Acute Abdomen and Appendicitis in 1010 Pediatric Patients With COVID-19 or MIS-C: A Multinational Experience from Latin America

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Background: To date, there are only sporadic reports of acute abdomen and appendicitis in children with coronavirus disease 2019 (COVID-19) and multisystem inflammatory syndrome in children (MIS-C).

Methods: Children 17 years of age or younger assessed in 5 Latin American countries with a diagnosis of microbiologically confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and children fulfilling MIS-C definition were included. For children with acute abdomen, we investigate main radiologic patterns, surgical treatment and intraoperative findings, outcomes.

Findings: One-thousand ten children were enrolled. Forty-two children (4.2%) had a clinical diagnosis of acute abdomen. Four (9.5%) were diagnosed with MIS-C and did not undergo surgery. The remaining 38 children (3.8%) underwent abdominal surgery due to suspected appendicitis, 34 of them (89.7%) had an intraoperative diagnosis of acute appendicitis (AA), while 4 of them had nonsurgical findings. Eight children died (0.8%), none of them being diagnosed with appendicitis. Children with AA were significantly older than those without (P < 0.0001). Children with complicated appendicitis had more frequently fever (85.7% vs. 60%), intestinal distension on the abdominal radiograph (7.1% vs. none), leukocytosis (85.7% vs. 40%) and high levels of C-reactive protein (35.7% vs. 5%), although differences were not statistically significant.

Conclusions: Our study showed that children may present with acute abdomen during COVID-19 or MIS-C, which is not always associated with intraoperative findings of appendicitis, particularly in case of MIS-C. Further studies are needed to better characterize children with acute abdomen during COVID-19 or MIS-C, to avoid delay in diagnosis of surgical conditions and at the same time, minimize unnecessary surgical approaches.

Key Words: COVID-19, SARS-CoV-2, appendicitis, children

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MATERIALS AND METHODS

Study Design and Participants
This study is part of an ongoing independent, unfunded project that aims to provide urgent information on COVID-19 and MIS-C in Latin American children. The project was presented during the first peak in Latin America and led to the publication of different papers describing an initial group of 409 children with confirmed COVID-19, antibiotic use in children with COVID-19 or with MIS-C, and the impact of sex on disease severity in children. For the current study, we aimed to assess the diagnoses of AA in children with COVID-19 or with MIS-C. We implemented the previously used dataset including specific variables for this aim: clinically diagnosed acute abdomen; abdominal ultrasound; abdominal radiograph; complete blood count and C-reactive protein (CRP); surgical findings; culture results from intraoperative specimens. Appendicitis with peritonitis or abdominal abscesses were considered as complicated. These adjunctive data were collected only for children with a clinical diagnosis of appendicitis, since the current emergency situation in Latin America and the burden on health workers, along with the lack of dedicated research resources in our Institutions, did not allow a comprehensive data collection for all children. The remaining variables were collected for all children and are those previously used and included: age, gender, symptoms, imaging, underlying medical conditions, need for hospital and neonatal intensive care unit/pediatric intensive care unit (PICU) admission, respiratory and cardiovascular support, other viral coinfections, drugs used to treat COVID-19, development of MIS-C and type of organ involvement, and outcome. SARS-CoV-2 infection was defined as a positive polymerase chain reaction (PCR) test on nasopharyngeal swab.

MIS-C due to SARS-CoV-2 was defined according to the Centers for Disease Control and Prevention criteria. The study was reviewed and approved by the CoviD in sOurth aMerIcan children—study GrOup core group and approved by the ethics committee of the coordinating center and by each participating center (Mexico: COMIN�ETICA-30072020-CEI0100120160207; Colombia: PE-CEI-FT-06; Peru: No. 42-IE TSI-ESSALUD-2020 and Costa Rica: CEC-HNN-243-2020). The study was conducted in accordance with the Declaration of Helsinki and its amendments. No personal or identifiable data were collected during the conduct of this study.

Statistical Analysis
Summary statistics were presented as counts and percentages. Crude comparisons between groups were evaluated with the chi-squared test or Fisher’s exact test, as appropriate. The association of relevant demographic characteristics and clinical factors with the diagnosis of appendicitis was assessed through logistic regression analysis; the effect size of covariates was expressed by odds ratios with 95% confidence intervals (CIs), and the presence of systematic differences (i.e., statistical significance) was assessed using the 2-sided Wald test. Standard errors were adjusted for clustering of patients within hospitals (m = 8). All data were analyzed using Stata version 15 (StataCorp. 2017. Stata Statistical Software: Release 15. College Station, TX: StataCorp LP). The significance level was set at 5%.

