UDC 616.24-002:616.98:578.834]-074-037 https://doi.org/10.26641/2307-0404.2020.3.214807

T.A.Pertseva [1],
K.O. Bielosludtseva [1],
T.V. Kirieieva [1],
L.I. Konopkina [1],
M.A. Krykhtina [1],
B.A. Basina [1],
N.N. Matykina [2],
N.A. Turchin [3]

COMMUNITY-AQUIRED PNEUMONIA ON THE BACKGROUND OF CORONAVIRAL DISEASE (COVID-19): PRINCIPLES OF DIAGNOSTICS AND DETERMINATION OF RISK FACTORS OF PATHOLOGICAL PROCESS AGGRAVATION

SE «Dnipropetrovsk medical academy of Health Ministry of Ukraine» [1]
V. Vernadsky str., 9, Dnipro, 49044, Ukraine
MNI"City Clinical Hospital No. 6" DCC [2]
Batumska str., 13, Dnipro, 49000, Ukraine
MNI "City Clinical Hospital No. 21 named after Prof. EG Popkova" DCC [3]
Kanatna, 17, Dnipro, 49006, Ukraine
ДЗ «Дніпропетровська медична академія МОЗ України» [1]
вул. В. Вернадського, 9, Дніпро, 49084, Україна
КНП «Міська клінічна лікарня № 6» ДМР [2]
вул. Батумська, 13, Дніпро, 49000, Україна
КНП «Міська клінічна лікарня № 21 ім. проф. Є.Г. Попкової» ДМР [3]
вул. Канатна, 17, Дніпро, 49006, Україна
e-mail: ukrxenia@gmail.com

Цитування: Медичні перспективи. 2020. Т. 25, № 3. С. 50-61
Cited: Medicni perspektivi. 2020;25(3):50-61

Key words: *community-acquired pneumonia, viral pneumonia, coronavirus disease, COVID-19, diagnosis, risk factors of aggravation*
Ключові слова: *негоспітальна пневмонія, вірусна пневмонія, коронавірусна хвороба, COVID-19, діагностика, фактори ризику обтяження*
Ключевые слова: *внебольничная пневмония, вирусная пневмония, коронавирусная болезнь, COVID-19, диагностика, факторы риска утяжеления*

Abstract. Community-aquired pneumonia on the background of coronaviral disease (COVID-19): principles of diagnostics and determination of risk factors of pathological process aggravation. Pertseva T.A., Bielosludtseva K.O., Kirieieva T.V., Konopkina L.I., Krykhtina M.A., Basina B.A., Matykina N.N., Turchin N.A. *The diagnosis of community-acquired pneumonia (CAP) on the background of COVID-19 is especially actual due to the prevalence of this pathology and the possible aggravation of the pathological process. The aim of our study was to improve the principles of CAP diagnostics on the background of COVID-19 and to determine risk factors for aggravating of the pathological process. Patients with respiratory symptoms who were hospitalized with suspected COVID-19 were examined. General clinical research methods were carried out, determination of SARS-CoV-2 virus RNA by PCR method, computer tomography (CT) to identify the features of lung tissue damage was performed. The main observation group consisted of 37 patients (men – 19 (51.4%), average age – 61 (57; 69) years) with pneumonia on the background of confirmed COVID-19. According to the severity of coronavirus disease, all patients of the main group were divided into 3 subgroups: subgroup 1 included 17 people with moderate COVID-19, subgroup 2 – 13 people with severe COVID-19, subgroup 3 – 7 people with critical COVID- 19 course. The levels of markers of systemic inflammation (C-reactive protein (C-RP) and fibrinogen) were also determined. Since patients with COVID-19 of moderate severity (which is characterized by the presence of community-acquired viral pneumonia) belong to the risk group of severe and critical course, it is suggested to consider the following risk factors for aggravating the pathological process as: temperature over 38.5°C, heart rate over 90 per minute, respiratory rate over 20 per minute, $SpO_2 \leq 93\%$; absolute lymphopenia (less than 0.9 G/L) and an increase in serum levels of C-RP more than 50 mg/L and fibrinogen more than 5 g/L.*

Реферат. Внебольничная пневмония на фоне коронавирусной болезни (COVID-19): принципы диагностики и определения факторов риска утяжеления патологического процесса. Перцева Т.А., Белослудцева К.О., Киреева Т.В., Конопкина Л.И., Крыхтина М.А., Басина Б.А., Матыкина Н.Н., Турчин Н.А. *Вопросы диагностики внебольничной пневмонии (ВП) на фоне COVID-19 приобретают особую актуальность в связи с распространенностью этой патологии и возможным утяжелением патологического процесса. Целью нашего*

