

To Cite:

Kramarov S, Yevtushenko V, Seriakova I, Palatna L, Shpak I, Voronov O, Shadrin V, Kyrytsia N, Dudnikova M, Kaminska T, Holovach O, Chemerkina N, Bolshakova L, Tsymbalenko A. Comparative characteristics of the clinical picture of COVID-19 in children in 2020 and 2021. *Medical Science*, 2021, 25(115), 2373-2382

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Peer-Review History

Received: 14 August 2021
 Reviewed & Revised: 17/August/2021 to 09/September/2021
 Accepted: 11 September 2021
 Published: September 2021

Peer-review Method

External peer-review was done through double-blind method.



DISCOVERY
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Comparative characteristics of the clinical picture of COVID-19 in children in 2020 and 2021

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ABSTRACT

Background: In Ukraine there have been two periods of increased incidence of COVID-19 in 2020 and 2021. The pandemic has wavy character, which may be due, to the high mutational activity, which leads to the rapid formation of new variants of the virus. *Materials and Methods:* There was an analysis of 530 case histories of children from birth to 18 years old, who were hospitalized with coronavirus disease in the period from June 2020 to May 2021. *Results:* In 2021 the share of children aged 1 to 5 increased significantly (from 26.2% to 41%) and the percentage of adolescent visitors decreased (from 24.7% to 15.8%). We found that the average number of patients in 2021 increased in some children with chronic controversial pathology (14.7% in 2021 and 5% in 2020). In 2021, the part with general symptoms and local manifestations of airway lesions significantly increased ($p < 0.05$) 81.15% in 2020). During the wave of 2021, 18 (9.5%) children were involved in intensive care units and the average in 2020 - only 7 (2%). *Conclusions:* During the second wave of coronavirus infection in Ukraine, we observed an increase in the proportion of young and preschool children among inpatients. In the clinical picture of the disease of patients during the second wave of COVID-19, we observed an increase in the absolute number and proportion of children with severe and complicated forms of the disease.

Keywords: children, COVID-19, waves 2020 and 2021

1. INTRODUCTION

The COVID-19 pandemic, which has swept the world since early 2020, continues and continues to spread. To date, sufficient information has been accumulated on certain epidemiological features of coronavirus disease. In particular, COVID-19 is known to affect all age groups, but in children the disease is usually mild and may be accompanied by nonspecific symptoms, especially in newborns. The incidence of children is 2% of all cases in China,

1.2% in Italy, 0.8% in Spain, 1.7% in the USA and 1% in Turkey (Ludvigsson, 2020; Tagarro et al., 2020; Tezer et al., 2020). Children under 10 make up 1% of all cases. According to the Korean Center for Disease Control and Prevention, in Korea, 6.3% of all cases that tested positive for SARS-CoV-2 were children under 18 years old.

In addition, statistics indicate a wavy nature of the spread of infection. In many countries so far, there have been two waves of coronavirus infection, manifested by an active increase in daily incidence in the first period, which was in 2020, then there was a decline and then a new episode with high daily incidence in 2021. Data from several studies indicate some clinical and epidemiological differences between the first and second waves. Differences in age range and severity of disease were reported, in particular. Thus, data from COVID-19 in Spain show that hospitalized patients during the second wave were younger and required fewer days of hospitalization. During the second wave frequency of gastrointestinal symptoms prevailed, despite the fact that many symptoms were similar in both periods morbidity (Iftimie et al., 2021). In addition, according to statistics, patients in Spain during the second peak of the disease were significantly less likely to receive invasive mechanical ventilation, anticoagulants and oxygen therapy, and more often received corticosteroids and non-invasive mechanical ventilation. A significant number of infants, children and women who were hospitalized during pregnancy or after delivery became an important epidemiological difference, according to the author of the study. However, it is noted that in general the course of coronavirus disease in these categories of patients was not severe and relatively favorable (Soriano et al., 2021).

