

Screening of COVID-19 in children admitted to the hospital for acute problems: preliminary data

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Summary. *Background:* The new Coronavirus identified in Whuan at the end of 2019 (SARS-CoV-2) belongs to the Beta Coronavirus genus and is responsible for the new Coronavirus 2019 pandemic (COVID-19). Infected children may be asymptomatic or present fever, dry cough, fatigue or gastrointestinal symptoms. The CDC recommends that clinicians should decide to test patients based on the presence of signs and symptoms compatible with COVID-19. *Material and methods:* 42 children (the majority < 5 years of age) were referred, to our Pediatric Department, as possible cases of COVID-19 infection. Blood analysis, chest X-ray, and naso-oro-pharyngeal swab specimens for viral identification of COVID-19 were requested. *Results:* None of the screened children resulted positive for COVID-19 infection. At first presentation, the most frequent signs and symptoms were: fever (71.4%), fatigue (35.7%) and cough (30.9%). An high C-reactive protein value and abnormalities of chest X-ray (bronchial wall thickening) were detected in 26.2% and 19% of patients, respectively. Almost half of patients (45.2%) required hospitalization in our Pediatric Unit and one patient in Intensive Care Unit. *Conclusions:* Testing people who meet the COVID-19 suspected case definition criteria is essential for clinical management and outbreak control. Children of all ages can get COVID-19, although they appear to be affected less frequently than adults, as reported in our preliminary survey. Further studies are needed to confirm our observations. (www.actabiomedica.it)

Key words: COVID-19, children, emergency, respiratory and gastrointestinal symptoms.

Introduction

On 9 January 2020, a novel coronavirus, 2019-nCoV, was officially identified as the cause of an outbreak of diffuse pneumonitis in the city of Wuhan in Hubei Province, China. The epidemic has progressed very quickly in the following weeks, and an increasing number of cases have occurred daily in many countries (1).

The highest infection rate occurs in adults; however, neonates, children, and adolescents can also be infected (3). People of all ages are susceptible to SARS-CoV-2 2019-nCoV infection (3). The 95% confidence interval of 2019-nCoV infections period varies from 1

to 14 days (on average from 3 to 7 days). The majority of COVID-19 positive children had a close contact with an infected case or were family cluster cases and their age, at onset of disease, ranged from 1.5 months to 17 years (4).

Approximately 90% of cases are associated with household or community exposure, and 10 % are associated with travel.

The clinical features are variable. Patients display no obvious clinical symptoms at diagnosis and are found by screening, because of close contacts with confirmed patients, or gradually present fever, fatigue, dry cough, accompanied by other upper respiratory symp-

toms including nasal congestion, runny nose, and/or gastrointestinal symptoms, such as nausea, vomiting and diarrhoea (3-5).

From a systematic review of the literature, Ludvigsson (6) identified 45 relevant scientific papers and letters related to COVID-19 in children. The data showed a prevalence from 1 to 5%. The majority of them had a milder infection than in adults, although severe cases have been reported.

Laboratory findings in children with confirmed infection are variable. Approximately one-quarter had white blood cell count $<5.5 \times 10^9/L$ and 3.5 percent had lymphocyte count $<1.2 \times 10^9/L$ (7). Procalcitonin was elevated (>46 pg/mL) in 64 % and C-reactive protein was elevated (>10 mg/L) in 20 % of children. Chest radiographs may be unremarkable or demonstrate bilateral consolidation.

In order to gain more insights into the outbreak of COVID-19, in our population of children and adolescents, we analyzed the clinical presentations, laboratory data and radiologic findings of patients who came to the Emergency Pediatric Department of Catanzaro (Italy), for an acute disease.

Patients and methods

The study was performed from 1 March 2020 to 13 April 2020. A total of 127 patients were enrolled in our survey.

Demographic, clinical, and laboratory data of patients (age, sex, location, date at symptom onset, travel history and information on relatives) were collected using a standardized electronic medical record.

