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LABORATORY MONITORING OF INDICES IN BURNT DURING INFECTION COVID-19

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***ABSTRACT*:** The results of laboratory and instrumental studies are analyzed in 46 victims with skin burns of various localization, area and depth of the lesion infected with COVID virus 19 hospitalized in the burn center of Saint-Petersburg Research Institute of Ambulance named after I.I. Dzhanelidze in 2020. The control group included 46 patients with similar severity lesions who were treated at the center in 2018. The data on the general condition of patients, clinical and biochemical blood tests, coagulogram, gas composition, general urine analysis, and X-ray data were assessed. It was found that in the groups of lightly and severely burned and patients in 75.9 and 64.9% of cases, respectively, X-ray examination and computed tomography of the chest organs did not reveal infiltrative changes in the lungs, despite the positive results of virological studies. In the second half of the incubation period, in comparison with the data obtained in the control group, deviations in the following indicators were stated: hemoglobin, hematocrit, leukocytes, neutrophils, lymphocytes, immature granulocytes, erythrocyte sedimentation rate, levels of total protein, creatinine and blood fibrinogen from 1.6% up to 18 times. In other analyzed parameters, no changes were noted. When comparing the data obtained in the second half of the incubation period with the results of laboratory studies of uninfected patients in the group of severely burned patients, significant differences were established among the thrombocyte readings (39.2% less), platelet count (42.9% less), and in the group of lightly burned — the number of erythrocytes (less by 11.8%), hemoglobin (less by 19.4%), hematocrit (less by 16.2%) and eosinophils (less by 71%), total protein (less by 5.6%) and creatinine (less by 12.2%). Providing medical care to patients during the pandemic caused by the new coronavirus infection COVID-19 is a challenge for the healthcare system. The results obtained are the first step towards understanding the features of the course of typical pathological processes caused by burn injury and the new coronavirus infection COVID-19.

Keywords: COVID-19; biochemical blood test; blood gas composition; infection; clinical blood test; coagulogram; coronavirus; burns.

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ЛАБОРАТОРНЫЙ МОНИТОРИНГ ПОКАЗАТЕЛЕЙ У ОБОЖЖЕННЫХ ПРИ ИНФИЦИРОВАНИИ COVID-19

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Резюме. Анализируются результаты лабораторных и инструментальных исследований у 46 пострадавших с ожогами кожи различной локализации, площади и глубины поражения, инфицированных вирусом COVID-19, госпитализированных в ожоговый центр Санкт-Петербургского научно-исследовательского института скорой помощи им. И.И. Джанелидзе в 2020 г. В группу контроля включено 46 пациентов с аналогичными по тяжести поражениями, лечившихся в центре в 2018 г. Оценены данные общего состояния пациентов, клинического и биохимического анализов крови, коагулограммы, газового состава, общего анализа мочи, а также данные рентгенологических исследований. Установлено, что в группах легко- и тяжелообожженных пациентов в 75,9 и 64,9% случаев соответственно при рентгенологическом исследовании и компьютерной томографии органов грудной клетки не были выявлены инфильтративные изменения в легких, несмотря на положительные результаты вирусологических исследований. Во второй половине инкубационного периода по сравнению с данными, полученными в контрольной группе, выявлены отклонения в показателях гемоглобина, гематокрита, лейкоцитов, нейтрофилов, лимфоцитов, незрелых гранулоцитов, скорости оседания эритроцитов, уровней общего белка, креатинина и фибриногена крови от 1,6% до 18 раз. В остальных анализируемых параметрах изменений не отмечено. При сравнении данных, полученных во второй половине инкубационного периода, с результатами лабораторных исследований неинфицированных пациентов в группе тяжелообожженных достоверные различия установлены среди показателей тромбокрита (меньше на 39,2%), уровня тромбоцитов (меньше на 42,9%), а в группе легкообожженных — числа эритроцитов (меньше на 11,8%), гемоглобина (меньше на 19,4%), гематокрита (меньше на 16,2%) и эозинофилов (меньше на 71%), общего белка (меньше на 5,6%) и креатинина (меньше на 12,2%). Оказание медицинской помощи пациентам в период пандемии, вызванной новой коронавирусной инфекцией COVID-19, является сложной задачей для системы здравоохранения. Полученные результаты являются первым шагом на пути понимания особенностей течения типовых патологических процессов, вызванных ожоговой травмой и новой коронавирусной инфекцией COVID-19.

Ключевые слова: COVID-19; биохимический анализ крови; газовый состав крови; инфекция; клинический анализ крови; коагулограмма; коронавирус; ожоги.

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BACKGROUND

Currently, the new coronavirus infection, COVID-19, continues to spread worldwide. In every country, people are infected, recovered, and deceased. In many large clinics, in parallel with treating such patients, fundamental and clinical studies are being conducted to assess the impact of new infection on the human body, including in combination with various somatic pathologies and injuries [1, 2].

