medium expression,[9] which suggests that the SARS-CoV-2 may more likely bind to the gastrointestinal tract compared with the lungs. No difference in expression levels between gender or age were reported. These data supported that gastrointestinal infection and potential fecal–oral transmission can last long after the respiratory samples have tested negative. Therefore, the stool specimens should be taken into consideration when it comes to case confirmation and discharge criteria.

Several studies have reported on the clinical characteristics of asymptomatic infection in children[3,10] and have showed that the duration of positive SARS-CoV-2 nucleic acid in pharyngeal swabs was no different from that in asymptomatic children. Still, data are limited about the changes of nucleic acid in stool specimens in symptomatic children. Our study demonstrated that nucleic acid testing results of anal swabs remain positive for 30 days after pharyngeal swab results turn negative in asymptomatic children.

This study has limitations, including the small sample size and failure to obtain stool specimens during their first few days of hospitalization. And we did not get RT-PCR Ct values over time for all patients due to limited conditions. However, our study can be considered as an evidence for the management of asymptomatic children infected with SARS-CoV-2, and we provide new evidence for current criteria for diagnosis and discharge. Therefore, prospective and large-sample studies are needed for further research on RNA replication in stools of asymptomatic children infected with SARS-CoV-2 to provide more credible evidence for clinical practice.

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REFERENCES

1. Utunen H, Ndiaye N, Piroux C, et al. Launch and global reach of an online COVID-19 course in multiple languages on OpenWHO in the first quarter of 2020. *JMIR Public Health and Surveillance. J Med Internet Res*. 2020;22:e19076.
2. Qiu H, Wu J, Hong L, et al. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. *Lancet Infect Dis.* 2020;20:689–696.
3. Xu Y, Li X, Zhu B, et al. Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nat Med.* 2020;26:502–505.
4. Xing YH, Ni W, Wu Q, et al. Prolonged viral shedding in feces of pediatric patients with coronavirus disease 2019. *J Microbiol Immunol Infect*. 2020;53:473–480.
5. Zhang T, Cui X, Zhao X, et al. Detectable SARS-CoV-2 viral RNA in feces of three children during recovery period of COVID-19 pneumonia. *J Med Virol.* 2020;92:909–914.
6. Wu Y, Guo C, Tang L, et al. Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. *Lancet Gastroenterol Hepatol.* 2020;5:434–435.
7. Han C, Duan C, Zhang S, et al. Digestive symptoms in COVID-19 patients with mild disease severity: clinical presentation, stool viral RNA testing, and outcomes. *Am J Gastroenterol*. 2020;115:916–923.
8. Cipriano M, Ruberti E, Giacalone A. Gastrointestinal infection could be new focus for coronavirus diagnosis. *Cureus.* 2020;12:e7422.
9. Li MY, Li L, Zhang Y, et al. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. *Infect Dis Poverty.* 2020;9:45.
10. Pan X, Chen D, Xia Y, et al. Asymptomatic cases in a family cluster with SARS-CoV-2 infection. *Lancet Infect Dis.* 2020;20:410–411.

GASTROINTESTINAL SYMPTOMS IN SEVERE COVID-19 CHILDREN

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Abstract: There are growing evidence of clinical manifestations other than acute respiratory syndrome in severe acute respiratory syndrome associated with coronavirus 2-infected children. In our multicenter retrospective analysis, we observed among 127 severe acute respiratory syndrome associated with coronavirus 2 positive children that the presence of gastrointestinal symptoms was more frequently associated with severe and critical phenotype ($P = 0.029$). Moreover, having gastrointestinal symptoms was more frequently reported in patients who developed cardiac impairment.

Key Words: child, COVID-19, SARS-CoV-2, gastrointestinal symptoms
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As of May 7, the Italian National Institute of Health reported 3752 cases of severe acute respiratory syndrome associated with coronavirus 2 (SARS-CoV-2) in Italian children <18 years of age, 140 of them requiring hospital admission.