исследования было усовершенствование принципов диагностики ВП на фоне COVID-19 и определение факторов риска утяжеления патологического процесса. Обследованы больные, которые были госпитализированы с подозрением на COVID-19. Проведены общеклинические методы исследования, определение РНК вируса SARS-CoV-2 методом ПЦР, проведена компьютерная томография (КТ) для идентификации особенностей поражения легочной ткани. Основную группу наблюдения составили 37 больных (мужчин – 19 (51,4%), средний возраст – 61 (57; 69) год с пневмонией на фоне подтверждённой COVID-19. Согласно тяжести коронавирусной болезни больные основной группы были разделены на 3 подгруппы: в подгруппу 1 вошли 17 человек с COVID-19 средней степени тяжести, в подгруппу 2 – 13 человек с COVID-19 тяжелого течения, в подгруппу 3 – 7 человек с COVID-19 критического течения. Также были определены уровни маркеров системного воспаления (С-реактивного протеина (С-РП) и фибриногена). Поскольку больные COVID-19 средней степени тяжести (для которой характерно наличие внебольничной вирусной пневмонии) относятся к группе риска тяжелого и критического течения, предлагается факторами риска утяжеления патологического процесса считать: температуру выше 38,5°С, частоту сердечных сокращений более 90 в минуту, ЧДД более 20 в 1 минуту, $SpO_2 \leq 93\%$; абсолютную лимфопению (менее 0,9 Г/л) и повышение сывороточных уровней С-РП (более 50 мг/л) и фибриногена (более 5 г/л).

Less than a year ago (at the end of 2019) all the humanity of the planet faced an extraordinary challenge – a new disease appeared and spread around the world, which by the name of the etiological factor (SARS-CoV-2) (from the English severe acute respiratory syndrome coronavirus-2) – "Severe acute respiratory syndrome caused by coronavirus-2") was called "coronavirus disease" (COVID-19). Today, the virus has crossed the borders of almost every country in the world. Millions of people fell ill, thousands of them died [9, 17]. Fortunately, most of the infected recovered [8, 9, 17].

Observing the peculiarities of the course of coronavirus disease, doctors noted that the clinical symptoms in patients are quite different, and the most significant problem with COVID-19 is the formation of complications, the development of which leads to premature death of the infected.

In patients from different regions of the world, the most common complication of coronavirus disease is lung damage, which is now interpreted as "community-acquired pneumonia" [14, 16, 18]. The term "non-hospital" is used due to the fact that the first manifestations of the pathology appear at home, even before the patient enters the hospital. Regarding the term "pneumonia", there are different opinions: some authors are inclined to this term, because they believe that lung damage occurs due to the action of an infectious agent – the virus SARS-CoV-2 [14, 16, 18], while others believe that the lesion of lung tissue on the background of COVID-19 can be interpreted as "pneumonitis", i.e. pathology of non-infectious nature [19]. However, issues related to both the interpretation of pathological changes and terminology are still being discussed, and clinical data are accumulatied rapidly.

Because information on non-infectious factors that could affect the formation of pathological changes in lung tissue in COVID-19 is still insufficient, and the etiological factor in the development of coronavirus disease against which pneumonia develops is well known, in this article the term "community-acquired pneumonia" is used.

If we consider the problem from this point of view, it should be noted that community-acquired pneumonia (CAP) remains an extremely important problem in world medicine in general. Mortality is quite high and almost does not change in recent years [1, 11, 14].

The existence of more than 100 species of pneumonia has been proven [15], although only a few of them cause the majority of cases. The most common cause of CAP are bacteria: pneumococcus (in some regions – almost 50% of cases), Escherichia coli (almost 20% of cases), intracellular pathogens (chlamydia, mycoplasma, legionella) (about 20% of cases), golden staphylococcus (up to 5% of cases), gram-negative bacteria (up to 5% of cases) [1, 11, 15]. Approximately in 15% of patients CAP is caused by various viruses: influenza virus, parainfluenza, rhinosinustial virus, coronaviruses, metapneumoviruses, etc. [10]. Even less often (in no more than 5% of cases) fungi (candida, pneumocystis) and the simplest microorganisms can be the etiological factors of CAP [15].

It should be noted that bacterial pneumonia in terms of symptoms, medical history, features of the course, objective data, the results of laboratory and instrumental research methods in general differs from similar manifestations of viral pneumonia [10, 15]. Thus, bacterial emergencies are usually characterized by an acute onset of the disease (often after hypothermia) with a body temperature above 38°C and productive cough, percussion – deaned or dull sound, auscultatory – harsh or weakened vesicular respiration, ringing small-bubbling rales, in indured part of the lung – bronchial respiration, crepitation; in peripheral blood – leukocytosis (more than

$10x10^9$/l), stab neutrophiles shift (more than 10%) and increase in ESR are almost always observed [13], and radiologically – infiltration of the pulmonary tissue within the lung lobe or segment [1, 13]. Viral CAP is more characterized by dry cough, rapid increase in shortness of breath, severe weakness, headache and muscle pain [11, 15]; in the anamnesis – contact with a patient with acute respiratory viral infection (SARS), auscultatory data are less pronounced than in bacterial CAP and are usually characterized by sacterred dry rales; laboratory - neutropenia, lymphopenia, and radiologically – bilateral reticulonodular areas of opacity with or without focal consolidations [10].

