

**CORONAVIRUS INFECTION IN CHILDREN**<sup>1</sup>Khabibullayeva Moxichexra Abdulkhamidovna, <sup>2</sup>Maxamatov Umidjon Shoirjonovich,<sup>3</sup>Muhammadaliyev Asadbek Yuldashali ugli, <sup>4</sup>Tolqinov Islamjon Ikromjon ugli

Laboratory physician of the Fergana branch of the Republican Scientific Center for Emergency Care<sup>1</sup>, Lecturer, Department of Nutrition, Child and Adolescent Hygiene, Fergana Institute of Public Health<sup>2</sup>, 4th year student of medical prophylaxis<sup>3</sup>, 4th year student of medical prophylaxis<sup>4</sup>

**ANNOTATION**

Currently, 7 coronaviruses that cause human disease are known, 3 of which over the past 20 years have caused epidemics with a large number of severe cases, a high mortality rate and infection from the primary focus to other countries, followed by the formation of epidemic foci. The last epidemic of coronavirus infection (CVI) COVID-19 (COrona VIRus Disease 2019) arose at the end of December 2019 in the province of Hubei, China and still continues. Objective of the research: comparative epidemiological and clinical characteristics of the new CVI and peculiarities of its course in children. An analysis of 64 publications in peer-reviewed journals and official sources of health care in Russia and China, WHO, devoted to epidemiologically significant CVI, including COVID-19. According to the literature, in all three epidemics of CVI, children, including newborns, were involved in the epidemic process. Almost all sources indicate a milder course of CVI in young children. Cases of perinatal infection are described. The review provides a comparative analysis of the clinical and epidemiological features of CVI in children using SARS, MERS as an example, gives basic approaches and recommendations for the diagnosis and treatment of COVID-19 with an assessment of the possibility of using antiviral drugs in children.

**Keywords:** *coronavirus, SARS, MERS, COVID-19, children, pneumonia, epidemic, pregnancy.*

Cases of pneumonia with low efficacy of antibiotic therapy were reported to the international information network ProMed on December 30, 2019 [1]. An outbreak of new coronavirus infection (CVI) (COVID19), which originated in Wuhan (Hubei province, China) and spread in the first two months of 2020 across all administrative regions of mainland China and more than 80 countries around the world, received unprecedented coverage in press and the Internet. As of March 7, 2020, more than 100 thousand cases were registered in the world with a total mortality rate of 3.4%.

In the Russian Federation, anti-epidemic measures have been taken to prevent the import and spread of the new coronavirus [2–5], however, the possibility of importing a new CVI remains high, while children of any age can be in the epidemiological focus. In this regard, pediatricians need to have an idea of the clinical and epidemiological features of CVI in childhood.

Cases of pneumonia with low efficacy of antibiotic therapy were reported to the international information network ProMed on December 30, 2019 [1]. An outbreak of new coronavirus infection (CVI) (COVID19), which originated in Wuhan (Hubei province, China) and spread in the first two months of 2020 across all administrative regions of mainland China and more than 80 countries around the world, received unprecedented coverage in press and the Internet. As of March 7, 2020, more than 100 thousand cases were registered in the world with a total mortality rate of 3.4% [2].

In the Russian Federation, anti-epidemic measures have been taken to prevent the import and spread of the new coronavirus [2–5], however, the possibility of importing a new CVI remains high, while children of any age can be in the epidemiological focus. In this regard, pediatricians need to have an idea of the clinical and epidemiological features of CVI in childhood.

Coronaviruses are a family of enveloped viruses containing a single-stranded positive RNA with 26-30,000 nucleotides. In most viruses, large ashlomeres (up to 20 nm) are integrated into the envelope, which are clearly distinguishable during microscopy and resemble the solar corona [7]. Currently, about 40 coronaviruses are known, 7 of which are pathogenic to humans. The family Coronaviridae includes the subfamilies Letivirinae (represented by one species) and Orthocoronavirinae, which unites 4 genera (alpha, beta, delta, gamma). The variety of coronaviruses is the result of three main reasons. First, the inaccuracy of the RNA-dependent RNA polymerase of coronaviruses leads to their mutation frequency of the order of one per 1000–10,000 nucleotides, which makes them especially variable [8]. Second, as a result of their unique random template switching, which is believed to be mediated by a mechanism of "copy selection", coronaviruses have a high frequency of homologous RNA recombination [9]. Third, coronaviruses have the largest genomes of any known RNA virus, which gives them additional flexibility in gene modification. The combination of these factors made it possible for the emergence of a variety of coronaviruses adapted to different hosts [10]. The first coronavirus was isolated from a chicken embryo in 1937 [11], and the first two human viruses (HCoV-229E and HCoV-OC43) were identified in the mid-1960s from patients with acute respiratory viral infection [12, 13] ... Until 2002, coronaviruses were considered the causative agents of mild respiratory diseases.

