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ЖУРНАЛ ГЕПАТО-ГАСТРОЭНТЕРОЛОГИЧЕСКИХ ИССЛЕДОВАНИЙ

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CLINICAL AND EPIDEMIOLOGICAL FEATURES IN PEDIATRIC PATIENTS IN WITH SARS-COV-2 INFECTION IN THE RYAZAN REGION

ANNOTATION

To study the clinical and laboratory features of the course of SARS-CoV-2 infection (COVID-19) in children of the Ryazan region. A retrospective study carried out with the participation of 55 children hospitalized at the City Clinical Hospital No. 11 (Ryazan) from April 2020 to March 2021 with a diagnosis of new coronavirus infection COVID-19. Among those hospitalized, there was a predominance of children over the age of 12 years (61.8%). Almost one third of patients had comorbid pathology. The most common comorbidities were obesity, CVS and CNS pathology. More than half of the hospitalized children (58.2%) had intrafamilial contact with laboratory-confirmed cases of COVID-19. The main clinical manifestations in the observed children were: symptoms of intoxication, respiratory tract lesions and gastrointestinal symptoms. In the dominant number of cases (63.6%), lung damage corresponded to mild (CT-1) severity. More than half of the children (63.6%) had a concomitant bacterial infection. IgM antibodies to Mycoplasma pneumoniae were detected by ELISA in 15 patients (27.3%). A direct correlation was found between the degree of lung damage and the level of CRP ($r = 0.31$, $p = 0.019$), ALT ($r = 0.30$, $p = 0.05$) and LDH ($r=0.27$, $p = 0.05$), as well as the presence of concomitant diseases ($r = 0.41$, $p = 0.002$). Against the background of the therapy, positive dynamics was noted in the condition of all patients. Lethal outcomes not recorded in the studied sample of patients.

Almost half of the patients (40%) had a comorbid pathology. The presence of concomitant bacterial infection was detected in 63.6% of children. Most patients are diagnosed with respiratory mycoplasmosis. A significant positive correlation was established between the degree of damage to the lung tissue and the presence of concomitant diseases, as well as deviations from the norm of a number of laboratory parameters (CRP, ALT, LDH). With timely treatment, most patients with viral lung disease caused by the new coronavirus infection COVID-19 had a favorable outcome of the disease.

Key words: new coronavirus infection, viral lung disease, community-acquired pneumonia, children

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КЛИНИКО-ЭПИДЕМИОЛОГИЧЕСКИЕ ОСОБЕННОСТИ У ПЕДИАТРИЧЕСКИХ БОЛЬНЫХ ИНФЕКЦИЕЙ SARS-COV-2 В РЯЗАНСКОЙ ОБЛАСТИ

АННОТАЦИЯ

Изучить клинико-лабораторные особенности течения инфекции SARS-CoV-2 (COVID-19) у детей Рязанской области. Проведено ретроспективное исследование с участием 55 детей, госпитализированных в Городскую клиническую больницу № 11 (Рязань) с апреля 2020 года по март 2021 года с диагнозом новой коронавирусной инфекции COVID-19. Среди госпитализированных преобладали дети старше 12 лет (61,8%). Почти у трети пациентов наблюдалась коморбидная патология. Наиболее частыми сопутствующими заболеваниями были ожирение, патология ССС и ЦНС. Более половины госпитализированных детей (58,2%) имели внутрисемейный контакт с лабораторно подтвержденными случаями COVID-19. Основными клиническими проявлениями у наблюдаемых детей были: симптомы интоксикации, поражения дыхательных путей и желудочно-кишечные симптомы. В преобладающем числе случаев (63,6%) поражение легких соответствовало легкой (КТ-1) степени тяжести. Более половины детей (63,6%) имели сопутствующую бактериальную инфекцию. Антитела IgM к Mycoplasma pneumoniae с помощью ИФА выявлены у 15 пациентов (27,3%). Была обнаружена прямая корреляция между степенью поражения легких и уровнем CRP ($r = 0,31$, $p = 0,019$), АЛТ ($r = 0,30$, $p = 0,05$) и ЛДГ ($r = 0,27$, $p = 0,05$), а также как наличие сопутствующих заболеваний ($r = 0,41$, $p = 0,002$). На фоне проведенной терапии отмечена положительная динамика в состоянии всех пациентов. Летальных исходов у исследуемой выборки пациентов не зафиксировано.