It should be emphasized that, depending on the specific pathogen (either bacterial or viral), certain features of the clinical course can be observed [5]. Thus, in bacterial CAP caused by pneumococcus and described by Hippocrates, sputum often has a "rusty" color, the patient has a fever, pain or in the chest under the shoulder blade, percussion – a dull sound over the lobe (or several lobes) of the lung, auscultation – crepitation, which is a manifestation of intraalveolar exudation [13]; often a complication of such pneumonia is exudative pleurisy. Legionnaires' pneumonia, which most often occurs after staying in an air-conditioned room or bathing in closed water, can be accompanied by abdominal pain, diarrhea, delirium [12]. In Klebsiella pneumonia, bloody sputum called "currant jelly" can be observed; such pneumonia often develops in patients with impaired consciousness and/or aspiration [15]. Staphylococcal pneumonia is characterized by the formation of a lung abscess (one large cavity) or abscess (many small cavities) [15]. Mycoplasmic pneumonia can be accompanied by enlargement of the lymph nodes of the neck, pain in the joints, infection of the tissues of the middle ear [12].

As for viral pneumonias, they are associated with epidemics or outbreaks of SARS. The clinical picture is dominated by signs of intoxication: hyperthermia, headache, body aches, nausea, vomiting, and radiological changes are most often characterized by damage to the interstitial tissue of the lungs. Typical signs of viral pneumonia on CT are usually bilateral lesions, characterized by changes in the nodular nature or small areas of consolidation of pulmonary tissue, mainly in the posterior basal segments [3, 4, 10].

Unfortunately, despite the existence of modern methods of identification of various pathogens (both bacterial and viral), in about half of cases the pathogen is not detected [1, 11], so the clinician often has to focus on clinical and anamnestic data, results of laboratory research methods, radiological signs. The issues of diagnosis of CAP on the background of COVID-19 become especially relevant due to the prevalence of this pathology, as well as the possible burden of the pathological process and, unfortunately, disappointing results.

In view of the above-mentioned purpose of our study was to improve the principles of diagnosis of CAP against COVID-19 and identify risk factors for the burden of the pathological process by establishing the diagnostic significance of clinical, anamnestic data, markers of systemic inflammation and radiological signs in hospital stage of patient management.

MATERIALS AND METHODS OF RESEARCH

We examined 50 patients who sought medical help in the admission departments of the Municipal Non-Profit Enterprises "City Clinical Hospital № 6" and "City Clinical Hospital № 16" of the Dnieper City Council from April to June 2020 due to suspected coronaviral disease and CAP associated with it. During the clinical examination of patients, the analysis of complaints, anamnesis data and objective status was performed.

Criteria for inclusion of patients in the screening were:

1) complaints, anamnestic data and clinical signs of acute upper respiratory tract infection;
2) complaints and clinical signs of lower respiratory tract infection, which could indicate the development of CAP;
3) consent to testing for coronavirus disease;
4) age – over 18 years.

The criteria for excluding patients from screening were:

1) presence of a confirmed alternative diagnosis (pulmonary tuberculosis, chronic thromboembolism of the pulmonary artery, etc.), in which clinical signs could mimic the manifestations of CAP;
2) presence of previously confirmed HIV infection;
3) decompensation of chronic comorbidities that could affect the results of research;
4) presence of previously diagnosed oncologic pathology.

At the screening stage in the admission departments of both treatment and prevention facilities (TPF), each patient was tested for the

presence of coronavirus SARS-CoV-2 (by "rapid" express-test, which is based on immune-histochemical reactions to determine antibodies to the virus in the blood for 15 minutes), a general blood test and chest X-ray in 2 projections was performed, HIV status (by rapid blood testing using "CITO TEST HIV ½" ("Pharmaco", Ukraine) was determined as well.

At the end of the screening phase, 10 patients showed a positive result of the "rapid" express-test for SARS-CoV-2, due to this they were immediately sent for further treatment to an infectious disease hospital (according to the order of the Department of Health Care of the Dnipropetrovsk Regional State Administration from 15.04.2020); one patient was diagnosed with HIV; in two people – signs of tuberculous lung lesion according to the radiograph of the chest, in this connection they were referred to a TB specialist. 37 patients who with negative results of a "rapid" express-test for SARS-CoV-2 at the screening stage but still suspected COVID-19 (in the presence of respiratory symptoms and in view of the coronavirus pandemic) were hospitalized and formed the main group of observation (men – 19 (51.4%), mean age – 61 (57; 69) years)).

