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Acute pancreatitis in children hospitalized with COVID-19

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Background: Limited data exists on the association or prevalence of pancreatitis in children with COVID-19.

Methods: This is a retrospective study of pediatric patients admitted to a large health system in New York (Northwell Health System) from March 1, 2020–June 1, 2020 during the COVID-19 pandemic.

Results: 8159 pediatric patients were admitted to our healthcare system during the study period, of which 112 were diagnosed with COVID-19 (1.37%). Thirteen were diagnosed with pancreatitis for a point prevalence of 0.16% (13/8159) for all patients admitted. Of the thirteen patients admitted with pancreatitis, two patients were COVID-19 positive for a point prevalence of 1.8% (2/112) among COVID-19 patients compared to 0.14% (11/8047) in the non-COVID-19 population.

Conclusions: This study shows that pancreatitis can occur in pediatric patients with COVID-19 and may be more common in the COVID-19 population.© 2020 IAP and EPC. Published by Elsevier B.V. All rights reserved.

Introduction

A recent study has shown adult patients with COVID-19 can present with acute pancreatitis [1]. In that study, idiopathic pancreatitis was statistically the most common etiology in COVID-19 patients and thus implicates SARS-CoV-2 in a causative role for acute pancreatitis. Although various case reports exist [2]–[3], no study to date has examined the association or prevalence of pancreatitis in children with COVID-19. Our study aimed to identify the point prevalence of acute pancreatitis within pediatric patients hospitalized in our large healthcare system in New York between March and June 2020, as well as describe the characteristics of these patients.

Methods

This is a retrospective study of patients less than 18 years old admitted to twelve hospitals within a large health system in New York (Northwell Health System) from March 1, 2020–June 1, 2020 during the COVID-19 pandemic. Institutional Review Board approval was obtained for this study.

Charts for all pediatric (age <18) admissions were searched for diagnostic lipase levels, cross sectional imaging (CT/MRI) evidence of pancreatitis, or charts ICD10 coded for pancreatitis. Charts were manually reviewed to ensure the correct diagnosis. Patients were included if they met the INSPIRE criteria; the accepted standard definition of pediatric pancreatitis [4], which requires two of the three following: elevated amylase or lipase >3 times the upper limit of normal, imaging showing characteristic findings of pancreatitis, and characteristic abdominal pain. Each chart was manually abstracted for etiologies of pancreatitis that have been previously described in pediatric patients [4–6]. Severity of pancreatitis was classified using the NASPGHAN algorithm [7]. SAS, Version 9.4 (SAS Institute, Cary, NC) was used to perform all analysis.

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Table 1
Patient characteristics and outcomes.