Почти половина пациентов (40%) имели сопутствующую патологию. Наличие сопутствующей бактериальной инфекции выявлено у 63,6% детей. У большинства пациентов диагностируется респираторный микоплазмоз. Установлена достоверная положительная корреляция между степенью поражения легочной ткани и наличием сопутствующих заболеваний, а также отклонениями от нормы ряда лабораторных показателей (СРБ, АЛТ, ЛДГ). При своевременном лечении у большинства пациентов с вирусным заболеванием легких, вызванным новой коронавирусной инфекцией COVID-19, исход болезни был благоприятным.

Ключевые слова: новая коронавирусная инфекция, вирусное заболевание легких, внебольничная пневмония, дети.

Background. COVID-19 is an acute infectious disease, caused by a member of the *Coronaviridae* family - *SARS-CoV-2*, which characterized by its ability to cause severe damage to the lung tissue in humans. The first case of COVID-19 infection was registered at the end of December 2019 in China (Hubei province, Wuhan city) [1]. The virus has spread at a rapid pace almost across the globe. By March 2020, the number of countries, with confirmed cases of COVID-19, reached 114, in connection with which the WHO declared a pandemic [2].

According to world statistics, at the time of this writing (September 2021), there were 222,969,174 confirmed cases of COVID-19 in 214 countries of the world, of which 197,776,410 were recovered, and the number of deaths reached 4,604,072 [3]. At the same time, the number of cases of COVID-19 among children and adolescents in the structure of morbidity in different countries is not large and does not exceed 16%. So, on the territory of the Russian Federation, patients aged 0-18 years with a confirmed diagnosis of COVID-19 make up 7.6% of the total [4]. In the United States, according to the American Academy of Pediatrics, children account for 15.1% of the total number of patients diagnosed with SARS-CoV-2 infection [5], and in China people under 19 years old account for 2.2% of COVID-19 cases [6].

The spectrum of clinical manifestations of COVID-19 is very diverse. Currently, many scenarios of the course of this disease have been described: from asymptomatic carriage to extremely severe forms characterized by the involvement of various organs and systems in the pathological process, the development of multiple organ failure and a high frequency of deaths [1,6]. At the same time, in children and adolescents the new coronavirus infection, in general, is proceeding relatively favorably. In contrast to the adult population, in the pediatric population asymptomatic and mild forms of the disease are mainly found [4,6,7]. The severity of clinical manifestations is most often due to the defeat of the terminal sections of the respiratory tract and the development of pneumonia [7,8,9].

According to a Russian study in 218 sick children, the development of COVID-19-associated pneumonia observed in 11.5% of cases, and the frequency of lung damage was significantly higher among infants and adolescents [7]. The authors noted, that in children of the first year of life an atypical course of the disease was mainly recorded, while for patients of

puberty age the manifest course of COVID-19 was more typical. In an American study W.R. Otto et al. report, that of 424 children, who tested positive for SARS-CoV-2, pneumonia was found in 77 (18.2%) patients, 24 children of which required respiratory support [8]. M. Jahangir and M. Nawaz indicate, that in patients (n=224) of pediatric wards with confirmed SARS-CoV-2 infection in 147 (65.6%) cases, radiographic changes were found, indicating the development of pneumonia, as a rule, of mild severity [9].

Some authors pay attention to the presence of comorbidity as the main risk factor for the development of COVID-19 pneumonia in children [9,10]. However, in a systematic review and meta-analysis by C.R. Jutzeler et al. [11] reported, that in a study involving 1,056 children and newborns with COVID-19, when performing computed tomography, changes in lung tissue indicating pneumonia were detected in 65% of patients, and the presence of concomitant pathology was detected in only 2 children. Insufficiency and inconsistency of data, as well as a limited number of works, devoted to the problem of lung damage in children with a new coronavirus infection, determine the relevance of this study.

