

Clinical Properties, Diagnostics and Treatment of Coronavirus Infections for Children

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Abstract

This article provides a review of the literature on the features of the course of coronavirus infection in children. It has been shown that COVID-19 in children is milder and often asymptomatic (1/5 to 1/3 cases). To date, the collection of additional qualitative data on the course and treatment of COVID-19 in children remains important to identify the most effective patient management algorithms. Correct observation, early detection of complications of the disease, as well as the possibility of timely treatment and limitation of the secondary spread of infection are important.

Keywords: COVID-19; children; infection; flow features.

For the first time, coronaviruses were described in 1966 by Tyrell and Bynoe as causative agents of acute respiratory infections [1]. The genome of coronaviruses (CoV) is represented by single-stranded (+) RNAs with the ability to rapidly mutate and recombine. The name of the family is associated with the structure of the virus, the spine-like processes of which resemble the sun's crown. After the receptor captures a fake molecule from the "crown", it is pushed by the virus into the cell, and the virus RNA follows it [2]. There are four subfamilies of coronaviruses: alpha, beta, gamma and delta coronaviruses. The SARS-CoV-2 virus is a beta coronavirus. The genome of the SARS-CoV-2 virus is highly homologous to the genome of the SARS-CoV virus, which caused acute respiratory distress syndrome (ARDS) in thousands of people in 2003. However, COVID-19 is characterized by a lower severity and mortality rate than SARSCoV-associated ARDS [3]. The hallmark of coronaviruses is that they are capable of rapid mutation and recombination, leading to the formation of new coronaviruses that can spread from animals to humans. This is exactly what happened in China in 2002: when the new severe acute respiratory syndrome coronavirus (SARS-CoV) appeared, it was believed that it was transmitted from civet cats or bats to humans [4,5]. The pathogenesis of COVID-19, according to a number of authors, is that this infection is associated with early functional depletion of the activity of cells of innate (NK cells) and acquired (CD8 + cytotoxic lymphocytes) immunity, although not everyone agrees with the theory of virus-induced inhibition of innate immunity [6,7]. Common circulating coronaviruses can be isolated in 4–6% of children hospitalized for acute respiratory tract infections [8] and from 8% of children receiving treatment on an outpatient basis [9]. Despite the high prevalence, starting from the first weeks of registration of infection in foci and

individual areas, and subsequently - during the period of an avalanche increase in the incidence in regions, countries and up to its global spread throughout the planet, researchers drew attention to the fact that the proportion of children among patients with COVID-19 is significantly lower than other age groups. According to recent studies, only 0.9% of positive cases were associated with COVID-19 in children under 15. The results showed that COVID-19 occurs in 0.39-12.3% of children [10]. Apparently, the diversity of statistics from 1 to 5% in the structure of patients with diagnosed cases of the disease, from 1 to 5% in the structure of patients with diagnosed cases of the disease, is determined by the differences in the cohorts tested for SARS-CoV-2 (Severe acute respiratory syndrome related coronavirus 2, severe acute respiratory syndrome associated with coronavirus 2) patients. In addition, it was also noted that children have a milder course of the disease and much less frequent complications and adverse outcomes [11,12,13,14,15,16]. The disease is also recorded in newborns. Little is known about mother-to-child transmission, but there are studies reporting positive cases among newborns born to mothers with confirmed COVID-19. In these cases, it is unclear whether the infection occurred intrapartum or perinatally (through secretions or milk), while there is no clear route of transmission [17,18,19]. Over the entire period, the world statistics of the pandemic recorded single deaths of the disease in children. The vast majority of all described cases of the disease in children are associated with contacts with sick adults. The most common symptoms in children are fever, unproductive cough, and signs of intoxication (myalgia, nausea, weakness) may appear. Some have rhinorrhea, nasal congestion, rarely - symptoms of gastrointestinal tract damage (abdominal pain, diarrhea, vomiting). Diarrhea in children with COVID-19 infection is more common than in adults. Recovery usually occurs within 1–2 weeks. At least 1/4 of children carry the infection asymptotically. Up to 10% of children require hospitalization. A severe course is noted on average in 1% of cases of COVID-19 infection in children, most often complicated forms of the disease develop against the background of severe concomitant diseases [20]. Risk factors for a severe course of the disease in children, regardless of the variant of coronavirus, are: unfavorable premorbid background (lung diseases, malformations, oncological diseases); immunodeficiency states of various origins; coinfection with respiratory syncytial virus, influenza virus, etc.

