SARS-CoV-2 Sequelae and Postdischarge Health Care Visits Over 5 Months Follow-up Among Children Hospitalized for COVID-19 or MIS-C

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Abstract: Although post-acute sequelae of COVID-19 among adult survivors has gained significant attention, data in children hospitalized for severe acute respiratory syndrome coronavirus 2 is limited. This study of commercially insured US children shows that those hospitalized with COVID-19 or multisystem inflammatory syndrome in children have a substantial burden of severe acute respiratory syndrome coronavirus 2 sequelae and associated health care visits postdischarge.

Key Words: COVID-19, long COVID, multisystem inflammatory syndrome in children, pediatrics, persistent symptoms, post-acute sequelae of COVID-19, severe acute respiratory syndrome coronavirus 2 sequelae

Post-acute sequelae of COVID-19 among adult survivors has gained significant attention.1 While evidence has also started emerging in pediatric patients they have been derived largely from either single institutions, self-reports, or short follow-up durations and/or extremely small sample sizes.2–10 Furthermore, reports of persistent symptoms or sequelae post-severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children severe enough to require hospitalization is limited, particularly in the United States.11 The limited data available to date from ex-US settings suggests that children hospitalized for COVID-19 have a higher rate of post-acute sequelae of COVID-19 than nonhospitalized children.10 In this study, we used de-identified administrative claims data for commercially insured children across the United States to describe SARS-CoV-2 sequelae and associated health care visits over 5 months postdischarge among children hospitalized for COVID-19. Since multisystem inflammatory syndrome in children (MIS-C) has emerged as a serious complication of infection with SARS-CoV-2, we separately examined children hospitalized with MIS-C.

Methods

We used de-identified administrative claims data available from Optum Labs for approximately 7 million commercially insured children 0–17 years of age across all states in the United States.11 The data contain medical (emergency, inpatient, outpatient) and pharmacy claims submitted by health care providers for third party reimbursement after delivery of services to insurance enrollees and have been used in prior studies of COVID-19.12–14 From this data source, we identified 2 mutually exclusive groups of children 0–17 years old hospitalized with a primary diagnosis of COVID-19 (ie, COVID-19 group) or a primary or secondary diagnosis of MIS-C (ie, MIS-C group) between March 1, 2020, and February 28, 2021 (see Figure, Supplemental Digital Content 1, http://links.lww.com/INF/E812). Since the latest complete claims data at the time of the analysis were until July 31, 2021, we were able to conduct a 5-month postdischarge follow-up. Hence, both groups were required to have continuous enrollment in the 5 months postdischarge to assess diagnoses for sequelae of SARS-CoV-2 (as defined in Table, Supplemental Digital Content 2, http://links.lww.com/INF/E812) and 5-month preadmission to assess whether sequelae were new diagnoses (ie, not observed in the 5 months to 14-day period before admission). Health care visits, overall and SARS-CoV-2 sequelae related, were also examined. Health care visits included inpatient, emergency room and outpatient (physician and outpatient hospital) visits and were deemed as SARS-CoV-2 sequelae related if the medical claim for that visit had at least 1 diagnosis for sequelae of SARS-CoV-2 (see Table, Supplemental Digital Content 2, http://links.lww.com/INF/E812). Sample characteristics including demographics, hospital length of stay and risk factors for severe COVID-19 (as defined in Table, Supplemental Digital Content 3, http://links.lww.com/INF/E812) were described. This study was deemed exempt from institutional board review given the use of a de-identified secondary dataset. All analyses were conducted using Python v3.6.15

Results

Out of approximately 7 million insured children in our dataset, 544 children were discharged after a hospitalization with COVID-19 and 219 children were discharged after a hospitalization with MIS-C (see Figure, Supplemental Digital Content 1, http://links.lww.com/INF/E812). After requiring continuous insurance enrollment in the 5 months preadmission and 5 months postdischarge, the final study sample included 372 children hospitalized with COVID-19 (mean age: 11.1, 47.3% male) and 183 children hospitalized with MIS-C (mean age: 9.1, 71.6% male) (Table 1). Children hospitalized with COVID-19 were more likely to be 12–17 years old, whereas those hospitalized with MIS-C were more likely to be 5–11 years old. Nearly half (45.4%) of the COVID-19 group and one-quarter (25.1%) of the MIS-C group had evidence of a risk factor for severe COVID-19 illness. The median length of stay was 4 days in both groups (Table 1). The median income in