At the inpatient stage, all patients in the main group underwent general clinical research methods, as well as PCR tests to verify coronavirus disease (determination of SARS-CoV-2 virus RNA in the collection of mucus from the respiratory tract) and computed tomography (CT) for identification features of lung tissue lesions. Levels of systemic inflammation markers were also determined – serum levels of C-reactive protein (C-RP) and fibrinogen [7], for which venous blood was taken on the first day of treatment (before antibacterial therapy or after a single dose of potentially effective antibiotic), and the results of findings were evaluated in comparison with reference laboratory values [4].

Formulation of clinical diagnoses of coronavirus disease and CAP on its background was carried out in accordance with national recommendations [1, 2].

All patients agreed to undergo the necessary research methods.

Statistical processing of the obtained results was performed using the methods of biometric analysis, which are implemented in the software packages "STATISTICA 6.0" (N 31415926535897) [5].

RESULTS AND DISCUSSION

According to the PCR test performed at the hospital stage, coronavirus disease was confirmed in all patients of the main group.

Signs of lung tissue damage according to chest radiography, which was performed at the screening stage, required their verification, as no patient had any reliable radiological signs of CAP. According to the results of CT of the thoracic cavity, all patients were diagnosed with CAP, which allowed to exclude a mild degree of severity of COVID-19 (this degree of severity is characterized by the absence of CAP). Subsequently, to clarify the severity of coronavirus disease, the criteria set forth in the Protocol "Provision of medical care for the treatment of coronavirus disease (COVID-19)" were used [2] (Table 1).

Thus, according to the severity of coronavirus disease, all patients of the main group were divided into 3 subgroups: subgroup 1 included 17 people with moderate COVID-19, subgroup 2 – 13 people with severe COVID-19, subgroup 3 – 7 people with critical course of COVID-19.

Regarding the division of patients into subgroups, it should be noted that in real medical practice to track the dynamics of infiltrative changes of the thoracic cavity on CT is quite problematic due to technical difficulties (usually due to the inability to perform this costly study). That is why most often we have to focus on other criteria for determining the severity of the disease (Table 1). Thus, subgroup 1 included patients in whom on hospitalization RR was lower than 30 (and made up 18 (16; 21)), the level of SpO_2 was higher than 93% (and made up 96 (94; 98)%), and clinical symptoms remained stable, which most likely indicated the absence of prolongation of the pathological process in the lungs. Subgroup 2 included patients in whom on hospitalization RR was also lower than 30 (and made up 20 (20; 21)) but the level of SpO_2 was lower than 94% (and made up 93 (92; 93)%), which required non-invasive oxygen therapy (indications for mechanical ventilation) were not observed), and the clinical course was accompanied by high fever (38.8 (38.7; 39.0)°C) and severe weakness. Subgroup 3 included 7 people in whom at the stage of hospitalization RR was the highest and amounted to 24 (23; 27), the level of SpO_2 was the lowest and amounted to 78 (74; 89)% (i.e. clinical symptoms were dominated by signs of respiratory failure); 5 of them later developed ARDS, due to which mechanical ventilation was performed, 1 person developed septicemia, confirmed by bacteriological blood test (the patient died on day 10 after hospitalization), and another 1 person developed multi-organ failure (the patient died on day 6 after hospitalization).

Analysis of demographic findings showed that almost 90% of patients were persons over 50 years of

age (Table 2). The majority of patients in the group on a whole were of 60-70 years, most of them had moderate coronavirus disease. Among people aged 50-59, the course of the disease was the most common, and in people over the age of 70, the course of moderate severity, severe and critical one were equally common (Table 2).

Table 1

Criteria of defining coronovirus disease severity [2]

Degree of coronovirus disease severity	Criteria
Diseases of moderate severity (in the presence of all three of these criteria). Patients belong to the risk group of severe and critical course	**respiratory rate (RR) < 30 per 1 minute; blood oxygen saturation according to pulse oximetry (SpO_2) > 93% or PaO_2 / FiO_2 ratio ≥ 300; the area of infiltrative lung lesions does not increase by more than 50% within 24–48 hours.**
Severe disease (if one or more of these criteria)	**RR ≥ 30 per 1 minute; SpO_2 ≤ 93% or PaO_2 / FiO_2 < 300 ratio; the area of infiltrative lung lesions increases by more than 50% within 24–48 hours.**
Diseases of critical course (in the presence of one or more of these criteria)	**acute respiratory distress syndrome (ARDS); sepsis; altered consciousness; multiorgan failure.**

In terms of gender, in subgroup 1 women dominated, while in subgroup 2 and 3 men dominated (Table 2).