The clinical forms of the course of COVID-19 infection in children in foreign publications are currently being considered according to the clinical recommendations of the Association of Chinese Physicians, published in March 2020. According to this classification, mild and moderate forms are predominantly found in children. However, a number of authors emphasize the possibility of radiological verification of pneumonia in a patient with good health. Such conditions are typical for the course of SARS-CoV-2 infection in adults and require X-ray monitoring of all patients with confirmed COVID-19 over time [21,22,23]. Comparison of clinical manifestations in children with COVID-19 (n = 36) with adult patients with COVID-19 (n = 135), as well as children with ARVI (n = 44) and influenza (n = 167), in one city showed that children with COVID-19 were less likely to have symptoms that characterize the severity of the disease: fever (36% of children and 86% of adults), cough (19% and 62%), pneumonia (53% and 95%), an increase in C-reactive protein (3% and 49%), severe course of the disease (0% and 23%; p < 0.0001). Some authors have described asymptomatic carriers in the pediatric population, which is of concern because infected

children can spread the disease asymptotically [24]. Dong et al. Reported that 4.4% of children were completely asymptomatic and 55.3% had mild forms such as rhinopharyngitis [25]. The occurrence of multisystem inflammatory syndrome in children has also been reported [25]. The syndrome was originally named "Kawasaki disease" and was later renamed Pediatric Multisystem Inflammatory Syndrome (PIMS), and it is similar to multisystem inflammatory vascular disease in adults with COVID-19. The disease is usually preceded by gastrointestinal symptoms, followed by systemic vasculitis with prolonged fever, accompanied by rash, palmar erythema, conjunctivitis, oral lesions and laterocervical lymphadenopathy, and sometimes complicated by myocarditis and / or severe coronaritis. PIMS has been registered in the UK, France, Italy and the US, but fortunately, treatment for Kawasaki vasculitis has proven to be effective.

The following classification system for COVID-19 for children has been proposed, depending on the severity of the disease (based on the clinical picture) [10, 27]

In the asymptomatic form: there are no clinical signs or symptoms, chest imaging is normal, the SARS-CoV-2 nucleic acid test result is positive.

Mild: Symptoms of an acute upper respiratory tract infection such as fever, cough, rhinorrhea, sneezing, fatigue, and myalgia. Physical examination reveals only a few congestions of the pharynx without auscultatory abnormalities. Some children may not have a fever, but only digestive symptoms such as nausea, vomiting, abdominal pain, and diarrhea. [28]

Moderate to severe: Typical signs and symptoms of pneumonia, such as fever, predominantly productive cough and / or wheezing, but no hypoxemia, dyspnea, or other signs of respiratory distress. In some cases, there may be no clinical signs or symptoms, but only positive results from computed tomography (CT).

In severe cases: fever, cough and shortness of breath (associated with central cyanosis and oxygen saturation <92%), tachypnea, or severe diarrhea. The disease usually progresses in 7-10 days. Signs of respiratory distress are present, such as shortness of breath, chest retraction, bradypnea, and, in rare cases, apnea. Cases of silent hypoxia without compensatory signs in children, in contrast to adults, have not been registered [29].

In the critical form: progression to acute respiratory distress syndrome (ARDS) or respiratory failure with complications such as intravascular disseminated coagulation, shock, encephalopathy, myocarditis, heart failure, and acute kidney disease.

A COVID-19 case may be suspected if there are clinical signs and symptoms in an appropriate epidemiological context (for example, in an endemic area), especially if contact with a confirmed COVID-19 case is known. The diagnosis can be confirmed by laboratory tests to detect viruses. It is important to establish the time of onset of infection based on an

incubation period of 2-14 days, on average 3-7 days [28]. A child may be suspected of contracting COVID-19 if at least one of the following exists: [23]

1. Fever, specific respiratory symptoms, digestive symptoms or fatigue.
2. Presumptive biological findings: normal leukocyte count, leukopenia, and elevated C-reactive protein (CRP) and procalcitonin (PCT) levels.
3. Specific imaging results (based on chest x-ray and computed tomography)

If suspected, laboratory confirmation is necessary, although some doctors recommend diagnosing if there are clinical signs and symptoms and contact with someone with COVID-19 [30].