The results of another study conducted by Japanese researchers indicate a lower proportion of severe cases during the second wave of the disease. The authors also note an increase in the proportion of young people among patients, as well as a lower number of comorbidities, a lower proportion of critically ill patients and a decrease in mortality during the second rise in COVID-19 incidence (Sho et al., 2021). At the same time, in another geographical region, India, the second wave of the disease was more severe. It began around mid-March 2021 and grew rapidly, peaking at more than 400,000 reported daily cases by the end of April. There are several factors that are considered as probable causes of the wave-like course of the infection. High mutational activity of SARS-CoV-2 is one of them, which, according to scientists, leads to the rapid formation of new strains of the virus. Some of them show more aggressive pathological properties compared to the original version, which was isolated in Wuhan at the beginning of the pandemic.

In particular, in October 2020 in the UK for the first time heard about a mutated type of coronavirus B.1.1.7 (Kupferschmidt, 2020). Its rapid spread is seen as a likely factor that has provoked a significant increase in the level of COVID-19 infection in the world. According to international reports about epidemiological lineages of SARS-CoV-2, the first statements about new strain B.1.1.7 in Ukraine began to appear in February 2021 and this coincides with the beginning of the increase in daily incidence of COVID-19. Ukrainian Ministry of Health reports that the second increase in morbidity in our country was accompanied by a large number of deaths. Thus, the evolution of COVID-19 entails changes in the epidemiological and clinical characteristics of the disease. The study and systematization of these changes are necessary to build adequate response to the pandemic.

Objective

To compare the epidemiological and clinical characteristics of pediatric patients who were hospitalized during the first and second waves of COVID-19.

2. MATERIALS AND METHODS

The study was one-center, retrospective, cohort. There was an analysis of case histories of children from birth to 18 years old, who were hospitalized at the Kyiv City Children's Clinical Infectious Diseases Hospital (Kyiv, Ukraine) with coronavirus disease in the period from June 2020 to May 2021. There were selected 530 case histories of children with confirmed cases of COVID-19. Among them were 340 patients who were treated during the first wave of incidence in the period from June to November 2020, and another 190 - in the period from February to May 2021, when there was a second rise in incidence in Ukraine.

In all patients, the final diagnosis according to the International Statistical Classification of Diseases of the Tenth Revision (ICD-10) was the diagnostic code U07.1 Verification of the diagnosis in the hospital was performed by single PCR examination of the nasopharyngeal smear, according to the current protocol. The PCR study was performed in the local laboratory of Kyiv City Children's Clinical Infectious Diseases Hospital. Confirmed case was when PCR tests SARS-Cov-2 were positive. Information was collected from patients' medical records, which included demographic data (age, sex), epidemiological information (contact with the patient), anamnestic data (comorbidities, prehospital disease), main clinical symptoms and their duration (including prehospital and hospital stages), results of laboratory and instrumental research, treatment and consequences of the disease.

Upper respiratory tract infection was determined in the presence of catarrhal manifestations and rhinorrhea or nasal congestion. Symptoms of a lower respiratory tract infection included shortness of breath and cough, as well as auscultatory changes such as shortness of breath or wheezing and / or changes in the parenchyma on a chest radiograph or computed tomography. To study the age-related clinical and epidemiological features, all patients were divided into two main periods - in 2020 we studied 340 case histories of children with COVID-19 and in 2021-190 cases. They were divided into five age groups: from birth to 1 month, from 1 to 12 months, from 1 to 5 years, from 6 to 9 years and from 10 to 18 years. Comorbid patients were also divided into a category of patients with concomitant pathology and complications.

Statistical processing of the results was performed using Microsoft Excel. Data were presented using methods of descriptive statistics. The median (M) and interquartile range (IQR, 1st - 3rd quartile) were determined. The significance of the difference between nonparametric parameters was determined using the Chi-square test or Fisher's exact test, for the parametric data used the Mann-Whitney test and Kruskal-Wallis test. The difference was considered significant when the error value $p < 0.05$.

3. RESULTS

The main characteristics of the cohort of patients studied are presented in table 1. The cohort included patients of all ages. Compared to 2020, in 2021 the share of children aged 1 to 5 increased significantly and the percentage of adolescent patients decreased. Also among patients in 2021 the share of children with chronic comorbidities increased. In 2021, in addition, the share of children whose probable place of infection was the children's team decreased, while the percentage of patients who had contact with patients within the family increased. The terms of hospitalization and the number of bed-days did not differ significantly in 2020 and 2021.