| Patient Characteristics | Patient 1 | Patient 2 | Patient 3 | Patient 4 | Patient 5 | Patient 6 | Patient 7 | Patient 8 | Patient 9 | Patient 10 | Patient 11 | Patient 12 | Patient 13 |
|-------------------------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| Age (years)             | 17        | 17        | 14        | 10        | 8         | 4         | 4         | 14        | 2         | 15        | 15        | 10        | 16        |
| Sex                     | M         | M         | M         | F         | F         | F         | F         | F         | F         | M         | F         | M         | M         |
| Race                    | Other     | Other     | White     | Other     | Hispanic  | Hispanic  | Black     | Black     | Black     | White     | Black     | Black     | Hispanic  |
| Pancreatitis Characteristics |          |           |           |           |           |           |           |           |           |           |           |           |           |
| Etiology                | Idiopathic| Idiopathic| Gallstone | Idiopathic| Idiopathic| Idiopathic| Idiopathic| Idiopathic| Drug Induced| Idiopathic| Idiopathic| Idiopathic|
| Diagnosis               | Lipase, Abdominal Pain Moderate | Lipase, Abdominal Pain Moderate | Lipase, Abdominal Pain Severe | Lipase, Abdominal Pain Moderate | Lipase, Abdominal Pain Severe | Lipase, Abdominal Pain Severe | Lipase, Abdominal Pain Mild | Lipase, Abdominal Pain Severe | Lipase, Abdominal Pain Mild | Lipase, Abdominal Pain Mild | Lipase, Abdominal Pain Mild | Lipase, Abdominal Pain Severe |
| NASPGHAN acute pancreatitis classification | Mild | Mild | Moderate | Mild | Moderate | Severe | Mild | Mild | Severe | Mild | Mild | Mild |
| Blood Cytology (Normal Range) | 16.68 | 16.72 | 7.93 | 7.14 | 6.2 | 9.26 | 12.02 | 14.9 | 8.11 | 12.64 | 1.81 | 11.36 | 91.49 |
| White Count k/UL | | | | | | | | | | | | | |
| 1-3yr (6-17) | 16.68 | 16.72 | 7.93 | 7.14 | 6.2 | 9.26 | 12.02 | 14.9 | 8.11 | 12.64 | 1.81 | 11.36 | 91.49 |
| 3-5yr (5.5-15.5) | | | | | | | | | | | | | |
| 6-10yr (4.5-14.5) | | | | | | | | | | | | | |
| 10-15yr (4.5-13.5) | | | | | | | | | | | | | |
| 15-20yr (4.5-12.5) | | | | | | | | | | | | | |
| Lipase (U/L) (12.70) | 470 | 2190 | 221.3 | 1078.4 | 2234.2 | 288.1 | 843.6 | >3000 | 888 | 1246.2 | 420 | 365.7 | 233.3 |
| LDH (U/L) (140-280) | 264 | 354 | 191 | 23 | 64 | 18 | 804 | 41 | 23 | 75 | 145 | | |
| AST (U/L) (5-40) | 11 | 30 | 7 | 16 | 5 | 10 | 14 | 13 | 33 | 18 | 11 | 14 | 45 |
| BUN (mg/dL) (7-20) | 5 | 97 | 7 | 16 | 5 | 10 | 14 | 13 | 33 | 18 | 11 | 14 | 45 |
| COVID-19 | Negative | Negative | Negative | Negative | Negative | Negative | Negative | Negative | Negative | Negative | Negative | Positive | Positive |
| Outcomes | Length of stay (days) | 6 | 3 | 4 | 13 | 3 | 3 | 16 | 2 | 29 | 9 | 2 | 5 | 25 |
| Mortality (yes/no) | No | No | No | Yes | No | No | No | No | Yes | No | No | No | No |
| Pancreas Necrosis (yes/no) | No | No | No | Yes | No | No | No | No | Yes | No | No | No | No |
| Mechanical Ventilation (yes/no) | Yes | No | Yes | No | No | Yes | No | Yes | No | Yes | No | No | Yes |

a Patient had Walker-Warburg congenital muscular dystrophy and congenital hydrocephalus with acute on chronic respiratory failure.
b Patient had history of hypoxic ischemic encephalopathy, adrenal insufficiency, chronic lymphocytic leukemia, seizure disorder.
c Other race was selected if patient did not identify as White, Black, or Hispanic/Latin.
Results

8159 pediatric patients were admitted to our healthcare system during the study period, of which 112 were diagnosed with COVID-19 (1.37%). All patients admitted during the study period were tested for COVID-19. 347 were tested for lipase in the non-COVID group (4.3%) and 38 were tested for lipase in the COVID group (33.9%). Thirteen patients were diagnosed with pancreatitis for a point prevalence of 0.16% (13/8159) for all patients admitted. Patient and clinical characteristics can be found in Table 1. Of the thirteen patients admitted with pancreatitis, two patients were COVID-19 positive for a point prevalence of 1.8% (2/112) among COVID-19 patients compared to 0.14% (11/8047) in the non-COVID-19 population.

The first COVID-19 patient was diagnosed with pancreatitis due to an elevated lipase level and epigastric abdominal pain. No etiology was identified and thus was classified as idiopathic. This patient required mechanical ventilation due to pulmonary involvement of COVID (computed tomography with lower lung ground glass opacities). He was intubated and extubated prior to the pancreatitis diagnosis, and his symptoms improved with supportive care. The second COVID-19 patient was a 10-year-old female who presented with fever, epigastric abdominal pain, nausea and vomiting. Her lipase was elevated to greater than three times the upper limit of normal, leading to a diagnosis of pancreatitis. Her COVID-19 IgG was positive. She was ultimately diagnosed with post-COVID Multisystem Inflammatory Syndrome in Children (MIS-C). Her symptoms improved with supportive care.

