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PARTICULARITIES OF RESPIRATORY MANIFESTATIONS OF COVID-19 INFECTION OF CHILDREN

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Keywords: *COVID-19, clinical signs, complications, respiratory syndrome, children.*

Introduction. *COVID-19 infection is common in the pediatric population, presenting a variety of respiratory manifestations and complications.*

Material and methods*. The study involved 64 children from the COVID-19 section, Institute of Mother and Child, with an average age of 2.04±0.4 years (variations 1 day-17 years), divided into 5 age groups: 0-1 month, 1-12 months, 1-3 years, 3-7 years, >7 years. The methodology of the study is directed to the assess the significance of clinical manifestations in the COVID-19 infection episode.*

Results. *As a result of 21 cases, this study discovered a higher frequency of the disease in infants. The nosological expression of the infection was dominated by pneumonia and unique cases of infection in four children with upper respiratory infections. Eleven children showed severe evolution, the moderate form being the dominant one. An almost constant feature in children in the study was a febrile syndrome, which in 31 cases was > 38.0°C. Every second child showed catarrhal respiratory signs, cough, and cyanosis in 66.1% of the children, chest circulation in 32.1% of the cases, wheezing in 6 children. COVID-19 infection in hospitalized children resulted in respiratory complications in 81.3% of cases and toxic infections – 23.4%.*

Conclusions. *Analyzing the age structure of children with COVID-19 infection, a higher frequency of the disease was found in infants. In hospitalized children with SARS-CoV-2 infection, the disease manifests primarily in a moderate form (70.3%). Despite the predominance of moderate forms of the disease, children are susceptible to develop the complications and severe forms of the SARS-CoV-2 infection.*

Cuvinte cheie: *COVID-19, manifestări clinice, complicații, sindrom respirator, copii*

PARTICULARITĂȚILE MANIFESTĂRILOR RESPIRATORII ALE INFECȚIEI COVID-19 LA COPII

Introducere. *Infecția COVID-19 este frecventă la populația pediatrică, prezentând o varietate de manifestări respiratorii și evoluând cu multiple complicații.*

Material și metode. *În studiu au fost implicați 64 de copii din secția COVID-19, a IMSP Institutul Mamei și Copilului, cu vârsta medie de 2,04±0,4 ani (variații de la 1 zi la 17 ani), repartizați în 5 categorii de vârstă: 0-1 lună, 1-12 luni, 1-3 ani, 3-7 ani, >7 ani. Metodologia studiului a urmărit aprecierea semnificației manifestărilor clinice la episodul de infecție COVID-19.*

Rezultate. *Studiul a constatat o frecvență mai mare a bolii la sugari – 21 copii. Expresia nosologică a infecției a fost dominată de pneumonie și, în cazuri unice (4 copii), infecții respiratorii superioare. Evoluție severă au prezentat 11 copii, forma moderată fiind dominantă. Un semn aproape constant la copiii din studiu a fost sindromul febril, care în 31 cazuri era >38.0°C Fiecare al doilea copil prezenta semne catarale respiratorii, tusea și cianoza la 66,1% dintre copii, tirajul toracic în 32,1% de cazuri și wheezing-ul la 6 copii. Infecția COVID-19 la copiii spitalizați s-a soldat cu complicații respiratorii în 81,3% dintre copii și toxiinfecțioase – 23,4% de cazuri.*

Concluzii. *Analizând structura de vârstă a copiilor cu infecție COVID-19, s-a constatat o frecvență mai mare a bolii la sugari. La copiii internați cu infecție SARS-CoV-2, boala se manifestă în primul rând într-o formă moderată (70,3%). În pofida predominanței formelor moderate ale bolii, copiii sunt susceptibili de a dezvolta complicații și forme severe de infecție cu SARS-CoV-2.*

INTRODUCTION

A sudden outbreak of a new type of pneumonia caused by coronavirus in Wuhan, China, at the end of 2019, wreaked havoc on both Chinese society and the global community. The SARS-CoV-2 infection has devastated social and economic life worldwide, thus reorienting the population's goals and priorities. Initially, specialized literature claimed that children and teens are less prone to complications and severe forms of infection. However, even if they have poor clinical manifestations, this group of people plays an important role in spreading the infection (1).