The diagnosis of coronavirus infection in children is established with a positive epidemiological history and in the presence of any 2 of the clinical symptoms with laboratory confirmation.

Epidemiological history: children who traveled or lived in the focus of coronavirus infection during the 14 days preceding the onset of the disease; children who have been in contact with people with a high fever or respiratory symptoms from foci of infection; children from family or other foci of a new viral disease; newborns from mothers infected with the new coronavirus infection.

Clinical manifestations

1. Fever (although many pediatric patients have a subfebrile or normal temperature), nonproductive cough, sore throat, diarrhea, papulovesicular rash, “coarse fingers” [31].
2. Typical lung changes on CT [32].
3. At the onset of the disease, normal indicators of the clinical analysis of blood (leukopenia and / or lymphopenia are possible) [33,34].
4. No other pathogens are identified that can cause similar clinical symptoms [34].

COVID-19 viral pneumonia in children is generally mild with characteristic changes on a computed tomogram (CT) of the lungs, which are monitored over time [35]. Many studies describe COVID-19 CT lesions that are nonspecific and have some similarities with other lung pathologies [36,67,38]. Children without symptoms may be diagnosed with pneumonia due to chest CT abnormalities. Atypical symptoms and nonspecific laboratory findings tend to complicate the diagnosis, especially if chest CT abnormalities are the only manifestations [39].

According to some authors, today in the clinical manifestation of COVID-19 in children, some manifestations are common, but much less often than in adults, some are rare, some symptoms are described in adults, but not described in children, others, on the contrary, are described in children and did not occur in adults. There are some that have been described in children in recent weeks. So: 1) often found in children: asymptomatic course; fever (only in half of cases - 40–56%); cough (about every second); d) sore throat / pharyngitis (in 40% of cases); mild diarrhea; coinfection (influenza A and B, M. pneumonia, RSV, RV, etc.); 2) rarely occur: rhinorrhea; wheezing; c) malaise / headache / myalgia; 3) often found in adults, there is no data on children: anosmia / hyposmia (in adults it is referred to as pathognomonic symptoms); conjunctivitis (RT-PCR +, Wu); 4) often found in children, it is not known about adults: "covid fingers" in the absence of other symptoms of the disease (fingers or individual phalanges with signs of cutaneous vasculitis, painful, outwardly similar to frostbite, are described in children in Spain, USA); 5) have recently been described: papulovesicular rash (as in chickenpox) has been described in patients of all ages in Italy and neurological complications (Guillain – Barré syndrome, strokes, polyneuropathies, including transient ones) [41-44].

Currently, there is no etiological treatment or prevention of COVID-19 [45]. Treatment for mild cases is aimed at eliminating current symptoms, and isolation to prevent person-to-person transmission of the virus is the most important preventive treatment. For moderate to severe COVID-19, therapeutic recommendations include supportive therapy, supplemental oxygen and, if bacterial infection (which is common in children) is suspected, empiric antibiotics [46]. very severe cases, accompanied by refractory hypoxia and respiratory failure, will require hospitalization in the intensive care unit for mechanical ventilation; Fortunately, children do not need this as often as adults [26,47,48].

The general principles of treatment include: bed rest, adequate caloric intake and adequate hydration, control of electrolyte balance and homeostasis, monitoring of vital functions and oxygen saturation, correction of respiratory disorders, if indicated - oxygen therapy, control blood and urine tests, blood gas analysis and repeated radiography of the lungs.

Among the main etiotropic drugs that were recommended and / or used for etiotropic therapy in children in the first 3 months of the epidemic were recombinant interferon alfa in the form of nebulizer inhalation, lopinavir / ritonavir, umifenovir, oseltamivir, ribavirin, intravenous immunoglobulins. In general, most publications recommend antiviral therapy in severe cases, but there is no reliable data on its effectiveness and safety in children with COVID-19 infection [20].

Corticosteroids are recommended for the treatment of complications of COVID-19 such as ARDS, septic shock, encephalopathy and bleeding disorders, and steroids are required for other specific pathologies. GCS are prescribed in a short course - for 3-5 days, the dosage for methylprednisolone - no more than 1-2 mg / kg per day [40].