Since the first outbreak, a global effort has been made to collect clinical and laboratory findings on patients with SARS-CoV-2 infection. The lower airway is the primary target of the infection; however, the disease spectrum in adults goes from asymptomatic subjects to sever illness including 5.0% subjects requiring intensive care unit (ICU) admission, 2.3% who underwent invasive mechanical ventilation, and 1.4% who died.[1] Data suggest that children are less likely to develop severe symptoms compared with adults.[2] Also, there are growing evidence of clinical manifestations other than acute respiratory syndrome in pediatrics suggesting that coronavirus diseases 2019 (COVID-19) spectrum and pathogenesis in children are yet to be unravel. In this report, we describe the results of our preliminary analysis of a cohort of hospitalized pediatrics COVID-19 patients focusing on mode of presentation, presence of comorbidities, severity of disease, and early outcome.

MATERIALS AND METHODS

We conducted a multicenter retrospective analysis of clinical record of SARS-CoV-2-infected children in 23 different sites in Italy.

TABLE 1. Association of Clinical Characteristics With Severity Score and ICU

	Asymptomatic, mild, or moderate		Severe or critical			Not ICU		ICU		
	N = 107		N = 20			N = 111		N = 8		
Characteristics	N	%	n	%	*P*[a]	N	%	n	%	*P*[a]
Age median (IQR, y)	1.6 (0.3, 7.9)		4.3 (0.3, 10.1)		0.393[b]	1.6 (0.3, 7.9)		5.5 (0.4, 10.1)		0.497[b]
Age group					0.845					0.854
Newborn	5	4.7	1	5.0		6	5.4	0	0.0	
Infant	44	41.1	7	35.0		44	39.6	3	37.5	
Children	42	39.2	8	40.0		46	41.4	3	37.5	
Adolescent	16	15.0	4	20.0		15	13.5	2	25.0	
Male	68	64.2	14	70.0	0.799	71	64.5	5	62.5	1.000
Presentation										
Fever	85	79.4	20	100.0	0.023	92	82.9	8	100.0	0.352
Respiratory symptoms	68	63.6	14	70.0	0.799	74	67.3	4	50.0	0.441
Respiratory symptoms only	46	43.0	7	35.0	0.624	44	39.6	2	25.0	0.468
Cough	52	48.6	9	45.0	0.812	57	51.4	2	25.0	0.812
Rhinorrhea	43	40.2	6	30.0	0.460	46	41.4	0	0.0	0.022
Wheezing	4	3.7	0	0.0	1.000	3	2.7	0	0.0	1.000
Dyspnea	5	4.7	5	25.0	0.009	7	6.4	2	25.0	0.114
GI symtomps	26	24.3	10	50.0	0.029	31	27.9	4	50.0	0.232
GI symptoms only	13	12.1	5	25.0	0.160	14	12.6	3	37.5	0.087
Vomit	6	5.6	6	30.0	0.004	6	5.4	6	75.0	0.004
Diarrhea	20	18.7	8	40.0	0.044	20	18.0	8	100	0.044
Abdominal pain	6	5.6	2	10.0	0.611	8	7.2	0	0.0	1.000
Comorbidities	14	13.1	6	30.0	0.088	16	14.4	3	37.5	0.115
Chronic cardiac conditions	3	2.8	2	10.0	0.176	4	3.6	1	12.5	0.298
GI disorder	2	1.9	2	10.0	0.117	2	1.8	1	12.5	0.190
Obese	1	0.9	2	10.0	0.064	3	2.7	0	0.0	1.000
Chronic kidney disease	2	1.9	0	0.0	1.000	2	1.8	0	0.0	1.000
Chronic neurologic disease	0	0.0	2	10.0	0.024	1	0.9	0	0.0	1.000
Immunologic condition	2	1.9	0	0.0	1.000	1	0.9	0	0.0	1.000
CXR positive	25	43.9	13	65.0	0.125	35	51.5	3	37.5	0.711
Complication	23	21.5	19	95.0	<0.001	35	31.5	7	87.5	0.003
Viral pneumonia	16	15.0	9	45.0	0.004	24	21.6	1	12.5	0.468
Bronchiolitis	8	7.5	1	5.0	0.570	9	8.1	0	0.0	0.522
Bacterial pneumonia	0	0.0	2	10.0	0.024	1	0.9	1	12.5	0.130
ARDS	0	0.0	2	10.0	0.024	1	0.9	1	12.5	0.130
Pleural effusion	0	0.0	1	5.0	0.157	0	0.0	1	12.5	0.067
Myocardial involvement	0	0.0	6	30.0	<0.001	2	1.8	4	50.0	<0.001
Bacteremia	0	0.0	1	5.0	0.157	0	0.0	1	12.5	0.067
Coagulation disorder	0	0.0	1	5.0	0.157	0	0.0	1	12.5	0.067
AKI	0	0.0	1	5.0	0.157	0	0.0	1	12.5	0.067
Liver dysfunction	0	0.0	1	5.0	0.157	0	0.0	1	12.5	0.067
Myositis	1	0.93	0	0.0	0.843	1	0.9	0	0.0	0.933

