Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Impact of Coronavirus Disease 2019 on the Pediatric Population with Aerodigestive Disease

Beate Beinvogl, MD, MPH, Alexandra Cohen, BA, Courtney DiFilippo, BS, Madeline Kane, BS, Samuel Nurko, MD, MPH, and Rachel Rosen, MD, MPH

Objective To determine the impact of the coronavirus disease 2019 (COVID-19) quarantine on baseline health, medication use, health anxiety, and healthcare use in pediatric patients with aerodigestive disease and to evaluate for associations of commonly prescribed medications with the risk of COVID-19 illness.

Study design Prospective study of patients presenting in person to pediatric neurogastroenterology clinics between July 2020 and March 2021.

Results Of 202 recruited patients, 71.3% were seen in the aerodigestive diseases center and 28.7% in the functional abdominal pain (FAP)/motility clinic. Of all patients, 25.1% reported improved overall health during quarantine; patients with aerodigestive disease (35.3%) reported higher rates of improved overall health compared with patients with FAP/motility disorders (3.6%, $P = .0001$). Patients with aerodigestive disease had fewer airway symptoms ($P < .05$) and less medication use during quarantine (inhaled steroids, $P < .05$ and albuterol, $P < .05$). Despite objective improvement, there was significant health-related anxiety, with greater anxiety scores reported during and at the end of quarantine ($P < .05$), with no difference between patient groups ($P > .11$). Patients continued to access healthcare during quarantine. In total, 28.7% of patients were seen in the emergency department (patients with FAP more than patients with aerodigestive disease, $P = .02$), and 19.8% were hospitalized. COVID-19 testing was performed in 58.4% of patients and 2.0% (n = 4) of the entire cohort tested positive.

Conclusions Patients with aerodigestive disease show improvement of airway symptoms and decreased use of medications during the pandemic, despite increased health-related anxiety. Despite complexities of accessing care due to the widespread lockdown, all patient groups continued to access healthcare. *(J Pediatr 2022;243:14-20)*.

In response to the emergence of the coronavirus disease 2019 (COVID-19) pandemic in early 2020, large areas of the US were placed under lockdown to slow down and prevent further spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) virus. In addition to its major impact on daily life and risks to health, this also affected access to care for patients both due to decreased availability and fear of exposure to the virus.[1-3] Pediatric patients with aerodigestive disorders were felt to be among the greatest risk of severe disease from the virus because of the risk of infection on lung health,[4] but no publications exist studying exactly how these patients have been affected.

The goal of this study was to better understand how the COVID-19 pandemic quarantine impacted patients with aerodigestive disease and to better understand their risks for COVID-19. The aims of this study were to understand the impact of the pandemic on baseline health and health-related anxiety in patients with aerodigestive disease; to determine the impact of COVID-19 on healthcare use; and to determine whether any commonly prescribed gastrointestinal medications were associated with testing positive for COVID-19.

Methods

This is a prospective questionnaire study of consecutive patients seen in-person in the aerodigestive, FAP, or motility clinic at a tertiary care hospital during the SARS-CoV2 pandemic between July 2020, after the clinics reopened, and March 2021. All patients presenting for in-person outpatient appointments to all 3 clinics were given a questionnaire to reduce risk of bias. Patients presenting for virtual visits were excluded from the analysis because the original goal of the questionnaire

COVID-19	Coronavirus disease 2019
FAP	Functional abdominal pain
PPI	Proton pump inhibitor
SARS-CoV2	Severe acute respiratory syndrome coronavirus 2

From the Aerodigestive Center and Center for Motility and Functional Gastrointestinal Disorders, Division of Pediatric Gastroenterology, Boston Children's Hospital, Boston, MA

Funded by the National Institutes of Health (NIH) R01 DK097112 (to R.R.). The authors declare no conflicts of interest.

Poster presentation at *Digestive Disease Week (DDW)* Virtual Conference, May 21-23, 2021; Poster presentation at the *North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN)* Virtual Conference, December 12-18, 2021.

https://doi.org/10.1016/j.jpeds.2021.12.022

Table I. Patient characteristics (n = 202)

