



## THE ROLE OF COVID-19 IN THE ACUTE RESPIRATORY PATHOLOGY FORMATION IN CHILDREN

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### ABSTRACT

The study of the etiology of acute respiratory infections in 4022 hospitalized children aged 1 month to 14 years revealed the involvement of coronavirus in 12.4% of cases (500 children) more often in combination with other pathogens. In the case of coronavirus infection, moderate forms of the infectious process prevail mainly in the form of rhino-pharyngo-tracheitis against the background of subfebrile and febrile temperatures with moderate symptoms of intoxication. Majority of the children had dyspeptic symptoms. Every third child may have a lower respiratory tract lesion (bronchitis, pneumonia).

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### Introduction

In March 2003, World health organization (WHO) declared a global epidemic called atypical pneumonia or Severe Acute Respiratory Syndrome (SARS). The disease, first reported in November 2002 in southern China. It spreaded in 30 countries including Asia, Europe, North and South America, Africa, and Australia within a few months. The cause of this epidemic which resulted in about 8.5 thousand cases with more than 800 deaths was the coronavirus (CoV), later called the SARS coronavirus (SARS-CoV). Coronaviruse belongs to the same genus of the family *Coronaviridae* and widely distributed in nature [1-4]. This infectious agent, first discovered in the 1930<sup>th</sup>, until recently were better known as pathogens of severe and often fatal disease among farm animals and poultry. The study of clinical and laboratory features of human coronavirus infection (COVID) started in 1965. It attracted exclusive scientific interest but its diagnosis was not included in the routine laboratory studies range in clinical practice [5].

In this regard, the features of the clinical course of respiratory COVID are insufficiently studied. Few data were obtained in experiments on volunteers infected with COVID [6, 7]. Isolated studies were devoted to the study of COVID in children [8, 9].

Until 2020, few studies on the role of COVID in acute respiratory pathology associate with the "common cold", which occurs quite easily – in the form of a short-term profuse runny nose [10, 11]. Only isolated reports indicate the possibility of involving not only the upper but also the lower respiratory tract, which is observed in young children, especially newborns [12].

The small number of studies on COVID is due to the lack of commercial coronavirus diagnostics, as well as the great complexity of isolation and cultivation of this infection [13, 14]. To diagnose coronavirus infection and to analyze the peculiarities of clinical symptoms of diseases caused by this virus has become possible only with the inclusion of a range of

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new diagnostics group specifier of the drug prepared in the Scientific and Research Institute RAMN (SRI RAMN) based on the COVID 229-E, which allows determining the whole group of pathogens coronavirus infection [15].

Currently, coronavirus infection has become the number one target for scientific and medical research in the world. Most authors are inclined to develop effective antiviral agents. In general, many interesting areas have been covered in recent years. Some scientists suggest using active phytopreparations in food to prevent coronavirus [16, 17]. There are works on the study of the venom activity of migalomorphic spiders [18], which concluded that the polypeptide combinations of the studied poisons have strong antiviral activity. The effect of other biologically active substances on antiviral activity has also been studied [19-22]. Formation of a significant immune response to various viral particles is also the normalization of the essential nutrients intake. The most important of which is the essential trace element zinc. The most noteworthy is the highly biologically active colloidal hellate forms presented in the diverse works [23-28]. The development of digitalization of medical wards [29-31] such as operations computer simulation and the use of an electronic pharmacist in postoperative therapy are worth noting [32].

However, in addition to fighting against the coronavirus, it is also necessary to study the impact of infection on the formation of pathologies in patients, including respiratory function – the most confirmed COVID system of the body. At the same time, it is very difficult to restore the respiratory system in children and the elderly.

**This work aimed** to study the role of COVID-19 in the formation of acute respiratory pathology in children.

## Materials and Methods

Experimental studies were conducted at the SRI RAMN in Saint Petersburg, Russia.

The specific weight and clinical manifestations of COVID were studied in 500 out of 4022 children aged 1 month to 14 years with acute respiratory infections who were hospitalized in the basic departments of the influenza clinic and acute respiratory disease (ARI) in children of the SRI RAMN. The etiology of diseases was determined by micro methods: Complement Binding Reaction (CBR), Hemagglutination Inhibition Reaction (HIR), and Indirect Hemagglutination Reaction (IHR), using paired blood sera and nasal secretions of patients [13, 14].

The COVID antigen for CBR was prepared from a strain of coronavirus adapted to the diploid cells of a human embryo lung. The antigen titer was 1:64-:128. Also, 16-32 complement-binding antigen units were used. HIR was performed with the COVID OS-43 (HCoV-OC43) strain and IHR was performed with the first developed erythrocyte diagnostic from the COVID 229E (HCoV-229E) strain.

The obtained data were compared with the results of a survey of adult patients, also hospitalized in the basic unit of research institute of influenza of the RAMS. The prevalence of coronavirus among different age groups of St. Petersburg was determined using extensive incidence rates per 1000 persons by the method of Y. G. Ivannikov [15].

## Results and Discussion

The inclusion of COVID diagnostic in the kit for determining the etiology of acute respiratory infections in hospitalized children allowed us to determine that COVID is not such a rare finding in the etiological spectrum of pathogens of these diseases in children. On average, it was observed in 12.4% of cases among the surveyed, more often diagnosed in children aged 0-2 years than in the older age group (Table 1).

These data were confirmed by an analysis of extensive morbidity indicators, which revealed that children are 5-7 times more likely to carry COVID than adults, and the prevalence rate decreased with the increasing age of the observed population. So, if every 5th preschool child is infected with COVID during the year, then among schoolchildren COVID was diagnosed only in every 8th child and only in 112 out of 1000 adults.