In the anamnesis in most of the surveyed (31 (83.8%)) epidemic signs of COVID-19 were detected. Thus, 18 (48.6%) patients came into contact at work or at home with persons with signs of respiratory infection, 5 (13.5%) persons attended various religious events the day before where a large number of people gathered, 3 (8, 1%) persons soon returned from abroad or border areas, and 2 (5.4%) were medical workers.

Most of the patients examined sought medical help and, accordingly, were hospitalized on day 6-10 of disease. Moreover, the later the patient sought medical help, the more severe the course of coronavirus disease he was diagnosed (Table 2).

The vast majority of patients with COVID-19 (25 people (67.6%)) had comorbidities and comorbid states. In 17 patients, two or more diseases and conditions were diagnosed, among which cardiac pathology without signs of decompensation prevailed (stage 1 hypertension, stage I heart failure, coronary heart disease (CHD)), obesity and type 2 diabetes mellitus; each of 8 people had one comorbid disease. The maximum number of concomitant diseases and conditions was in patients of subgroups 2 and 3 (Table 3).

In a careful individual analysis of clinical, anamnestic and laboratory data of patients with COVID-19 who developed CAP, we identified certain features.

The acute onset with fever was characteristic of all hospitalized for coronavirus disease, but later it had its own characteristics. Thus, in 30 patients (81.1%) it was preceded by a prodromal period, which is recognized as a characteristic manifestation of any viral pneumonia [10], however, in almost 20% of our patients (every fifth patient) such signs were not detected – the clinical symptoms of CAP developed acutely and rapidly. However, most often 1-2 days before the rise in temperature, patients developed pain in the joints and muscles – in 10 (27%) cases), throat irritation or sore throat – in 19 (51.3%) cases), nasal congestion – in 8 (21.6%) cases), general weakness – in 30 (81.1%) cases).

Table 2

Demographic and general indicators of patients with coronavirus disease, *Me (25%;75%)*

Indicator	Main group	Subgroups of patients			p
		1	2	3	
Average age, years	**61 (57; 69)**	**61 (59; 66)**	**57 (51; 70)**	**65 (58; 70)**	**p_{1-2}=0.966 p_{1-3}=0.996 p_{2-3}=0.721**
Distribution by age: abs. (% in group or subgroup)					
under 50 years	**5 (13.5)**	**3 (17.6)**	**1 (33.3)**	**1 (14.3)**	**p_{1-2-3}=0.071**
50–59 years	**10 (27.0)**	**2 (11.8)**	**6 (46.2)**	**2 (28.6)**	
60–69 years	**13 (35.1)**	**9 (52.9)**	**3 (23.1)**	**1 (14.3)**	
70 years and more	**9 (24.3)**	**3 (17.6)**	**3 (23.1)**	**3 (42.8)**	
Distribution by gender, abs. (% in group or subgroup):					
Men	**19 (51.4)**	**4 (23.5)**	**10 (76.9)**	**5 (71.4)**	**p_{1-2-3}=0.007**
women	**18 (48.6)**	**13 (76.5)**	**3 (23.0)**	**2 (28.6)**	
Day of disease on hospitalization	**8 (7; 10)**	**7 (6; 8)**	**8 (7; 10)**	**9 (7; 10)**	**p_{1-2}=0.526 p_{1-3}=0.400 p_{2-3}=0.572**

Notes: p – significance of differences between subgroups, 1, 2, 3 – corresponding subgroups of patients.

On hospitalization body temperature in the main group generally was higher than 38°C. Patients of subgroups 2 and 3 had the highest rates (Table 4). Most likely, the severity of the temperature reaction (above 38.5°C) can be considered a factor that is associated with a more severe course of COVID-19. It should also be added that the response to the action of antipyretics in patients was insignificant (0.5-1°C) and short-run (usually the effect lasted no more than 2-3 hours).