Characteristics	Total N (%)	Patients with aerodigestive disease, n (%)	Patients with FAP/motility disease, n (%)	*P* value*
Number of patients	202	144 (71.3)	58 (28.7)	–
Sex (% female)	98 (48.5)	**54 (37.5)**	**44 (75.9)**	<.01
Age, y, mean ± SD	6.5 ± 6.5	**4 ± 4.8**	**12.9 ± 6**	<.01
Age, y, range	0.1-25	0.2-22	0.1-25	
Age, y, median	3.5	2	15	
Ethnicity				
White	180 (89.1)	127 (93.1)	53 (91.4)	.35
Black	17 (8.4)	14 (9.7)	3 (5.2)	.22
Hispanic	15 (7.4)	9 (6.3)	6 (10.3)	.24
Asian	13 (6.4)	10 (6.9)	3 (5.2)	.46
Other	12 (5.9)	10 (6.9)	2 (3.4)	.56
Community				
Suburban	102 (50.5)	70 (48.6)	32 (55.2)	.44
Urban	41 (20.3)	30 (20.8)	11 (19.0)	.85
Rural	38 (18.8)	28 (19.4)	10 (17.2)	.84
Comorbidities				
Neurologic	58 (28.7)	39 (27.1)	19 (32.8)	.26
Cardiac	46 (22.8)	35 (24.3)	11 (18.9)	.27
Genetic syndrome	45 (22.3)	28 (19.4)	17 (29.3)	.09
Aspiration	90 (44.6)	**83 (57.6)**	**7 (12.1)**	<.01
Feeding tube present	86 (42.6)	**70 (34.7)**	**16 (7.9)**	**.01**
Household members				
Other children <18 y	127 (62.8)	92 (63.9)	35 (60.3)	.34
Number of siblings	1.6 ± 0.8 (1-5)	1.6 ± 0.8	1.5 ± 0.8	.92
Number of adults	2.1 ± 0.8 (1-7)	2.1 ± 0.7	2.1 ± 0.9	.12
Essential workers				
Younger parent	52 (25.7)	33 (22.9)	19 (32.8)	.09
Older parent	73 (36.1)	49 (34.0)	24 (41.4)	.17
Equal quarantining of parents (if >2)	103 (51.0)	79 (54.9)	24 (41.4)	.05
Subjects spending time in >1 home	12 (5.9)	9 (6.3)	3 (5.2)	.52
Child care				
In-home, any member	35 (12.3)	29 (20.1)	6 (10.3)	.06
Out of home, any member	24 (11.9)	19 (13.2)	5 (8.6%)	.22
Grocery shopping in-store by any family member	151 (74.8%)	105 (72.9%)	46 (79.3)	.42
Change in overall health during quarantine (n = 175)				
Unchanged	104 (59.4)	68 (57.1)	36 (64.3)	.41
Improved	44 (25.1)	**42 (35.3)**	**2 (3.6)**	<.01
Worse	27 (15.4)	**9 (7.5)**	**18 (32.1)**	<.01

Statistically significant values ($P < .05$) are shown in bold.
*χ^2 for proportions, *t* test for means.

was to assess for parental concerns related to in-person healthcare utilization and the feasibility of in-person clinics.

Patients/families were surveyed about demographics, comorbidities, baseline airway and gastrointestinal symptoms, medication use, risk factors for exposure to and testing for SARS-CoV-2, healthcare use, and health-related anxiety (rated on a Likert scale 0-10, with 0 representing no and 10 representing most severe anxiety) before and during the pandemic. Patients were considered positive for COVID-19 if they tested positive by polymerase chain reaction testing. If a question was not answered, it was considered negative. This study was part of a prospective quality initiative whose aim was to determine healthcare use to understand clinical needs.

Statistical Analyses

Values are expressed as mean and SD. Means were compared using *t* tests. Proportions were compared using χ^2 analyses or the McNemar test for related samples. Statistical analysis was performed using SPSS (SPSS Inc), version 27.

Results

Of the 202 subjects participating in this study, 144 (71.3%) were seen in the aerodigestive diseases center, 37 (18.3%) in the motility clinic, and 21 (10.4%) in the FAP clinic. Surveys were completed by parents in 91% of cases and by patients themselves in 9%, a mean of 7.7 ± 1.6 months (range 4-11 months) into the quarantine. Baseline characteristics are detailed in Table I. Patients seen in the aerodigestive diseases center were younger, more likely to be male, and have aspiration and feeding-tube dependency. Otherwise, there was not difference in baseline characteristics or comorbidities between groups (Table I).