Aim: to study the clinical and laboratory features of the course of SARS-CoV-2 infection (COVID-19) in children of the Ryazan region.

Materials and research methods. A single-center pilot observational study carried out with the participation of 55 children (30 boys, 25 girls), hospitalized at the City Clinical Hospital No. 11 (Ryazan) from April 2020 to March 2021 with a diagnosis of new coronavirus infection COVID-19. The diagnosis verified according to modern clinical and laboratory criteria for etiological diagnostics, including the detection of ribonucleic acid (RNA) of SARS-CoV-2 in the material of a smear from the oropharynx and nasopharynx by polymerase chain reaction (PCR), as well as taking into account modern clinical and radiological criteria for viral lung damage using specialized methods of radiation diagnostics.

The inclusion criteria for the study were: age from 1 month up to 17 years; the diagnosis verified by the detection of SARS-CoV-2 RNA by the PCR method: new coronavirus infection COVID-19; the presence of signs of damage to the lung tissue, typical for pneumonia of viral etiology, according to the X-ray computed tomography (X-ray CT) of the chest. C-reactive protein (CRP), alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), creatinine phosphokinase-MB (CPK-MB), serum ferritin determined in all patients. Statistical processing performed using the Pandas, SciPy libraries and the Python programming language. Given the limited number of observations, the absence of a normal distribution, the methods of nonparametric statistics were used. For quantitative variables, the median and quartiles were calculated, the data are presented as Me [P25; P75], for qualitative variables the determination of absolute values and their shares (in %) was carried out. For the correlation analysis, the Spearman rank correlation coefficient (r) was calculated with an estimate of the significance level (p). Differences were considered statistically significant at $p<0.05$.

Results. All patients with COVID-19 admitted to an infectious diseases hospital for emergency indications. Most of them were delivered by the transport of the territorial center of disaster medicine from the regional hospitals of the region (22 patients, 40.0%), $^1/_3$ of children (17 patients, 30.9%) were admitted by the referral of the district pediatrician, ambulance teams were delivered from home 14 children (25.5%), 2 children (3.6%) were hospitalized on self-referral without a referral from medical organizations.Twenty children (36.4%) were admitted to the hospital in the first 3 days from the onset of the disease, 19 (34.6%) children – on 4-6 days, 12 (21.8%) – on 7-10 days, 2 (3.6%) – on the 11-14 days and 2 (3.6%) – after 14 days from the moment the first clinical symptoms appeared.During the analysis of the gender-age structure of the studied group of patients (table 1), there were no significant differences in the incidence of COVID-19 depending on gender. The youngest patient was 1 month old, the oldest - 17 years 11 months old. Among those hospitalized, there was a predominance of children over the age of 12 years (34 patients, 61.8%).

Table 1

Distribution of patients with COVID-19 by age and sex

Age groups	Gender		Total
	Boys	Girls	
0-12 months	4 (7.3%) 4	1 (1.8%)	5 (9.1%)
1-5 years	5 (9.1%)	1 (1.8%)	6 (10.9%)
5-12 years	2 (3.6%)	8 (14.6%)	10 (18.2%)
12-18 years	19 (34.5%)	15 (27.3%)	34 (61.8%)
Total:	30 (54.5%)	25 (45.5%)	55 (100%)

Various comorbidities had 17 (30.9%) patients, the structure of which is shown in table 2. Moreover, a combination of obesity with pathology of the cardiovascular system had 5 children (9.1%).

Table 2

The structure of comorbid pathology in the observed patients

Nosology	Quantity	
	n	%
Bronchial asthma	2	3,6%
Bronchopulmonary dysplasia in history	1	1,8%
Obesity	9	16,4%
Pathology of Central Nervous System	3	5,5%
Arterial hypertension	4	7,3%
Congenital heart defects	3	5,5%

More than half of the hospitalized (32 children, 58.2%) had intrafamilial contact with laboratory-confirmed cases of COVID-19 in relatives, in 23 (41.8%) patients the source of infection could not be identified (fig. 1).