RESULTS
Study Population
A total of 1010 children were enrolled: 941 children (93.2%) with COVID-19 and 69 children (6.8%) with MIS-C: Peru (n = 391, 38.7%), Costa Rica (n = 303, 30%), Argentina (n = 260, 25.7%), Colombia (n = 44, 4.4%) and Mexico (n = 12, 1.2%).

The demographic and clinical characteristics of the 1010 study patients, and according to the final diagnosis of appendicitis or not, are summarized in Table 1. Four hundred ninety-four (48.9%) were female. A total of 323 (32%) children were admitted to the hospital and 47 (4.7%) required admission to a PICU.

Forty-two children (4.2%) had a clinical diagnosis of acute abdomen. Of them, 4 (9.5%) were diagnosed with MIS-C and did not undergo surgery. The remaining 38 children (3.8%) of the study population underwent abdominal surgery due to suspected appendicitis, 34 of them (89.7%) had an intraoperative diagnosis of AA, while 4 of them had nonsurgical findings (mesenteric adenitis in 2 cases, and normal abdominal findings in the remaining 2). The 2 children with mesenteric adenitis but no appendicitis who underwent surgery, were eventually diagnosed with MIS-C with myocarditis. Eight children died (0.8%), none of them being diagnosed with appendicitis. Further details are described in Table 1.

Characteristics of Children With Acute Appendicitis
Children with AA were significantly older than those without (P < 0.0001) and did not experience a delay at diagnoses, compared with the other group (Table 1).

Table 2 describes details of the cohort of children with appendicitis and according to the presence of surgical complications or not (peritonitis, abdominal abscesses). Children with complicated appendicitis had more frequently fever (85.7% vs. 60%), intestinal distension on the abdominal radiograph (7.1% vs. none), leukocytosis (85.7% vs. 40%) and high levels of CRP (35.7% vs. 5%), although differences were not statistically significant probably due to the overall low number of children with appendicitis. On multivariate analyses (Table 3), age >5 years was associated with a higher risk of appendicitis (P < 0.001, 95% CI: 4.17–32.83), while the presence of upper respiratory tract symptoms with a reduced risk (P = 0.019, 95% CI: 0.02–0.71).

DISCUSSION
Abdominal pain is one of the clinical manifestations in children with COVID-19 and the MIS associated with SARS CoV-2 infection. According to available literature, it has been shown that patients with MIS-C could present in up to 30% as an acute abdomen. To our knowledge, this is the first multinational study assessing the outcomes of AA in children with COVID-19 and MIS-C. We found that a non-negligible percentage of children with COVID-19 or MIS-C presented with the acute abdomen (42 children, 4.2%) and 34 had AA. Interestingly, 4 children underwent surgery without finding surgical reasons for the abdominal pain, suggesting that COVID-19 and MIS-C can both present with acute abdomen and simulate appendicitis. In fact, a recent case series clearly showed that MIS-C can have a similar presentation with acute enteritis or acute abdomen for surgical reasons and the conditions may be misdiagnosed.

There are reports of case series of pediatric patients with AA during COVID-19 and MIS-C which describe the relationship between this infection and delays in diagnosis and management. In our study, we found a low prevalence of diagnosis of AA (4.2%) but higher than other reported series. Gastrointestinal symptoms were present in a third of all COVID-19 patients and present in all patients with the diagnosis of AA. Similar findings were reported by Tullie et al and Meyer et al. However, we did not find that a delay in the diagnosis of appendicitis in these patients was associated with...
TABLE 1. Characteristics of the Study Sample, Overall and by Diagnosis of Appendicitis