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the zip-code of residence was $58,580 in both groups (see Table, Supplemental Digital Content 4, http://links.lww.com/INF/E812). Table (Supplemental Digital Content 4, http://links.lww.com/INF/E812) also shows the characteristics of the overall population of commercially insured children from which our study groups were derived for comparison. For instance, the MIS-C group was more likely to be 5–11 years old, male and reside in the Midwest compared with the overall population. Over 90% of children in both groups had at least 1 SARS-CoV-2 sequelae related health care visits with a median of 6 visits in the 5 months postdischarge (Table 1). Nearly one-quarter (23.7%) of the children hospitalized with COVID-19 had 15 or more visits related to SARS-CoV-2 sequelae over the 5-month follow-up. The median time from discharge to the last visit related to SARS-CoV-2 sequelae was 18.4 weeks and 15.4 weeks in the COVID-19 and MIS-C group, respectively; at least 25% of the children hospitalized with COVID-19 or MIS-C have a substantial burden of SARS-CoV-2 sequelae and associated health care visits postdischarge. Over one-quarter of the children in both groups continued to have a SARS-CoV-2 sequelae related health care visit in month 5 after discharge. Among the COVID-19 group, 20.4% were readmitted and 18.0% had an emergency room visit related to SARS-CoV-2 sequelae in the 5 months after their index hospitalization; corresponding rates were lower in the MIS-C group (Table 1). The overwhelming majority of postdischarge outpatient visits in both groups were related to SARS-CoV-2 sequelae. The median number of outpatient visits in the 5-month postdischarge period was substantially higher than in the 5-month preadmission period in both groups (COVID-19: 9.5 vs. 4.0; MIS-C: 6.0 vs. 2.0) (data not shown).

As shown in Figure 1, the type of SARS-CoV-2 sequelae occurred at different rates across the 2 groups and were less likely to be new diagnoses in the COVID-19 versus MIS-C group. For example, the overall rate of cardiovascular-related sequelae in the COVID-19 group was 22.6% with three-quarters newly diagnosed while the rate in the MIS-C group was 49.7% with nearly all newly diagnosed. In addition, the subtypes of these sequelae were different between the 2 groups (see Table, Supplemental Digital Content 5, http://links.lww.com/INF/E812). For instance, the rates of peri-/myocarditis (16.9% vs. 4.6%) and cardiac arrhythmias (19.1% vs. 8.1%) were higher in the MIS-C versus COVID-19 group. Median time to the last visit during the follow-up period for each sequelae also varied considerably (see Table, Supplemental Digital Content 5, http://links.lww.com/INF/E812).

**DISCUSSION**

This study of commercially insured US children shows that those hospitalized with COVID-19 or MIS-C have a substantial burden of SARS-CoV-2 sequelae and associated health care visits postdischarge. Over one-quarter of the children in both groups continued to have a SARS-CoV-2 sequelae related health care visit in month 5 after discharge, thus suggesting that recovery may take months. The reasons for follow up visits differed between patients with acute COVID-19 and MIS-C; patients with COVID-19 were more likely to have follow up visits for respiratory, neurologic and mental health reasons while those with MIS-C were more likely to have visits for cardiovascular, gastrointestinal and inflammatory conditions.

It is worth noting that our study sample was drawn from a population of commercially insured children captured in the data source that represent approximately 20% of all US children with private insurance. Unlike prior studies on long COVID in children that have relied primarily on self-reports by patients and/or parents, the strength of our study is that it relied on diagnosis codes

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**TABLE 1.** Patient Characteristics and Postdischarge Health Care Visits Over 5 Months of Follow-up Among Children Hospitalized With COVID-19 and MIS-C