COVID-19 is a viral infectious disease caused by a specific virus., in 10% to 15% of patients with COVID-19, the infection progresses to an acute respiratory syndrome, the so-called cytokine storm. This progression enables parallels to be drawn with a burn disease when, as a result of massive ingestion of tissue decay products into the bloodstream, it causes hyperactivation of the cytokine cascade [3, 4]. A scientific hypothesis proposes that during the infection process with COVID-19, neutrophils begin to form extracellular traps causing organ damage. In patients with a severe course of new coronavirus infection, there is a progression of pulmonary inflammation, high levels of pro-inflammatory cytokines in the blood serum, and extensive damage to the lungs develops against their microthrombosis [5, 6]. Leukocytes are a source of leukotrienes, platelet aggregation factors, proteases, and oxidants. This reaction of the release of biologically active and aggressive cellular components causes fibrin loss in the alveoli, hyaline membrane formation, and microthrombosis in the vascular bed of the lungs [7]. The acute process ends with primary hypoxemia, impaired ventilation function, and bronchial tree drainage. The addition of secondary bacterial microflora supports the progression of processes and the development of pneumonia. Pneumonia can be reversible, which avoids death in the acute period, but it can cause a serious complication in the form of organized pulmonary fibrosis [2].

COVID-19 is a systemic infection affecting the hematopoietic system and hemostasis [8]. Lymphopenia is one of the manifestations of infection and has the prognostic potential [9]. The numerical ratio of neutrophils to lymphocytes and the peak ratio of platelets to lymphocytes have prognostic value in identifying the severity of the disease course. The evaluation of the dynamics of the lymphocyte count and other markers of inflammation, such as lactate dehydrogenase (LDH), C-reactive protein, and interleukin-6 (IL-6), can predict the development of critical conditions and contribute to the timely provision of medical care [10]. Biomarkers, such as serum procalcitonin and ferritin, are poor predictors of COVID-19. One of the most common complications of coronavirus infection is hypercoagulation. The gradual increase in D-dimer levels during disease progression is closely associated with worsening the patient's condition and poor prognosis. Other markers of hypercoagulation, such as prolonged prothrombin time (PT) and activated partial thromboplastin time, increased fibrin degradation products, and severe thrombocytopenia, lead to the development of disseminated intravascular coagulation syndrome [11–13]. Assessing the dynamics of blood biomarkers during COVID-19 infection can help clinicians implement an individualized approach to treatment [14].

The burn department has the highest infectious risk of COVID-19 due to the unpredictable possibility of emergency hospitalization of patients with an unknown epidemiological history. Algorithms to manage such patients have been proposed, which are similar in most countries [15]. Over the past 25 years, considerable experience has accumulated in understanding the pathogenesis of the development of complications of burn disease. Clinicians must provide complete medical care under particular conditions in cases involving extensive burns combined with new coronavirus infection.

This study aimed to analyze the results of laboratory and instrumental studies in COVID-19 patients with skin burns of various lesion localizations, areas, and depths.

MATERIALS AND METHODS

The study was based on the results of the examination and treatment of 46 burn patients with a confirmed diagnosis of novel coronavirus infection (COVID-19), hospitalized at the burn center of the I.I. Dzhanelidze Saint Petersburg Research Institute of Emergency Medicine (SPRIEM) from April to November 2020. All the patients were distributed into two groups depending on the severity of the burn injury, including 29 minor-burned patients (without the development of a burn disease) and 17 severely burned patients (with the development of a burn disease). The control group (CG) consisted of 29 and 17 mild and severely burned patients, respectively, who were also treated in the intensive care unit of the SPRIEM burn center in 2018. For a comparative analysis, we used the results of a group of burn patients infected with COVID-19, obtained in half 2 of the incubation period (InP). This period is the most significant concerning assessing the impact of new coronavirus infection on the condition of burn patients.

In the analyzed sample of patients, the nonparametric Mann–Whitney test did not reveal significant intergroup differences between age, total burn area, and deep burn area (Table 1).

Blood and urine laboratory parameters were assessed at three control points selected considering the InP of new coronavirus infection, corresponding to 14 days. Point 1 was within the interval from 7 to 10 days before the start of the proposed InP. The InP (14 days) was divided into equal intervals of 7 days to determine more accurately the possible changes in the laboratory parameters analyzed. Half 1 (days 1–7) and 2 (days 7–14) of the InP corresponded to control points 2 and 3. The list of laboratory examinations performed during the study is presented in Table 2.

In addition, the state of the red bone marrow lineage (normoblasts, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, the width of the histogram of the erythrocyte distribution relative to the average volume (variation coefficient), red cell distribution width (standard deviation)), and leukocyte (level of basophils) and platelet (count of large platelets, mean platelet volume, platelet distribution width) links with hematopoiesis were assessed.