Antibiotics are recommended for secondary chest infections associated with COVID-19. Most studies suggest the use of broad-spectrum antibiotics. Given the incidence of mycoplasma infections in children [24] and the well-described anti-inflammatory properties of azithromycin, this antibiotic may be preferred for children with COVID-19 and bacterial superinfection.

Patients with fever $> 38.5^{\circ}\text{C}$, causing discomfort - physical methods, physical methods of cooling, paracetamol in age-related dosages. Antitussives, expectorants, mucolytics, including numerous patented drugs with various herbal ingredients, are not recommended for routine use due to their ineffectiveness. The appointment of mucolytic and expectorant drugs (ambroxol, acetylcysteine, carbocysteine) is recommended only for viscous, difficult to separate sputum [20].

Immunomodulatory therapy includes intravenous administration of methylprednisolone (1-2 mg / kg / day) for 3-5 days, but not for long-term use. Intravenous immunoglobulin can be used in severe cases when indicated, but its effectiveness needs further evaluation. The recommended dose is 1.0 g / kg / day for 2 days or 400 mg / kg / day for 5 days [4, 23].

An important question, to which there is currently no unambiguous answer, is whether all children infected with SARSCoV-2 need antiviral and immunomodulatory therapy, especially given the high proportion of asymptomatic forms and the large number of side effects of antiviral drugs lopinavir / ritonavir and ribavirin.

Conclusions. Thus, according to most authors, COVID-19 in children is easier and often asymptomatic (from 1/5 to 1/3 of cases). To date, it remains important to collect additional high-quality data on the course and treatment of COVID-19 in children in order to highlight the most effective patient management algorithms. Proper monitoring, early detection of complications of the disease, as well as the possibility of timely treatment and limiting the secondary spread of infection are important.

References:

- [1] Tyrrell DA, Bynoe ML. Cultivation of viruses from a high proportion of patients with colds. *Lancet*. 1966; 1 (7428): 76–77. doi: 10.1016 / s0140-6736 (66) 92364-6
- [2] Larina V. N., Golovko M. G., Larin V. G. The effect of coronavirus infection (covid-19) on the cardiovascular system. *RGMU Bulletin* 2, 2020, 5-13.
- [3] Abaturov A.E., Agafonova E.A., Krivusha E.L., Nikulina A.A. Pathogenesis of COVID-19. *Zdorov'eRebenka*. 2020; 15 (2): 133-144. doi: 10.22141 / 2224-0551.15.1.2020.200598
- [4] Melekhina E.V., Gorelov A.V., Music A.D. Clinical features of the course of COVID-19 in children of different age groups. Literature review by early April 2020. *Practical issues of pediatrics*. 2020; 15 (2): 7–20. (In Russian). DOI: 10.20953 / 1817-7646-2020-2-7-20.

