ASSESSMENT OF THE FUNCTIONAL STATE OF THE RESPIRATORY SYSTEM AFTER RECOVERING FROM VIRAL INFECTION IN CHILDREN

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Abstract. *Increasing attention is being given to the issue of prolonged COVID-19 and the development of symptoms in children who have previously recovered from the coronavirus infection in the global medical literature. The emergence of new symptoms related to SARS-CoV-2 infection and their prolonged persistence are becoming increasingly relevant for both the population and the healthcare system. While respiratory organ changes are the most common, there are also numerous extrapulmonary manifestations.*

This article examines the specific features of viral respiratory tract involvement in children with acute respiratory viral infections (ARVI). It provides detailed insights into the clinical and radiological manifestations of lung damage in children caused by COVID-19.

Keywords: *children, respiratory system, pulmonary pathohistology, long-term manifestations of COVID-19.*

Аннотация. *В мировой медицинской литературе все больше внимания уделяется проблеме продолжительного течения COVID-19 и развитию симптомов у детей, которые ранее переболели коронавирусной инфекцией. Возникновение новых симптомов, связанных с инфекцией SARS-CoV-2, и их продолжительное сохранение становятся все более актуальными как для населения, так и для системы здравоохранения. Хотя изменения в органах дыхания являются наиболее распространенными, также существует множество внелегочных проявлений.*

Данная статья рассматривает особенности вирусного поражения дыхательных путей у детей с острыми респираторными вирусными инфекциями (ОРВИ). Подробно освещаются вопросы клинических и рентгенологические проявления поражения легких у детей, вызванные COVID-19.

Ключевые слова: *дети, дыхательная система, патогистология легких, долгосрочные проявления COVID-19.*

Relevance of the problem: Reducing the negative impact of various infectious agents on health and preventing the development of associated diseases, particularly in children, is a priority in the advancement of modern pediatrics [12, 23]. The respiratory system of children, being at the "borderline" and directly in contact with the external environment, is highly susceptible to viral infections [7,10]. Prolonged persistence and shedding have been described for several respiratory viruses, including SARS-CoV [1] and MERS-CoV [4]. Cases of SARS-CoV-2 persistence in the respiratory tract have been reported since the early stages of the pandemic, confirmed by positive results of RNA virus detection using nucleic acid amplification tests [8, 13]. This disease is characterized by a high level of respiratory tract involvement, frequent development of pneumonia in patients, severe respiratory failure, and a high mortality rate, especially among those admitted to intensive care units [7].

Initially, COVID-19 was believed to be an acute infection with complete resolution of mild and moderate forms within 2-3 weeks. However, over time, increasing evidence suggests that clinical manifestations can persist for more than 6 months [1].

Research objective: The aim of this study is to review the current information on the epidemiology, clinical features, and possible pathogenetic mechanisms of long-term consequences of coronavirus infection.

The analysis included literature reviews, meta-analyses, systematic reviews, and clinical studies. The selection process focused on the most informative and up-to-date articles. The depth of the search was not limited, as the absolute number of identified studies was published within the last 2 years [8].

Type II alveolar cells (ATII) in the lungs are the main target of SARS-CoV-2, which determines the development of diffuse alveolar damage (the predominant type of lung involvement in patients with COVID-19 [21]) and damage to the microcirculatory bed with abnormalities in the blood coagulation system.

The term "viral (interstitial) pneumonia" essentially reflects the development of diffuse alveolar damage. In turn, severe diffuse alveolar damage is synonymous with the clinical concept of "acute respiratory distress syndrome" (ARDS) [17] .

Observations over a 2-year period in patients who have recovered from COVID-19 have shown that impairments in various organs and systems are not limited to the acute phase of the disease. Understanding the consequences of past infection and persistent respiratory disorders has been established [3,15] .

It has been noted that after 6 months from the acute phase of the infection, individuals who have recovered complained of dyspnea, fatigue and muscle weakness, anxiety or depression, and sleep problems, which correlated with the severity of the previous illness [10].

According to the recommendations of the British Pediatric Service, the following children may be considered at increased risk of complicated COVID-19 infection: those with chronic bronchopulmonary diseases (oxygen-dependent BLD, cystic fibrosis with significant respiratory problems, interstitial lung disease, severe bronchial asthma); children with respiratory complications of neuromuscular disorders; patients with immunodeficiency conditions. The development of acute respiratory failure is one of the most common complications of severe viral pneumonia [11].

Reports indicate the recurrence of dyspnea symptoms even several weeks after discharge, with the dyspnea being more pronounced compared to the pre-COVID-19 illness [8,21].