Statistical processing of the results obtained was performed using MS Office Excel (Microsoft, USA) and Statistics 17.0 (StatSoft, USA) software. The median (*Me*)

Table 1. The test scores of both groups burned, Me (Q25; Q75)
Таблица 1. Исследуемые показатели обожженных обеих групп, *Me* (Q25; Q75)

Parameter	Control group	COVID-19	*p*
Severely burned			
Age	55 (37.5; 64.5)	54 (47.5; 58)	0.919
Total burn area	35 (35; 45.5)	40 (31; 54)	0.540
Deep burn area	14 (8; 18)	15 (7.5; 29.5)	0.658
Mildly burned			
Age	58 (51.5; 62.5)	55 (41.5; 69.5)	0.618
Total burn area	10 (8; 14.5)	8 (4; 21.5)	0.523
Deep burn area	3 (1.5; 4)	4 (0.5; 10.5)	0.248

Table 2. List of laboratory indicators in patients suffering from skin burns and COVID-19
Таблица 2. Перечень лабораторных показателей у больных, страдающих ожогами кожи и COVID-19

Clinical blood test		
erythrocytes	neutrophils	eosinophils
hemoglobin	lymphocytes	platelets
hematocrit	monocytes	ESR
leukocytes	immature granulocytes	
Biochemical blood test		
ALT	glucose	total bilirubin
AST	total protein	creatinine
Coagulogram		
INR	prothrombin time	
Quinck prothrombin activity	fibrinogen	
Gas composition of the blood		
BE b	pO_2	SO_2
FiO_2	pO_2t	pH
patient temperature	pCO_2t	lactate
General urine analysis		
relative density	bilirubin	nitrites
transparency	glucose	urobilinogen
color	ketone bodies	leukocytes (microscopy)
protein	acidity (pH)	erythrocytes (microscopy)

Note: ALT — alanine aminotransferase; AST — aspartate aminotransferase; INR—international normalized ratio; BE b — buffer bases; FiO_2 —concentration of oxygen in the inhaled air; pO_2 — partial pressure of oxygen in the blood; pCO_2t — partial pressure of oxygen in the blood, converted to body temperature; pCO_2t — partial pressure of carbon dioxide in the blood, converted to body temperature; ESR — erythrocyte sedimentation rate; SO_2 — blood concentration of oxygen; pH — hydrogen indicator.

was used as an average indicator with boundaries equal to the 25th (Q_{25}) and 75th (Q_{75}) quartiles. The significance of differences between related and unrelated data samples was determined using the *t*-Wilcoxon and *U*-Mann – Whitney tests, respectively. The alternative hypothesis was accepted at $p < 0.05$.

RESULTS AND DISCUSSION

Stage 1 of the study included an analysis of the treatment results of 17 patients with extensive deep skin burns, in whom the COVID-19 virus infection was laboratory confirmed. The average patient age was 53 (37.5; 64.5) years, while the total area of the burn and the area of deep skin lesions corresponded to 40% (31; 54) and 15% (7.5; 29.5) of the body surface. When assessing the incidence of pneumonia in this group of burn patients, it was revealed that in the incubation period (14 days from collecting the material from the pharynx/upper respiratory tract for diagnosing (polymerase chain reaction) the COVID-19 virus), signs of infiltration confirmed by X-ray examination and the results of computed tomography of the chest organs were detected only in 4 (23.5%) patients, including three cases of bilateral polysegmental pneumonia and one case with damage to the lower lobe of the right lung; two patients (11.7% of the total number of cases) were diagnosed with bilateral lower lobe and right-sided middle lobe pneumonia before the InP. In 11 (64.7%) patients, there were no specific symptoms characteristic of new coronavirus infection caused by the COVID-19 virus and no signs of infiltrative lung lesions in the InP. However, in two burn patients from this group, foci of lung tissue infiltration were detected, which regressed by the beginning of the presumed incubation period (14 days from obtaining a positive test result for coronavirus).

When infected with the COVID-19 virus, respiratory dysfunction is one of the major pathognomonic symptoms. It was established that in the group of severely burned patients, only 5 (29.4%) of 17 were on artificial lung ventilation (ALV) at the time of transfer from the institute to a hospital repurposed for the treatment of those infected with the coronavirus. Patients were transferred to ALV within 14 days from a positive COVID-19 result in all these cases. Mechanical ventilation was provided in the ventilation mode with pressure support with the average values of oxygen concentration in the inhaled gas mixture of 35 ± 12%, spontaneous inspiration support pressure of 12 ± 4 cm of the water column, and positive end-expiratory pressure of 5 ± 0.5 cm of the water column. Blood oxygen saturation (SpO_2) was maintained at 97%–99%. In 11 (64.7%) cases, the patients could independently maintain the necessary blood SpO_2 level of more than 95%. In one case, additional oxygen insufflation through nasal catheters in a volume of 4–5 l/min was required. The average body temperature increased insignificantly in half 2 of the InP to 37.05°C, which was 0.95% higher than the results obtained at control point 1 (half 1 of the InP). An analysis of the venous blood gas composition in severely burned patients with a positive test result for COVID-19 is presented in Table 3.

It was established that all patients with extensive burns and a verified diagnosis of COVID-19 infection tended to be b deficiency of – 0.65 mmol/l and –1.3 mmol/l for halves 1 and 2 of the InP, respectively. However, these changes were within the reference values of 0 ± 2.3 mmol/L.