- [5] Luk HKH, Li X, Fung J, Lau SKP, Woo PCY. Molecular epidemiology, evolution and phylogeny of SARS coronavirus. *Infect Genet Evol.* 2019 Jul; 71: 21-30. DOI: 10.1016 / j.meegid.2019.03.001
- [6] Zheng M, Gao Y, Wang G, et al. Functional exhaustion of antiviral lymphocytes in COVID-19 patients. *Cell MolImmunol.* 2020; 17 (5): 533-535. doi: 10.1038 / s41423-020-0402-2.
- [7] Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet.* 2020; 395 (10229): 1033-1034. doi: 10.1016 / S01406736 (20) 30628-0
- [8] Gaunt ER, Hardie A, Claas EC, Simmonds P, Templeton KE. Epidemiology and clinical presentations of the four human coronaviruses 229E, HKU1, NL63, and OC43 detected over 3 years using a novel multiplex real-time PCR method. *J ClinMicrobiol.* 2010 Aug; 48 (8): 2940-7. DOI: 10.1128 / JCM.00636-10
- [9] Taylor S, Lopez P, Weckx L, Borja-Tabora C, Ulloa-Gutierrez R, Lazcano-Ponce E, et al. Respiratory viruses and influenza-like illness: epidemiology and outcomes in children aged 6 months to 10 years in a multi-country population sample. *J Infect.* 2017 Jan; 74 (1): 29-41. DOI: 10.1016 / j.jinf.2016.09.003
- [10] Ioana M Ciuca. COVID-19 in Children: An Ample Review Risk ManagHealthc Policy. 2020; 13: 661-669. doi: 10.2147 / RMHP.S257180
- [11] Zaplatnikov A.L., Svintsitskaya V.I. COVID-19 and children. *Breast cancer.* 2020; 1 (*): 1-3.
- [12] Liu W., Zhang Q., Chen J. et al. Detection of COVID-19 in Children in Early January 2020 in Wuhan, China. *N Engl J Med.* 2020.https: // www.nejm.org/doi/10.1056/NEJMc2003717. DOI: 10.1056 / NEJMc2003717.
- [13] Chan J.F., Yuan S., Kok K.H. et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet.* 2020; 395: 514-523.
- [14] Zhang Y.P. The epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) in China. *Chin J Epidemiol.* 2020; 41: 145-151.
- [15] Cao Q., Chen Y.C., Chen C.L., Chiu C.H. SARS-CoV-2 infection in children: Transmission dynamics and clinical characteristics. *J Formos Med Assoc.* 2020 Mar 2; 119 (3): 670–673. DOI: 10.1016 / j.jfma.2020.02.009.
- [16] Lu X., Zhang L., Du H. et al. SARS-CoV-2 infection in children. *N Engl J Med.* 2020 Mar 18; [e-pub]. DOI: .1056 / NEJMc2005073
- [17] Centers for Disease Control and Prevention. Care for Breastfeeding Women. Available from: <https://www.cdc.gov/coronavirus/2019-ncov/hcp/care-for-breastfeeding-women>. Accessed April 01, 2020
- [18] Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *TranslPediatri.* 2020; 9 (1): 51-60. doi: 10.21037 / tp.2020.02.06
- [19] Fan C, Lei D, Fang C, et al. Perinatal transmission of COVID-19 associated SARS-CoV-2: should we worry? *Clin Infect Dis.* 2020: ciaa226. doi: 10.1093 / cid / ciaa226.

- [20] Aleksandrovich Yu.S., Baybarina E.N., Baranov A.A., et al. Management of children with a disease caused by a new coronavirus infection (SARS-CoV-2). *Pediatric Pharmacology*. 2020; 17 (2): 103-118. doi: 10.15690 / pf.v17i2.2096
- [21] Livingston E, Bucher K. Coronavirus disease 2019 (COVID-19) in Italy. *JAMA*. 2020 Mar 17. DOI: 10.1001 / jama.2020.4344
- [22] Wei M, Yuan J, Liu Y, Fu T, Yu X, Zhang ZJ. Novel coronavirus infection in hospitalized infants under 1 year of age in China. *JAMA*. 2020 Feb 14. DOI: 10.1001 / jama.2020.2131,
- [23] Chen ZM, Fu JF, Shu Q, Chen YH, Hua CZ, Li FB, et al. Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus. *World J Pediatr*. 2020 Feb 5. DOI: 10.1007 / s12519-020-00345-5
- [24] Xia W, Shao J, Guo Y, Peng X, Li Z, Hu D. Clinical and CT features in pediatric patients with COVID-19 infection: different points from adults. *PedPulmonol*. 2020; 55: 1169-1174. doi: 10.1002 / ppul.24718
- [25] Schroeder AR, Wilson KM, Ralston SL. COVID-19 and Kawasaki disease: finding the signal in the noise. *HospPediatr*. 2020; hpeds. 2020–000356. doi: 10.1542 / hpeds.2020-000356
- [26] Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 Among Children in China, ”. *Pediatrics*. 2020; 145 (6): e20200702. doi: 10.1542 / peds.2020-0702
- [27] Fang F, Zhao D, Chen Y. Recommendations for the diagnosis, prevention, and control of the 2019 novel coronavirus infection in children (first interim edition). *ZhonghuaErKeZaZhi*. 2020; 145.
- [28] Shen K, Yang Y, Wang T, et al; Global Pediatric Pulmonology Alliance. Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts ’consensus statement. *World J Pediatr*. 2020; 1-9. doi: 10.1007 / s12519-020-00343-7,
- [29] Guan WJ, Liang WH, Zhao Y, et al. Comorbidity and its im pact on 1590 patients with Covid-19 in China: a nationwide analysis. *EurRespir J*. 2020; 55 (5): 2000547. doi: 10.1183 / 13993003.00547-2020
- [30] Global surveillance for COVID-19 caused by human infection with COVID-19 virus Interim guidance; March 20, 2020. Available from: [www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-\(2019-ncov\)](http://www.who.int/publications-detail/global-surveillance-for-human-infection-with-novel-coronavirus-(2019-ncov)). Accessed June11, 2020
- [31] Gao Y, Li T, Han M, et al. Diagnostic utility of clinical laboratory data determinations for patients with the severe COVID-19. *J Med Virol*. 2020; 0.1002 / jmv.25770. doi: 10.1002 / jmv.25770
- [32] Li W, Cui H, Li K, et al. Chest computed tomography in children with COVID-19 respiratory infection. *PediatrRadiol*. 2020; 50 (6): 796-799. doi: 10.1007 / s00247-020-04656-7.].
- [33] Henry BM, Lippi G, Plebani M. Laboratory abnormalities in children with novel coronavirus disease 2019. *ClinChem Lab Med*. 2020; j / cclm.ahead-of-print / cclm-2020-0272 / cclm-2020-0272. xm. doi: 10.1515 / cclm-2020-0272.
- [34] Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet*. 2020; 395 (10223): 507-513.doi: 10.1016 / S0140-6736 (20) 30211-7.