Table 1 Demographic and epidemiological data of patients for 2020 and 2021

Parameters	2020 (n=340)	2021 (n=190)	P
Age n(%):			
0-1 months	29 (8.5%)	16 (8.4%)	p=0.966
1-12 months	85 (25%)	41 (21.6%)	p=0.375
1-5 years	89 (26.2%)	78 (41%)	p<0.001
6-9 years	53 (15.6%)	25 (13.2%)	p=0.449
10-18 years	84 (24.7%)	30 (15.8%)	p=0.017
Sex n(%):			
Boys	183 (53.8%)	102 (53.7%)	p=0.976
Girls	157 (46.2%)	88 (46.3%)	p=0.976
Contact with patients n (%):			
Family members	220 (64.7%)	128 (67.4%)	p=0.536
Children's team	18 (5.3%)	2 (1.0%)	p=0.014
Unknown	102 (30.0%)	60 (31.6%)	p=0.706
Hospitalization Day, M (IQR)	3 (1-5)	3 (2-5)	p=0.631
Bed-days, M (IQR)	6 (3-9)	6 (4-8)	p=0.107
Concomitant pathology n (%):	17 (5%)	28 (14.7%)	p<0.001
Allergological	3	6	p=0.759
Endocrine	3	4	p=0.763
Hematological	2	5	p=0.585
Nephrological	1	2	p=0.870
Neurological	3	6	p=0.759
Oncological	1	1	p=0.716
Adiposity	4	4	p=0.432

In the structure of concomitant pathology, allergic diseases were manifested by allergic dermatitis, bronchial asthma and atopic dermatitis; endocrine pathology was represented by aplasia of the thyroid gland, type I diabetes mellitus, Itsenko-Cushing syndrome, rickets; hematological diseases - Minkowski-Shofar anemia, severe iron deficiency anemia; 1 patient had congenital

kidney disease (hypoplasia), another 1 - congenital malformation of the brain; also one case of Down syndrome, cerebral palsy, mental retardation, epilepsy; one child had medulloblastoma of the cerebellum with metastases, 8 patients - obesity, 2 - meningococcal infection, meningococemia. A comparison of the frequency of clinical symptoms in patients with coronavirus infection in 2020 and 2021 is presented in table 2.

Table 2 Comparative characteristics of clinical symptoms in patients with coronavirus infection in 2020 and 2021

Symptoms	2020	2021	P
Fever, n (%)	310 (91.2%)	186 (97.9%)	p=0.003
Weakness, n (%)	300 (88.2%)	185 (97.3%)	p=0.0003
Decreased appetite, n (%)	251 (73.8%)	185 (97.3%)	p<0.00001
Rhinitis, n (%)	139 (40.9%)	139 (73,2%)	p<0.0001
Sore throat, n (%)	67 (19.7%)	53 (27.9%)	p=0.031
Cough, n (%)	219 (64.4%)	104 (54.7%)	p=0.029
Diarrhea, n (%)	24 (7.1%)	16 (8.4%)	p=0.57
Headache, n (%)	20 (5.8%)	32 (16.8%)	p=0.00005
Shortness of breath, n (%)	13(3.8%)	12 (6.3%)	p=0.194
Myalgia, n (%)	18 (5.2%)	7 (3.7%)	p=0.402
Abdominal pain, n (%)	13 (3.8%)	14 (7.3%)	p=0.075
Anosmia, n (%)	27 (7.9%)	8 (4.2%)	p=0.097
Rash, n (%)	17 (5.0%)	8 (4.2%)	p=0.68

Symptoms included fever, general weakness, loss of appetite, and cough in most patients. Compared to 2020, in 2021 the frequency of patients with general symptoms (fever, headache, weakness, loss of appetite) and local manifestations of airway lesions (rhinitis, cough) (p <0.05 according to the Pearson Chi-square criterion) increased. Among laboratory and instrumental research methods, most patients of both study groups were covered by clinical blood tests, biochemical tests (ALT, AST), markers of inflammation (C-reactive protein (CRP), procalcitonin), coagulation tests (international normalized ratio). and X-ray of the chest cavity (table 3).

