

Annals of Clinical and Medical Case Reports

Clinical Paper

ISSN 2639-8109 | Volume 9

Clinical and Evolutionary Features of SARS CoV-2 Infection (COVID-19) in Children

Jugulete G^{1,2*}, Safta M¹, Gheorghe E¹, Borcoş B¹ and Merişescu M^{1,2}

¹National Institute for Infectious Diseases-Prof. Dr. Matei Bals, Bucharest, Romania

²Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

*Corresponding author:

Jugulete Gheorghita,
National Institute for Infectious Diseases-Prof.
Dr. Matei Bals, Carol Davila University of Medicine
and Pharmacy, Bucharest, Romania
E-mail: georgejugulete@yahoo.com

Received: 02 Jun 2022

Accepted: 14 Jun 2022

Published: 20 Jun 2022

J Short Name: ACMCR

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Citation:

Jugulete G, Clinical and Evolutionary Features of SARS CoV-2 Infection (COVID-19) in Children. Ann Clin Med Case Rep. 2022; V9(8): 1-6

Keywords:

COVID-19; Mortality; Comorbidities

1. Abstract

Starting with December 2019 the medical world has faced a new challenge as a consequence of a new type of coronavirus-2019-nCoV, similar to several familiar strains that determine a comparable symptomatology (SARS- severe acute respiratory syndrome, MERS- Middle East severe acute respiratory syndrome), subsequently named SARS CoV-2, while the disease it causes- COVID-19. The virus is of animal origin and through an intermediate host (probably also a mammal) it suffered genetic changes thus acquiring human cells receptors. In consequence, SARS CoV-2 virus affects both children and even more frequently where it determines more severe clinical forms of disease. In children, COVID-19 has various clinical forms, from asymptomatic ones to severe ones, complicated by multisystem inflammatory syndrome (MIS-C Multisystem Inflammatory Syndrome – Child or PIMS - TS (Paediatric Multisystem Inflammatory Syndrome temporally associated with COVID-19) that sometimes can lead to death [5].

In the present article we aim to analyse the paediatric cases of SARS CoV-2 admitted on the Infectious Diseases Clinical Ward IX, in National Institute for Infectious Diseases „Prof. Dr. Matei Bals” during March 2020-February 2021. In the respective period of time 225 children were admitted for SARS CoV-2 infection with various clinical forms of disease. We monitored the following parameters: age, sex, clinical onset picture, clinical form of disease, comorbidities and evolution under treatment. Of all hospitalized cases, 10,2% presented comorbidities, the most affected age group was 1-5 years and the percentage of male patients was sensitively higher- 53,3%. The clinical onset picture of COVID-19 in children

was polymorphous with the predominance of systemic symptomatology (fever, chills, altered general state, lack of appetite, fatigue) as well the presence of a clinical picture characteristic for upper respiratory tract infections (nasal obstruction, rhinorrhoea, cough, odynophagia, dysphagia, dysphonia) sometimes accompanied by difficulty in breathing and digestive manifestations (nausea, vomiting, diarrhoea). The onset of disease differed based on the children's ages. Thus, in small children the onset consisted mainly in digestive manifestations while in older children and adolescents respiratory signs occurred. In what concerns the clinical forms of disease, most cases presented medium forms (55,1%). Severe cases were less common (4,8%) and there was only one PIMS (with favourable evolution under treatment). All paediatric cases admitted in our clinic evolved favourably and no death was recorded.

2. Introduction

Common human coronaviruses (4 serotypes: 229E, NL63, OC43 and HKU1) cause in immunocompetent individual's light or moderate infections of the upper respiratory tract, clinically manifested by fever, altered general state, rhinorrhoea, odynophagia, cough, headache). In immunocompromised persons and in those of extreme ages coronaviruses can determine lower respiratory tract infections such as pneumonia or bronchitis. Most people get infected with one or several of these viruses at some point in their lives thus the adult population presents serotype protective neutralizing antibodies. Transmission of the infection is predominantly airborne but also through direct contact with contaminated objects or surfaces. While coronaviruses have suffered genetic mutations as a consequence of successive passage from one host to another (mammal, human) this resulted in new coronaviruses with dif-

ferent pathogenesis and increased virulence in humans that cause more and more severe forms of diseases. Hence in 2012, SARS CoV2 that causes severe acute respiratory syndrome (SARS) led, in approximately one year, to 8427 cases and 813 deaths (9,65 mortality rate). The first cases were discovered in Hong-Kong and subsequently the infection spread throughout 37 other countries. SARS may have several clinical forms- early stage of diseases (two or more symptoms: fever, chills, myalgia, headache, diarrhoea, odynophagia, dysphagia or rhinorrhoea), light or moderate respiratory disease (Fever $> 38^{\circ} \text{C}$ and one or more clinical signs of respiratory infections: cough, difficulty breathing) and severe respiratory disease (it meets the clinical criteria of light/moderate infections and one of the following: X-ray evincing pneumonia or acute respiratory distress syndrome or autopsy findings in accordance with pneumonia or acute respiratory distress syndrome without an identifiable cause of severe acute respiratory syndrome).