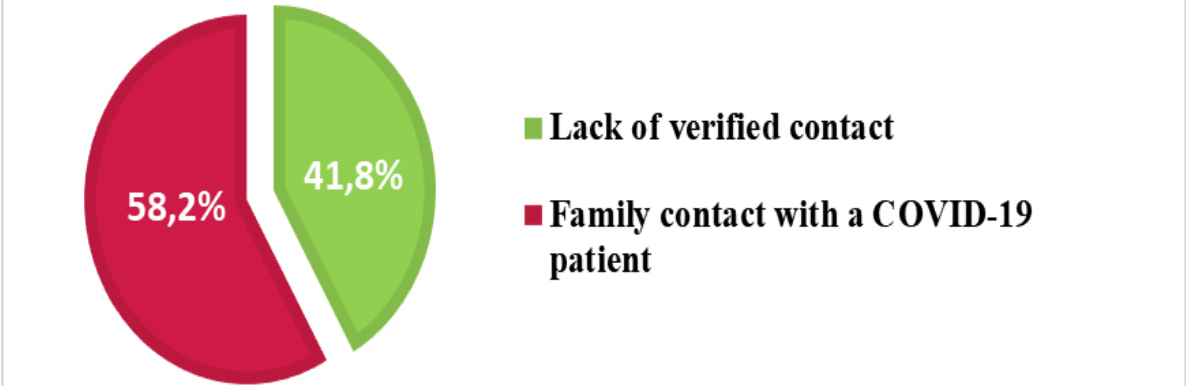

Figure 1. Data on contacts with laboratory-confirmed cases of COVID-19 in patients' relatives

At the time of admission, the condition of the majority of patients was assessed as moderate (53 patients, 96.4%), 2 (3.6%) children were in a serious condition. The severity was due to the presence of respiratory disorders and the severity of the intoxication syndrome. The main clinical symptoms, observed in children with COVID-19 associated pneumonia, are presented in table 3.

Table 3

The clinical symptoms in the observed patients

Clinical symptoms	Number	
	n	%
Intoxication symptoms		
Fever	48	87,3%
Weakness/lethargy	31	56,4%
Decreased appetite	26	47,3%
Headache	28	50,9%
Myalgia	3	5,5%
Tachycardia	37	67,3%
Respiratory tract symptoms		
Cough	53	96,4%
Sore throat	8	14,5%
Difficulty in nasal breathing	27	49,1%
Auscultators changes in the lungs (dry/wet rales)	11	20,0%
Shortness of breath	26	47,3%
Tachypnea	19	34,5%
Gastrointestinal symptoms		
Nausea	4	7,3%
Vomiting	5	9,1%
Abdominal pain	2	3,6%
Diarrhea	3	5,5%
Other		
Disturbances of taste and / or smell	17	30,9%
Skin rashes	1	1,8%

Among the clinical symptoms of infectious toxicosis, fever of varying severity was most often recorded, which was observed in 48 (87.3%) patients. In most cases, the body temperature reached subfebrile

values (22 patients, 40.0%), febrile fever observed in 20 (36.4%) patients, and fever increase of more than 39.1°C (high febrile fever) at the time of admission was noted in six children (10.9%). In 7 (12.7%) patients thermometry indices corresponded to the norm. The median body temperature was 37.9°C [37.4; 38.5]. Other intoxication symptoms were rate: weakness/lethargy (31 patients, 56.4%), decreased appetite (26 patients, 47.3%), headache (28 patients, 50.9%), myalgia (3 patients, 5.5%).

A common symptom of respiratory tract damage was dry or unproductive cough (53 patients, 96.4%). Dyspnea was present in 26 (47.3%) patients. In 9 (16.3%) patients, there were symptoms of respiratory failure of 1-2 degrees.