Table 3 Comparative characteristics of laboratory and instrumental data for 2020 and 2021

Indicators	2020	2021	P
Leukocytes (10 ⁹ / l), M (IQR)	8.4 (6-11.9)	7.7 (5.5-10.3)	p = 0.02202
Neutrophils (%), M (IQR)	34 (26-49)	48 (32.3-68.95)	p = 0.0012
Lymphocytes (%), M (IQR)	40 (24-50)	42.65 (24.15-53.95)	p = 0.65272
Platelets (10 ⁹ /l), M (IQR)	255 (212-312)	224 (174-281)	p < 0.00001
ESR (mm / h), M (IQR)	6 (5-8)	6 (5-9)	p = 0.5157
CRP> 6 mg / l, n (%)	130 (38.2)	58 (30.5)	p = 0.075
Procalcitonin (ng / ml), M (IQR)	0.0415 (0.027-0.064)	0.053 (0.036-0.06925)	p = 0.60306
ALT (U / l), M (IQR)	20 (17-27.75)	20 (17-25.25)	p = 0.78716
AST (U / l), M (IQR)	32.25 (24.6-44)	32.5 (25-43.8)	p = 0.034
EOM, M (IQR)	1.05 (1.04-1.05)	1.06 (1.05-1.06)	p < 0.00001
Fibrinogen (g / l), M (IQR)	3.4 (2.4-4.2)	3.3 (2.6-4.2)	p = 0.9124
X-ray of the lungs, n (%):	260 (76.4%)	147 (77.4%)	p = 0.815
Unchanged	49(18.8%)	35(23.8%)	p = 0.235
With changes in the parenchyma	211(81.15%)	112(76.2%)	p = 0.235

There was no significant difference between indicators of laboratory research methods in the period of outbreaks in 2020 and 2021 (according to the Mann-Whitney test). The results of the general clinical blood test in most patients at the initial examination were within normal limits. Leukopenia ($<4 \times 10^9 / l$) was observed in 12 (3.5%) patients of the 2020 group and 16 (8.4%) patients in 2021, leukocytosis ($> 10 \times 10^9 / l$) in 109 (32%) patients and 48 (25%) respectively. Thrombocytopenia ($<150 \times 10^9 / l$) was observed in 16 (4.7%) patients, and increased platelet count ($> 420 \times 10^9 / l$) - in 28 (8.2%) patients from the study cohort in 2020, while in the group this year thrombocytopenia was observed in 31 (16.3%) patients and thrombocytosis in 9 (4.7%) patients. The erythrocyte sedimentation rate (ESR) at hospitalization in most of children was within the reference values. Only 60 (17.6%) patients in 2020 and 23 (12%) patients in the 2021 group had a higher 10 mm / h. The study of C-reactive protein was performed in 150 (44%) cases and 66 (34.7%), respectively. Of these, 114 (76%) and 58 (87.8%) cases exceeded 6 mg / l. Procalcitonin levels were determined in 67 patients and 64 patients, respectively and ranged from 0.011 to 0.4 ng / ml. Relatively higher rates of transaminases were observed in children of younger age groups (from 0 to 1 month and from 1 to 12 months). Determination of EOM was performed in 87 (25.5%) and 61 (32%) patients, respectively. The rate ranged from 1 to 1.12 (median 1.05). The study of fibrinogen levels was performed in 167 (49%) and 159 (83.6%) children, respectively. Fluctuations of the indicator occurred in the range of 1.6 - 7.88 g / l (median 3.4 g / l).