Epidemiological data from the early stages of the pandemic suggest that children present a much milder course of the disease than adults do. A mild clinical presentation or asymptomatic nature of the pediatric infection with SARS-CoV-2 might generate false data, especially when limited testing capabilities mask a tendency toward more severe cases of the disease in the population (2). However, imaging and laboratory data of post-COVID children demonstrate a different reality, even if the clinical manifestations are less pronounced. A predominance of uneven infiltrations, consolidations, and, to a lesser extent, ground-glass opacities are reported from patients' chest imaging examinations (3).

The pandemic has serious and multifaceted consequences for young children, including impaired mental health, delayed or stopped progress in schooling, complications due to delayed necessary medical care, malnutrition, poverty, and domestic violence (2).

In comparison with the other viruses, SARS-CoV-2 viral ribonucleic acid (RNA) is subject to replication errors and mutations, reducing its virulence. Therefore, children could be infected more frequently with a virus of the second or third generation, leading to milder cases. Recent evidence suggests that the cellular receptor for the angiotensin 2 converting enzyme (ACE2) and transmembrane protease-serine 2 (TMPRSS2), which are needed for SARS-CoV-2 to enter cells and be distributed in various organic tissues, may be different in children and adults. In children, ACE2 receptors may have a different structure, concentration, or ability to connect to the virus (4).

Children with COVID-19 present a variety of symptoms. The most common are fever, fatigue, headache, catarrhal respiratory signs with nasal congestion, serous rhinorrhea at onset, dry cough and then with sputum, gastrointestinal symptoms like diarrhea, and general symptoms (5, 6, 7). Although most children and young people suffer from mild or asymptomatic forms of the disease, severe cases and associated complications have recently been reported. A wide range of signs and symptoms found in children vary from fever and systemic inflammation to myocardial damage, resulting in tissue injury and shock in some patients, to the development of coronary artery dilatation/aneurysms.

Aim of the study. The objective of this study was to describe the characteristics of clinical signs of respiratory system in children hospitalized with COVID-19 infection in the Institute of Mother and Child.

Hypothesis of the study. It is suggested that children do not appear to be at higher risk of severe illness, but it needs more studies on the role of comorbidities in the severity of pediatric COVID-19 infection.

MATERIAL AND METHODS

Data collection

A retrospective descriptive study with medical charts was performed during the period March-July 2021, that included 64 children from the COVID-19 department of the Institute of Mother and Child, with a mean age of 2.04±0.4 (variations from one day to 17 years). The study methodology expected the assessment of the following information: the onset of the disease, general symptoms (febrile syndrome, fatigue, headache), catarrhal respiratory signs (nasal congestion, serous rhinorrhea at onset, cough), and complications developed during the disease within the COVID-19 infection episode.

Eligibility Criteria

All children who were confirmed SARS CoV-2 positive by molecular biology tests and/or rapid tests for the detection of SARS-CoV-2 antigen.

Data processing

All collected data were introduced into the Excel program, and the statistical data was calculated using the Epi Info program, based on different criteria.

Confirmation of the clinical diagnosis was made according to the National Clinical Protocol “Coronavirus infection of new type (COVID-19)” criteria in the new type of coronavirus infection and was based on positive molecular biology tests and/or rapid tests for the detection of SARS-CoV-2 antigen (7, 8, 9, 10).

RESULTS

The distribution of children in the study showed a high share of infants – 21 children (32.8%: 95%CI 21.6-45.7) and episodic cases in school-children – 5 children (7.8%: 95%CI 2.6-17.3). Newborns were distributed with a uniform frequency – 12 children (18.8%: 95%CI 10.1-30.5), children aged 1-3 years – 13 (20.3%: 95%CI 11.3-32.2), and preschoolers – 13 children (20.3%: 95%CI 11.3-32.2). Among the patients included in the study were children with chronic diseases such as congenital heart defects (2 patients), cystic fibrosis, neurological disorders (one patient), and allergic diseases (two patients each).

Children have a smaller variety of activities. Therefore, they are primarily infected in their family community, which is also confirmed in our study, where 34 children (53.1%: 95%CI 40.2-65.7) were confirmed after their parents had been tested and the results proved to be positive.