The oxygen partial pressure in the blood in burn patients with confirmed COVID-19 virus infection in halves 1 and 2 of the InP was close to the lower limit of the reference values (40–60 mm Hg) and had no significant deviations. However, the pCO2 value turned out to be below the lower

Таблица 3. Показатели газового состава венозной крови тяжелообожженных с верифицированным COVID-19, *Me* (Q25; Q75)
Table 3. Indicators of venous blood gas composition of severely burnt with verified COVID-19, *Me* (Q25; Q75)

Parameter	Control group	Half 1 of InP	Half 2 of InP
BE b, mmol/l	–0.1 (–2.85; 1.3)	–0.65 (–4.25; 1.9)	–1.3 (–3.2; 1.4)
FiO_2, %	21 (21; 32.5)	21 (21; 28.75)	21 (21; 30.0)
Patient temperature, °C	37.2 (36.7; 37.7)	36.7 (35.98; 37.55)	37.05 (36.73; 37.3)
pO_2, mm Hg	43.7 (36.3; 46.85)	39.1 (28.35; 45.65)	40.05 (36.03; 46.18)
pO_2t, mm Hg	41 (36.8; 43.75)	38.5 (27.08; 44.75)	40.5 (35.13; 46.85)
pCO_2t, mm Hg	44.2 (37.25; 50.7)	41.55 (38.25; 43.85)	41.6 (36.85; 46.55)
SO_2, %	77.3 (68.85; 83.8)	68.15 (42.15; 80.65)	77.2[1] (63.38; 80.8)
pH, n	7.4 (7.36; 7.42)	7.38 (7.32; 7.43)	7.39 (7.33; 7.41)
Lactate, mmol/l	1.6 (1.21; 1.82)	2.4 (1.6; 3.05)	1.9[2] (1.75; 2.45)

Note: [1] — Wilcoxon *t*-test: differences compared to the results obtained in the half 1 of the incubation period (InP); [2] — Mann – Whitney *U*-test: differences compared to the results obtained in the control group, $p < 0.05$.

limit of the norm (46–58 mm Hg) by 9.7% and 9.6% in halves 1 and 2 of InP, respectively. There were also no significant differences in this parameter between the study points in halves 1 and 2 of the InP. An assessment of the blood oxygen saturation indicator enabled it to state its increase in half 2 of the InP to 77.2%, which is 13.3% ($p < 0.05$) higher than the results obtained at control point 1. Exceeding the level of permissible values (0.6–1.4 mmol/l) was noted when assessing the blood level of lactate. The maximum content of metabolites was recorded in half 1 of InP (2.4 mmol/l, 71.4% above the upper limit of the norm), and it decreased to 1.9 mmol/l (35.7% above the upper limit of the norm). In half 2 of the InP, significant differences were detected only in the level of lactate in venous blood in severely burned COVID-19 patients and in the CG examined.

The results of clinical blood tests in patients with extensive skin burn with positive test results for COVID-19 indicate the presence of deviations from the reference values at all points of the study of the counts of erythrocytes, hemoglobin, hematocrit, leukocytes, neutrophils, lymphocytes, and the value of syncytium forming units (Table 4).

Exceeding the permissible values (less than 0.03 × 109/l) of immature granulocytes was noted only outside the InP and in its half 2 by 16.7% and 18.3 times, respectively. There were wave-like dynamics of erythrocytes in patients with extensive burn injury and verified COVID-19. The maximum value was noted at a period up to 14 days from the positive test result for coronavirus (outside the InP), namely, 3.48 × 1012/l, which was 4.2 and 0.6% ($p > 0.05$) higher compared with the halves 1 and 2 of InP. There were no significant changes in the erythrocyte counts in the analyzed patient group. The dynamics of hemoglobin counts were positive and linear. Outside the InP and in its half 1, its value corresponded to 97 g/l, followed by an increase of 2% ($p > 0.05$) in its half 2.

For all patients with extensive skin burns, hemoconcentration is characteristic, which, during the intensive infusion therapy and intravascular destruction of erythrocytes, was replaced by hemodilution. Before transferring to a specialized infectious diseases hospital repurposed to treat COVID-19 patients, the hematocrit count in severely burned patients corresponded to the value of 30.7%, which is 0.6% and 2.8% ($p > 0.05$) less than the results obtained outside the InP and its half 1.

Wound infection and developing intoxication cause the development of a systemic inflammatory response. This is manifested as an increase in the level of leukocytes (norm 4–7 × 109/l) and neutrophils (norm 47%–72%), the values of which in half 2 of the InP reached 9.9 × 109/l and 75.6%, respectively, which was 41.4% and 5% above the upper limit of normal. The dynamics of the blood level of lymphocytes also had a wave-like course. In half 1 of the InP, the indicator analyzed was close to the lower limit of the norm (19–37%) and amounted to 18.7%, which was 29.9% and 24.7% ($p > 0.05$) higher than the results obtained in the halves 1 and 2 of the InP. ESR tended to a significant increase. The maximum value was noted in half 2 of the InP and corresponded to a value of 55 mm/h, which was 37.5% and 28.8% ($p > 0.05$) higher than the value at the control points 1 and 2 (outside the InP and in its half 1).