Blood oxygen saturation indices, as a rule, corresponded to normal values (Me=98 [96; 99]), decrease in saturation <95% had 5 patients (9%) (fig. 2)

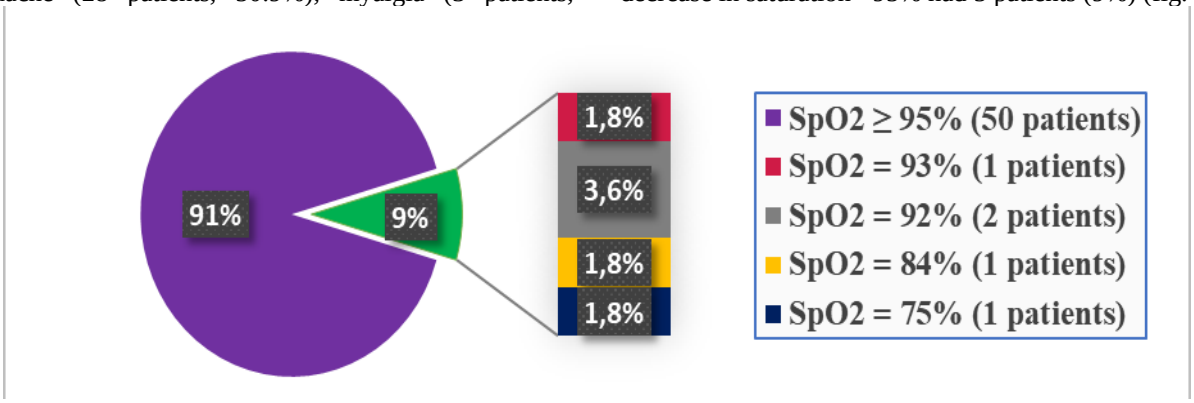

Figure 2. Indicators of blood oxygen saturation in patients with COVID-19

In an objective study, 11 (20%) patients showed auscultatory changes in the lungs in the form of dry or wet rales. An increase in the respiratory rate (tachypnea) in 19 patients (34.5%) revealed, tachycardia – in 37 patients (67.3%). In an objective study, 11 (20%) patients showed auscultatory changes in the lungs in the form of dry or wet rales.

Catarrhal inflammation of upper respiratory tract had 28 (50.9%) children. At the same time, difficulty in nasal breathing was noted in 27 (49.1%) patients, 8 (14.5%) patients actively complained of sore throat. Disturbances of taste and smell registered mainly among children of the older age group (17 patients, 30.9%). Significantly less frequently, gastrointestinal symptoms were detected: nausea - 4 patient (7.3%), single vomiting – 5 (9.1%), diarrhea – 3 (5.5%), diffuse abdominal pain – 2 (3.6%). One patient has an urticarial-type skin rash (1.8%).

The presence of lung tissue lesions typical for pneumonia of viral etiology was established on the basis of computed tomography data of the chest organs. In the dominant number of cases (35 patients, 63.6%), lung damage corresponded to mild (CT-1) severity.

Changes in laboratory parameters in patients with COVID-19 associated pneumonia presented in table 4.

Hematological abnormalities in most patients were represented by leukopenia (33 patients, 60.0%), absolute lymphopenia (28 patients, 50.9%) and neutropenia (22 patients, 40.0%). A change in the number of platelets was observed in 18 patients, thrombocytopenia occurred in 15 (27.3%) of them, thrombocytosis was observed in 3 (5.5%) cases. ESR acceleration was registered in 23 (41.8%) hospitalized children. An increase of CRP had 19 (34.6%) patients, ALT (alanine aminotransferase) and LDH (lactate dehydrogenase) - in 11 (20.0%), AST (aspartate aminotransferase) - in 14 (25.5%), CPK-MB (creatine phosphokinase-MB) - in 24 (34.6%). The serum ferritin in the overwhelming majority of patients was in the range of normal values, hyperferritinaemia observed in 15 (27.3%) patients.

Pathological changes in the coagulogram recorded in 8 (14.5%) cases, 5 (9.1%) children had an increase in the D-dimer level ≥ 500 ng/L, 2 of them also had a decrease in the level of fibrinogen in the blood, isolated hypofibrinogenemia occurred in 1 (1.8%) patient, hyperfibrinogenemia - in 2 (3.6%).