Amongst confirmed cases through laboratory tests, 12.9% were asymptomatic, 43.1% had mild symptoms, 40.9% had moderate symptoms, and 2.9% had severe symptoms or critical illness. The proportion of severe or critical cases was higher in children under 1 year of age (3, 6, 7, 10, 11). In children included in the study, the course of SARS-CoV-2 infection is acute and evolves with moderate severity manifestations in 58±0.7% of cases. The study looked at hospitalized children who had a progressive illness that increased to a severe illness and required specialized treatment. For them, clinical symptoms developed with marked fever, general symptoms with toxi-infectious syndrome that were recorded most frequently in newborns (58.3%: 95%CI 27.7-84.8) and infants (52.4%: 95%CI 29.8- 74.3) (fig. 1).

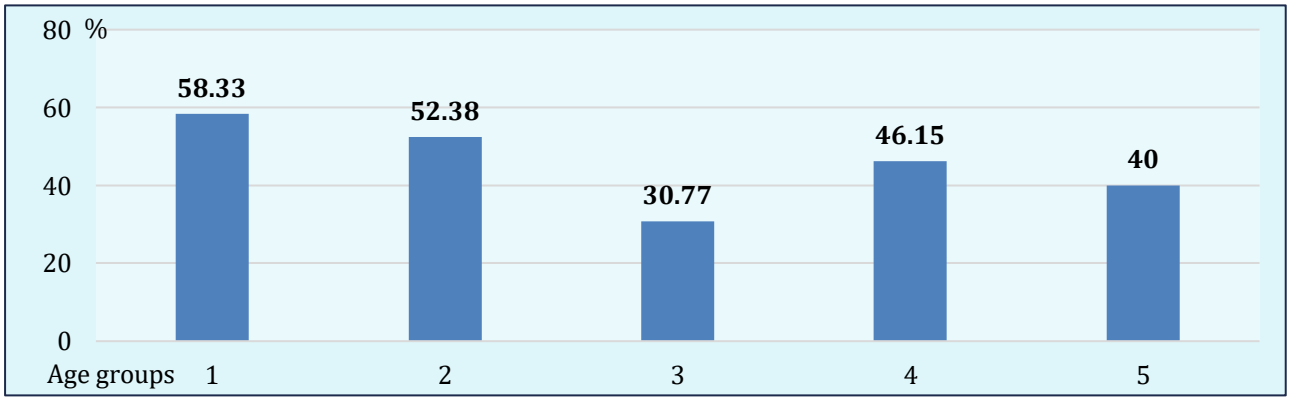

Figure 1. Severe onset of COVID-19 infection depending on the child's age.

Febrile syndrome was recorded in 48.4%: 95%CI 35.8-61.3, χ^2=3.18, p>0.5, but subfebrility in 51.6%: 95%CI 38.7-64.3 cases of children with COVID-19 infection. Febrile syndrome is recorded as the only symptom in more than 30% of patients (3, 7), and it is more common in hospitalized children (71.8%) than in those who received treatment at home (27.4%).

In our study, respiratory manifestations in children with SARS-CoV-2 infection were dominant (fig. 2). Catarrhal respiratory signs were seen in 50%: 95%CI 37.2-62.8 cases, χ^2=3.5, p>0.4. Cough was the most common symptom (63.5%: 95%CI 52.2-78.2) and was reported predominantly in preschool children, χ^2=5.5, p>0.05. Cough syndrome was the most frequent symptom in infants, ante-preschoolers, and preschoolers, but very rare in children up to one month of age.

Hospitalized children with COVID-19 infection presented moderate perioral and periorbital cyanosis (67.9%: 95%CI 83.1-99.4, χ^2=5.1, p>0.74). Generalized cyanosis with marbled skin has characterized severe cases of the disease (3.6%: 95%CI 0.61-16.9). Most cases of cyanosis were found in newborns with SARS-CoV-2 infection. Moderate cyanosis predominates in all age groups, but generalized cyanosis is more common in preschool children with COVID-19 infection.