In COVID-19 patients with extensive skin burns, compared with the CG in half 2 of InP, significant ($p < 0.05$) differences in thrombocrit and platelet levels were revealed, which were 42.8% and 39.2% lower, respectively.

Table 4. Indicators of clinical blood test the tyazheloobozhzhennykh with the verified COVID-19, *Me* (Q25; Q75)
Таблица 4. Показатели клинического анализа крови тяжелообожженных с верифицированным COVID-19, *Me* (Q25; Q75)

Parameter	Control group	Outside InP	Half 1 of InP	Half 2 of InP
Erythrocytes, $\times 10^{12}$/L	3.37 (3.03; 3.76)	3.48 (3.01; 4)	3.34 (3.2; 4.55)	3.46 (3.13; 3.97)
Hemoglobin, g/l	101 (95.5; 109.5)	97 (88; 105.5)	97 (91; 128)	99 (88; 111)
Hematocrit, %	31.7 (29.7; 34.4)	30.9 (27.15; 33.25)	31.6 (28.4; 39.2)	30.7 (27.95; 35.1)
Leukocytes, $\times 10^9$/L	10.7 (10.2; 14.87)	11 (9.75; 16.1)	10.66 (7.2; 12.62)	9.9 (7.25; 13.49)
Neutrophils, %	76.9 (68.7; 81.05)	74.6 (57.9; 81.2)	73.3 (62.5; 81.4)	75.6 (68.3; 77.3)
Lymphocytes, %	9 (6; 16)	18.7 (10; 29.35)	14.4 (8; 24.3)	15 (7.5; 19.85)
Monocytes, %	7 (6; 11)	6.9 (5.95; 10.9)	7.4[1] (4.75; 11.2)	7.1 (4.5; 8.75)
Immature granulocytes, $\times 10^9$/L	0.8 (0.2; 1.4)	0.035 (0.02; 0.1)	0.03 (0.02; 0.05)	0.55[1, 2] (0.04; 1.48)
Eosinophils, %	1.2 (1; 3)	1 (0.7; 1.4)	1 (0.25; 3.45)	1.65 (0.1; 2.7)
Thrombocrit,%	0.51 (0.39; 0.64)	0.22 (0.19; 0.3)	0.27[1] (0.22; 0.38)	0.31[1, 3] (0.19; 0.41)
Platelets, $\times 10^9$/L	497 (343.5; 686)	226 (194; 505)	263 (200; 438)	284[3] (222; 435)
ESR	60 (42; 65)	40 (17.5; 57.5)	42.5 (28.5; 55)	55[1] (25; 65)

Note: [1] — Wilcoxon *t*-test: differences compared with the results obtained outside the incubation period (InP); [2] — differences compared with the results obtained in the half 1 of the InP; [3] — Mann – Whitney *U*-test: differences compared with the results obtained in the CG, $p < 0.05$.

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Таблица 5. Показатели биохимического анализа крови тяжелообожженных с верифицированным COVID-19, *Me* (Q25; Q75)
Table 5. Indicators of biochemical blood test the tyazheloobozhzhennykh with the verified COVID-19, *Me* (Q25; Q75

Parameter	Control group	Outside InP	Half 1 of InP	Half 2 of InP
ALT, U/l	28.7 (15.45; 55.1)	24 (16.58; 40.93)	24.8 (20.58; 47.3)	19.3[1] (12; 36.9)
AST, U/l	24 (16.65; 55.8)	22 (15.4; 39.4)	27.85 (14.58; 40.38)	20.9[1] (12.9; 29;15)
Glucose, mmol/l	5.83 (5.14; 6.79)	5.11 (4.66; 6.4)	5.42 (4.25; 5.72)	5.25 (4.64; 7.0)
Total protein, g/l	57.4 (53.6; 60.9)	53.8 (49.25; 59.45)	51.6 (47.7; 58.3)	50.1 (45.55; 56.75)
Total bilirubin, mcmol/l	7.9 (5.98; 8.63)	8.2 (6.55; 14)	8.3 (6.2; 10)	5.7 (4.75; 11.85)
Creatinine, mcmol/l	51 (42; 64.5)	37 (28.5; 53)	54 (32; 64)	59 (30.5; 67.5)

Note: [1] — Wilcoxon *t*-test: differences compared to the results obtained in the half 1 of the incubation period (InP), $p < 0.05$.

The course of burn disease and infection with COVID-19 affected the main homeostasis systems of the body and was accompanied by changes in several parameters of the biochemical blood test (Table 5).

It was established that the total protein level in severely burned patients with verified COVID-19 tended to decrease at all follow-up points. Its minimum value (50.1 g/l) was noted in half 2 of the InP, which was 6.9% and 2.9% ($p > 0.05$) less than the results obtained in the control point 1 (outside the InP) and the control point 2 (half 1 of the InP). The creatinine level was characterized by a minimum value outside the InP (37 μmol/l), followed by an increase of 45.9% and 59.4% ($p > 0.05$) in its halves 1 and 2 of the InP, respectively.

