Commentary

Commentary on Clinical Characteristics of Children Infected with SARS-CoV-2 in Italy

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Received: 20 July 2021; **Accepted:** 27 July 2021; **Published:** 12 August 2021

Citation: Isabella Tarissi De Jacobis, Rosa Vona, Camilla Cittadini, Alessandra Marchesi, Laura Cursi, Andrea Campana, Lucrezia Gambardella, Alberto Villani, Elisabetta Straface. Commentary on Clinical Characteristics of Children Infected with SARS-CoV-2 in Italy. Journal of Pediatrics, Perinatology and Child Health 5 (2021): 164-167.

Abstract

SARS-CoV-2 is a highly contagious respiratory virus that in December 2019 emerged in Wuhan (Hubei Province, China) and spread rapidly worldwide. Despite the high number of people affected, data on clinical features and prognostic factors in children and adolescents are limited. Children become less ill than adults and most of them contract the infection through close contact with their parents or family members. In this short communication, we commented data of our study on an Italian pediatric population with COVID-19, published on the Italian Journal of Pediatrics.

Keywords: Pediatric Population; COVID-19; Gender; Inflammation; Thrombocytosis

Abbreviations: ACE2: Angiotensin-converting enzyme 2; CRP: C-reactive protein; LDH: Lactate dehydrogenase; MIS-C: Multisystem inflammatory syndrome

In December 2019, a new coronavirus (SARS-CoV-2) emerged in Wuhan (Hubei Province, China) and spread rapidly worldwide. SARS-CoV-2, is a highly contagious respiratory virus that can be transmitted from an infected person or an asymptomatic carrier through respiratory droplets, tear fluid and close contacts. On February 11, 2020, the World Health Organization (WHO), officially named respiratory disease caused by this virus, COVID-19. The incubation period for COVID-19 is variable. It has been estimated that the median incubation period is 5.1 days and that 97.5% of infected patients will develop symptoms within 11.5 days of infection. Italy was one of the European countries most affected by the COVID 19. By 16 April 2020, 1,123 children, up to 9 years of age, and 1,804 adolescents, aged between 10 and 19 years old were tested positives for COVID-19. Despite the high number of people affected, data on clinical features and prognostic factors in children and adolescents are limited. Children become less ill than adults and most of them contract the infection through close contact with their parents or family members. In the pediatric population, COVID 19 appears to be mild or asymptomatic [1-2]. Compared to adults, children manifest a mild disease that often do not need hospitalization and have a lower chance of developing interstitial pneumonia, which is among the most serious complications of the infection. There are various hypotheses on the low susceptibility of children to infection: i) a more efficient immune response due to the stimulation given by typical age vaccinations; ii) a lower expression of the angiotensin-converting enzyme 2 (ACE2) receptor to which the virus would bind to enter cells; iii) an "immaturity" of the ACE2 receptor, which makes it difficult for the virus to enter the body [3]; and iv) external factors (before the lockdown, children less likely than adults to visit places that could have facilitated the spread of the virus, such as railway stations and airports) [4].

Recently, on the Italian Journal of Pediatrics we published a study conducted on 66 patients (35 males and 31 females) with mean age of 6.8 years (range ≤ 1-18 years) and admitted with COVID-19 to Bambino Gesù Children's Hospital of Rome (Italy) in the period from the end of February to July 2020 [5]. This study was aimed to evaluate the clinical characteristics of children with COVID-19 in Italy, taking into account gender differences. Our study was performed in accordance with Good Clinical Practice and the Declaration of Helsinki principles for ethical research. All patients analyzed in this study contracted the infection from their parents and were hospitalized. The date of disease onset was defined as the day when the symptoms were noticed. All patients underwent nasopharyngeal, eye, urine and stool swab. The presence of SARS-CoV-2 in respiratory specimens was detected by real-time reverse transcription (RT-PCR) methods. Analyses by gene amplification reaction and RT-PCR were also carried out to exclude evidence of other viral infections, including influenza, respiratory syncytial virus, avian influenza, para-influenza, adenovirus and rhinovirus. To compare medians and range of values between two groups (males and females) we used the Mann-Whitney´s U test.