Baseline Health and Medication Use

When we compared the presence of selected symptoms before and during the quarantine period, there was a decreased incidence of airway symptoms across all patients during the quarantine period compared with before,

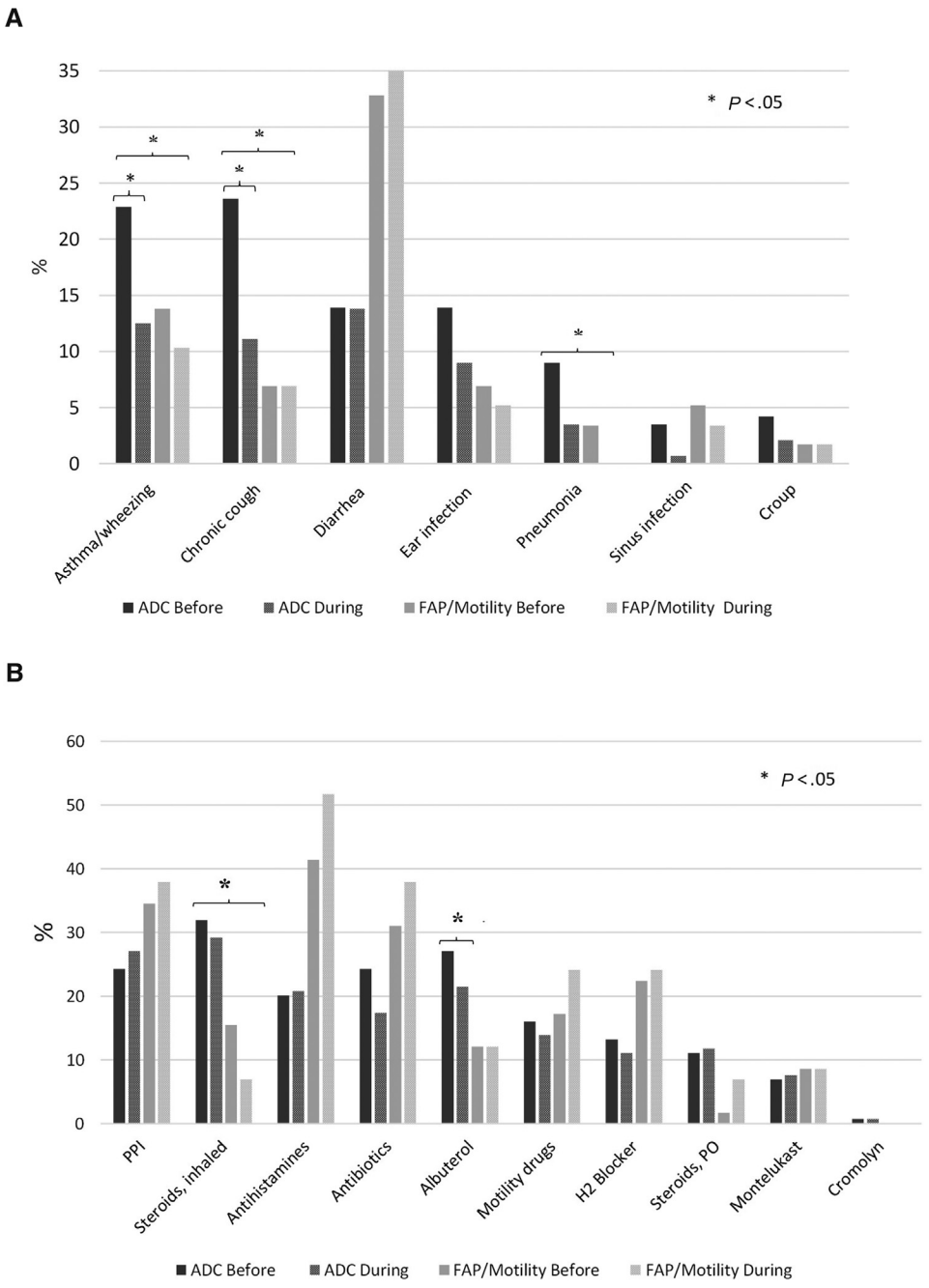

Figure 1. Symptoms and medication use before and during quarantine. **A,** Symptom prevalence before and during the COVID-19 quarantine (by cohort). *P* value based on McNemar test for related samples. **B,** Medication use before and during the COVID-19 quarantine (by cohort). *P* value based on McNemar test for related samples. *ADC*, aerodigestive; *PO*, per oral.

including wheezing ($P < .01$), chronic cough ($P < .01$), and pneumonia ($P = .04$) (Figure 1, A).

Change in overall health status during quarantine compared with before (unchanged, improved, or worse) are detailed in Table I. Of note, 27 patients were born during quarantine and unable to answer this question and therefore not included in the analysis. Although most patients reported no change in their overall health status, there were notably greater reports of subjective improvement in the patients with aerodigestive disease group (35.3%) compared with the FAP/motility group (3.6%) ($P = .0001$), and notably greater rates of worsening of overall health in the FAP/motility group (32.1%) compared with the patients with aerodigestive disease group (7.5%, $P = .001$, Table I).