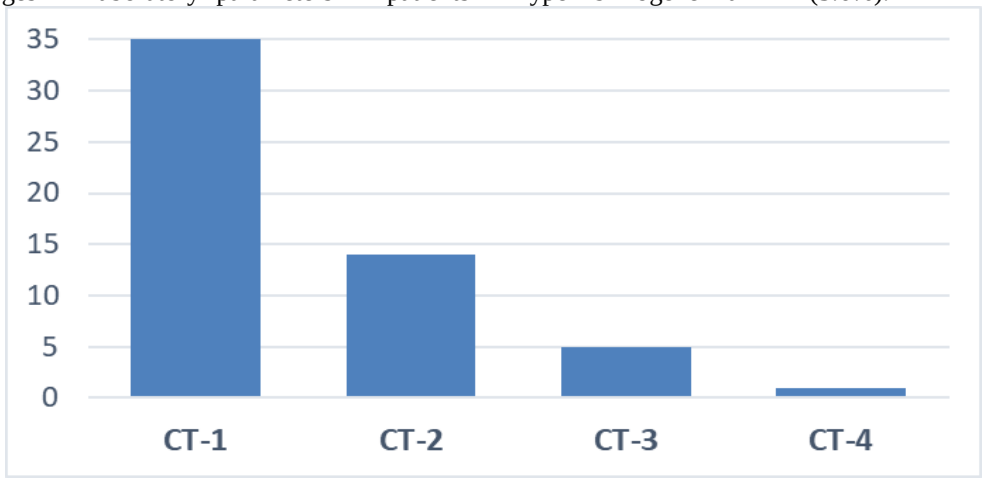

Figure 3. Grades of lung involvement on chest CT

Table 4

The Laboratory Test Results of patients with COVID-19

Deviation of indicators		n	%	Me [P_{25}; P_{75}]
Complete blood count	Leukopenia (10^9/L)	33	60,0%	5,7 [4,7; 6,8]
	Leukocytosis (10^9/L)	7	12,7%	
	Abs.neutropenia (10^9/L)	22	40,0%	2,9 [2,1;4,5]
	Abs.neutrophilia (10^9/L)	10	18,2%	
	Abs. lymphopenia (10^9/L)	28	50,9%	1,9 [1,5; 3,0]
	Abs. lymphocytosis(10^9/L)	6	10,9%	
	Thrombocytopenia (10^9/L)	15	27,3%	184 [248; 146]
	Thrombocytosis (10^9/L)	3	5,5%	
	ESR acceleration (mm/h)	23	41,8%	12 [7; 18]
Blood biochemistry	ALT >40 U/L	11	20,0%	22 [16; 35]
	AST >40 U/L	14	25,5%	29 [21; 42]
	LDH >576 U/L	11	20,0%	462 [365; 532]
	CPK-MV >24 U/L	24	43,6%	24 [20,2; 33,8]
	CRP ≥ 6 mg/L	19	34,6%	24[12; 48]
	↑ Ferritin (ng/ml)	15	27,3%	75 [34; 175]
Coagulogram	Fibrinogen >4 g/L	2	3,6%	3,2 [2,61; 3,5]
	Fibrinogen <2 g/L	3	5,5%	

In 35 (63.6%) children, the presence of concomitant bacterial infection revealed. The main pathogens detected by throat swab culture are shown in figure 4