Hypercoagulation is known to occur in COVID-19 patients, and thrombosis of microvessels in tissues results in their obligate lesion and the development of fibrosis. We have not revealed significant differences in most coagulogram parameters in patients with extensive skin burns and COVID-19 infection, except for the fibrinogen level. Its counts throughout the entire follow-up period exceeded the upper limit of the reference values (2–4 g/l), reaching a maximum in half 2 of the InP (7.02 g/l), which was 46.6 and 15.6% ($p < 0.05$) higher than the results obtained at the control point 1 (outside the InP) and the control point 2 (half 1 of the InP), respectively (Table 6).

At stage 2 of the study, the results of laboratory and instrumental studies in minor-burned patients associated with new coronavirus infection COVID-19, i.e., without developing a burn disease, were evaluated. The retrospective study included 29 such patients. The average indicators of age, total burn area, and volume of deep skin lesions for this group of cases were 55 (41.5; 69.5) years, 8% (4; 21.5), and 4% (0.5; 10.5), respectively.

It was established that pneumonia, confirmed by X-ray examination and the results of computed tomography of the chest organs, was diagnosed in InP in 3 (10.3%) patients of this group. At the same time, for up to 14 days (presumptive InP) from the positive result of the study for coronavirus, radiographic signs of lung tissue lesions were not detected. In 2 (6.9%) burn patients, signs of pneumonia persisted, diagnosed using computed tomography of the chest organs before COVID-19 InP (up to 14 days from the positive result of the polymerase chain reaction). In 22 (75.9%) patients, radiological examinations revealed no changes in the lung tissue.

COVID-19 patients with minor burns showed abnormal erythrocytes, hemoglobin, hematocrit, and ESR (Table 7).

Таблица 6. Показатели коагулограммы тяжелообожженных с верифицированным COVID-19, *Me* (Q25; Q75)
Table 6. Coagulogram indices of severely burnt with verified COVID-19, *Me* (Q25; Q75)

Parameter	Control group	Outside InP	Half 1 of InP	Half 2 of InP
INR	1.09 (1.02; 1.18)	1.11 (1.03; 1.2)	1.11 (1.05; 1.22)	1.14 (1.12; 1.29)
Prothrombin activity according to Quick, %	886 (78; 93.5)	85 (75.5; 92)	84 (73.5; 92.25)	83 (69.5; 84.5)
PT, s	14.1 (13.5; 15.15)	13.3 (12.3; 14.35)	13.25 (12.48; 14.63)	13.6 (13.35; 15.4)
Fibrinogen, g/l	6.81 (5.78; 7.1)	4.79 (3.88; 7.46)	6.07[1] (4.34; 8.39)	7.02[1, 2] (6.25; 81.9)

Note: [1] — Wilcoxon *t*-test: differences compared to the results obtained outside the incubation period (InP); [2] — differences compared with the results obtained in the half 1 of the InP, $p < 0,05$.

Table 7 indicates that the dynamics of the level of erythrocytes is characterized by a gradual increase with a minimum value outside the COVID-19 InP equal to 3.66 × 1012/l, which is 8.5% less than the lower limit of the reference values (4–5 × 1012/l). The blood hemoglobin level, as well as the hematocrit, in half 2 of the InP, compared with the data obtained outside it, increased by 3.2% and 7% ($p > 0.05$), respectively, but remained below the norm. The dynamics of changes in the ESR value were characterized by a wave-like nature. At control point 1 (outside the InP), its maximum value was noted as 50 mm/h, which is 88.7% and 42.9% ($p < 0.05$) higher than the results in halves 1 and 2 of the InP. Comparison of the data obtained in half 2 of the InP with the CG results enabled the establishment of significant differences only in the levels of erythrocytes, hemoglobin, and hematocrit.

In minor-burned patients with burn injury and COVID-19, the characteristics of the dynamics of laboratory blood parameters were revealed. Thus, there was a deviation from the reference values in the total protein levels, aspartate aminotransferase, and creatinine. Outside the COVID-19 InP, the total protein level corresponded to 62.05 g/l, which was 3.6% and 1.5% ($p > 0.05$) lower than the values obtained in halves 1 and 2 of the InP. A similar tendency was noted in the changes in AST. The dynamics of AST were nonlinear, with an increase in control point 2 (half 1 of the InP) and a decrease in the control point 3 (half 2 of the InP). The maximum increase in the indicator was noted in its half 1 (31.7 units/l), which was 2.3% higher than the permissible values. Changes in the creatinine level were characterized by a significant ($p < 0.05$) increase from 53.5 μmol/L at control point 1 (outside InP) to 65 μmol/L at control point 3 (half 2 of InP), respectively (Table 8).

Comparison of the results of laboratory parameters in the next day after the transfer (half 2 of InP) of infected minor-burned patients to a specialized infectious diseases hospital with CG data revealed significant ($p < 0.05$) differences in the level of total protein and creatinine by 5.6% and 12.1%, respectively.

G. Lippi, M. Plebani, B.M. Henry [16], N. Tang, D. Li, X. Wang, Z. Sun [17], A.A. Zaitsev, S.A. Chernov, E.V. Kryukov, et al. [18] indicate the presence of aspects of the course of the new coronavirus infection COVID-19, associated with increased aggregation of formed elements and enhanced thrombogenesis. We established that the international normalized ratio and prothrombin time values are characterized by minimal changes that are not beyond the reference values (Table 9).