In this study a causative etiology could not be found in the majority (77%, 10/13) of patients. Idiopathic pancreatitis was diagnosed in both COVID-19 patients and in eight non-COVID-19 patients (100% vs 80%). Outcomes regarding length of stay, development of pancreas necrosis, need for mechanical ventilation, and mortality can be found in Table 1. Two patients died during the study period and both were COVID-19 negative (18% vs 0%). Both patients had significant underlying comorbidities. Four patients without COVID-19 and one with COVID-19 required mechanical ventilation during their hospital stay (36% vs 50%). One patient without COVID-19 developed pancreatic necrosis (9% vs 0%).

Discussion

In summary, our study shows that pancreatitis can occur in pediatric patients with COVID-19 and may be more common in the COVID-19 population. The mechanism for the development of pancreatitis in this population is unclear; perhaps due to a direct cytopathic effect from the COVID-19 virus, as has been implicated in other viral causes of pediatric pancreatitis [6], or as a result of the ischemic and systemic inflammatory states that can occur with MIS-C [8]. In order to better understand the role of COVID-19 in the development of pancreatitis, these potential mechanisms warrant further investigation. However, this study highlights the possible association of pancreatitis in pediatric COVID-19 patients, and this diagnosis should be entertained in patients presenting with COVID-19 and abdominal pain.

Authors contributions

Conception and design (AJT). Analysis and interpretation of the data (KS, YL, DW, KLR, AJT). Drafting of the article (KS, YL, DW, KLR, AJT). Critical revision of the article for important intellectual content (KS, YL, DW, KLR, AJT). Final approval of the article (KS, YL, DW, KLR, AJT).

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References

[1] Inamdar S, Benias PC, Liu Y, Sejpal DV, Satapathy SK, Trindade AJ. Prevalence, risk factors, and outcomes of hospitalized patients with COVID-19 presenting as acute pancreatitis. Gastroenterology 2020;159:2266–8. https://doi.org/10.1053/j.gastro.2020.08.044.
[2] Alloway BC, Yaeger SK, Mazzacaro RJ, Villalobos T, Hardy SG. Suspected case of COVID-19 associated pancreatitis in a child. Radiology Case Reports 2020;15(8):1309–12.
[3] Stevens JP, Brownell JN, Freeman AJ, Bashaw H. COVID-19-associated multi-system inflammatory syndrome in children presenting as acute pancreatitis. J Pediatr Gastroenterol Nutr DOI: 10.1097/mpg.0000000000003260.
[4] Morinville VD, Husain SZ, Bai H, Barth B, Ahlors R, Durham PR, Freedman SD, et al. Definitions of pediatric pancreatitis and survey of current clinical practices: report from INSPPFIRE (international study group of pediatric pancreatitis: in search for a cure). J Pediatr Gastroenterol Nutr 2012;55(3):261.
[5] UC A, Alvey, Husian Sohail Z. Pancreatitis in children. Gastroenterology 2019;156(7):1969–78. https://doi.org/10.1053/j.gastro.2018.12.043.
[6] Pohl JF, UC A. Pediatric pancreatitis. Curr Opin Gastroenterol 2015;31(5):380–6.
[7] Abu-El-Haija M, Kumar S, Szabo F, Werlin S, Conwell D, Banks P, et al. Classification of acute pancreatitis in the pediatric population: clinical report from the NASPGHAN pancreas committee. J Pediatr Gastroenterol Nutr 2017;64(6):984–90.
[8] Ahmed Mubbasheer, Advani Shailesh, Moreira Axel, Zoretic Sarah, Martinez John, Chorath Kevin, Acosta Sebastian, et al. Multisystem inflammatory syndrome in children: a systematic review. EClinicalMedicine 2020;26:100527.