| Characteristic                                      | All (n = 1010) | Appendicitis | No (n = 976) | P value |
|-----------------------------------------------------|----------------|--------------|--------------|---------|
|                                                    | n   | %   | n   | %   | n   | %   | n   | %   |         |
| Female sex                                          | 494 | 48.9 | 13  | 38.2 | 481 | 49.3 | 0.205 |         |
| Age group                                           |     |      |     |      |     |      |     |      |         |
| 0 yr                                                | 202 | 20.0 | 0   | 0    | 202 | 20.7 | <0.001 |         |
| 1–2 yr                                              | 229 | 22.7 | 0   | 0    | 229 | 23.5 |         |         |
| 3–5 yr                                              | 146 | 14.5 | 5   | 14.7 | 141 | 14.4 |         |         |
| 6–11 yr                                             | 259 | 25.6 | 22  | 64.7 | 237 | 24.3 |         |         |
| 12–17 yr                                            | 174 | 17.2 | 7   | 20.6 | 167 | 17.1 |         |         |
| Delay between onset and diagnosis                   |     |      |     |      |     |      |     |      | 0.061   |
| 0–1 d                                               | 448 | 44.4 | 20  | 58.8 | 428 | 43.9 |         |         |
| 2–7 d                                               | 469 | 46.4 | 14  | 41.2 | 455 | 46.6 |         |         |
| >7 d                                                | 93  | 9.2  | 0   | 0    | 93  | 9.5  |         |         |
| Likely index case                                    |     |      |     |      |     |      |     |      | 0.220   |
| Yes                                                  | 290 | 28.7 | 14  | 41.2 | 276 | 28.3 |         |         |
| No                                                   | 723 | 71.3 | 14  | 58.8 | 696 | 71.7 |         |         |
| Medical history                                      |     |      |     |      |     |      |     |      |         |
| Known history of BCG vaccine                        | 760 | 75.2 | 34  | 100.0| 726 | 74.4 | 0.001  |         |
| Pre-existing medical conditions                      | 153 | 15.2 | 7   | 20.6 | 146 | 15.2 | 0.196  |         |
| Long-term immunosuppressants at the time of diagnosis| 11  | 1.1  | 0   | 0    | 11  | 1.1  | 1.000  |         |
| Primary or secondary immunodeficiency                | 8   | 0.8  | 0   | 0    | 8   | 0.8  | 1.000  |         |
| Chemotherapy over the last 6 months                  | 8   | 0.8  | 0   | 0    | 8   | 0.8  | 1.000  |         |
| Intensive care during hospital stay                  | 323 | 32.0 | 34  | 100.0| 289 | 29.6 | <0.001 |         |
| Intensive care during hospital stay                  | 47  | 4.7  | 1   | 2.9  | 46  | 4.7  | 1.000  |         |
| Symptoms                                             |     |      |     |      |     |      |     |      |         |
| Pyrexia (≥38.0°C/100.4°F)                            | 692 | 68.5 | 24  | 70.6 | 668 | 68.4 | 0.791  |         |
| Upper respiratory tract infection                    | 468 | 46.3 | 3   | 8.8  | 465 | 47.6 | <0.001 |         |
| Diarrhea and/or vomiting                             | 321 | 31.8 | 5   | 14.7 | 216 | 22.1 | 0.328  |         |
| Lower respiratory tract infection                    | 217 | 21.5 | 5   | 14.7 | 212 | 21.7 | 0.328  |         |
| Headache                                            | 105 | 10.4 | 1   | 2.9  | 104 | 10.7 | 0.246  |         |