Signs of respiratory distress were predictable given the severity of respiratory failure. Dyspnea was perceived in 14.1%: 95%CI 6.4-26.2 cases, and chest circulation in every third child, 32.8%: 95%CI 20.3-45.9. The severe form of the disease has been noted most frequently in younger children, from birth to 7 years old.

The most common clinical symptom by stetoacustic evaluation is coarse breathing (97%: 95%CI 87.7-99.6). Pathological respiratory sounds are not characteristic respiratory manifestations in the COVID-19 infection. The wheezing dry rales are heard in every fourth child from the study, crackling rales in 14%: 95%CI 6.4-26.2 cases; less often, moist rales that have been found in 5.4%: 95%CI 1.12-14.9 cases. A total of 4% of the children with SARS-CoV-2 infection had oxygen saturation values (measured by pulsoxymetry) of 95.6±0.3% with a minimum of 90% and a maximum of 98%. Among them, 11 children (22%: 95%CI 11.5-36 cases) needed respiratory support from the mask and nasal cannulas. Compared to the age of the children, the lowest SpO_2 was appreciated in antepreschool children (94.8±0.5%), the others having SpO_2 higher than 95%, F stat = 2.9, p<0.04.

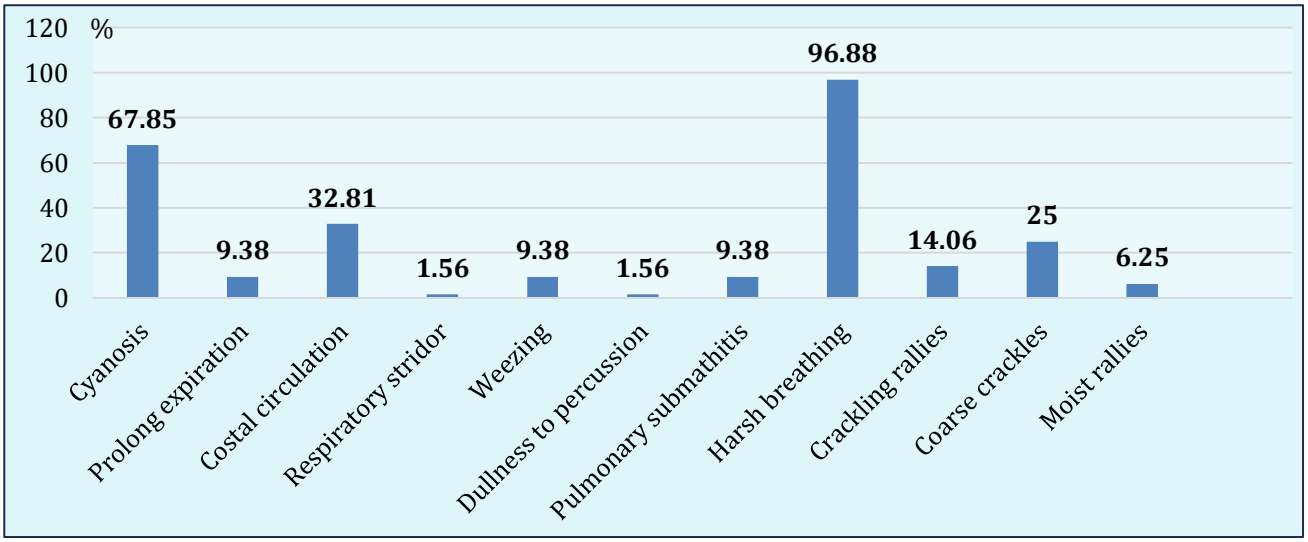

Figure 2. Frequency of clinical respiratory manifestation in children with COVID-19 infection.

The most common clinical symptom by stetoacustic evaluation is coarse breathing (97%: 95%CI 87.7-99.6). Pathological respiratory sounds are not characteristic respiratory manifestations in the COVID-19 infection. The wheezing dry rales are heard in every fourth child from the study, crackling rales in 14%: 95%CI 6.4-26.2 cases; less often, moist rales that have been found in 5.4%: 95%CI 1.12-14.9 cases. A total of 4% of the children with SARS-CoV-2 infection had oxygen saturation values (measured by pulsoxymetry) of 95.6±0.3% with a minimum of 90% and a maximum of 98%. Among them, 11 children (22%: 95%CI 11.5-36 cases) needed respiratory support from the mask and nasal cannulas. Compared to the age of the children, the lowest SpO_2 was appreciated in antepreschool children (94.8±0.5%), the others having SpO_2 higher than 95%, F stat = 2.9, p<0.04.