In accordance with the results of instrumental examinations among 260 patients of the outbreak in 2020 and 147 patients in 2021, there is a tendency to reduce the frequency of detection of parenchymal changes in radiography. The most frequent changes recorded on the radiograph were interstitial lesions, which were described in 171 (81.15%) of 211 patients in 2020 and in 90 patients (80.3%) of the cohort studied in 2021, peribronchial infiltration - in 30 (14.2%) and 20 (17.8%), respectively, the share of the lesion - in 10 (4.65%) and 2 (1.9%) patients, respectively. The frequency of radiological changes in the lung parenchyma at the initial examination was the lowest in the group of children in the first month of life, and the highest - in the age group 6-9 years of both study groups. In children of the first month of life, the frequency of detection of radiological changes in the parenchyma was significantly lower than in older children (10-18 years) ($p = 0.011$ by the criterion of Chi-square).

According to the National Institutes of Health Coronavirus Disease 2019 (COVID-19) Treatment Guidelines) the severity of the condition is interpreted by the following indicators: Asymptomatic or asymptomatic infection: Presence of a positive SARS-CoV-2 test by virological test (ie nucleic acid amplification test [NAAT] or antigen test), but no symptoms corresponding to COVID-19.

Mild disease: No signs and symptoms of COVID-19 (eg fever, malaise, sore throat, cough, muscle aches, headache, vomiting, nausea, loss of taste and smell and diarrhea), but no shortness of breath or changes in the chest during imaging by instrumental methods of research.

Moderate disease: Detection of signs of upper respiratory tract disease during clinical evaluation or imaging and oxygen saturation (SpO_2) $\geq 94\%$.

Severe disease: Detection of signs of lower respiratory tract disease during clinical evaluation or imaging and oxygen saturation $SpO_2 < 94\%$, the ratio of partial pressure of oxygen in the arteries to the proportion of inhaled oxygen (PaO_2 / FiO_2) < 300 mm Hg. Century, Respiratory rate > 30 breaths / min or pulmonary infiltrates $> 50\%$.

Critical disease: Septic shock and / or dysfunction of many organs and severe respiratory failure.

Taking into account the above criteria, estimating the frequency of severity of coronavirus outbreaks in 2020 and 2021, Figure 1 and Table 4 show that the severity of the disease prevailed in the current year compared to last year almost 5 times (9.5% vs. 2%) ($p < 0.001$) and almost three times lower rate of mild severity compared to 2020 (2% vs. 5.6%).

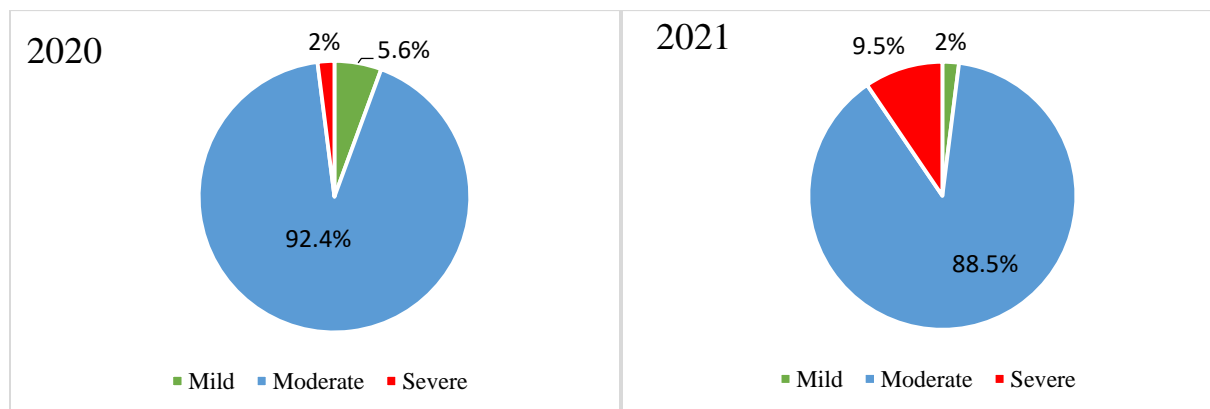


Figure 1 Frequency distribution of the severity of coronavirus infection outbreaks in 2020 and 2021

Table 4 Frequency distribution of the severity of coronavirus infection outbreaks in 2020 and 2021