Middle East Respiratory Syndrome (MERS) is a disease caused by another coronavirus (MERS CoV) identified in 2012 in Jordan. Most patients developed severe respiratory diseases with fever, cough and difficulty in breathing. Some infected patients presented mild symptoms or had no symptoms at all. The evolution was severe with Multiple Organ System Failure and an increased mortality rate (30%). In December 2019 the first cases with the new coronavirus infection were reported in China (Wuhan region in Hubei province). The number of infected patients increased rapidly thus setting off an epidemic that subsequently morphed into a pandemic.

The epidemic extended rapidly in all China than in other countries in Asia (Japan, The Republic of Korea, Singapore, Vietnam, Nepal, Malaysia, Taiwan, Thailand), Australia, Europe and North America (United States of America and Canada). The new coronavirus-2019-nCoV (later known as SARS- CoV-2) is a new coronavirus strain unidentified before in humans that causes the affection named COVID-19. Genetic studies have demonstrated that SARS-CoV-2 is of animal origin (viral zoonosis- snakes, bats) and through an intermediate host it acquires human cells receptors. The pandemic evolved in successive waves (6 so far) without a specific season but with a predominant specific strain for each of them (strains β , γ , μ , δ , omicron). In Romania, the first cases of infection with the new coronavirus were registered in March 2020. COVID-19 has various clinical forms, from asymptomatic to severe ones, some with evolution to multiple organ failure and death. Severe clinical forms are frequently met in patients with comorbidities (cardio-vascular diseases, diabetes, renal impairment, obesity, tumours). In children with SARS-CoV-2, the infection is usually asymptomatic or mild but more severe clinical cases have been observed especially in patients with associated risk factors (obesity, type 1 or 2 diabetes, cardiovascular diseases, chronic pulmonary diseases, including asthma, chronic renal diseases, including dialysis, chronic liver diseases, immunosuppression, human

deficiencies, HIV/AIDS, prolonged usage of immunosuppressors) [1].

One life-threatening complication is Multisystem Inflammatory Syndrome associated to COVID-19 (MIS-C or PIMS-TS) that can occur in SARS-CoV-2 infection in children and adolescents, especially at the recovery time. The diagnosis is established based on the assessment of the presence of the inflammatory syndrome (certified by laboratory investigations) associated with multiple organ failure (renal, cardiac, haematological, respiratory, gastrointestinal, dermatological, neurological). These cases featured in Literature during the first pandemic waves when severe forms of diseases in children were also registered, with an incidence rate of approximately 1 to 5000 cases of COVID-19 [5,6]. The first cases were documented in USA and Italy, both in previously healthy children as well as in those with comorbidities.

3. Material and Methods

We aim to analyse COVID-19 cases in children and to highlight the clinical particularities of SARS-Cov-2 in this population group. In this context, the authors have undertaken a clinical retrospective study on COVID-19 paediatric cases admitted in the National Institute for Infectious Diseases „Prof. Dr. Matei Bals”, Bucharest in April 2020-March 2022. The following parameters were monitored: age, sex, clinical onset picture, evolution, complications and comorbidities. We also surveyed the occurrence of Multiple Organ System Failure as well as the rate of death caused by COVID-19 in children.

4. Results and Conclusions

During the study period a number of 243 paediatric COVID-19 infections were recorded out of an overall of 1655 hospitalized patients (14,68%). All cases of SARS CoV2 in children evolved favourably, without deaths but two cases, however, presented Multiple Organ System Failure with favourable evolution under treatment. Graphic no.1 evinces the distribution in waves of admissions, with a peak registered in January-March 2022. The gradual increase in the number of cases was the consequence of a highly contagious strain selection.

The analysis of SARS CoV-2 associated deaths showed that on our ward the rate of mortality was zero in children while in adult patients it reached 1,75% (29/1.655) out of the overall admitted cases and 2,05% (29/1.412) reported to the number of adult patients. The data obtained in our study correlates with data reported by literature [9].