The difference between the results obtained outside the InP and its half 2 was 2.8% and 2.8% ($p > 0.05$), respectively. Prothrombin activity, according to Quick, was characterized by wave-like changes. Its minimum value was noted in half 2 of the InP (88.5%), which is 2.8% and 4.3% ($p > 0.05$) less compared to control point 1 (outside the InP) and control point 2 (half 1 of the InP). The level of fibrinogen was the only parameter in which changes were

Таблица 7. Показатели клинического анализа крови легкообожженных с верифицированным COVID-19
Table 7. Indicators of clinical blood test of the lightly burned with verified COVID-19

Parameter	Control group	Outside InP	Half 1 of InP	Half 2 of InP
Erythrocytes, $\times 10^{12}$/L	4.56 (4; 4.73)	3.66 (3.44; 4.18)	3.94 (3.19; 4.61)	4.02^2 (3.47; 4.45)
Hemoglobin, g/l	139 (118; 147.5)	108.5 (95; 121.25)	108 (93; 139.75)	112^2 (63.5; 135)
Hematocrit, %	43.1 (36.7; 44.45)	33.75 (30; 38.63)	36 (30.4; 49.95)	36.1^2 (32.05; 42.4)
Leukocytes, $\times 10^9$/L	9.2 (6.83; 10.82)	7.9 (5.2; 10.35)	7.7 (6.74; 9.91)	7.79 (5.47; 10.5)
Neutrophils, %	63.5 (56.85; 70)	63.65 (56.45; 75.95)	62.8 (52.35; 71.83)	59 (49.9; 72.12)
Lymphocytes, %	22 (28.35; 18.25)	20.5 (11.23; 25.43)	21.3 (16.13; 29.53)	24.3 (12.95; 33.8)
Monocytes, %	10.2 (8.2; 11.65)	10.25 (8.45; 11.83)	9.25 (8; 13.18)	10.55 (7.55; 12.9)
Immature granulocytes, $\times 10^9$/L	0.03 (0.02; 0.07)	0.03 (0.02; 0.09)	0.03 (0.02; 0.05)	0.03 (0.02; 0.06)
Eosinophils, %	2.2 (1; 3.4)	1.15 (0.48; 2.92)	1.6 (0.23; 2.83)	1.4^2 (0.35; 2.23)
Thrombocrit, %	0.34 (0.28; 0.41)	0.28 (0.23; 0.47)	0.33 (0.24; 0.39)	0.3 (0.25; 0.36)
Platelets, $\times 10^9$/L	366 (285.5; 423)	286 (212.8; 445.5)	300 (247.8; 448.3)	313.5 (247.3; 397)
ESR, mm/h	25 (17.5; 40.5)	50 (30; 58)	26.5^1 (7.25; 42.75)	35^1 (9; 45)

Note: ^{1} — Wilcoxon *t*-test: differences compared with the results obtained outside the incubation period (InP); ^{2} — Mann – Whitney *U*-test: differences compared with the results obtained in the CG, $p < 0{,}05$.

Таблица 8. Показатели биохимического анализа крови легкообожженных с верифицированным COVID-19, *Me* (Q25; Q75)
Table 8. Indicators of the biochemical blood test of the lightly burned with verified COVID-19, *Me* (Q25; Q75)

Parameter	Control group	Outside InP	Half 1 of InP	Half 2 of InP
ALT, U/l	18.8 (13.15; 27.2)	17.25 (12.85; 37.73)	29.95[1] (16.73; 50.6)	16.35[2] (11.33; 24.53)
AST, U/l	19 (14.7; 22.1)	26.8 (18.5; 56.4)	31.7 (12.25; 55.4)	21.25[1, 2] (15.58; 27.95)
Glucose, mmol/l	5.21 (4.83; 5.92)	5.54 (4.74; 6.87)	5.43 (4.46; 6.69)	5.23 (4.64; 6.31)
Total protein, g/l	66.8 (63.05; 70.35)	62.05 (58.66; 68.38)	64.4 (56.4; 67.3)	63[3] (57.18; 66.2)
Total bilirubin, mcmol/l	7.15 (6.35; 9.23)	7.2 (6; 10.33)	7.55 (4.73; 13.92)	7.4 (4.95; 10.5)
Creatinine, mcmol/l	74 (68; 85.5)	53.5 (41.5; 70.25)	60 (51; 68.25)	65[1, 3] (51.5; 73)

Note: [1] — Wilcoxon *t*-test: differences compared with the results obtained outside the incubation period (InP); [2] — differences compared with the results obtained in the half 1 of the InP; [3] — Mann – Whitney *U*-test: differences compared with the results obtained in the CG, $p < 0.05$

Таблица 9. Показатели коагулограммы легкообожженных с верифицированным COVID-19, *Me* (Q25; Q75)
Table 9. Coagulogram indices of the lightly burned with verified COVID-19, *Me* (Q25; Q75)