From a medication perspective, there was a significant decrease in the use of inhaled steroids during the pandemic among all patients ($P < .05$, Figure 1, B). Of

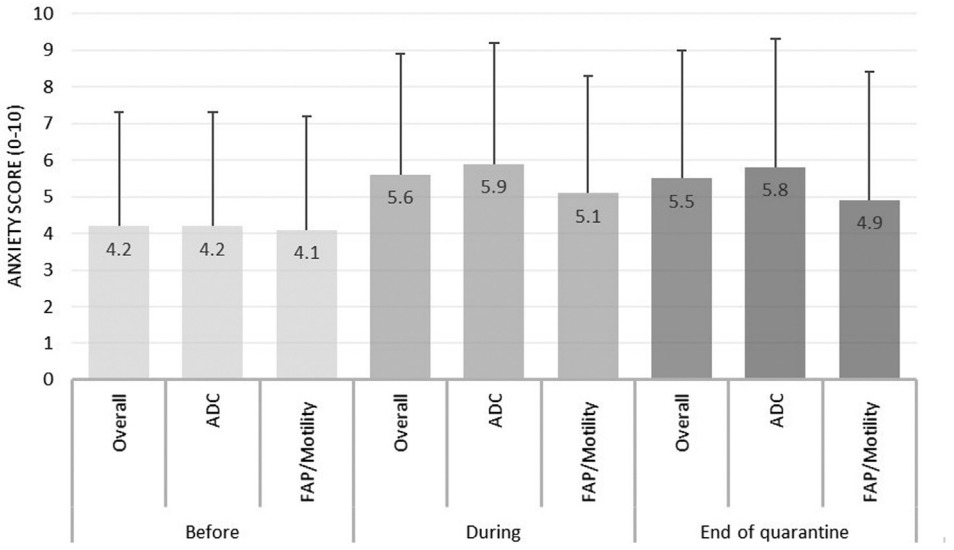

Figure 2. Health-related anxiety scores before and during COVID-19 quarantine.

patients receiving inhaled steroids before the quarantine (n = 55), 12 of 55 (21.8%) discontinued steroids, and only 3 of 147 (2.0%) patients were newly started during quarantine.

Health-Related Anxiety

Anxiety scores (0-10) increased significantly during quarantine ($P < .05$) compared with before and remained high through the end of quarantine. There was no difference in anxiety scores between the patients with aerodigestive disease and patients with FAP/motility disorder groups at any time point (Figure 2).

Healthcare Use

Despite complexities of accessing care due to the widespread lockdown, all patient groups continued to access healthcare. Fifty-eight of 202 (28.7%) patients were seen in the emergency department; notably, patients with FAP/motility disorders presented to the emergency department more frequently than patients with aerodigestive disease (41.4% compared with 22.9%) ($P = .02$); however, the number of outpatient visits per month during the study period was similar between groups ($P = .43$). Forty of 202 (19.8%), were hospitalized during the study period with no difference in hospitalization rates between the patients with aerodigestive disease and FAP/motility groups ($P = .56$). Of all patients, 84 of 202 (41.6%) saw their primary care physician for an in-person visit and 61 of 202 (30.2%) for a virtual visit at one point during the quarantine study period, with no significant difference in the visits per month between the groups for both in-person visits ($P = .43$) or virtual visits ($P = .87$) during the study period. The most common reasons for seeking care