In what concerns the onset clinical picture of SARS CoV-2 in children it has been observed to be polymorphous and particularised based on the child's age. Thus in small children (under the age of 1) digestive symptomatology predominated (lack of appetite, vomiting, diarrhoea, acute dehydration syndrome) accompanied by fever. In pre-school children symptomatology is polymorphous with the occurrence of upper respiratory tract infections. In school-

aged children and adolescents the clinical picture of upper respiratory tract infections (fever, rhinorrhea,odynophagia, dysphagia, cough). Rarely have we encountered systemic type manifestations in children (sweats, exanthema, arthralgias, headaches) such as agenesia and anosmia that are specific to the adult patient (chart no. 1, 2).

Assessing the admitted cases and correlating them with the onset of the clinical picture we reached the conclusion that most children presented respiratory symptomatology (62%) and a low percentage of associated clinical manifestations (digestive and respiratory - 14%). This is explained by the small number of hospitalized children below the age of one who mainly presented a digestive clinical picture (Chart no. 3). The data obtained from our study correlate to the data reported by other authors in literature [2, 4, 8]. In what concerns distribution by sex of COVID-19 cases in children, as (Chart no. 4) evinces there is no statistically significant difference between the number of male or female paediatric cases. There are studies in adult patients that highlight a predominant affection in males, especially severe and critical forms with increased mortality compared to females [3, 7].

From the analysis of the cases studied, it was observed that SARS CoV-2 infection in children predominated in the age groups 1-5 years and 6-14 years. This can be explained by the fact that the 0-1 age group is more protected by the family and their contacts more diminished compared to the other age groups. We also recorded fewer cases in adolescents, which can be explained by the introduction of vaccination in this age group (chart no. 5). A percentage of 9.87% (24/243) of the cases presented various comorbidities at the time of hospitalization (obesity, chronic haematological, metabolic, neurological, autoimmune, neurological and oncological diseases). (Chart 6) shows that, among the associated comorbidities COVID-19 in children, the best represented were obesity (62.5%), haematological diseases (25%) and oncological affections (20.8%). In the group of children analysed, comorbidities were in a much lower percentage than in hospitalized adult patients, which explains the low number of severe and critical clinical forms in paediatric patients [7, 8].

From the standpoint of clinical forms of COVID-19 it was found that most cases in children were mild and moderate while in adult's severe forms predominated due to multiple comorbidities encountered in this population group. Compared to adults, in children the severity of the disease is not correlated with the age but it is associated with the presence of comorbidities. (Chart no. 7) displays a comparison between the clinical forms of SARS CoV-2 infection in children and in adults, the data being similar with the one in literature [4, 8]. We must mention that we haven't registered critical forms of COVID-19 in children but in two situations it was complicated by PIMS.

The number of SARS CoV-2 infections is higher in adults with more severe clinical forms due to comorbidities that are more frequent in these patients. Along with the emergence of COVID-19 vaccines, the number of cases decreased, more viral and contagious strains appeared but with mild clinical manifestations, so that during the last pandemic wave we registered less severe forms of diseases but we had to face more paediatric cases, especially in children under the age of 5 (decreased rate of vaccination in this age group).

Graph 8 shows the main complications associated with SARS CoV-2 infection in children. It is observed that the best represented are the digestive ones (acute diarrheal disease - 41.9%, acute dehydration syndrome - 75.5%, stomatitis - 17.2% and hepatic cytolysis syndrome - 27.9%) as well as the haematological (anaemia - 26.3%, lymphopenia - 34.5%, neutropenia - 22.2% and thrombocytopenia - 34.5%). We also recorded a significant percentage of cases with acute interstitial pneumonia (37.3%) and ENT involvement - 60.9% (pharyngitis, laryngitis, otitis, anosmia). Cardiac impairment (myocarditis, pericarditis, heart rhythm disorders) was present in 2.4% of cases and only 2 children presented with PIMS, with a favourable evolution under the established treatment. The data obtained in our study are similar to those obtained by other authors and reported literature [1, 3]. It is also reported that in paediatric patients- digestive, haematological and ENT complications predominate compared to adults where respiratory, cardiac and metabolic complications are mainly present [7].