Table 3

The presence of comorbidities and comorbid conditions in the examined patients with coronavirus disease

Супутні хвороби і стани	Основна група	Підгрупи		
		1	2	3
Diseases of the cardiovascular system, abs. (% in group or subgroup)	**27 (73.0)**	**10 (58.8)**	**10 (76.9)**	**7 (100)**
Adiposity, abs. (% in group or subgroup)	**9 (24.3)**	**2 (11.7)**	**3 (23.1)**	**4 (57.1)**
Diabetes, abs. (% in group or subgroup)	**6 (16.2)**	**1 (5.8)**	**2 (15.4)**	**3 (42.8)**
COPD, abs. (% in group or subgroup)	**1 (2.7)**	**1 (5.8)**	**0 (0.0)**	**0 (0.0)**
Alcohol abuse, abs. (% in group or subgroup)	**1 (2.7)**	**1 (5.8)**	**0 (0.0)**	**0 (0.0)**

Cough was observed in 29 (78.4%) patients. Its feature was the absence of sputum production in 20 (69%) of people or the discharge of a small amount – in 9 (31%) of people. Most often it was characterized by a paroxysmal course, exacerbated by deep breathing, laughter, crying, with changes in ambient temperature. In 5 (13.5%) individuals, cough was accompanied by discomfort or mild chest pain.

The leading syndrome in the clinical symptoms of patients in subgroup 2 and 3 was respiratory failure, which was manifested by severe shortness of breath with high RR and low (in subgroup 2) or extremely low (in subgroup 3) level of SpO_2 (Table 4).

Our attention was drawn to the fact that in patients with COVID-19 with a decrease in the level of SpO_2 there was no corresponding increase in RR, especially in patients of subgroup 3, in whom the level of SpO_2 did not exceed 90%, and in no patient RR exceeded 30 per 1 minute. It is possible that this phenomenon is a pathogenetic feature of coronavirus lesion of the lung and can be used as a differential diagnostic indicator in determining the severity of the disease or as a marker of the burden of the pathological process.

Regarding saturation, its level in subgroup 3 was significantly lower than in subgroups 1 and 2, being the main manifestation of ARDS.

On auscultation over the lungs of patients of the main group, most often harsh breathing (in 33 (89.2%) cases) and a small number of soft rales on both sides (in 15 (40.5%) cases) was heard. Crepitation in patients with COVID-19 was not heard.

Table 4

Some clinical findings of patients with coronavirus disease on hospitalization, *Me (25%;75%)*

Findings	Main group	Subgroups			p
		1	2	3	
Body temperature, ºC	38.5 (38.1; 38.9)	38.0 (37.9; 38.6)	38.8 (38.7; 39.0)	38.9 (38.5; 40.0)	p_{1-2}=0.007 p_{1-3}=0.017 p_{2-3}=0.700
HBR per 1 minute	90 (85; 100)	88 (80; 94)	90 (86; 100)	110 (100; 125)	p_{1-2}=0.248 p_{1-3}=0.004 p_{2-3}=0.012
RR per 1 minute	20 (18; 21)	18 (16; 21)	20 (20; 21)	24 (23; 27)	p_{1-2}=0.001 p_{1-3}=0.000 p_{2-3}=0.000
SpO_2, %	93 (92; 96)	96 (94; 98)	93 (92; 93)	78 (74; 89)	p_{1-2}=0.000 p_{1-3}=0.000 p_{2-3}=0.001

Notes: the same as in table 1.

In most of the examined patients ***a normal total number of leukocytes without stab neutrophils shift*** was observed (Table 5). Slight leukocytosis was observed in only two patients of subgroup 2. More than half of patients of subgroup 3 (4 (57.1%)) had leukopenia with relative lymphopenia, which is usually a characteristic feature of severe viral infection [4, 10].

The results of counting the absolute number of lymphocytes were of informative value. The laboratory norm of this finding should be from 1,2 to 3,0 G/l whereas in all patients examined, ***absolute lymphopenia*** was revealed. The lowest rates were in persons of subgroup 3, which indicates an impairment of protective mechanisms and can be used as a differential diagnostic finding of severe COVID-19.

The level of ESR did not exceed the reference values, even in patients with severe and critical disease, which also indicates the peculiarities of the systemic response in COVID-19.

Of particular interest is the assessment of serum C-RP levels in patients with coronavirus disease. It is generally accepted that the indicator is a highly sensitive and nonspecific marker of the acute phase of the inflammatory process and reflects the degree of tissue damage [7]. Its level in the examined patients exceeded the generally accepted norm, which is <5 mg/l in 31 (83.8%) cases. Therewith, if

the median level of C-RP in subgroup 1 exceeded the reference values only by 2 times, then in subgroup 2 and 3 – by 16 and 17 times, respectively (Table 5). In addition, individual analysis showed that in a slightly larger number of patients with moderate COVID-19, the level of C-RP was in the range from 5 to 50 mg/l, while in patients with severe and critical course it was often higher than 50 mg/l, which indicates the diagnostic value of the marker.