Degree of severity, n (%)	2020	2021	P
Mild	19 (5.6%)	4 (2%)	p=0.060
Moderate	314 (92.4%)	168 (88.5%)	p=0.131
Severe	7 (2%)	18 (9.5%)	p<0,001

The course of the disease in most patients was not accompanied by life-threatening symptoms. In the cohort of patients of the current year, 18 (9.5%) children were treated in the intensive care unit (ICU) and among patients in 2020 - 7 (2%) (Table 5). In the distribution of severe cases by age, the predominance of complications was observed among the age groups 1-5 years and 10-18 years. During the outbreak of 2021, there was a significant increase in the number of complicated cases among older children with comorbidities. Among these conditions, the leading symptoms of severity were neurological disorders (convulsive syndrome), respiratory failure at the level of 1-2 degrees and in 2 patients at hospitalization there were manifestations of septic shock on the background of concomitant meningococemia.

Table 5 Distribution of complicated cases by age and concomitant pathology

Complications	2020	2021	P
Complicated course, total n (%)	7 (2.06%)	18 (9.5%)	p=0.0001
Thrombosis of the right internal jugular vein, n (%)	1 (0.3%)	0	p=0.102
Respiratory failure, n (%)	4 (1.2%)	16 (8.4%)	p=0.00003
Respiratory failure 1st. , n (%)	1 (0.3%)	10 (5.3%)	p=0.062
Respiratory failure 2st. , n (%)	3 (0.9%)	6 (3.2%)	p=0.246
Multisystem inflammatory syndrome (MIS-C), n (%)	1 (0.3%)	0	p=0.102
Septic shock, n (%)	1 (0.3%)	1 (0.5%)	p=0.275
Neurological complications, n (%)	0	1 (0.5%)	p=0.612

Oxygen support was performed in a total of 25 patients with signs of respiratory failure (Pearson's test p = 0.0001). Patients received oxygen through a face mask or nasal cannula. Non-invasive and invasive lung ventilation was not performed in this cohort of patients. Specific antiviral therapy for SARS-CoV-2 was not prescribed among either cohort of patients. Antibacterial therapy was performed more often in 2021 (Pearson's test p <0.001). Antithrombotic drugs were prescribed in 5 cases. Among them, 4 children received enoxaparin. In one case, the drug was prescribed for the treatment of acute thrombosis of the right jugular vein, in the other three situations enoxaparin was used for prophylactic purposes. In another case, aspirin was prescribed to a child with COVID-19 infection and symptoms corresponding to MIS-C syndrome. The frequency of administration of inhaled beta-agonists (salbutamol) and inhaled corticosteroids increased in 2021 (Pearson's test p = 0.0002) (table 6).

Table 6 Distribution of inpatient treatment characteristics by years

Parameters	2020 (n=340)	2021 (n=190)	P
Treatment in ICU, n (%)	7 (2%)	18 (9.5%)	p=0.0001
Treatment, n (%):			
Oxygen support	7 (2%)	18 (9.5%)	p=0.0001
Antibacterial therapy	153 (45%)	120 (63%)	p<0,001
Corticosteroids	3 (0.9%)	4 (2%)	p=0.237
Anticoagulants	2 (0.6%)	3 (1.5%)	p=0.258
Inhalation bronchodilators	6 (1.76%)	16 (8.4%)	p=0.0002
Bed-days, M (IQR)	6 (3-9)	6 (4-8)	
Fatalities	0	0	

4. DISCUSSION

Analyzing and comparing the structure of COVID-19 incidence in children during the outbreak seasons of 2020-2021. We observed during the second wave of incidence of coronavirus infection in Ukraine, among children undergoing inpatient treatment, an increasing number of young and preschool children. Among the possible explanations for such a redistribution of the age structure, in our opinion, may be the weakening in this period of quarantine measures (opening of preschools), due to age, relatively low level of personal hygiene in children in this category. This assumption certainly requires further study and analysis, but there are isolated reports where researchers also point to the growing role of children in the epidemiology of COVID-19 after the easing of quarantine measures. In particular, a study conducted in the United Kingdom covering 9,334,392 adults under the age of 65 found that the risk of infection in adults living with children increased significantly during the second outbreak compared to the first one. The authors note that the second outbreak in the country took place against the background of the weakening of quarantine and the opening of children's schools and preschools (Forbes et al., 2021). Other researchers are also inclined to believe that the weakening of quarantine had a significant impact on childhood morbidity of COVID-19 during the second peak (Krajcar et al., 2020; Soriano et al., 2021; Taksande et al., 2020).