Severe forms of COVID-19 infection in children have been reported less frequently. Complications such as MIS-C (Multisystem Inflammatory Syndrome in Children), Kawasaki-like disease, septic shock, metabolic acidosis, irreversible clotting dysfunction, and diabetes have been reported in those with a severe course of SARS-CoV-2 infection. Presence of respiratory complications has been demonstrated in 52 children (81.3%: 95%CI 69.5-89.9), but toxi-infectious ones – in 15 children (23.4%: 95%CI 13.8-35.7). Despite the fact that moderate forms of the disease prevail, children are susceptible to developing complications and severe forms of the SARS-CoV-2 infection.

SARS-CoV-2 virus infection remains associated with other respiratory virus infections that are dangerous to children's lives and health. A false positive dynamic can delay the establishment of the correct treatment with the risk of developing a series of complications from the respiratory system as well as other systems. Thus, in the context of the current pandemic with the SARS-CoV-2 virus, even the trivial catarrhal signs with which we are accustomed in the case of respiratory disorders should be thoroughly analyzed, and finally, yet importantly, testing of children should be performed.

DISCUSSIONS

The impact of COVID-19 on the pediatric population is incompletely understood (1). Children infected with SARS-CoV-2 (3, 9-11) are less likely to develop symptomatic or serious diseases. Among symptomatic children, the most common clinical features were fever and respiratory symptoms, followed by gastrointestinal manifestations.

In our study, we described the characteristics of the evolution of COVID-19 infection in children, with an evaluation of the evolutionary peculiarities in different age groups. Analyzing the age structure shows that infants were the most likely to get sick. Although some instances were asymptomatic, the majority had mild to severe symptoms, which needed specialized care. Respiratory syndrome manifested itself mainly with both subjective and objective signs along with the change in the auscultatory picture.

The rate of premature delivery has increased, and SARS-CoV-2 infection is proportionately higher in premature neonates, which appears to be related to premature delivery (3, 10, 11). In our study, children up to one month of age developed more severe forms with complications. Disease might affect newborns who acquired the infection from their mothers, suggesting a possible perinatal-peripartum transmission. Our analysis showed that pediatric patients acquired infections mainly through close contact with their parents or other family members.

Among the patients included in the study were children with comorbidities such as cystic fibrosis (1 patient), carious malformations (2 patients), neurological disorders (1 patient), coagulation abnormalities (3 patients), allergic conditions (2 patients), prematurity (2 patients), and a case of death on the background of COVID-19 due to comorbidities (multiple birth defects).

Other findings (7, 8, 10, 11) included respiratory failure (40%), fever (10%), feeding intolerance (30%), melena (10%), and renal failure (5%). All infants had elevated inflammatory biomarkers and received steroids and IVIG. Two infants died. We speculate that maternal SARS-CoV-2 and transplacental antibodies cause multisystem inflammatory syndrome in neonates (MIS-N). Further studies are needed to confirm whether immunomodulation may be beneficial in some cases.

CONCLUSIONS

1. Analyzing the age structure of children with COVID-19 infection, a higher frequency of the disease was found in infants. An almost constant sign in the children in the study was febrile syndrome, which in 48.4% of cases was >38.0°C. Catarrhal respiratory signs and fever were constant signs. Cough, dyspnea, and cyanosis remain the main clinical signs, the last predominantly in newborns. Every second child presents catarrhal respiratory signs (50%), cough and cyanosis in 66.1% of children, chest circulation in 32.1% cases of COVID-19 infection.
2. In hospitalized children with SARS-CoV-2 infection, the disease manifests primarily in a moderate form (70.3%). Despite the predominance of moderate forms of the disease, children are susceptible to developing complications and severe forms of the SARS-CoV-2 infection.

CONFLICT OF INTERESTS

Authors declare no conflict of interests.

ETHICAL APPROVAL

No the opinion from the ethics committee.

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