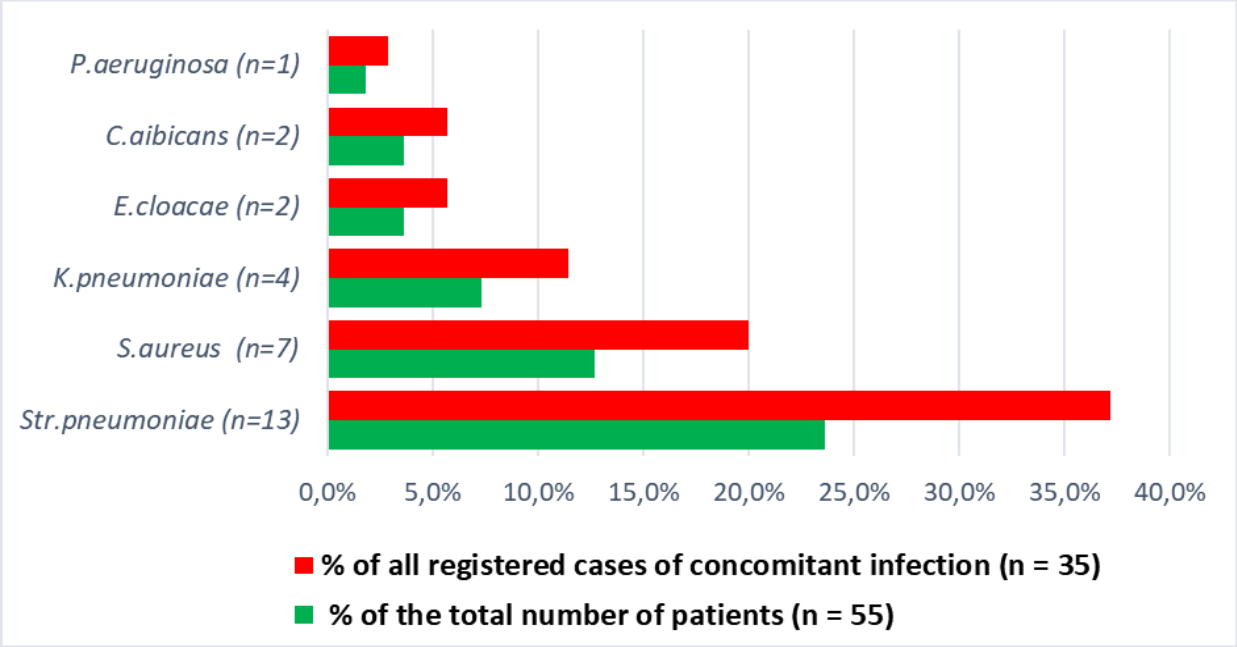

Figure 4. Results of bacteriological examination of throat swab

IgM antibodies to *M. pneumoniae* detected by ELISA in 15 patients (27.3%), 6 child have a combination of mycoplasma and pneumococcal infections (10.9%).

Treatment of patients with COVID-19 associated pneumonia carried out in accordance with current clinical guidelines and included antiviral drugs, non-steroidal anti-inflammatory drugs, mucolytic, anticoagulants and glucocorticosteroids. Three patients needed to oxygen therapy. In the presence of concomitant infection, antibacterial drugs were prescribed according to the sensitivity of the isolated pathogen. Against the background of the therapy, positive dynamics noted in the all patients. Temperature normalization noted on the 7-10th day of inpatient treatment. Among other clinical manifestations, ageusia, anosmia and cough persisted the longest. By the time of discharge, the symptoms of coughing had been stopped in all patients, however, sense of smell and taste recovered only in 3 of 17 children. The average length of stay in the hospital was 15±5 bed-days.

Complete regression of laboratory changes achieved in 19 patients (34.5%). Most of the children (53

patients, 96.4%) were discharged in satisfactory condition under the further supervision of a local pediatrician at the place of residence. To search for significant relationships between the degree of lung tissue damage (according to chest CT data) and laboratory parameters, the Spearman rank correlations were assessed. A direct correlation was found between the degree of lung damage and the level of CRP ($r = 0.31$, $p = 0.019$). A similar relationship was observed for ALT ($r = 0.30$, $p = 0.05$) and LDH ($r = 0.27$, $p = 0.05$). A statistically significant positive correlation was also established between the degree of lung tissue damage and the presence of concomitant diseases ($r = 0.41$, $p = 0.002$).

Conclusions: Among hospitalized patients with community-acquired pneumonia associated with the new coronavirus infection COVID-19, there was a predominance of children over the age of 12 years (61.8%). Almost half of the patients (40%) had concomitant diseases, among which the most common were obesity, cardiovascular diseases, and pathology of central nervous system. The presence of concomitant bacterial infection detected in 63.6% of children. Most patients diagnosed with respiratory mycoplasmosis. A significant positive correlation was established between the degree of lung damage and the presence of concomitant diseases, as well as deviations from the norm of a number of laboratory parameters (CRP, ALT, LDH). With timely treatment, most patients with viral lung disease caused by the new coronavirus infection COVID-19 have a favorable outcome of the disease

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