In the clinical picture of the disease of patients undergoing inpatient treatment during the second wave of the rise in the incidence of COVID-19, we observed an increase in the absolute number and proportion of children with severe and complicated forms of the disease. Severe course was observed in 18 (9.5%) patients, mainly in the age groups 1-5 years and 10-18 years ($p < 0.001$), which correlates with the data of the study in China (Bo Zhou et al., 2021), where the severe course was recorded in 15 (7.46%) patients and, similarly to our work, was characterized by manifestations of respiratory failure, drop in oxygen saturation below 92% and the presence of concomitant background pathology. General symptoms (weakness 97.3%, fever 97.9%, loss of appetite 97.3%, headache 16.8%) and respiratory symptoms (cough 54.7%, runny nose 73.2%) were presented relatively more often in the clinical picture during the second wave. The data obtained by us correspond to the symptoms presented in the literature, although the frequency of some clinical symptoms in our work was slightly higher compared to the published meta-analyses. In the Mark et al., (2021) study, the most common symptoms were fever (73%), cough (38%), rhinitis (36%), respiratory distress (26%), refusal to eat (24%), vomiting, and diarrhea (14%).

Changes in the disease clinic in our study were associated with an increase in patients requiring intensive care (2% during the first peak and 9.5% during the second one) and respiratory support (2% during the first outbreak and 9.5% during the second one). It should be noted that in some studies, the authors, by contrast, register an increase in mild and asymptomatic forms of the disease among children during the second wave (Brookman et al., 2021; Krajcar et al., 2020). We consider several factors that may have influenced the changes in the clinical characteristics of the disease among hospitalized patients in the direction of increasing the severity of the disease. On the one hand, during the first wave of morbidity, parental anxiety and the lack of strict hospitalization criteria could contribute to the high frequency of hospitalization of children with mild forms of the disease.

In the future, the growing awareness of the population and the improvement of algorithms for inpatient care contributed to a more reasonable hospitalization in the presence of objective indications. In favor of this hypothesis, in particular, the results of the analysis of clinical symptoms of our cohort of patients. During the first peak of morbidity, 8.8% of children who were hospitalized did not show fever, while during the second wave the share of these children decreased to 2.1%. The same trend was with other common symptoms, such as weakness and loss of appetite. At the same time, the percentage of patients with shortness of breath increased among hospitalized children (6.3% during the second wave versus 3.8% during the first wave). This means that during the second outbreak, the children sought hospital care in the presence of more severe symptoms. The increase quantity of severe patients was also associated with an increase in patients with concomitant pathology. As is known from previous studies, chronic pathology is one of the risk factors for severe and complicated COVID-19 in children (Parsons & Van L Tran, 2021).

Observations among pediatric patients also often indicate the effect of age on the severity of COVID-19. In particular, some studies indicate that the age of patients older than 10 years is associated with severe disease. Thus, according to a cohort study conducted in the United States, which covered 20,714 pediatric cases of COVID-19, children aged 12-18 years accounted for the majority (50.3%) of severe forms of the disease (Preston et al., 2021). However, there are studies that do not support this thesis. In particular, in a European multicenter study, the authors did not find an increase in the risk of ICU hospitalization of children older than 10 years with coronavirus disease, compared with younger age groups (Götzinger et al., 2021).