- [35] Namazova-Baranova L.S., Baranov A.A. Coronavirus infection in children (as of February 2020). *Pediatric Pharmacology*. 2020; 17 (1): 7-11. doi: 10.15690 / pf.v17i1.2076)
- [36] Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis*. 2020; 20 (4): 425-434. doi: 10.1016 / S1473-3099 (20) 30086-4
- [37] Ji LN, Chao S, Wang YJ, et al. Clinical features of pediatric patients with COVID-19: a report of two family cluster cases. *World J Pediatr*. 2020: 1–4. doi: 10.1007 / s12519-020-00356-2.
- [38] Ng M, Lee E, Yang J, et al. Imaging Profile of the COVID-19 Infection: radiologic findings and literature review. *Radiology*. 2020; 2 (1): e200034. doi: 10.1148 / ryct.2020200034
- [39] *J Clin Virol*. Clinical features of pediatric patients with coronavirus disease (COVID-19) 2020 Jun; 127: 104377. doi: 10.1016 / j.jcv.2020.104377
- [40] Namazova-Baranova L.S. Coronavirus infection (COVID-19) in children (as of April 2020). *Pediatric Pharmacology*. 2020; 17 (2): 85–94. doi: 10.15690 / pf.v17i2.2094,
- [41] Liu W, Zhang Q, Chen J, et al. Detection of Covid-19 in Children in Early January 2020 in Wuhan, China. *N Engl J Med*. 2020; 382 (14): 1370-1371. doi: 10.1056 / NEJMc2003717.
- [42] Zheng F, Liao C, Fan QH, et al. Clinical characteristics of children with Coronavirus Disease 2019 in Hubei, China. *Curr Med Sci*. 2020; 40 (2): 275-280. doi: 10.1007 / s11596-020-2172-6.
- [43] Marzano AV, Genovese G, Fabbrocini G, et al. Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicenter case series of 22 patients. *J Am Acad Dermatol*. 2020; S01909622 (20) 30657-5. doi: 10.1016 / j.jaad.2020.04.044.
- [44] Genovese G, Colonna C, Marzano AV. Varicella-like exanthem associated with COVID-19 in an 8-year-old girl: a diagnostic clue? *Pediatr Dermatol*. 2020. doi: 10.1111 / pde.14201
- [45] Bouadma L, Lescure F, Lucet J, Yazdanpanah Y, Timsit JF. Severe SARS-CoV-2 infections: practical considerations and management strategy for intensivists. *Intensive Care Med*. 2020; 46 (4): 579-582. doi: 10.1007 / s00134-020-05967-x
- [46] Jin YH, Cai L, Cheng ZS, et al. A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). *Mil Med Res*. 2020; 7 (1): 4. doi: 10.1186 / s40779-020-0233-6
- [47] Xu XW, Wu XX, Jiang XG, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ*. 2020; 368: m606. doi: 10.1136 / bmj.m606,
- [48] Sun D, Li H, Lu X, et al. Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: a single center’s observational study. *World J Pediatr*. 2020. doi: 10.1007 / s12519-020-00354-4