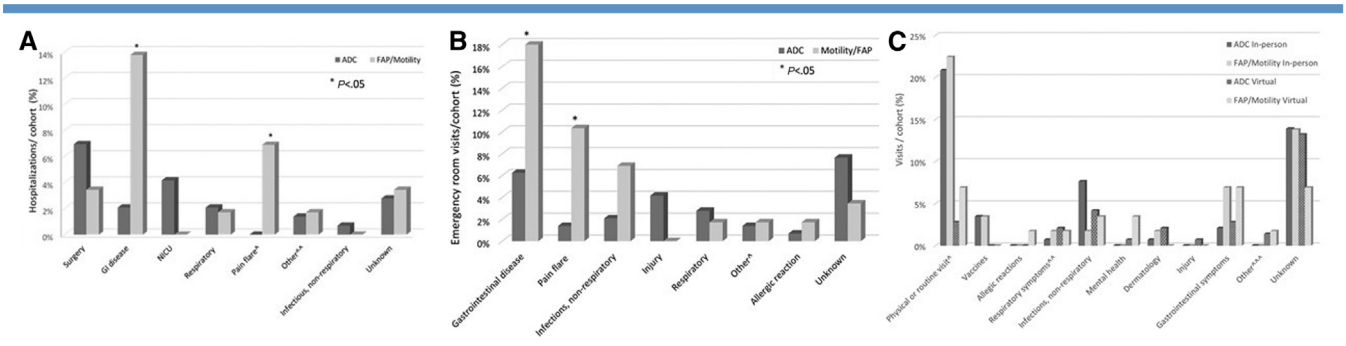

Figure 3. Healthcare use during the COVID-19 quarantine including reasons for **A,** Hospitalization. ^Pain flares including abdominal pain and migraines. ^^Other: anxiety, supraventricular tachycardia, pulmonary stenosis. **B,** Visits to the emergency department. ^Other routine check, procedure complications, anxiety. **C,** Primary care visits. ^Routine well-child visits and admission/emergency department follow-up. ^^Infections and noninfectious respiratory symptoms. ^^^Medication adjustment, elevated lead level. *NICU*, neonatal intensive care unit.

are summarized in Figure 3, A-C. There was no significant difference in healthcare use between families with greater (anxiety score >5) and lower (anxiety score ≤5) anxiety scores ($P > .05$).

COVID-19 Exposure and Illness

Overall, 96 of 202 (47.5%) subjects knew someone who had COVID-19; and 49 of 202 (24.3%) had a relative with COVID-19. Seven of 202 (3.5%) patients had a direct COVID-19 contact. A total of 118 of 202 (58.4%) patients were tested for COVID-19 at one point during the study period, and 4 of 118 (3.4%) tested positive, of whom 3 (75%) were patients with aerodigestive disease. Patients also were asked if they had symptoms of COVID-19 but were not tested (due to the paucity of testing availability at the time of questionnaire administration), and 9 of 202 (4.5%) patients responded affirmatively to this question. There was no significant difference in the rate of COVID-19 testing between the cohort of patients with aerodigestive disease (79/144, 54.9%) and those with FAP/motility disease (39/58, 67.2%) ($P = .12$). COVID-19 positivity was more prevalent among patients with aerodigestive disease (3/144, 2.1%) compared with patients with FAP/motility disorders (1/58, 1.7%) but this did not reach statistical significance ($P = .68$). All patients who tested positive COVID-19 were symptomatic at the time of testing, symptoms that were reported to be fever, cough, and/or nasal congestion. None of the patients who tested positive were hospitalized, and all recovered fully with supportive care. One patient required increase of pulmonary medications for a mild exacerbation of cystic fibrosis.

We investigated whether there was an association between medication use and likelihood of contracting COVID-19. All 4 patients who tested positive for COVID-19 were taking proton pump inhibitors (PPIs) at the time of testing. The use of PPIs ($P = .01$) and inhaled steroids ($P = .04$) was associated with testing positive for COVID-19 (Table II; available at www.jpeds.com).

There were no significant associations with COVID-19 illness and race ($P = .37$), geographics ($P = .07$), living with siblings younger than age 18 years ($P = .55$), having in-home ($P = .57$) or out-of-home childcare ($P = .56$), comorbidities (neurologic [$P = .33$]), cardiac ($P = .65$), genetic ($P = .22$), presence of aspiration ($P = .23$), or presence of a feeding tube ($P = .21$).

Discussion

We show that respiratory symptoms improved and that use of airway medication decreased in patients with aerodigestive disease during quarantine with no change in gastrointestinal symptoms. We found increased overall health-related anxiety regardless of patient cohort during and at the end of, compared with before, the quarantine period. Although limited by the small number of patients who were COVID-19 positive, we show an association of active PPI and inhaled steroid use with COVID-19 positivity.

Our study shows that respiratory symptoms including wheezing, chronic cough, and pneumonia decreased significantly during quarantine among the patients in the aerodigestive disease cohort. This is not surprising, given the greater rate of chronic respiratory symptoms in this population, the likelihood that patients were home-bound in the setting of the quarantine, and the pervasive mask use, particularly in the Northeast of the US. Our results are supported by other pediatric studies showing improved asthma control with decreased asthma exacerbations during the lockdown.[5,6] Overall improvement of health during quarantine was reported in 26% of all patients, with a greater proportion of improvement among the group of patients with aerodigestive disease (37%) compared with the FAP/motility group (3.7%), also reflecting the likely beneficial effect of having less environmental triggers for respiratory symptoms in the group of patients with aerodigestive disease.