Parameter	Control group	Outside InP	Half 1 of InP	Half 2 of InP
INR	1.03 (0.97; 1.08)	1.04 (0.99; 1.13)	1.04 (0.99; 1.08)	1.07[2] (1.02; 1.12)
Prothrombin activity according to Quick, %	95 (86.8; 102.3)	91 (83; 99.5)	92.5 (88; 97.75)	88.5[2] (83; 96.25)
PT, s	12.9 (12.3; 13.55)	12.4 (11.85; 13.5)	12.35 (11.88; 12.98)	12.75 (12.05; 13.43)
Fibrinogen, g/l	5.79 (5.07; 6.46)	6.74 (5.12; 7.71)	5.55[1] (3.65; 6.99)	5.49[1] (4.85; 6.12)

Note: [1] — Wilcoxon *t*-test: differences compared with the results obtained outside the incubation period (InP); [2] — Mann – Whitney *U*-test: differences compared with the results obtained in the CG, $p < 0.05$; INR—international normalized ratio.

significant, and the dynamics of its count were characterized by a gradual decrease. The maximum fibrinogen level was noted outside the COVID-19 InP (6.74 g/l), which was 21.4% and 23.2% ($p < 0.05$) higher compared to the data obtained in its halves 1 and 2, respectively. Comparison of the results in half 2 of InP and CG revealed significant differences in INR and prothrombin activity according to Quick, namely by 3.8% and 6.8% ($p < 0.05$), respectively.

CONCLUSION

In severely burned patients with verified COVID-19 in the incubation period, in 64.9% of cases, X-ray examination and computed tomography of the chest organs do not reveal infiltrative changes in the lungs, despite the positive results of the study (polymerase chain reaction). A similar tendency was noted in the minor-burned patient group, as 75.9% had no signs of lung damage during radiological studies.

When evaluating the clinical blood test parameters in half 2 of the incubation period in patients with extensive skin burns, deviations from the reference values of erythrocytes (by 13.5%), hemoglobin (by 23.8%), hematocrit (by 23.3%), leukocytes (by 41.4%), neutrophils (by 5%), lymphocytes (by 21.1%), immature granulocytes (by 18.3 times), and ESR (by 5.5 times) were revealed. In the group of minor-burned patients, there were changes in the level of hemoglobin (by 13.8%), hematocrit (by 9.8%), leukocytes (by 11.8%), and ESR (by 3.5 times). Such aspects are obviously due to the dynamics of the development of wound infection and the general reaction of the body to a skin burn. They are not associated with the addition of new coronavirus infection, which is confirmed by the results of the comparison with CG. When comparing the data obtained in half 2 of the incubation period with the results of laboratory studies of severely burned patients of the CG, significant differences were established among the thrombocrit (less by 39.2%) and platelet (less by 42.9%) levels. In the group of minor-burned patients, those in the counts of erythrocytes (less by 11.8%), hemoglobin (less by 19.4%), hematocrit (less by 16.2%), and eosinophils (less by 71%) were registered.

In the half 2 of the incubation period in severely burned patients, there was a deviation from the reference values of total protein and creatinine levels by 21.7% and 1.7%, respectively. A similar tendency was noted in minor-burned patients. The maximum changes in total protein and creatinine corresponded to 1.6% and 8.3%. When comparing the data obtained in half 2 of the incubation period with the results of laboratory studies of the CG, significant differences were established only in the minor-burned group in terms of total protein (less by 5.6%) and creatinine (less by 12.2%).

In the group of mild and severely burned patients infected with the COVID-19 virus, in half 2 of the incubation period, a deviation in the level of blood fibrinogen by 68.5% and 75.5%, respectively, was revealed compared with the upper limit of the reference values. No significant differences were revealed when comparing the data obtained in half 2 of the incubation period of mildly and severely burned patients with the results of laboratory studies of uninfected patients.

With an additional study of indicators of the state of the red lineage of the bone marrow (normoblasts, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, the width of the histogram of the distribution of erythrocytes relative to the average volume (variation coefficient), red cell distribution width (standard deviation)), as well as leukocyte (level of basophils) and platelet (count of large platelets, mean platelet volume, platelet distribution width) links of hematopoiesis, no deviations from the reference values before the incubation period, as well as in its halves 1 and 2, were noted.

CONCLUSION

Providing medical care to patients during the pandemic caused by new coronavirus infection, COVID-19, is a complex task for the healthcare system. After receiving a positive diagnostic result (polymerase chain reaction) for COVID-19, the approved routing system for infected patients implies the transfer of such a category of patients to repurposed infectious disease hospitals. Given the long incubation period and the high incidence of the disease's asymptomatic course, the number of infected patients is increasing many times due to contact patients and staff of the departments where the carrier is detected. Our attempts to summarize the characteristics of the burn disease course, the general reaction of the body, and laboratory parameters in COVID-19 infection, and to assess the impact of this viral infection on the wound process under a limited period of follow-up of such patients, are not possible. The results obtained are the first step toward understanding typical pathological processes caused by burn injury and the new coronavirus infection, COVID-19.

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