COVID-19 pneumonia is characterized by prolonged fever, intoxication, cough, and 58.2% of children complained of dyspnea or a sense of breathlessness. In 45.5% of cases, oxygen saturation dropped to 90%, and 13.6% of children developed severe respiratory failure (SpO2 < 90%). Chest X-ray examinations more frequently revealed bilateral lung involvement (54.6%). In cases of unilateral involvement, the left and right lungs were affected with equal frequency [6,19].

According to available statistics, complications are less common in children and asymptomatic or mild forms of COVID-19 are more frequently reported. However, severe forms of the disease do occur, primarily in children with underlying conditions [3,17].

In the majority of hospitalized children, the severity of COVID-19 was moderate (53.6%), mild forms accounted for 27.5%, and severe forms for 18.8%. Infants in their first month of life more often experienced the disease in a mild form, while severe cases of the new coronavirus infection were more frequently observed in patients aged 7-14 years and 14-18 years[9,14].

In adults, moderate to severe dyspnea was more often reported by women than men in the intensive care unit group (53.8% compared to 21.1%), while the proportions did not significantly

differ among patients in general wards (24.2% and 20.0%). Among all patients whose ethnic background was known, 8 (42.1%) out of 19 participants of Black Asian and minority ethnic groups reported moderate or severe dyspnea compared to 18 (25.0%) out of 72 White patients [5,11].

Vibholm L.K. et al. demonstrated that SARS-CoV-2 RNA can be detected in oral and nasopharyngeal swabs up to 105 days after clinical recovery. Simultaneously, patients showed a higher level of activity of specific CD8 T lymphocytes, suggesting ongoing immune response stimulation in the presence of viral persistence [16,17]. Li N. et al. analyzed data from 22 patients with laboratory-confirmed COVID-19. All patients showed clinical recovery, positive dynamics in chest CT scans, and no need for continued therapy. However, in all cases, prolonged detection of SARS-CoV-2 RNA in upper respiratory tract swabs was found for more than 50 days after recovery. The average shedding period was 76 days, with a maximum of 112 days [6]. Studies have reported cases of prolonged detection of SARSCoV-2 in upper respiratory tract samples for up to 4 months in quantitative PCR tests [14]. In a study by Salmon-Ceron D. et al., RT-PCR testing of nasopharyngeal swabs for SARS-CoV-2 remained positive in 11 out of 43 patients after two months from the onset of the disease, and in three patients, it remained positive after 3 months [18]. Although SARS-CoV-2 is primarily transmitted through respiratory droplets and clinically manifests as respiratory organ involvement, it should be noted that due to the wide distribution of ACE-2 receptors in the body, COVID-19 is a systemic infection.

When studying the functional state of the lungs after recovering from COVID-19, a predominance of changes in lung diffusion capacity (DLCO) is indicated in 35-39% of cases, while restrictive and obstructive types are observed less frequently. In a prospective cohort of 114 patients, residual changes were observed in 62% of patients based on CT data after 6 months. This included 35% of the entire cohort showing "fibrosis-like" features such as parenchymal stripes, irregular borders between regions (bronchovascular, pleural, or mediastinal), traction bronchiectasis, and honeycombing. The remaining patients with residual changes exhibited ground-glass opacities and thickening of the interstitial tissue. A decrease in gas exchange was observed in 26% of patients [20,24].

In most cases, a combination of several symptoms is observed, and in some cases, the symptoms may change over time, indicating the development of functional impairments in other organs and systems [22].

Y. Li et al. (2021) demonstrated changes resembling nonspecific interstitial pneumonia in the late phase of diffuse alveolar damage [2,14]. Some of these changes may persist in the long term. Focal visceral pleural fibrosis is a consequence of prior inflammation. Lymphoid infiltration of the pleura has been described in some patients with COVID-19 [4,16]. Small areas of fibrosis, usually a few millimeters in size, appear to form in areas of organizing pneumonia. Several authors suggest that severe lung involvement in COVID-19 can lead to the subsequent development of interstitial lung fibrosis [18].

Thus, it is evident that the period of SARS-CoV-2 infectivity likely varies depending on several factors. One of the most significant factors contributing to prolonged persistence and infectivity is the state of the immune system.

Conclusion: In this article, we have discussed the potential long-term consequences of COVID-19 and the pathogenetic mechanisms associated with their development. The presented data indicate consistent findings from studies conducted in different countries and confirm the

widespread prevalence and significant duration of post-COVID sequelae. Children who have experienced COVID-19 should receive follow-up care to assess and dynamically monitor their health status, and if necessary, implement therapeutic, preventive, and rehabilitation measures.

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