The first official report of an outbreak of new CVI was received on December 31, 2019. The fish market in Wuhan was considered the primary focus of infection, and therefore the disease was initially considered zoonotic [38]. During January, more than 11 thousand cases with a mortality rate of 2.5-3% were registered on the territory of mainland China. The disease was characterized by an increase in body temperature, respiratory manifestations, frequent development of pneumonia and ARDS. On January 30, 2020, WHO declared an emergency related to an outbreak of new CVI of international concern [41]. The disease is called COVID-19 (Corona Virus Disease), and the virus itself is SARS-CoV-2.

The new coronavirus is believed to be a recombinant virus between the bat coronavirus and an unknown coronavirus, while its genetic sequence is 79.5% similar to that of SARS-CoV. It has been reported that SARS-CoV-2 uses the same receptor to enter the cell as SARS-CoV [42]. The virus is assigned to the II pathogenicity group, like the SARS-CoV and MERSCoV viruses. The pathogenesis of new CVI is not well understood. There are currently no data on the duration and strength of immunity in relation to the new coronavirus. Immunity in infections caused by other members of the coronavirus family is unstable and re-infection is possible.

The incubation period for COVID-19 was initially defined as 2-14 days (average 3-7 days) [43]. Similar terms are indicated in the temporary guidelines of the Ministry of Health of the Russian Federation [4]. However, later there were suggestions that the maximum incubation period could be up to 24 days [44, 45]. Reuters reported the case of a 70-year-old man 27 days after exposure. [46]

The main source of infection is patients infected with SARS-CoV-2 with or without clinical symptoms, incl. in the incubation period. A 6-month-old child with coronavirus disease 2019 (COVID-19) without clinical manifestations had persistently positive nasopharyngeal swabs before the 16th day of observation [47]. This case highlights the difficulty in establishing the true incidence of COVID-19, as people with asymptomatic disease can shed the virus for a long time. These patients can play an important role in human-to-human

transmission of the virus in society. The routes of transmission are airborne and contact (contact with the mouth, nose or conjunctiva of the eye through contaminated hands) [4, 43].

Among all cases of COVID-19 registered in China, the proportion of children under the age of 18 was 2.4% [48]. Known cases do not allow an objective assessment of the characteristics of the disease in children and their susceptibility to a new type of coronavirus.

Based on the National Guidelines for the Diagnosis and Treatment of Respiratory Infections Caused by the Novel Coronavirus (China, 4th Edition), as well as the clinical experience of research centers, Children's Hospital and Zhejiang University, where 10 cases of COVID-19 in children have been reported. Recommendations for the diagnosis and treatment of respiratory infections caused by the novel coronavirus in children were written [43].

An analysis of COVID-19 cases in children under 1 year of age showed that all 9 children, including 7 girls, were from family foci and epidemiologically linked to Wuhan. An increase in body temperature was noted in 4 children. None of the cases required hospitalization in the ICU and mechanical ventilation, and no one developed complications [49]. According to Z.M. Chen et al., The age of 10 sick children ranged from 112 days to 17 years, 3 out of 10 were diagnosed with pneumonia. Infection of children most often occurred through intrafamily contact.

The majority of children had a low body temperature, in some children the disease proceeded without an increase in body temperature. Lethargy and coughing were noted, which could be accompanied by nasal congestion, runny nose, diarrhea, headache, etc. Shortness of breath, cyanosis and other symptoms usually occurred after 1 week of illness, which was accompanied by symptoms such as malaise or anxiety, decreased appetite and activity. The deterioration of the condition of some children in connection with the development of respiratory failure has been described, in severe cases - the development of septic shock, metabolic acidosis and irreversible impairment of blood coagulation and coagulation [43]. In most children, the prognosis of the disease is favorable; in mild cases, recovery occurs within 1–2 weeks after the onset of the disease [43].

So far, no deaths have been reported for children under 9 years of age. In the age group of 10–19 years, the mortality rate is 0.2% [52].

According to the temporary recommendations of the Ministry of Health of the Russian Federation, risk factors for the development of a serious illness in children, regardless of the variant of coronavirus, are: early age; unfavorable premorbid background (chronic lung diseases, etc.); immunodeficiency states of various origins. Monoinfection caused by the SARS-CoV-2 virus often occurs in the form of mild to moderate damage to the upper respiratory tract, while coinfection with other respiratory viruses (respiratory syncytial, rhinovirus, bocavirus, adenovirus) aggravates the course of the disease and leads to damage lower parts of the respiratory tract (pneumonia, bronchiolitis) [4].

Maternal hypoxemia caused by severe COVID-19 can lead to intrauterine asphyxia, premature birth and other risks. Neonates, especially premature infants, require close monitoring.

To date, 9 cases of COVID-19 have been described in the 3rd trimester of pregnancy. In all cases, delivery was performed by caesarean section. PCR studies were carried out in 6 cases: no coronavirus RNA was found in amniotic fluid, umbilical cord blood and breast milk [53]. Currently, the presence of the disease in the mother is not a contraindication to breastfeeding, provided that preventive measures are taken (washing hands, using a medical mask, reducing the time of contact with the baby).