Table 5

Some findings of general inflammation in patients with coronavirus disease on hospitalization, *Me (25%; 75%)*

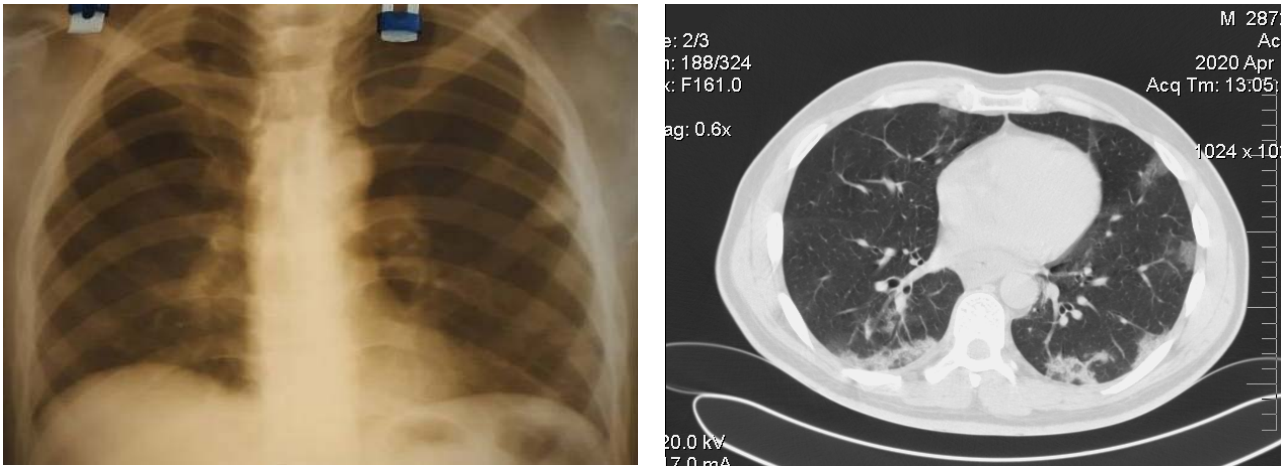
Findings	Main group	Subgroups of patients			p
		1	2	3	
Total number of leukocytes, G/l	**5.0 (4.0; 6.0)**	**5.6 (4.1; 6.7)**	**5.1 (4.3; 7.8)**	**3.9 (2.3;4.2)**	**p_{1-2}=0.278 p_{1-3}=0.001 p_{2-3}=0.004**
Distribution by number of leukocytes, abs. (% in group or subgroup)					
< 4,0 G/l	**8 (21.6)**	**3 (17.6)**	**1 (7.7)**	**4 (57.1)**	
4–9 G/l	**27 (73.0)**	**14 (82.4)**	**10 (76.9)**	**3 (42.9)**	**p_{1-2-3}=0.038**
> 9 G/l	**2 (5.4)**	**0 (0)**	**2 (15.4)**	**0 (0)**	
Relative number of stab neutrophils, %	**4 (2; 5)**	**4 (2; 6)**	**3 (1; 6)**	**4 (2; 5)**	**p_{1-2}=0.697 p_{1-3}=0.710 p_{2-3}=0.999**
Relative number of lymphocytes, %	**19.0 (18; 21)**	**18.0 (18; 20)**	**22.0 (20; 26)**	**15.0 (11; 20)**	**p_{1-2}=0.031 p_{1-3}=0.089 p_{2-3}=0.011**
Absolute number of lymphocytes, G/l	**0.86 (0.69; 1.17)**	**0.99 (0.59; 1.14)**	**0.92 (0.80; 1.16)**	**0.45 (0.34; 0.80)**	**p_{1-2}=0.506 p_{1-3}=0.002 p_{2-3}=0.009**
ESR, mm/g	**9.0 (8; 16)**	**8.5 (7; 10)**	**9.0 (7; 10)**	**10.0 (9; 12)**	**p_{1-2}=0.681 p_{1-3}=0.118 p_{2-3}=0.159**
C-RP, mg/l	**39.1 (5.4; 94.0)**	**11.2 (4.7; 27.8)**	**82.0 (19.25;97.5)**	**85.3 (16.9; 101.3)**	**p_{1-2}=0.222 p_{1-3}=0.318 p_{2-3}=0.999**
Distribution by C-RP, abs. (% in group or subgroup)					
< 5 m/l	**8 (21.6)**	**6 (35.3)**	**1 (7.7)**	**1 (14.3)**	**p_{1-2-3}=0.021**
5–49 mg/l	**14 (37.8)**	**9 (52.9)**	**4 (30.8)**	**1 (14.3)**	
50-99 mg/l	**10 (27.0)**	**1 (5.9)**	**6 (46.2)**	**3 (42.9)**	
≥ 100 mg/l	**5 (13.5)**	**1 (5.9)**	**2 (15.4)**	**2 (28.6)**	
Fibrinogen, g/l	**4.7 (3.84; 6.80)**	**4.4 (3.84; 4.84)**	**5.4 (3.91; 6.80)**	**6.1 (3.37; 7.50)**	**p_{1-2}=0.768 p_{1-3}=0.599 p_{2-3}=0.660**
Розподіл за фібриногеном, абс. (% у групі чи підгрупі)					
< 2 g/l	**1 (2.7)**	**0 (0)**	**0 (0)**	**1 (14.3)**	**p_{1-2-3}=0.103**
2–4 g/l	**11 (29.7)**	**7 (41.2)**	**3 (23.1)**	**1 (14.3)**	
4–7,4 g/l	**20 (54.1)**	**9 (52.9)**	**9 (69.2)**	**2 (28.6)**	
≥ 7,5 g/l	**5 (13.5)**	**1 (5.9)**	**1 (7.7)**	**3 (42.9)**	