In our study, we also did not observe an association of severity with older patients. In our cohort of patients, the increase in the number of severe forms occurred even against the background of a relative decrease in the proportion of adolescents. Regarding the severity of children 1 year of age, among 90% of cases the disease was characterized by upper respiratory tract and no complications and in 10% of patients the disease was accompanied by comorbidities such as anemia, congenital kidney disease,

ricketts and cerebral palsy, but also not accompanied by a complicated course. According to the literature, the most severe coronavirus infection occurs in infants and adolescents. Children with chronic severe pathologies that may worsen the course of COVID-19 are at risk. Most often, infants with SARS-CoV-2 suffer from disorders of the gastrointestinal tract, which can occur in the form of hemorrhagic form (Parsons & Van L Tran, 2021). In a study limited to the age group of children under 12 months in Wuhan, the disease was asymptomatic or mild in 9%, moderate in 87% and severe in 4% of patients. The critical condition was caused by diseases in the form of atrial septal defect, intussusception, hypogammaglobulinemia and traumatic brain injury (Liu et al., 2020). During the systematic examination of 63 infants under 3 months of age with laboratory-confirmed SARS-CoV-2 infection, 5% of patients were asymptomatic, 92% were hospitalized in moderate to severe condition, 20% were hospitalized in the intensive care unit and 3% required mechanical ventilation (Leibowitz et al., 2021).

Another component that may play a role in changes in epidemiological and clinical data is the spread of new strains, but there is currently no evidence that types such as B.1.1.7 are associated with increasing severity of coronavirus (Graham et al., 2021). Due to the daily situation report of the Robert Koch Institute, the first case of B.1.1.7 was recorded in Germany at the end of December 2020, while in Ukraine the first mention was registered in February 2021. According to recent studies, strain B.1.1.7 causes more deaths, especially in non-hospitalized patients, compared to the "classic" strain of the virus (Davies et al., 2021; Frampton et al., 2021). Analyzing the features of the clinical picture and course in children, there are not important difference. However, anosmia and agenesia, among the most specific symptoms of coronavirus disease, were less common in patients with strain B.1.1.7, while sore throat was more frequent (Maechler et al., 2020). A survey in the UK found that the most common symptoms in patients with B.1.1.7 were sore throat, cough, fatigue, myalgia and fever.

The study was conducted retrospectively, based on data from a single center and does not include data on patients who were hospitalized. Further analysis of such studies in the future will provide an opportunity to determine the trends and prospects of the epidemic process in the pediatric category of patients and to optimize the algorithms for combating the infection.

5. CONCLUSION

The proportion of children with chronic comorbidities increased in 2021 (14.7% in 2021 and 5% in 2020). In 2021 the share of children with a probable place of infection decreased by 4.3%, while the number of patients who had contact with ill within the family increased by 2.7%. Clinical symptoms included fever, general weakness, loss of appetite, and cough. In 2021, the amount of patients with general symptoms (fever, weakness, loss of appetite, headache) and local manifestations of airway disease (rhinitis, cough) increased significantly ($p < 0.05$). There was a tendency to reduce the frequency of parenchymal changes (76.2% in 2021 and 81.15% in 2020). Severe course was observed in 18 (9.5%) patients, mainly in the age groups 1-5 years and 10-18 years ($p < 0.001$), which correlates with the data of the study in China (Bo Zhou et al., 2021), where the severe course was recorded in 15 (7.46%) patients and, similarly to our work, was characterized by manifestations of respiratory failure, drop in oxygen saturation below 92% and the presence of concomitant background pathology. The increase in the quantity of patients with severe forms of the disease in 2021 was accompanied by an increase in the frequency of prescribing antibacterial drugs by 18%, antithrombotic drugs by 0.9% and inhaled bronchodilators (beta-agonists and corticosteroids) by 6.6%. The revealed clinical and epidemiological features of COVID-19 during two waves indicate the possible influence of mutations of the microorganism on them.

Acknowledgement

Authors would like to thank all participants of this study.

Author Contributions

All authors contributed to the research and/or preparation of the manuscript.

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study.

Ethical approval

The study was approved by the Biomedical Ethics Committee of Kyiv City Children's Clinical Infectious Diseases Hospital (Minutes No. 1 dated 08.03.2020). The article is recommended for publication by the Biomedical Ethics Committee of the Bogomolets National Medical University (Minutes No. 24 dated 31.08.2021).

Conflicts of interest

The authors declare that they have no conflict of interest.

Funding

This study has not received any external funding.

Data and materials availability

All data associated with this study are present in the paper.

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