Our retrospective study, based on medical record data,

highlighted that: i) compared to adults, children get less COVID-19 and less severe clinical manifestations; ii) 20% males and 22.5% females with COVID-19 were asymptomatic; iii) fever and cough were the most common manifestations (fever: 37% males and 38% females; cough: 17% males and 22.5% females), followed by diarrhea (14% males and 9.6% females) and headache (11% males and 9.6% females); iv) convulsions (2.8% males and 12.9% females) and vomit (2.8% males and 6.4% females) were less frequent; v) cases of pneumonia were present only in male (5.7%) and vi) co-infections with Rhinovirus (8.6%), Campylobacter (2.8%), Enterovirus (2.8%) and E. Coli (2.8%) were present only in males, while Epstein-Barr virus (6.4%) and Herpes virus (3.2%) were present only in females. Interestingly, we found that all ages of childhood were susceptible to COVID-19: from a few days of life to 18 years. In particular, we found that females with COVID-19, although not significantly, were older than males (median age: 8.1 years vs 5.98 years) and required more days of hospitalization (median days 9.50 vs 7.24). Moreover, from medical records we found lymphopenia in both sexes and high lactate dehydrogenase (LDH) values in females from 1 to 10 years old (317.5U/L vs 266.6U/L). In particular, LDH is a cytoplasmic enzyme present in all major organ systems and is released into the peripheral blood after cell death. Increased serum LDH levels are associated with pulmonary disease such as obstructive diseases, microbial pulmonary diseases and interstitial lung diseases such as acute respiratory distress syndrome [6]. During hospitalization some male patients (5 males) developed mild thrombocytosis (median number of platelets: 607 x 10^3/UL) and exhibited increased inflammation evaluated in term of high C reactive protein (CRP) values (median of values: 2.55 mg/dL). Platelets have been increasingly recognized as an important component of the immune response to infections. An increase in their number above the normal range (thrombocytosis) has often been considered a sign of normal inflammatory reaction. Importantly, compared to primary thrombocytosis, the reactive thrombocytosis is not associated with higher risk of cardiovascular or thrombotic events [7]. CRP is an inflammatory marker that plays an important role in host defense against invading pathogens [8] and it has been found elevated in severe and critically adult patients with COVID-19 [9].

To date, there are no specific protocols to guide treatment of children with COVID-19 and lots of therapies are being under investigation. In our study we found that 20 children (11 males and 9 females) did not receive any therapy because asymptomatic and apyretic; 13 males and 5 females were treated only with paracetamol as needed; 4 males and 7 females were treated with paracetamol and antibiotics; 4 males and 2 females were treated only with antibiotics and 3 males only needed oxygen. Moreover, in addition to paracetamol and antibiotics, 2 females were treated with corticosteroid (they manifested bronchiolitis or cough); 1 female with anti-rheumatic drugs; 3 females with anti-inflammatory drugs and 2 females with heparin (they showed high values of inflammatory parameters and one of them was suffering from rheumatoid arthritis). One year later of pandemic COVID-19, despite awareness of this infection has increased around the world it is difficult to estimate its long-term impacts on children's health. The post-acute sequelae of COVID-19 recognized as multisystem inflammatory syndrome (MIS-C) and “long-COVID”, can seriously affect children of all ages. There is increasing evidence that restrictive measures aimed at limiting the pandemic are having a significant impact on child’s mental health. In

children and adolescents "long-COVID" is mainly represented by psychological disorders [10], especially eating disorders. During lockdown, measure to prevent the virus spreading such as social Isolation, distance learning and imposing travel restrictions, have engendered emotional distress, fear, and anxiety amongst the children and their caregivers [11]. Although children become less ill than adults they can play an important role in the transmission of infection and in the dynamics of outbreaks and could be a key target population for effective measures to control outbreaks. It is therefore important that clinical trials for vaccine therapy and development include pediatric considerations.

Acknowledgments

We thank all patients involved in the study. Authors reviewed and approved the final manuscript for publication.

Conflicts of Interest

The authors declare that they have no conflicts of interests.

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