About one-third (31.0%) of patients with FAP/motility disorders experienced symptom exacerbation. These exacerbations may be due to social isolation, less opportunities to use coping strategies such as distraction, and limited access to care, including psychological services, that occurred as the pandemic continued. This contrasts with finding that patients with disorders of the gut–brain interaction, such as irritable bowel syndrome, showed that 57% had significant improvement of all symptoms during the early quarantine period.[7]

We also found that health anxiety was high during the pandemic, a finding that is consistent across other studies.[8,9] We show no difference in anxiety between patients with aerodigestive conditions vs functional gastrointestinal and motility disorders. It is possible that the reasons for increased anxiety were different between the patients with aerodigestive disease and FAP/motility populations. This may be due to the overall increase in health-related anxiety across the population due to having any chronic condition,[4] or the increase in underlying comorbid anxiety as frequently seen in patients with irritable bowel syndrome.[10] This study concluded in March 2021, before the COVID-19 vaccine availability to the general public or teenagers, which may have played a role in persistently high levels of anxiety.

Of the 4 patients who had COVID-19 infections, none were hospitalized. Symptoms of COVID-19 included cough, fever, and nasal congestion, typical symptoms previously reported in the pediatric population, as reported.[11] Early in the pandemic, chronic pulmonary disease was considered a risk factor for severe disease, although more recent studies have suggested that it does not increase morbidity or mortality related to COVID-19.[5,12] We also did not detect a statistically significant difference in the incidence of COVID-19 in the greater-risk patients with aerodigestive disease cohort compared with patients with FAP/motility disorders.

We did find a possible association of PPI use with COVID-19 positivity. Studies in adults early in the pandemic found increased odds for a positive COVID-19 test (aOR 2.15 [95% CI 1.9-2.4] for once-daily dosing and an aOR of 3.67 [95% CI 2.9-4.6] for twice-daily dosing) when compared with those not taking PPIs.[13] Our findings suggest that acid

suppression may increase the risk of viral infections, although this will require larger studies to confirm.[14-20] This concept of increased infection risk with acid suppression use is not novel. The PPI-induced risk of bacterial pulmonary infections is thought to be related to bacterial dysbiosis, local mucosal secretory alterations, and the anti-inflammatory effects of PPIs.[14,21] In patients with aerodigestive disease in whom aspiration is particularly common, the alteration of the gastric micro-organisms with PPI use may be particularly concerning.[22] Although studies on acid suppression and SARS-CoV-2 are conflicting, data in adults suggest that low gastric pH ≤3 impairs the infectivity of a similar severe acute respiratory syndrome coronavirus 1, compared with greater gastric pH values, which did not inactivate the virus.[23] This may be relevant for COVID-19 because SARS-CoV-2 is known to enter the body via both the respiratory and gastrointestinal systems.[13,24,25] A meta-analysis of 8 studies published by Yan et al found no difference in risk of COVID-19 infection in adult patients on or off PPI therapy but suggested that PPIs may have a role in progression to severe disease and secondary infections.[13,26-30]

We also found that receiving inhaled corticosteroids during the pandemic was associated with COVID-19 positivity, although again our data are limited, given the small number of patients who were positive for COVID-19 in this cohort. If the findings are confirmed in a larger studies, it would reinforce the recommendations not to use steroids unless patients are symptomatic with COVID-19 and requiring supplemental oxygen.[31-33] In symptomatic patients, steroids have been shown to reduce coronavirus replication, reduce the risk of acute respiratory distress syndrome, and improve pulmonary function testing.[34-39] Previous studies show that inhaled corticosteroids increase the risk of pneumonia and lower respiratory infections in adults with asthma.[40] In vitro studies have suggested that steroids can impair antiviral innate immune responses[41,42] and that inhaled corticosteroids use may lead to delayed virus clearance.[43,44] Little is known about the risk of contracting COVID-19 when using inhaled corticosteroids because most of the studies focus on disease severity rather than test positivity. A study of 77 676 adults conducted in Spain showed a prevalence of 16.1% for inhaled respiratory medication use among those who tested positive for SARS-CoV2 compared with 8% in the overall study population, although it is unclear whether these inhaled medications included steroids. Further analysis in this large cohort showed a hazard ratio of 1.41 (0.81-2.45) of contracting COVID-19 disease while on inhaled medications, adjusting for age, sex, comorbidities, residence, and other medication use.[45] In contrast, a study of Korean adults showed only a 1.6% prevalence of inhaled corticosteroids use among those who tested positive for COVID-19 with no significant association of inhaled corticosteroids use and clinical outcomes.[46] Finally, a recent meta-analysis showed no increase for severe COVID-19 disease, arguing that it is safe to continue inhaled corticosteroids use to control underlying disease.[47]