According to the international protocol, nasopharyngeal swab specimens for the detection of 2019-nCoV were requested. A duplex one-step real-time reverse transcription polymerase chain reaction (RT-PCR), using specific target genes (E, RdRp, N), was used to confirm the 2019-nCoV positivity (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance>). Influenza virus A and B were routinely tested on respiratory swabs.

Informed consent was obtained from the parents or guardians of children for the publication of clinical and laboratory data.

Data presentation

The following variables: age, sex, clinical features, onset of symptoms, laboratory indices and imaging, were collected and reported as number, frequency (%), and median (interquartile range). Laboratory indices and chest X-ray descriptions, in our patients and in children and adolescents with COVID-19 infections reported in the literature, are also presented.

Results

Of the 127 children and adolescents admitted to the Pediatric Emergency room, 42 patients (20 males and 22 females) were suspected to have a COVID-19.

Demographic data and clinical features of these patients are summarized in Table 1. The median age was 6.2 years (1 months-17.8 yrs) and half of them (52.3%) were between 1 mo. to 5 yrs of age. A high personal risk history for suspected COVID-19 was present in five patients (11.9%). In three children a personal history of prematurity, bronchodysplasia or sickle cell anemia was reported.

The average time of symptoms onset was 2.7 days. Fever was present in 71.4%, cough in 30.9%, and fatigue in 35.7% of our children and adolescents.

Laboratory investigations and the reported radiologic findings are summarized in table 2. The most common abnormalities on chest X-ray were bronchial wall thickening in 8 patients (19%) and nodular or reticulonodular opacities in 2 patients (4.7%). 45.2% required hospitalization in our Pediatric Unit and 1 patient required intensive care support.

None of our patients resulted positive for SARS-CoV-2 infection.

Discussion

The Centers for Disease Control and Prevention (CDC) and several other government health agencies emphasize that fever and respiratory symptoms are the criteria for suspecting a cases of 2019-nCoV infection. Based on the current WHO criteria (8), patients are suspected to have an infection in pres-

Table 1. Demographic data and clinical presentations

Age, sex and clinical features	
	Age
Median (range)	6.21 yrs (1 months-17.8 yrs)
Distribution - n. (%)	
1 month-5 yrs	22 (52.3%)
6 - 10 yrs	10 (23.8%)
11 - 15 yrs	4 (9.6%)
16 - 18 yrs	6 (14.3%)
Sex	
Male - n. (%)	20 (47.6%)
Female - n. (%)	22 (52.3%)
Onset of symptoms (median and range)	2.7 days (1- 15 days)
Signs and symptoms	
Fever — n. (%)	30 (71.4%)
	Body temperature - n. (%)
37.5-38.0°C	22 (52.4%)
38.1-39.0°C	7 (16.6%)
>39.1°C	1 (2.4%)
Dyspnea - n. (%)	10 (23.8%)
Cough - n. (%)	13 (30.9%)
Rhinorrhea - n. (%)	7 (16.6%)
Pharyngeal erythema - n. (%)	9 (21.4%)
Conjunctivitis - n. (%)	2 (4.7%)
Headache - n. (%)	2(4.7%)
Diarrhea - n. (%)	2 (4.7%)
Fatigue - n. (%)	15 (35.7%)
Vomiting - n. (%)	5 (11.9%)
Abdominal pain - n. (%)	6 (14.3%)
Oxygen saturation <94% - n. (%)	4 (9.5%)

ence of the following epidemiological and clinical characteristics:

a. Epidemiological history: 1) Children with a travel or residence history in an areas with persistent local transmission within 14 days prior to disease onset; 2) Children with a history of contacting patients with fever or respiratory symptoms who had a travel or residence history in an areas with persistent local transmission within 14 days prior to disease onset; 3) Children with a history of contacting confirmed or suspected cases infected with 2019-nCoV within 14

days prior to disease onset; 4) Newborns delivered by suspected or confirmed 2019-nCoV-infected mothers.

b. Clinical presentations: 1) fever or respiratory symptoms (e.g., cough, dyspnea, pharyngitis, flu-like symptoms) or digestive symptoms (e.g., vomiting, nausea and diarrhea) or fatigue.