| Abdominal surgery                                    | 42  | 4.2  | 33  | 97.1 | 9   | 0.9  | <0.001 |         |
| Chest radiograph                                     |     |      |     |      |     |      |     |      | 0.257   |
| Positive (pneumonia* and/or ARDS†)                   | 93  | 9.2  | 4   | 11.8 | 89  | 9.1  |         |         |
| Not performed                                       | 723 | 71.6 | 27  | 79.4 | 696 | 71.3 |         |         |
| Drug administration                                  |     |      |     |      |     |      |     |      |         |
| Systemic corticosteroids                             | 90  | 8.9  | 2   | 5.9  | 88  | 9.0  | 0.761  |         |
| Intravenous immunoglobulin (IVIG)                   | 60  | 5.9  | 3   | 8.8  | 57  | 5.8  | 0.449  |         |
| Hydroxychloroquine                                  | 9   | 0.9  | 0   | 0    | 9   | 0.9  | 1.000  |         |
| Ostealumir                                          | 8   | 0.8  | 0   | 0    | 8   | 0.8  | 1.000  |         |
| Lopinavir or ritonavir                               | 3   | 0.3  | 0   | 0    | 3   | 0.3  | 1.000  |         |
| Noncorticosteroid immunosuppressants                 | 3   | 0.3  | 0   | 0    | 3   | 0.3  | 1.000  |         |
| Favipiravir                                          | 2   | 0.2  | 0   | 0    | 2   | 0.2  | 1.000  |         |
| Remdesivir                                          | 2   | 0.2  | 0   | 0    | 2   | 0.2  | 1.000  |         |
| MIS-C diagnosis                                     |     |      |     |      |     |      |     |      | 0.300   |
| No                                                   | 941 | 93.2 | 31  | 91.2 | 910 | 93.2 |         |         |
| Yes, with no cardiac or joint involvement           | 33  | 3.3  | 1   | 3.2  | 32  | 3.3  | 1.000  |         |
| Yes, with cardiac involvement§                      | 23  | 2.3  | 0   | 0    | 23  | 2.4  | 1.000  |         |
| Yes, with joint involvement                          | 11  | 1.1  | 0   | 0    | 11  | 1.1  | 1.000  |         |
| Yes, with cardiac and joint involvement§            | 2   | 0.2  | 0   | 0    | 2   | 0.2  | 1.000  |         |
| Tocilizumab administration to treat MIS-C           | 8   | 0.8  | 0   | 0    | 8   | 0.8  | 1.000  |         |
| Current status                                       |     |      |     |      |     |      |     |      | 0.040   |
| All symptoms resolved                                | 989 | 97.9 | 32  | 94.1 | 957 | 98.1 |         |         |
| Dead¶                                                | 8   | 0.8  | 0   | 0    | 8   | 0.8  |         |         |
| Still symptomatic                                    | 7   | 0.7  | 0   | 0    | 7   | 0.7  |         |         |
| Long-term sequelae                                   | 6   | 0.6  | 2   | 5.9  | 4   | 0.4  |         |         |
| Country                                              |     |      |     |      |     |      |     |      | 0.737   |
| Peru                                                 | 391 | 38.7 | 11  | 32.4 | 380 | 38.9 |         |         |
| Costa Rica                                           | 305 | 30.0 | 14  | 41.2 | 291 | 29.6 |         |         |
| Argentina                                            | 260 | 25.7 | 8   | 23.5 | 252 | 25.8 |         |         |
| Colombia                                             | 44  | 4.4  | 1   | 2.9  | 43  | 4.4  |         |         |
| Mexico                                               | 12  | 1.2  | 0   | 0    | 12  | 1.2  |         |         |