There are several limitations to our small study without a healthy control group. We intended to determine the impact of COVID-19 on patients with aerodigestive disease, so we chose 2 multidisciplinary clinics that see patients with chronic neurogastroenterology diseases at a tertiary care center. Not unexpectedly, the patients with aerodigestive disease group, which has a greater prevalence of respiratory symptoms, were younger, which presents another limitation to the comparison. The number of patients who tested positive for COVID-19 was low, which limits the power of this study, but even with low numbers, we still found significant associations. Our findings indicate the need for larger studies to evaluate the effect of medications on COVID-19 infection risk or viral illnesses in general. The low observed rate of positivity for COVID-19 among our cohort may be due to the study having been conducted early in the pandemic, with limited testing availability or due to the strict quarantine measures, whereby children with chronic illness were especially sheltered during this time. Although we know the testing rates were high in our population, we do not know why patients were tested. Finally, the health-related anxiety levels may be an underestimate because all patients were recruited during an in-person visit, which may present a subset with less-severe underlying medical conditions or less patient/parental anxiety and therefore more willing to come for a clinic visit rather than meet via telemedicine.

In conclusion, the COVID-19 pandemic has had a significant impact on pediatric patients with aerodigestive disease. Although about one-half of patients had no change to their overall health status, one-third experienced overall improved health, including a decrease of respiratory symptoms. The rate of COVID-19 positivity was low in this study cohort, but all affected patients had a mild disease course and recovered fully. There was a significant increase in overall health-related anxiety reported by patients during and at the end compared with before the quarantine period. ■

Submitted for publication Sep 24, 2021; last revision received Nov 30, 2021; accepted Dec 15, 2021.

References

1. Lazzerini M, Barbi E, Apicella A, Marchetti F, Cardinale F, Trobia G. Delayed access or provision of care in Italy resulting from fear of COVID-19. Lancet Child Adolesc Health 2020;4:e10.
2. Vogt T, Zhang F, Banks M, Black C, Arthur B, Kang Y, et al. Provision of pediatric immunization services during the COVID-19 pandemic: an assessment of capacity among pediatric immunization providers participating in the vaccines for children program—United States, May 2020. MMWR Morb Mortal Wkly Rep 2020;69:859-63.
3. Dopfer C, Wetzke M, Zychlinsky Scharff A, Mueller F, Dressler F, Baumann U, et al. COVID-19 related reduction in pediatric emergency healthcare utilization—a concerning trend. BMC Pediatr 2020;20:427.
4. Shen K-L, Yang Y-H, Jiang R-M, Wang T-Y, Zhao D-C, Jiang Y, et al. Updated diagnosis, treatment and prevention of COVID-19 in children: experts' consensus statement (condensed version of the second edition). World J Pediatr 2020;16:232-9.
5. Farzan S, Rai S, Cerise J, Bernstein S, Coscia G, Hirsch JS, et al. Asthma and COVID-19: an early inpatient and outpatient experience at a US children's hospital. Pediatr Pulmonol 2021;56:2522-9.
6. Hurst JH, Zhao C, Fitzpatrick NS, Goldstein BA, Lang JE. Reduced pediatric urgent asthma utilization and exacerbations during the COVID-19 pandemic. Pediatr Pulmonol 2021;56:3166-73.