AKI indicates acute kidney injury; ARDS, acute respiratory distress syndrome; CXR, chest radiograph; GI, gastrointestinal; ICU, intensive care units; IQR, interquartile range.

From February 21, 2020, to May 1, 2020, subjects less than 18 years of age with a positive result on high throughput sequencing or real-time reverse transcriptase-polymerase chain reaction assay of nasal/pharyngeal swab specimens were included.

The study was approved by the ethical committees of the coordinating center in Milan (protocol number 2020/ST/061).

Data regarding recent exposure history, clinical symptoms or signs, and laboratory findings on admission were extracted using a common clinical record form. Radiologic assessments and laboratory testing were performed according to the clinical care needs of the patient.

The Student's *t* test, the χ^2 method, and Fisher's exact test were used as appropriate for statistical analysis to compare continuous and categorical variables. A *P* value <0.05 was chosen as cutoff for significance. Data were analyzed with StataMed (version 12.0).

RESULTS

Overall, 127 children were included; 44 were female (34.9%) and the median age was 4.8 years (interquartile range, 0.3–8.5); 57 (45%) <12 months of age.

Eight of 127 (6.7%) were admitted in ICU, 14 of 127 (12%) required oxygen therapy, 5 (4%) were noninvasive ventilation, and 1 patient required mechanical ventilation during the hospitalization.

The severity of the COVID-19 in our children was defined using previously published criteria[3]; 7.9%, 48.8%, and 27.7% of their clinical features were defined respectively as asymptomatic, mild, or moderate accounting for 84.4% of our cohort; 8.7% was severe and 7.1% was critical.

Age class, sex, and ethnic group did not show a different distribution among the severity categories (*P* = 0.57, 0.62, and 0.375 Fisher exact test; Table 1).

Twenty of 127 patients (15.7%) had at least 1 comorbidity. Five (3.9%) had chronic cardiac condition, 4 (3.1%) had gastrointestinal (GI) disorder, 3 (2.4%) were obese, 2 (1.6%) had chronic kidney disease, chronic neurologic disorder, and immunologic condition, respectively. Only 1 medically complex patient (defined as children who required long-term dependence on life support) was included. Comorbidities distribution was not different among severity classes (*P* = 0.08 Fisher exact test). Moreover, the ICU

admission rate was similar in patients with comorbidities and those without ($P = 0.115$ Fisher exact test).

The most common symptoms reported on admission were fever (82.7%), cough (48%), and rhinorrhea (38%). Seventy-seven of 127 (60.6%) presented with respiratory symptoms (cough, rhinorrhea, wheezing, and dyspnea).

Thirty-six out 127 (28.3%) had GI symptoms (vomit, diarrhea, abdominal pain), of them twenty-eight (22%) had diarrhea, 12 (9,4%) vomit, and 8 (6.3%) abdominal pain.

The presence of GI symptoms at the admission was differently distributed throughout severity classes ($P = 0.006$). Having GI symptoms was more frequently associated with severe and critical phenotype ($P = 0.029$). Interestingly, a history of GI symptoms was positively associated with cardiac involvement as clinical complications, in presence of other symptoms ($P = 0.007$) or alone ($P = 0.004$).

