predictor of a worse prognosis and an increased likelihood of death [18]. In the above-cited study of patients with COVID-19, conducted at the Wuhan Jin Yin Tang Hospital, with the participation of 99 infected people, it was shown that 52% of those infected had elevated glucose levels, and in some patients with viral pneumonia, infection with the virus was accompanied by an increase in the concentration glycated hemoglobin [16].

Goal and tasks

To assess the incidence of hyperglycemia and diagnosis of newly diagnosed diabetes mellitus in patients with COVID-19 and acute lung damage at the age of 41–80 years, hospitalized in a repurposed infectious diseases hospital in Moscow with a diagnosis of pneumonia.

Material and methods

The observational study analyzed laboratory and clinical diagnostic data of 278 patients who did not have, according to the anamnesis and the presented medical reports, signs of impaired glucose tolerance and manifest forms of diabetes mellitus, including 163 men and 115 women aged 41–80 years admitted to hospital for diagnosis and treatment in the period from 12.04.2020 to 10.11.2020 with diagnoses according to ICD-10: U07.1 Coronavirus infection. In the selected groups of patients, the initial and subsequent levels of fasting blood glucose were analyzed, after 8 hours without food, on a stationary automatic analyzer and using portable glucometers using diagnostic test strips. The concentration of glucose and ketones in urine was determined by a semi-quantitative method. The dynamics of indicators was assessed when pathological values of glucose concentration were detected. Glucose levels above 6.4 mmol/L were considered pathological.

Results

In patients aged 41–80 years hospitalized with covid-19 infection and pneumonia, fasting hyperglycemia was diagnosed in 31–47%, glucosuria in 1.9–6.1%, ketonuria - 20.4-46.2% of cases, in different age groups. In 16.6–31.3% of cases in patients with covid-19, after treatment and regression of changes in the lungs, there was a

normalization of glucose levels, but in 14.8–16.7% of cases persisted, and in 9–13% of them, after an additional study, newly diagnosed diabetes mellitus was diagnosed. Hyperglycemia was significantly more often detected in patients with arterial hypertension of 2–3 degrees of severity and with a tendency to reliability, in patients with obesity 2–3 degree. Lipid metabolism disorders (hypertriglyceridemia and hypercholesterolemia), characteristic of changes in carbohydrate metabolism with impaired glucose tolerance and diabetes, were significantly more often diagnosed in patients with covid-19 than in the group of patients with acute and chronic lung pathology without proven infection with this virus, but only in the group of patients age period 41–60 years.

Conclusion

Covid-19 infection complicated by pneumonia occurs in persons aged 41–80 years with a high incidence of hyperglycemia and ketonuria. The incidence of newly diagnosed diabetes mellitus in such patients is 9–13%.

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