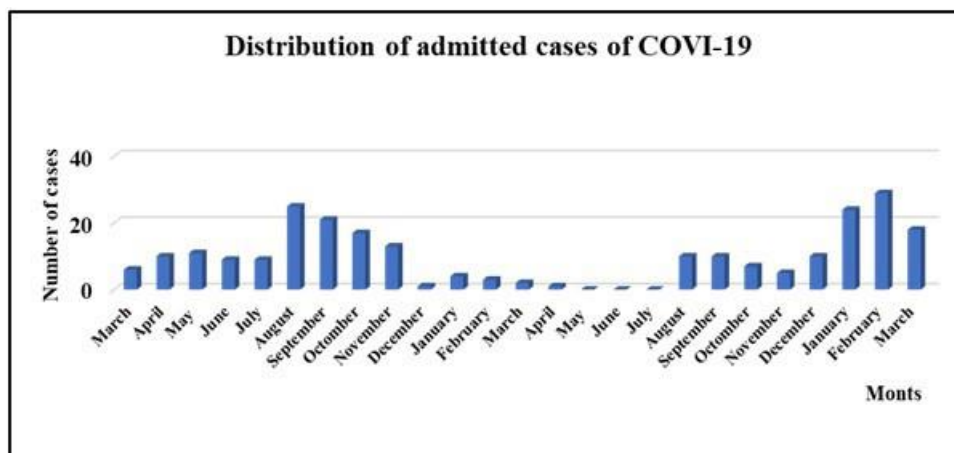


Chart no.1: Distribution of admitted cases of COVID-19

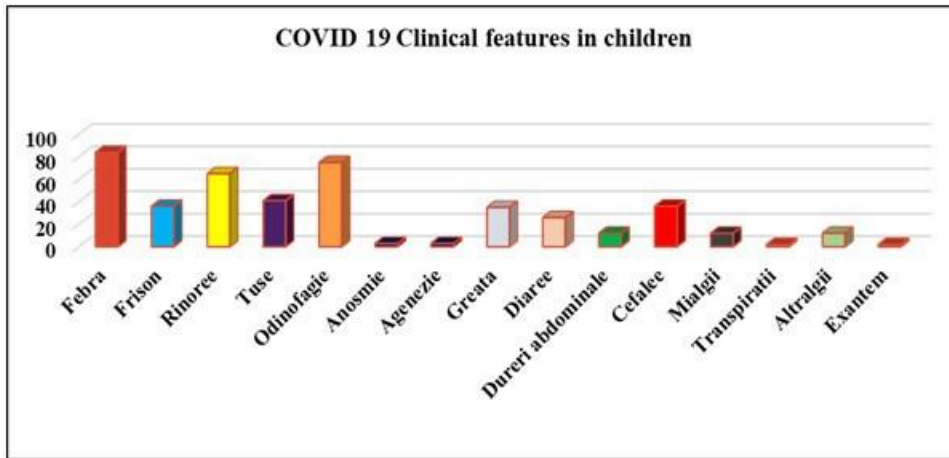


Chart no.2: COVID-19 Clinical features in children

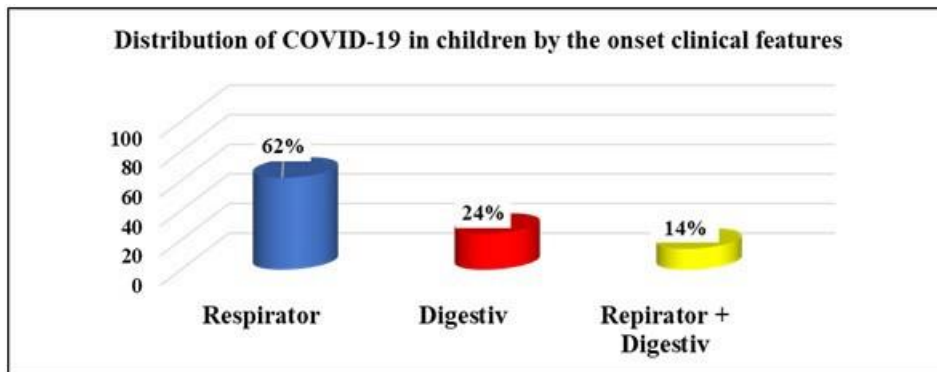


Chart no.3: Distribution of COVID-19 in children by the onset clinical features

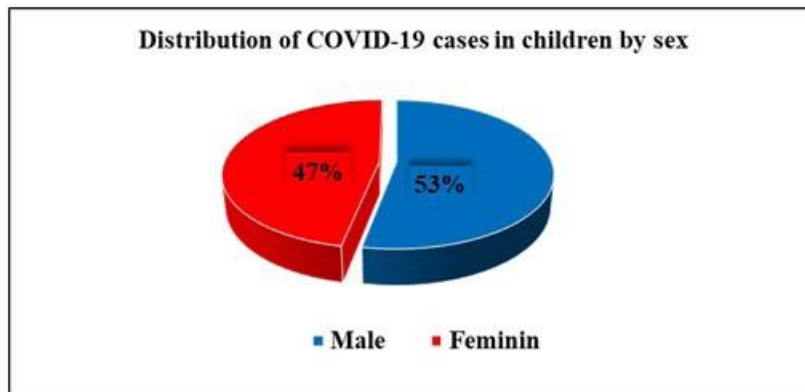


Chart no.4: Distribution of COVID-19 in children by sex

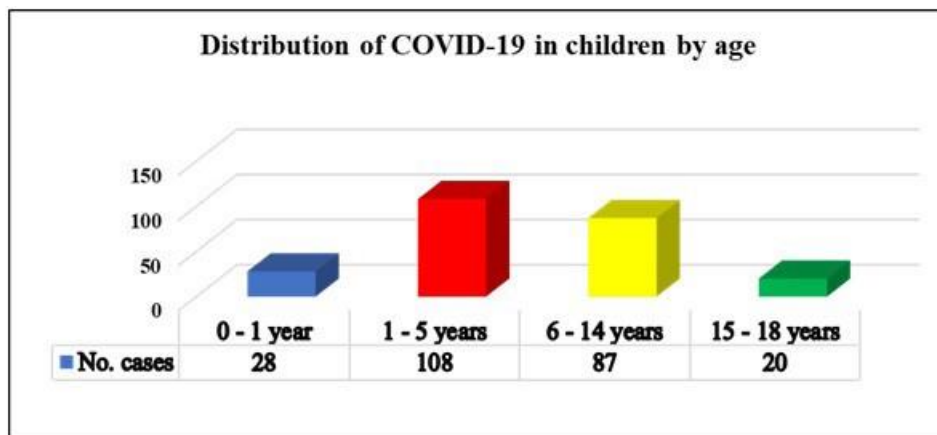


Chart no.5: Distribution of COVID-19 cases in children by age

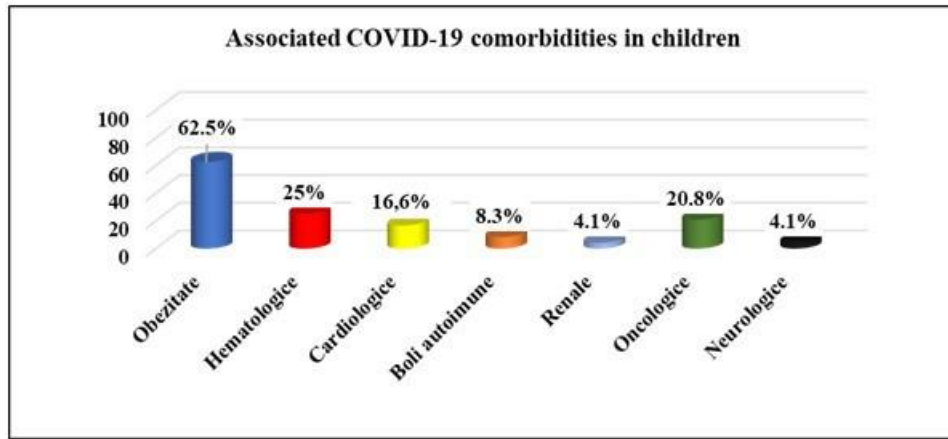


Chart no.6: Associated COVID-19 comorbidities in children

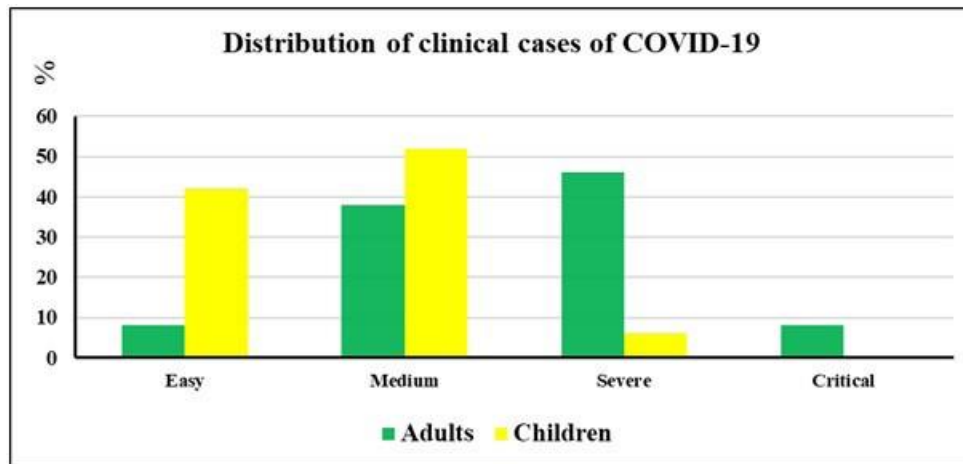


Chart no.7: Distribution of clinical cases of COVID-19

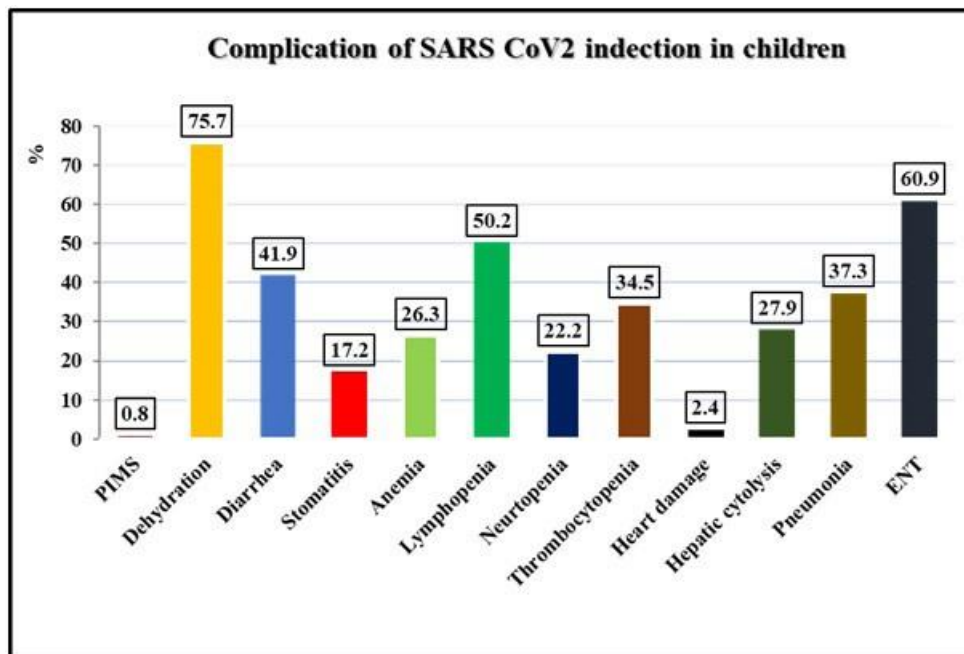


Chart no.8: Complications of SARS CoV-2 infection in children

5. Conclusions