Roughly, a third of the children presented lower respiratory tract complications as viral pneumonia and bronchiolitis. Viral pneumonia was more frequently reported in severe phenotype ($P = 0.004$), while admission rate to ICU was equally distributed among these patients. Chest radiogram was performed in 77 patients (65%) on admission, and infiltrates were found in 38 of 77 (50%). Respectively, 20 and 15 patients had bilateral and monolateral infiltrates, for 3 of them it was not specified. In 4 of 77 (5.2%), atelectasis and pleural effusion were found. The presence of infiltrates at the chest radiogram did not correlate with severity clinical score or ICU admission rate ($P = 0.125$ and 0.71 Fisher exact test, respectively).

DISCUSSION

In the present study, we reported that most SARS-CoV-2-infected children had fever and respiratory symptoms. Similarly, Shekerdemian et al[4] reported that most of the patients included in the North American Pediatric Intensive Care Unit cohort presented respiratory symptoms, but they also state that only 1 child of their cohort presented GI symptoms, speculating that these may be associated with milder clinical presentation.

In children, common circulating human coronaviruses can cause GI symptoms in up to 57% of cases, and this presentation is more common in children than adults.[5] Increasing evidence showed that the GI tract may represent a target for SARS-CoV-2 due to the expression of the angiotensin-converting enzyme 2, a major virus receptor. We reported, differently to published data, that a history of gastrointestinal (GI) was positively correlated with a worst severity score (severe and critical) and a higher ICU admission rate. The same result was found, in an pooled analyses of adult cohorts, where GI were correlated to increased odds of critical disease and higher prevalence of complications.[6]

Interestingly, in our cohort having GI was more frequently reported in patients who developed cardiac impairment as complications of SARS-CoV-2 infection. The development of hyperinflammatory syndromes and Kawasaki-like disease in children exposed to SARS-CoV-2 infection has been recently brought to attention. Riphagen et al[7] reported 8 cases of hyperinflammatory syndrome with cardiac involvement, all of them presenting with fever and significant GI symptoms (diarrhea, vomit, abdominal pain), according to our current results and to what we have previously reported.[8]

In recent studies,[4,9] comorbidities have been frequently reported in patients requiring admission to ICU. In the North American Pediatric Intensive Care Unit cohort, authors reported that up to 80% of patients included had comorbidities. The most common comorbidity reported was medically complex defined as long-term dependence on technologic support.[4] In agreement with this cohort, Parri et al, in a SARS-CoV-2 positive cohort of pediatric patients admitted at Italian Emergency Departments, reported that 9 patients of 100 need mechanical ventilation and, among them, 6 (66%) had comorbidities.[9]

In the present study, only 20 (16%) children with previous medical condition were included, 3 of them required ICU. The presence of preexisting medical conditions was not different in severe and critical patients when compared with mild, moderate, and asymptomatic ones. Moreover, the ICU admission rate was similar in patients with and without comorbidities.

There are several limitations to our study. First, the limited sample size. Second, children have been classified using a severity score previously applied to other pediatric cohorts, which is mainly designed on respiratory symptoms and lung involvement. The score criteria could explain the higher frequency of viral pneumonia among severe phenotype but not among patients requiring ICU admission. However, critical cases are defined not only by the progression to respiratory failure (acute respiratory distress syndrome) but also to life-threating organ dysfunction (shock, myocardial injury, acute kidney injury). Therefore, in the present study, the subset of critical patients includes not only patients with respiratory failure but also with other life-threating conditions. Finally, there are evidences that COVID-19-related multisystemic inflammatory syndrome could be a complication in the disease spectrum. Although a better understanding of timing between GI and its onset would be of great interest, we could not provide such information in the current study.

CONCLUSIONS

The intention of this short report is to bring to attention that COVID-19 disease spectrum in children is far from been described in a universally shared way. Other manifestations from respiratory are often the cause of severe illness, as we reported. Having preexisted medical conditions is not associated with worse outcome and consequently, severe clinical presentation must be considering also in previously healthy children.