*Forty-five cases of interstitial disease, 31 cases of consolidation, 4 cases of pleural effusion and 13 unspecified diagnoses.

†Three cases of interstitial disease, 3 cases of consolidation and 10 unspecified diagnoses.

§Eight mycoplasmas, 4 rhinoviruses, 1 cytomegalovirus, 1 Epstein–Barr virus and 1 unspecified virus.

‡Ten cases of pericardial effusion, 6 cases of coronary dilatation, 5 cases of myocarditis and 4 cases of “other” cardiac involvement.

¶Mean time from symptom onset to death was 14 ± 8 days, ranging from 3 to 27.

ARDS indicates acute respiratory distress syndrome; BCG, bacillus Calmette–Guérin; COVID-19, coronavirus disease 2019; IgG, immunoglobulin G; MIS-C, multisystem inflammatory syndrome; PCR, polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.
TABLE 2. Characteristics of the Study Patients Diagnosed With Appendicitis, Overall and by Presence of Complications

| Characteristic                          | All (n = 34) | Complicated appendicitis | P value |
|----------------------------------------|-------------|-------------------------|---------|
|                                        |             | Yes (n = 14) | No (n = 20) |         |
|                                        | n %         | n %          | n %         |         |
| Female sex                             | 13 38.2     | 5 35.7       | 8 40.0      | 0.800   |
| Age group                              |             |              |             | 0.302   |
| 3–5 yr                                 | 5 14.7      | 2 14.3       | 3 15.0      |         |
| 6–11 yr                                | 22 64.7     | 11 78.6      | 11 55.0     |         |
| 12–17 yr                               | 7 20.6      | 1 7.1        | 6 30.0      |         |
| Pre-existing medical conditions        | 7 20.6      | 1 7.1        | 6 30.0      | 0.198   |
| Intensive care during hospital stay    | 1 2.9       | 0 0.0        | 1 5.0       | 1.000   |
| Symptoms                               |             |              |             | 0.255   |
| Pyrexia (≥38.0°C/≥100.4°F)             | 24 70.6     | 12 85.7      | 12 60.0     | 0.141   |
| Upper respiratory tract infection      | 3 8.8       | 1 7.1        | 2 10.0      | 1.000   |
| Lower respiratory tract infection      | 5 14.7      | 0 0.0        | 5 25.0      | 0.063   |
| Headache                               | 1 2.9       | 0 0.0        | 1 5.0       | 1.000   |
| Acute abdomen                          | 33 97.1     | 14 100.0     | 19 95.0     | 1.000   |
| Chest radiograph                      |             |              |             | 0.097   |
| Negative                               | 3 8.8       | 1 7.1        | 2 10.0      |         |
| Positive (pneumonia and/or ARDS)       | 4 11.8      | 0 0.0        | 4 20.0      |         |
| Not performed                          | 27 79.4     | 13 92.9      | 14 70.0     |         |
| Abdominal ultrasound                   |             |              |             | 0.097   |
| Appendicitis                           | 4 11.8      | 0 0.0        | 4 20.0      |         |
| Mesenteric adenitis                    | 2 5.9       | 0 0.0        | 2 10.0      |         |
| Abdominal distension                   | 1 2.9       | 0 0.0        | 1 5.0       |         |
| Fluid                                  | 1 2.9       | 0 0.0        | 1 5.0       |         |
| Hepatic abscess                        | 1 2.9       | 1 7.1        | 0 0.0       |         |
| Not performed                          | 25 73.5     | 13 92.9      | 12 60.0     |         |
| Abdominal radiograph                   |             |              |             | 0.412   |
| Distended bowel loop                   | 1 2.9       | 1 7.1        | 0 0.0       |         |
| Not performed                          | 33 97.1     | 13 92.9      | 20 100.0    |         |
| Microbiologic findings                 |             |              |             | 0.328   |
| Negative                               | 10 29.4     | 2 14.3       | 8 40.0      |         |
| Escherichia coli                       | 4 11.8      | 2 14.3       | 2 10.0      |         |
| E. coli + Enterobacter cloacae         | 1 2.9       | 0 0.0        | 1 5.0       |         |
| Not detected                           | 19 55.9     | 10 71.4      | 9 45.0      |         |
| White blood cells                      |             |              |             | 0.008   |
| ≤15.0 × 10⁹/L                          | 14 41.2     | 2 14.3       | 12 60.0     |         |
| >15.0 × 10⁹/L                         | 20 58.8     | 12 85.7      | 8 40.0      |         |
| C-reactive protein                     |             |              |             | 0.111   |
| <100 mg/L                              | 10 29.4     | 3 21.4       | 7 35.0      |         |
| ≥100 mg/L                              | 6 17.6      | 5 35.7       | 1 5.0       |         |
| Not detected                           | 18 52.9     | 6 42.9       | 12 60.0     |         |
| Respiratory support                    |             |              |             | 0.008   |
| Oxygen support                         | 5 14.7      | 1 7.1        | 4 20.0      | 0.379   |
| Mechanical ventilation                 | 1 2.9       | 0 0.0        | 1 5.0       | 1.000   |
| Administration of inotropes           | 2 5.9       | 0 0.0        | 2 10.0      | 0.501   |
| Coinfections detected in respiratory samples(s) | 1 2.9       | 0 0.0        | 1 5.0       | 1.000   |
| Drug administration                    |             |              |             | 0.501   |
| Systemic corticosteroids               | 2 5.9       | 0 0.0        | 2 10.0      |         |
| Intravenous immunoglobulin (IVIG)      | 3 8.8       | 0 0.0        | 3 15.0      | 0.251   |
| MIS-C diagnosis (no cardiac/joint involvement) | 3 8.8       | 0 0.0        | 3 15.0      | 0.251   |
| Current status                         |             |              |             | 0.501   |
| All symptoms resolved                  | 32 94.1     | 14 100.0     | 18 90.0     |         |
| Long-term sequelae                     | 2 5.9       | 0 0.0        | 2 10.0      |         |
| Country                                |             |              |             | 0.061   |
| Peru                                   | 11 32.4     | 5 35.7       | 6 30.0      |         |
| Costa Rica                             | 14 41.2     | 3 21.4       | 11 55.0     |         |
| Argentina                              | 8 23.5      | 6 42.9       | 2 10.0      |         |
| Colombia                               | 1 2.9       | 0 0.0        | 1 5.0       |         |

ARDS indicates acute respiratory distress syndrome; MIS-C, multisystem inflammatory syndrome.

A higher incidence of complications (41.1%). Complications rate in Israel were reported in 22% associated with parental concern in contracting COVID-19 in the hospital, inadequate clinical evaluation and settings for clinical evaluation (telemedicine), and the lack of healthcare worker’s instructions in regard to the time to seek medical advice.