In Italy, the National Institute of Health (ISS; updated to 9 April 2020) reported 136,110 cases of COVID-19. The higher positive numbers were registered in the North of Italy (2). In Calabria Region 785 case of COVID-19 were registered, with an incidence rate of 40,32 per 100,000 of inhabitants (2).

Children represent the 2% of COVID-19 diagnosed cases in China (9), 1.2% of cases in Italy (10), and 5% of COVID-19 in the USA (11).

None of our tested children and adolescents for SARS-CoV-2 resulted positive. These results could be attributed to several factors: the low incidence of positive cases among children living in our Region (about 1.2% of the total registered in Italy); the early activation. in our region, of procedures and recommendations for reducing the viral transmission (e.g. schools closure, social distancing); to the different response of immune system in children (12); to the different environmental factors (13,14), and the absence of additional risk factors (such as: associated chronic diseases, smoking, air pollution exposure).

Children often experience respiratory infections in winter, and may have higher levels of antibody against virus than adults. Furthermore, children's immune system is still developing, and may respond to pathogens differently to adults (11).

It has been also speculated that children are less sensitive to 2019-nCoV because the maturity and function (e.g., binding ability) of angiotensin converting enzyme II (ACE2) may be lower than that in adults (15). ACE2 receptors are involved in the protective mechanisms of the lung to SARS-CoV infection, as indicated by recent evidence (16,17).

Environmental factors, such as temperature, humidity, chemical and biological contaminants can play an important role in progression and spread of SARS-CoV infection (17,18). Higher temperatures and higher relative humidity (38°C, and >95% RH) have been found to reduce virus viability (18). In addition,

Table 2. Laboratory findings and imaging features

Laboratory indices	Values N. and range	Data reported in children with COVID-19 (*)
C-reactive protein (CRP)	52 (3-169) mg/L	Elevated C-reactive protein in 19.3% of cases.
Procalcitonin (PCT)	0.47 (0.05-3.5) ng/ml	Elevated procalcitonin levels in 49.8% of cases.
Aspartate aminotransferase (AST)	39 (21-94) IU/L	Increased liver enzymes in 19.2% of cases.
Alanine aminotransferase (ALT)	30 (13-40) IU/L	Increased liver enzymes in 19.2% of cases.
Creatine kinase (CK)	164 (59-508) IU/L	N.A.
Lactate dehydrogenase (LDH)	242 (135-640) IU/L	May be a predictors of disease severity.
Chest X-ray	N. and %	
Bronchial wall thickening	8 (19%)	In the early stage of pneumonia cases, chest images show multiple small patchy shadows and interstitial changes, remarkable in the lung periphery. Severe cases can further develop to bilateral multiple ground-glass opacity, infiltrating shadows, and pulmonary consolidation, with infrequent pleural effusion.
Nodular or reticulonodular opacities	2 (4.7%)	
Interstitial abnormalities	1 (2.4%)	

Legend: (*) From: de Souza TH et al. Clinical Manifestations of Children with COVID-19: a Systematic Review. medRxiv preprint doi: <https://doi.org/10.1101/2020.04.01.20049833> and Chen ZM et al. Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus. World J Pediatr.2020. Feb5; *N.A.* not available.

chemical and biological contaminants can promote the permanence and the spread of the virus, even over long distances (19).

In conclusion, testing people who meet the COVID-19 suspected case definition is essential for clinical management and outbreak control. The CDC recommends that clinicians should decide to test patients based on the presence of signs and symptoms compatible with COVID-19.