Although the lot of children with COVID-19 wasn't very large (243 cases) we can safely assume that a series of particularities of this affection have emerged. SARS CoV-2 infection in children has a polymorphous clinical picture, where two types of onset predominate (digestive and respiratory manifestations), depending on the age group (in small children digestive manifestations are more present while in older children and adolescents - the respiratory ones). The clinical forms of disease in children are easier compared to adults this being explained by low percentage of comorbidities in paediatric patients. However, we registered several cases mainly with ENT affections, especially at the last pandemic wave as a consequence of the selection of a strain with a higher degree of infectiousness but with reduced severity of disease. We didn't record any critical forms of COVID-19 or any death in the studied lot.

SARS CoV-2 infection in children is more frequent in ages under 5 as vaccinations is absent in this age group, without a statistically significant difference, based on the children's sex. Paediatric COVID-19 cases presented a large picture of complications, the recurring ones being the digestive ones, ENT and haematological ones. A low percentage of children presented cardiac complications and two had PIMS with favourable evolution. Anti-COVID vaccination demonstrated that severe and critical cases diminished in adults as well as in children from the age groups that could undergo vaccination (over 12 years of age at the time of the study). The introduction, on a large scale, of COVID 19 vaccination in all age groups represents one of the most effective methods of specific prophylaxis along with non-specific methods (hand washing, physical distancing, protection mask). Subsequent studies, based on acquired clinical experience, will establish the particularities of SARS CoV-2 infection in children, useful to identify the most successful methods of diagnosis and treatment of COVID-19.

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