Note: the same as in Table 1.

The level of fibrinogen in the examined patients exceeded the reference values (2-4 g/l) in more than half of the persons (25 (67.6%)). Thus in subgroup 1 and 2 the is indicator, generally, was within 2-7.4 mg/l, whereas in three patients (40%) of subgroup 3 it exceeded a diagnostic maximum (7.5 g/l) and to determine its level was technically impossible (Table 5).

X-ray changes according to CT data were detected in all patients examined. They were mostly bilateral fine-focal in nature.

Thus, patient P., 51 years old on hospitalization (i.e. severe course of COVID-19 was referred to subgroup 2 because against respiratory symptoms (unproductive cough, shortness of breath) and fever up to 38.7°C for 7 days), the level of SpO_2 was 92%, and RR – 24 per minute. At the same time, only a small number of scattered dry rales were heard over the lungs on auscultation, and no signs of pneumonia were found on the radiograph of the chest (Fig. A). CT scan allowed to verify the clinical diagnosis and detect signs of pneumonia (Fig. B), and obtained after 4 days positive PCR result on COVID-19 confirmed the suspected etiology of the disease. Thus, the clinical diagnosis of the patient was as follows: confirmed coronavirus disease (COVID-19) of severe course, community-acquired bilateral viral pneumonia, respiratory failure of the II degree.



A **B**

Radiological data of a patient with severe COVID-19 on hospitalization (male P., 51 years old):
A - radiograph of the chest in frontal projection: bilateral strengthening of the vascular pattern in the basal areas, dilation of the roots of the lungs, blurred contours;
B - computed tomography: in the parenchyma of both lungs areas of consolidation of lung tissue by type of "frosted glass" are defined, small nodules, in the lower parts - areas of consolidation of the lung parenchyma (mainly - subpleural)

This clinical case demonstrates that patients with provisional or confirmed COVID-19 have an urgent need for CT of the thoracic cavity, even in the absence of convincing auscultatory and radiological signs of pneumonia. This method is more accurate, highly sensitive and highly specific for the diagnosis of viral pneumonia. The presence of signs characteristic of coronavirus lung damage on CT not only helps to verify the diagnosis, but also indicates the need for hospitalization and helps in determining place of treatment.

CONCLUSIONS

1. At the initial examination of all patients with suspected coronavirus disease, it is necessary to pay attention to the set of clinical symptoms and laboratory findings, which are most likely indicate the likelihood of aggravation of the pathological process with the development of community-acquired viral pneumonia. In this regard the most significant are complaints of fever above 38°C and dry cough; on taking case-history – epidemic data and prodromal period; objectively – the prevalence

of respiratory failure syndrome and minimally pronounced changes over the lungs on auscultation; decrease in saturation, which is not accompanied by a corresponding increase in RR; laboratory – leukopenia, absence of stab neutrophils shift, normal or reduced ESR, as well as elevated levels of markers of systemic inflammation (C-RP and fibrinogen) in the serum.

2. If a patient with suspected COVID-19 has high fever and/or signs of respiratory failure in the absence of convincing auscultatory and radiological signs of pneumonia, it is recommended to perform chest CT, which is a highly sensitive and highly specific method of verification of CAP viral pneumonia, which, in the end, allows the doctor to determine the need for patient's hospitalization. Characteristic CT signs of community-acquired viral pneumonia against COVID-19 are small nodular lesions, areas of consolidation of pulmonary tissue by the type of "frosted glass", in the lower parts (mainly subpleural) – areas of consolidation of the lung parenchyma.

3. Since patients with moderate COVID-19 (which is characterized by the presence of community-acquired viral pneumonia) belong to the risk group of severe and critical course [2], it is proposed to consider the risk factors of the pathological process: temperature above 38.5°C, heart rate – more than 90 per minute, RR – more than 20 per minute, SpO2 ≤93%; absolute lymphopenia (less than 0.9 G/l) and increased serum C-RP (over 50 mg/l).

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

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The article was received
2020.08.25