GI symptoms seem to be a clinical warning for children evaluated in any clinical settings when SARS-CoV-2 infection is suspected, independently of comorbidities.

Pathogenetic mechanisms causing severe phenotypes in SARS-CoV-2-infected children need to be deepened by multidisciplinary approach as well we need more data to define a suitable clinical severity score for COVID-19 in children.

REFERENCES

1. 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.
2. Bi Q, Wu Y, Mei S, et al. Epidemiology and transmission of COVID-19 in 391 cases and 1286 of their close contacts in Shenzhen, China: a retrospective cohort study. *Lancet Infect Dis*. 2020;20:911–919.
3. Dong Y, Mo X, Hu Y. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. *J Pediatr Cit*. May 17, 2020. Available from: www.aappublications.org/news.
4. Shekerdemian LS, Mahmood NR, Wolfe KK, et al. Characteristics and outcomes of children with coronavirus disease 2019 (COVID-19) infection admitted to US and Canadian Pediatric Intensive Care Units. *JAMA Pediatr*. 2020. Available from: https://doi.org/10.1001/jamapediatrics.2020.1948.
5. Zimmermann P, Curtis N. Coronavirus infections in children including COVID-19: an overview of the epidemiology, clinical features, diagnosis, treatment and prevention options in children. *Pediatr Infect Dis J*. 2020;39:355–368.
6. Mao R, Qiu Y, He J-S, et al. Manifestations and prognosis of gastrointestinal and liver involvement in patients with COVID-19: a systematic review and meta-analysis. *Lancet Gastroenterol Hepatol*. May 17, 2020. Available from: https://www.thelancet.com/journals/langas/article/PIIS2468-1253(20)30126-6/fulltext.

7. Riphagen S, Gomez X, Gonzalez-Martinez C, et al. Hyperinflammatory shock in children during COVID-19 pandemic. *Lancet*. 2020;395:1607–1608.
8. Wolfler A, Mannarino S, Giacomet V, et al. Acute myocardial injury: a novel clinical pattern in children with COVID-19. *Lancet.* 2020;4:E26-E27. Doi:10.1016/S2352-4642(20)30168-1.
9. Parri N, Lenge M, Buonsenso D; Coronavirus Infection in Pediatric Emergency Departments (CONFIDENCE) Research Group. Children with Covid-19 in Pediatric Emergency Departments in Italy. *N Engl J Med*. 2020;383:187–190.

SARS-COV-2 ENCEPHALITIS IN A 20-YEAR OLD HEALTHY FEMALE

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Abstract: We report a 20-year-old female with SARS-CoV-2 encephalitis who presented with 4 days of upper respiratory symptoms, fevers and sudden acute altered mental status. An extensive work up led to the most likely cause for the neurologic decompensation to be viewed as SARS-CoV-2 symptomology.

Key Words: coronavirus, COVID-19, encephalitis, altered mental status, critical care

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The seventh member of the family of coronaviruses that infect humans, SARS-CoV-2, first became a concern for Chinese health officials in late December 2019.[1] By March 11, 2020, the World Health Organization classified SARS-CoV-2 a pandemic, due to concern for the alarming rate of spread and severity of the disease.[2] As the pandemic has progressed, most literature has focused on the respiratory illness associated with the virus. However, extra-pulmonary manifestations are being increasingly described particularly in pediatric patients.

At time of publication, there were a limited number of case reports focused on SARS-CoV-2 encephalopathy. A retrospective case series by Mao et al indicated that neurologic symptoms are common in SARS-CoV-2 patients with up to 36% of patients demonstrating neurologic involvement. Primarily, these manifestations include acute stroke, consciousness impairment and skeletal muscle injury, all seen more commonly in individuals classified as having severe disease.[3] We present a case of SARS-CoV-2 related encephalopathy in a previously healthy 20-year old female with otherwise mild disease to highlight one of the lesser-discussed, but severe manifestations of SARS-CoV-2.