| Patient characteristics | Children Hospitalized With COVID-19 (N = 372) | Children Hospitalized With MIS-C (N = 183) |
|-------------------------|---------------------------------------------|---------------------------------------------|
| Age, mean (SD)          | 11.10 (5.82)                                 | 9.12 (4.62)                                 |
| 0–4 yr                  | 82 (22.0%)                                   | 32 (17.5%)                                  |
| 5–11 yr                 | 71 (19.1%)                                   | 92 (50.3%)                                  |
| 12–17 yr                | 219 (58.9%)                                  | 59 (32.2%)                                  |
| Gender                  |                                             |                                             |
| Female                  | 196 (52.7%)                                  | 52 (38.4%)                                  |
| Male                    | 176 (47.3%)                                  | 131 (71.6%)                                 |
| 1 or more CDC risk factors for severe COVID-19 | 169 (45.4%) | 46 (25.1%) |
| Length of stay, median (IQR) (d) | 4.00 (2.0–7.0) | 4.00 (3.0–6.0) |
| Postdischarge healthcare visits over 5 mo | | |
| Children with SARS-CoV-2 sequelae related health care visit(s) | 337 (90.6%) | 180 (94.8%) |
| No. SARS-CoV-2 sequelae related healthcare visits, median (IQR) | 6.00 (3.0–15.0) | 6.00 (4.0–8.0) |
| 0                       | 35 (9.4%)                                    | 3 (1.6%)                                    |
| 1–4                     | 147 (39.5%)                                  | 87 (47.5%)                                  |
| 5–9                     | 60 (16.1%)                                   | 58 (31.7%)                                  |
| 10–14                   | 42 (11.3%)                                   | 26 (14.2%)                                  |
| 15+                     | 88 (23.7%)                                   | 9 (5.0%)                                    |
| Weeks from discharge to the last visit related to SARS-CoV-2 sequelae, median (IQR) | 18.4 (11.4–20.7) | 15.4 (8.1–18.9) |
| Children with any hospital readmission(s) | 79 (21.2%) | 4 (2.2%) |
| Any readmission related to SARS-CoV-2 sequelae | 76 (20.4%) | 4 (2.2%) |
| Children with any postdischarge ER visit(s) | 75 (20.2%) | 26 (14.2%) |
| Children with SARS-CoV-2 sequelae related postdischarge ER visit(s) | 67 (18.0%) | 24 (13.1%) |
| Children with any postdischarge outpatient visit(s) | 359 (96.5%) | 182 (99.5%) |
| Children with SARS-CoV-2 sequelae related postdischarge outpatient visit(s) | 334 (89.8%) | 180 (98.4%) |
| Count of any postdischarge outpatient visit(s) per patient, median (IQR) | 9.5 (4.0–21.0) | 6.0 (4.0–9.0) |
| Count of postdischarge outpatient visits per patient related to SARS-CoV-2 sequelae, median (IQR) | 6.0 (3.0–14.0) | 6.0 (4.0–8.0) |

CDC indicates Centers for Disease Control and Prevention; ER, emergency room; IQR, interquartile range; SD, standard deviation.
entered by health care providers in medical claims. However, given that claims data are used primarily for billing purposes they may have resulted in our study underreporting SARS-CoV-2 sequelae, especially for milder symptoms not affecting reimbursement. Also, claims data do not permit an accurate assessment of whether there was worsening of symptoms or conditions that the children already had prior to admission. For example, while several of the hospitalized children also had mental health diagnoses preadmission in our study, it is possible that they experienced worsening of the symptoms postdischarge. At the same time, we were also unable to assess whether the mental health diagnoses observed postdischarge were truly associated with being hospitalized with COVID-19 or

FIGURE 1. Type of SARS-CoV-2 sequelae over 5 months postdischarge among children hospitalized with COVID-19 and MIS-C.
reflected the negative impact that the pandemic itself has had across children and adolescents. However, other studies have also shown depression, anxiety and other mood symptoms to be higher among postdischarge children with COVID versus healthy controls.\(^\text{10,17}\)

While our study did not include a control group of patients without COVID-19, our study did assess and report separately whether or not each of the sequelae were new diagnoses identified postdischarge (ie, not observed for the patient in the 5 months to 14-day period before the hospital admission). Even for the patients who had diagnoses for a given sequela both before and after the hospitalization, it is possible that COVID-19 exacerbated the severity or persistence of the symptom post-hospitalization; however, we are unable to assess this in medical claims data. Hence, for comprehensiveness our study also reported overall rates of SARS-CoV-2 sequelae (including incident and prevalent diagnoses). Finally, although we found that over 90% of previously hospitalized patients had evidence of sequela-related healthcare visits, these findings should be tempered by the fact that hospitalization for COVID-19 remains relatively rare among children in general, which is also the case for our study population of approximately 7 million children.

In summary, this study provides important new data on the long-term burden of severe COVID-19 in US children drawing from a geographically and sociodemographically diverse population followed for 5 months. As the number of pediatric hospitalizations for COVID-19 continues to increase in the United States our results point to the ongoing need for monitoring and mitigating its long-term burden in children.

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