An universal testing during the COVID-19 outbreak should be taken into consideration because is very important to understand the children's role in spreading the virus in their communities, to determine hospital isolation practices and bed assignments, to inform pediatric emergency care, and to guide the use of personal protective equipment.

Conflict of interest: Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article

References

- Zhu N, Zhang D, Wang W, et al. China Novel Coronavirus Investigating and Research Team. N Engl J Med. 2020;382:727-373.
- Task force COVID-19 del Dipartimento Malattie Infettive e Servizio di Informatica, Istituto Superiore di Sanità. Epidemia COVID-19, Aggiornamento Nazionale: 9 aprile 2020.
- Cai J, Xu J, Lin D, et al. A Case Series of children with 2019 novel coronavirus infection: clinical and epidemiological features. [published online ahead of print, 2020 Feb 28]. Clin Infect Dis. 2020; ciaa198. doi:10.1093/cid/ciaa198.
- The Society of Pediatrics of Hubei Medical Association, The Society of Pediatrics of Wuhan Medical Association, Hubei Pediatric Medical Quality Control Center. Suggestions on the diagnosis and treatment of novel coronavirus infection in children in Hubei province. CJCP. 2020;22:96-99.
- Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020;395:497-506.
- Ludvigsson JF. Systematic review of COVID-19 in children show milder cases and a better prognosis than adults. [published online ahead of print, 2020 Mar 23]. Acta Paediatr. 2020;10.1111/apa.15270. doi:10.1111/apa.15270.
- Lu X, Zhang L, Du H, et al. SARS-CoV-2 Infection in Children [published online ahead of print, 2020 Mar 18]. N Engl J Med. 2020;NEJMc2005073. doi:10.1056/NEJMc2005073
- World Health Organization. Global surveillance for COVID-19 caused by human infection with COVID-19 virus. Interim guidance 20 March 2020, pp.1-20. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/surveillance-and-case-definitions>.
- Zhang Y. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) – China, 2020. Chinese J Epidemiol. (by The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team) 2020.
- Livingston E, Bucher K. Coronavirus Disease 2019 (COVID-19) in Italy. JAMA. 2020 doi:

- 10.1001/jama.2020.4344 [published Online First: 2020/03/18].
11. Severe Outcomes Among Patients with Coronavirus Disease 2019 (COVID-19) — United States, February 12–March 16, 2020. (CDC COVID-19 Response Team). *Morbidity and Mortality Weekly Report* March 18, 2020;69.
12. Dong Y, Mo X, Hu Y, et al. Epidemiological Characteristics of 2143 Pediatric Patients With 2019 Coronavirus Disease in China. *Pediatrics*. 2020;e20200702. doi:10.1542/peds.2020-0702.
13. Kroumpouzos G, Gupta M, Jafferany M, et al. COVID-19: A Relationship to Climate and Environmental Conditions? *Dermatol Ther*. 2020;e13399.
14. Després VR, Huffman JA, Burrows SM, et al. Primary biological aerosol particles in the atmosphere: a review. *Tellus B: Chemical and Physical Meteorology*. 2012; 64:1. *Anal Bioanal Chem* (2016) 408:6337–6348
15. Fang F, Luo XP. Facing the pandemic of 2019 novel coronavirus infections: the pediatric perspectives. *Zhonghua Er Ke Za Zhi*. 2020;58:81–85.
16. Li W, Moore MJ, Vasilieva N, et al. Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. *Nature*. 2003;426: 450–454.
17. Zhou P, Yang X, Wang X, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020;579:270–273.
18. Kroumpouzos G, Gupta M, Jafferany M, et al. COVID-19: A Relationship to Climate and Environmental Conditions? *Dermatol Ther*. 2020;e13399.
19. Després VR, Huffman JA, Burrows SM, et al. Primary biological aerosol particles in the atmosphere: a review. *Tellus B: Chemical and Physical Meteorology* 2012;64:15598–15656.

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