About the management of AA, 81% of our patients underwent surgery as the preferred modality of treatment; this differs from the practice reported in some hospitals that suggest conservative management of patients with the diagnosis of SARS-CoV-2 and acute abdomen. Some centers have used more conservative approaches for uncomplicated cases of AA in patients with
COVID-19, including home care and nonoperative management with antibiotics.23

Reports of patients with AA and MIS-C has been described as part of the clinical features of the inflammatory syndrome.4,22,24 In our study, we found 4 patients with MIS-C and a clinical diagnosis of the acute abdomen who were treated with nonoperative management with no overall complications, suggesting that appendicitis was not the cause of abdominal pain. Interestingly, we also found 4 children who underwent but had not intra-operative findings of appendicitis, suggesting that the inflammatory response was the cause of pain rather than appendicitis. Two of these patients had mesenteric adenitis and were eventually diagnosed with MIS-C, supporting the evidence that AA may be one of the presenting symptoms of MIS-C and the difficulty in distinguishing the 2 conditions.

Our study has some limitations to address. We could not determine the time from diagnosis and the surgical management, limiting the result of the association between delayed treatment and complications. The small number of patients with AA and COVID-19 could be less than the real number of patients with these 2 conditions because a large proportion of children have not been tested with PCR test on nasopharyngeal test due to unavailability of them during certain periods of the pandemic, as may have happened in low-to-middle income countries settings worldwide. Despite these limitations, this study provides the largest overview of AA in children with COVID-19 and MIS-C to date.

In conclusion, our study found that both MIS-C and COVID-19 can present acute abdomen, with or without appendicitis. Further studies are needed to better recognize these cohorts of children and optimize diagnosis and both conservative or surgical treatment.

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### TABLE 3. Multivariable Logistic Regression Analysis of Appendicitis Diagnosis (n = 1010)

| Characteristic                                      | Odds ratio | P value | Lower bound | Upper bound |
|-----------------------------------------------------|------------|---------|-------------|-------------|
| Sex                                                  |            |         |             |             |
| Male                                                 | Ref.       |         |             |             |
| Female                                               | 0.60       | 0.067   | 0.35        | 1.04        |
| Age group                                            |            |         |             |             |
| ≤5 yr                                                | Ref.       |         |             |             |
| >5 yr                                                | 11.71      | <0.001  | 4.17        | 32.83       |
| Hospitalization                                      |            |         |             |             |
| No                                                   | Ref.       |         |             |             |
| Yes, without intensive care                          | 5.07       | 0.024   | 1.24        | 20.71       |
| Yes, with intensive care                             | 1.29       | 0.749   | 0.27        | 6.15        |
| Pyrexia (≥38.0/≥100.4°C/F)                           |            |         |             |             |
| No                                                   | Ref.       |         |             |             |
| Yes                                                  | 2.55       | 0.289   | 0.45        | 14.41       |
| Upper respiratory tract infection                    |            |         |             |             |
| No                                                   | Ref.       |         |             |             |
| Yes                                                  | 0.13       | 0.019   | 0.02        | 0.71        |
| Lower respiratory tract infection                    |            |         |             |             |
| No                                                   | Ref.       |         |             |             |
| Yes                                                  | 0.29       | 0.299   | 0.03        | 3.00        |
| Headache                                             |            |         |             |             |
| No                                                   | Ref.       |         |             |             |
| Yes                                                  | 0.15       | 0.177   | 0.01        | 2.36        |
| Chest radiograph abnormalities (pneumonia and/or ARDS)|            |         |             |             |
| No                                                   | Ref.       |         |             |             |
| Yes                                                  | 2.13       | 0.323   | 0.48        | 9.53        |
| Oxygen support, mechanical ventilation and/or CPAP    |            |         |             |             |
| No                                                   | Ref.       |         |             |             |
| Yes                                                  | 0.98       | 0.974   | 0.27        | 3.59        |
| Administration of systemic corticosteroids            |            |         |             |             |
| No                                                   | Ref.       |         |             |             |
| Yes                                                  | 0.57       | 0.343   | 0.18        | 1.81        |
| MIS-C diagnosis                                      |            |         |             |             |
| No                                                   | Ref.       |         |             |             |
| Yes                                                  | 0.57       | 0.252   | 0.22        | 1.49        |

Covariates that predict the outcome perfectly (immunosuppressants/immunodeficiency/chemo and diarrhea/vomiting) were excluded from the model.

ARDS indicates acute respiratory distress syndrome; CPAP, continuous positive airway pressure.
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