CASE REPORT

A 20-year-old female with past medical history of obesity and anxiety presented to the emergency department with 4 days of nasal congestion, fever, ageusia, insomnia and altered mental status (specifically, confusion with performing routine daily activities, hypervigilance and obsessive thinking). The patient had a family history notable for panic disorder in both parents and schizophrenia in a maternal aunt. On initial evaluation, the patient was oriented to person and place. She responded to questions appropriately, although with slight delay. Psychiatry consult recommended administration of lorazepam for anxiety, after which her mental status began to deteriorate and she was no longer able to answer questions.

Workup revealed a positive COVID-19 polymerase chain reaction (PCR) obtained by nasopharyngeal swab, a negative head CT, and CXR with faint right lower lung field opacity. Inflammatory markers were elevated with initial CRP 4.67 mg/dL (0–0.4 mg/dL), Ferritin 563 ng/mL (15–150 ng/mL) and D-Dimer 316 ng/mL DDU (0–230 ng/mL DDU). Thyroid levels resulted borderline with T4 Serum 11.6 µg/dL (4.6–12 µg/dL) and TSH 0.29 µlU/mL (0.27–4.2 µlU/mL). All other initially obtained labs were within normal limits. Patient was treated with levofloxacin, due to penicillin allergy, and acyclovir while awaiting cultures from cerebral spinal fluid.

On hospital day 2, the patient's mental status further deteriorated in the setting of persistent fevers. She was alert but could not confirm that she was oriented x3. Her speech was repetitive, confused and stuttering, and she did not follow verbal directions. She was tremulous but able to move all extremities purposefully, and demonstrated urinary incontinence. As day 2 progressed her mental status progressed to catatonia. Video EEG demonstrated generalized slowing. Magnetic resonance imaging (MRI) brain was unremarkable. Testing for anti-NMDA receptor antibodies, anti-GAD antibodies, VGKC antibodies, Interleukin-1 Beta, Interleukin-6, Interleukin-10, Interleukin-2, ANA, ANCA, lactic acid, ammonia, C3, C4, Beta-2 glycoprotein IgA, Beta-2 glycoprotein IgM, anti-DNAse B and Antistreptolysin antibody were all within normal limits. Serum Thyroperoxidase antibodies were elevated at 1499 IU/mL (≤34.9 IU/mL). Results of elevated thyroid function tests were discussed with endocrinology and thought to be likely Hashimoto's thyroiditis; however, in the setting of normal TSH and T4, no acute intervention was recommended. Cerebrospinal fluid (CSF) demonstrated cell count of 0 µ/L (0 µ/L), protein 18 mg/dL (15–45 mg/dL) and glucose 74 mg/dL (45–75 mg/dL), with negative PCR and Gram stain, and so both levofloxacin and acyclovir were discontinued.

Given the clinical picture and laboratory findings, our working diagnosis was Hashimoto's Encephalopathy versus SARS-CoV-2 Encephalopathy. Subsequently, 1 g/day methylprednisolone was started. The patient did not demonstrate any improvement with steroids, and began to have auditory hallucinations with questionable visual hallucinations. Methylprednisolone was discontinued after the second day of administration, hospital day 6, due to concern for psychiatric deterioration secondary to steroid administration. Psychiatry recommended olanzapine 2.5 mg oral disintegrating tablet nightly for what they assessed to be delirium.

Lovenox 40 mg SQ BID for deep vein thrombosis prophylaxis was started on hospital day 4. Patient became intermittently tachypneic to the 50s and high flow nasal cannula was trialed. No significant improvement in her respiratory symptoms was demonstrated and it was subsequently discontinued. Repeat chest radiograph showed low lung volumes, trace bibasilar markings, no new consolidations or effusions, and no signs of fluid in the fissures. She remained with altered mental status, persistent fevers, insomnia, tremulousness and was adequately maintaining her airway.

Neurology recommended repeat MRI brain with and without contrast and repeat lumbar puncture for further evaluation of non-improving altered mental status. Peripherally inserted central catheter team was also consulted for initiation of TPN due to