**Table 1. The specific weight of coronaviruses in the etiology of acute respiratory infections in children of different ages.**

Age	Surveyed children	Positive COVID test					
		Total		Including:			
				Mono		Mixed	
		a.u.	%	a.u.	%	a.u.	%
0-11 months	1113	146	13.1*	42	3.8	104	9.3
1-2 years	1215	157	12.9	28	2.3	129	10.6
3-6 years	964	120	12.4	20	2.1	100	10.3
> 7 years	730	77	10.5	8	1.1	69	9.6

\* the differences are significant compared to the older age group.

**Table 2. The frequency of respiratory lesions at COVID in children (RSV – Respiratory syncytial virus, PI – Parainfluenza, MP – Mycoplasma pneumonia).**

Etiology of infection	Surveyed children	Including bronchopulmonary lesions			
		bronchitis		pneumonia	
		a.u.	%	a.u.	%
COVID (mono)	98	33	33.7	16	16.3
COVID + influenza	183	37	20.2*	27	14.8
COVID + adeno infection	86	25	29.1**	14	16.2
COVID + RSV	74	36	48.6*	10	13.5
COVID + PI	27	12	44.4	8	29.6
COVID + MP	32	15	46.8	7	21.8

\* differences are significant compared to mono-infection.

\*\* differences are significant compared to the second infection

COVID-19 specific weight practically do not depend on the level of respiratory tract damage, somewhat prevailing in individuals with pneumonia. COVID-19 was observed mainly in the form of mixed infections. The ratio of mono and mixed infections was 1:4, of the latter, associations with influenza or adenovirus infection prevailed, and in bronchitis – with influenza and RSV infection.

Children of the first two years of life dominated among the 500 patients with COVID-19 (61% of cases). Approximately one in three children admitted to the hospital and among children in their first year of life and more often, there was a lesion of the bronchi or lungs (Table 2).

The incidence of bronchitis was highest in cases of simultaneous corona involvement with RSV, parainfluenza viruses (PI), and Mycoplasma pneumonia (MP), but rarer in corona-influenza associations. The frequency of involvement in the infectious process of the lungs was also maximal in acute respiratory infections caused by a combination of coronavirus with parainfluenza and Mycoplasma pneumonia.

According to statistical data, COVID-19 was registered from January 2020 with fluctuations in individual months from 1.8 to 28.6%, but the highest rises in the COVID-19 were observed in February, May, and August. During the same period, there was an increase in the level of immunological response in patients (the average geometric multiplicity of increase in serum antibodies increased to 6.5 versus 4.0 in relatively quiet months). Obtained results correlate with the data of many authors reporting the seasonal distribution COVID-19 (with predominance in March-May), the periodicity of the growth of this infection without clear patterns in time [33].

Diseases mainly occurred in a moderate form and began with both catarrhal symptoms in the nasopharynx and dyspeptic manifestations against the background of normal or subfebrile temperature, followed by its increase by 3-4 days in some cases to the maximum numbers (39.0 C). Symptoms of intoxication (malaise, anxiety, decreased appetite, nausea) were moderate. As well as an increase in body temperature which persisted for 4-5 days. Only in isolated cases (6 children under 1 year of age), the disease occurred with severe intoxication (severe anxiety, repeated vomiting), the presence of which was not always accompanied by high fever. Most children at the beginning of the disease often had intestinal syndrome in various manifestations, in young children – frequent regurgitation or vomiting, more often repeated, and short — term enteric liquid stools for 2-5 days, and in older age-nausea, vomiting and 1-2-fold liquefied stools. However, attempts to detect other viral or pathogenic intestinal flora by bacteriological or serological methods of examination of children were unsuccessful.

Catarrhal manifestations in the nasopharynx occurred in almost all children, absent in mono-COVID-19 only in 8.1% of cases. Basically, as with the flu, it was mucosal-serous discharge from the nose and dry unobtrusive painless, and sometimes painful cough, which becomes more humid in a few days. Approximately one in every 5-6 children had otitis media. In contrast to the flu, these symptoms persisted for a longer time:  $7.2 + 0.61$  days – with an uncomplicated course of COVID-19,  $11.6 + 0.64$  days – with bronchitis.

Every third child with bronchitis noted obstructive syndrome with a predominance of spastic or mixed forms of obstruction which persisted in children with flu for 4-6 days.

Clinical manifestations of mixed infection had features of both combined infections with the more aggressive one dominating. A reliable clinical sign of participation in the infectious process of COVID-19 was the detection of any dyspeptic manifestations described in mono-infection in a child with respiratory symptoms.

No specific patterns were found in the dynamics of laboratory parameters (hematological and biochemical). They corresponded to the severity of the disease and depended on the nosological diagnosis.

In cases with pneumonia in coronavirus (mono - or mixed), the disease was usually acute against the background of a higher (from the first days of the disease) temperature, accompanied by adynamia, pallor, and the appearance of symptoms of respiratory insufficiency. Infiltration was mainly segmental (1-2 segments more often than the upper lobe of the right lung). A more severe course of the disease was observed in cases of participation in the etiology of adenovirus and Mycoplasma infections

COVID-19 occurs in individuals with no or low titers of specific antibodies in both the blood and nasal secretions and is highly contagious. Thus, when analyzing 592 cases of nosocomial infections, it was found that in the etiological spectrum of these diseases, coronavirus dominated along with adenovirus being detected in about 20% of cases, mainly among children aged 6-11 months.

## Conclusion

Thus, the results indicate a certain significance in the etiological spectrum of infectious respiratory diseases in children caused by coronavirus infection, which became so significant in 2020 because of COVID-19. WHO declared a World pandemic and the virus covered most countries and all regions of Russia [33, 34].

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