In February 2020, a report on perinatal coronavirus pneumonia was published in China (the diagnosis was confirmed 30 hours after the birth of the child).

Experience in studying the epidemiology of CVI has shown that children of almost any age are susceptible to coronavirus infection. The inclusion of children in the epidemic process occurs mainly through intrafamilial contacts. Children with SARS and MERS-CVI most often suffered from mild illness, but with both infections, there were deaths. However, in most cases in children, CVI occurs in the form of mild ARVI. Signs of a severe course of CVI can be the appearance of shortness of breath, difficulty breathing and a decrease in oxygen saturation. It is impossible to unambiguously predict the dynamics of the spread of COVID-19; it is necessary to be prepared for such negative predictive scenarios as mutations of the virus in favor of increasing its virulence. In this regard, for any contact with ARVI, pediatricians must have epidemiological alertness and follow the recommendations for prevention. In addition, it is necessary to resolve the issue of providing all pediatricians with pulse oximeters. In an unfavorable epidemiological scenario, the priority will be the timely identification of patients with pneumonia, as well as equipping the ICU with the resources necessary for adequate oxygen support.

Currently, there is no vaccine against the new CVI and drugs with proven prophylactic and therapeutic efficacy. Therefore, to prevent infection of children with SARS-CoV-2, it is necessary to take the usual preventive measures, including thorough hand washing, using soap and / or alcohol-based hand sanitizers, rinsing the nose and gargling, and avoiding contact with sick people.

You can follow the update of information about COVID-19 on the websites of Rosпотребнадзор and the Ministry of Health of Russia, WHO, where the main regulatory documents for the diagnosis, treatment, and prevention of new CVI are posted.

## REFERENCES

1. Undiagnosed pneumonia - China (Hubei): request for information <https://promedmail.org/promed-post/?id=c6864153> Date of treatment from 11.02.2020
2. WHO. Coronavirus disease 2019 (COVID-19) Situation Report - 46. <https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200306-sitrep-46-covid-19.pdf> Date of treatment 03/06/2020
3. Rosпотребнадзор. Resolution of the Chief Sanitary Doctor of the Russian Federation No. 5 of March 2, 2020 "On additional measures to reduce the risks of importation of coronavirus infection." [https://rospotrebnadzor.ru/upload/iblock/494/postanovlenie\\_5-ot-02.03.2020-o-dopolnitelnykh-merakh-posnizheniyu-riskov-zavoza-koronavirusnoy-infektsii\\_1\\_\\_1\\_.pdf](https://rospotrebnadzor.ru/upload/iblock/494/postanovlenie_5-ot-02.03.2020-o-dopolnitelnykh-merakh-posnizheniyu-riskov-zavoza-koronavirusnoy-infektsii_1__1_.pdf) Date of treatment 03/07/2020

4. Ministry of Health of the Russian Federation. Interim guidelines "Prevention, diagnosis and treatment of new coronavirus infection (2019-nCoV)" Version 2 (3.02.2020). <https://www.garant.ru/products/ipo/prime/doc/73406661/> Date of treatment 03/06/2020.
5. Ministry of Health of the Russian Federation Information bulletin on the situation and measures taken to prevent the spread of diseases caused by the new coronavirus <https://www.rosminzdrav.ru/news/2020/01/30/13246-informatsionnyy-byulleteno-situatsii-i-prinimaemyh-merah-pone-dopuscheniyurasprostraneniya-zabolevaniy-vyzvannyh-novym-koronavirus> Date of access from 17.02.
6. Government of the Russian Federation Order of February 3, 2020 No. 194-r <http://static.government.ru/media/files/yv5Oy7YPB9oeeJeoycsaeW9sQ1xFSj29.pdf> Date of treatment 17.02.2020
7. Woo PC, Lau SK, Huang Y, Yuen KY. Coronavirus diversity, phylogeny and interspecies jumping. *ExpBiolMed* (Maywood). 2009; 234: 1117-1127. doi: 10.3181 / 0903-MR-94
8. Duffy S, Shackelton LA, Holmes EC. Rates of evolutionary change in viruses: patterns and determinants. *Nat. Rev. Genet.* 2008; 9: 267-276. doi: 10.1038 / nrg2323
9. Pasternak AO, Spaan WJ, Snijder EJ. Nidovirus transcription: how to make sense? *J. Gen. Virol.* 2006; 87: 1403-1421. doi: 10.1099 / vir.0.81611-0
10. Woo PC, Lau SK, Yuen KY. Infectious diseases emerging from Chinese wet-markets: zoonotic origins of severe respiratory viral infections. *Curr. Opin. Infect. Dis.* 2006; 19: 401-407. doi: 10.1097 / 01.qco.0000244043.08264.fc

