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BRIEF REPORT

ACTA PÆDIATRICA NURTURING THE CHILD WILEY

COVID-19 in Italian paediatric patients: The experience of a tertiary children's hospital

Coronavirus disease (COVID-19) caused by the novel SARS-CoV-2 has spread worldwide since its onset in Wuhan in December 2019. In Italy, COVID-19 rapidly increased in February 2020 and by May 12, 2020, 2.0% of the confirmed cases were under 18 years and 3.7% of those had been hospitalised.[1] This case series report reviews the demographic characteristics, clinical course, laboratory findings, radiological features and treatment of children admitted with COVID-19 to a tertiary care hospital in Italy.

The study included the children with COVID-19 admitted between the March 15, 2020, and May 6, 2020, at the Bambino Gesù Children's Hospital. Diagnosis of SARS-CoV-2 infection was defined by the detection of virus RNA through real-time polymerase chain reaction on naso-pharyngeal swab. Family cluster was defined as the presence of a family member (mother, father, household) with certain or suspected diagnosis of SARS-CoV-2 infection at the time of the admission in the hospital.

The institutional ethics board approved the study, and written informed consent was provided by the parents.

In total, 43 patients were identified with a median age of 7 years. Patients' characteristics are presented in Table S1. Thirty-eight of forty-three children belonged to a family cluster. In 14/38 (37%) of cases, the family member was a healthcare worker.

The symptoms at the admission are reported in Table S1.

Of 43 patients, 5 children (12%) developed new symptoms during hospitalisation including the following: respiratory symptoms requiring supplemental oxygen for 3 days in a 7-year-old boy, mild diarrhoea with spontaneous resolution of ileal thickening detected on ultrasound in a 12-year-old girl, conjunctival hyperaemia without SARS-CoV-2 detected on ocular surface in a 6-year-old boy and the hyperinflammatory syndrome in 15- and 14-year-old boys. These two patients were admitted with fever and cough at the onset of the disease; after 2 days and 3 weeks from the admission, respectively, they developed abdominal pain, diarrhoea, high fever associated to lymphopenia, high levels of inflammatory indexes (C-reactive protein, ferritin, D-dimer) and a progressive mild heart failure. The transfer to the PICU was necessary. The clinical course and treatment of these two patients will not be discussed in this brief report.

Patient's laboratory findings at the admission are presented in Table S1.

During the hospitalisation, lymphopenia and neutropenia were observed in 16/43 (37%) and 11/43 (26%) of patients, respectively. The C-protein remained negative in 32/43 (74%) children. Transient and self-limited thrombocytopenia (112×10^9/L) was detected in the child who presented the respiratory deterioration, as described above.

The imaging was performed in 15/43 (35%) cases with suspected lower respiratory tract infections (Table S1). Chest X-ray was performed in 14/43 (33%) patients while only 5/43 (12%) children were subjected to chest CT scan. In 2/43 (5%) children over the age of 12 years the CT scan showed more extensive lung involvement than the X-ray, with ground glass opacities: one monolateral and one bilateral. Brain magnetic resonance imaging identified pneumonia in a patient without respiratory symptoms after afebrile seizures extended to the chest.

In our cohort, ten patients were treated with different combination of medications (Table S1).

Because of the co-administration of drugs that potentially could prolong QT, routine ECGs were performed every 48-72 hours. In all these patients, the QT interval remained in the normal range.

A 15-year-old girl, affected by a connective tissue disorder in therapy with Hydroxychloroquine (HCQ) and Mycophenolate, was treated with a combination of HCQ and lopinavir-ritonavir. We observed bradycardia (HR 50-60 bpm) likely related to drug-drug interaction between the two drugs (HCQ and lopinavir-ritonavir). The heart rate returned to the normal rate after discontinuation of lopinavir-ritonavir.

In general, our data suggest that SARS-CoV-2 infection in children may be mild or atypical compared to adult patients, strengthening the hypothesis that paediatric cases may be underdiagnosed and misdiagnosed. Multiple hypothesis have been proposed to justify the different clinical presentation of COVID-19 between adults and children; still today, there is no a univocal explanation. Noteworthy, although a small percentage is reported, paediatric patients may develop a hyperinflammatory syndrome that needs to be carefully evaluated for a prompt treatment. Notably, adults have a much higher prevalence of increased C-reactive protein, suggesting a much milder immunological response and less immune-mediated

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tissue damage in children.[3] In our study, we did not find a correlation between the lymphocyte count and the course of the disease. One asymptomatic child with COVID-19 had pneumonia, which suggests specific paediatric imaging criteria so that lower respiratory tract infections are detected. The treatment strategy for children with COVID-19 is based on adult experience. The combination therapy with azithromycin and hydroxychloroquine is supported by the evidence, albeit of small size, that hydroxychloroquine treatment is significantly associated with viral load reduction/disappearance in COVID-19 patients and that its effect is reinforced by azithromycin.[4] Antiviral treatment has been used in only one immunocompromised patient but data on its efficacy in children with COVID-19 are missing.[2] Pending on a paediatric clinical trial, we included lopinavir-ritonavir in our guidelines.

In our experience, and according with the literature,[5] although children are just as susceptible to COVID-19 as adults, they appear to have a milder clinical course. We observed that the major pattern of viral transmission was intra-family; therefore, the risk of family cluster transmission from children harbouring virus and the impact to community-based epidemic prevention should be taken into consideration in policy making for epidemic control.

CONFLICT OF INTEREST

We have no conflicts of interest.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.