7. Strisciuglio C, Martinelli M, Lu P, Bar Lev MR, Beinvogl B, Benninga MA, et al. Overall impact of COVID-19 outbreak in children with functional abdominal pain disorders: results from the first pandemic phase. J Pediatr Gastroenterol Nutr 2021;73:689-94.
8. Lee J, Solomon M, Stead T, Kwon B, Ganti L. Impact of COVID-19 on the mental health of US college students. BMC Psychol 2021;9:95.
9. Khubchandani J, Sharma S, Webb FJ, Wiblishauser MJ, Bowman SL. Post-lockdown depression and anxiety in the USA during the COVID-19 pandemic. J Public Health (Oxf) 2021;43:246-53.
10. Beinvogl B, Palmer N, Kohane I, Nurko S. Healthcare spending and utilization for pediatric Irritable Bowel Syndrome in a commercially insured population. Neurogastroenterol Motil 2021;33:e14147.
11. Mantovani A, Rinaldi E, Zusi C, Beatrice G, Saccomani M, Dalbeni A. Coronavirus disease 2019 (COVID-19) in children and/or adolescents: a meta-analysis. Pediatr Res 2021;89:733-7.
12. Palla J, Laguna TA. Management of chronic pulmonary disease in the time of coronavirus disease 2019. Curr Opin Pediatr 2021;33:294-301.
13. Almario C, Chey W, Spiegel B. Increased risk of COVID-19 among users of proton pump inhibitors. Am J Gastroenterol 2020;115:1707-15.
14. Stark CM, Nylund CM. Side effects and complications of proton pump inhibitors: a pediatric perspective. J Pediatr 2016;168:16-22.
15. Eusebi LH, Rabitti S, Artesiani ML, Gelli D, Montagnani M, Zagari RM, et al. Proton pump inhibitors: risks of long-term use. J Gastroenterol Hepatol 2017;32:1295-302.
16. Freedberg DE, Kim LS, Yang Y-X. The risks and benefits of long-term use of proton pump inhibitors: expert review and best practice advice from the American Gastroenterological Association. Gastroenterology 2017;152:706-15.
17. Freedberg DE, Lamousé-Smith ES, Lightdale JR, Jin Z, Yang Y-X, Abrams JA. Use of acid suppression medication is associated with risk for *C. difficile* infection in infants and children: a population-based study. Clin Infect Dis 2015;61:912-7.
18. Brown KE, Knoderer CA, Nichols KR, Crumby AS. Acid-suppressing agents and risk for *Clostridium difficile* infection in pediatric patients. Clin Pediatr (Phila) 2015;54:1102-6.
19. Canani RB, Cirillo P, Roggero P, Romano C, Malamisura B, Terrin G, et al. Therapy with gastric acidity inhibitors increases the risk of acute gastroenteritis and community-acquired pneumonia in children. Pediatrics 2006;117:e817-20.
20. Eom C-S, Jeon CY, Lim J-W, Cho E-G, Park SM, Lee K-S. Use of acid-suppressive drugs and risk of pneumonia: a systematic review and meta-analysis. CMAJ 2011;183:310-9.
21. Rosen R, Amirault J, Liu H, Mitchell P, Hu L, Khatwa U, et al. Changes in gastric and lung microflora with acid suppression: acid suppression and bacterial growth. JAMA Pediatr 2014;168:932.
22. Rosen R, Hu L, Amirault J, Khatwa U, Ward DV, Onderdonk A. 16S community profiling identifies proton pump inhibitor related differences in gastric, lung, and oropharyngeal microflora. J Pediatr 2015;166:917-23.
23. Darnell MER, Subbarao K, Feinstone SM, Taylor DR. Inactivation of the coronavirus that induces severe acute respiratory syndrome, SARS-CoV. J Virol Methods 2004;121:85-91.
24. Trottein F, Sokol H. Potential causes and consequences of gastrointestinal disorders during a SARS-CoV-2 infection. Cell Rep 2020;32:107915.
25. Xiao F, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for gastrointestinal infection of SARS-CoV-2. Gastroenterology 2020;158:1831-3.e3.
26. Israelsen SB, Ernst MT, Lundh A, Lundbo LF, Sandholdt H, Hallas J, et al. Proton pump inhibitor use is not strongly associated with SARS-CoV-2 related outcomes: a nationwide study and meta-analysis. Clin Gastroenterol Hepatol 2021;19:1845-54.e6.
27. Lee S, Ha E, Yeniova A, Moon S, Kim S, Koh H, et al. Severe clinical outcomes of COVID-19 associated with proton pump inhibitors: a nationwide cohort study with propensity score matching. Gut 2021;70:76-84.
28. Luxenburger H, Sturm L, Biever P, Rieg S, Duerschmied D, Schultheiss M, et al. Treatment with proton pump inhibitors increases the risk of secondary infections and ARDS in hospitalized patients with COVID-19: coincidence or underestimated risk factor? J Intern Med 2021;289:121-4.
29. Liu JJ, Sloan ME, Owings AH, Figgins E, Gauthier J, Gharaibeh R, et al. Increased ACE2 levels and mortality risk of patients with COVID-19 on proton pump inhibitor therapy. Am J Gastroenterol 2021;116:1638-45.
30. Yan C, Chen Y, Sun C, Ahmed MA, Bhan C, Guo Z, et al. Will proton pump inhibitors lead to a higher risk of COVID-19 infection and progression to severe disease? A meta-analysis. Jpn J Infect Dis 2021. https://doi.org/10.7883/yoken.JJID.2021.074
31. Chow N, Fleming-Dutra K, Gierke R, Hall A, Hughes M, Pilishvili T, et al. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019—United States, February 12–March 28, 2020. MMWR Morb Mortal Wkly Rep 2020;69:382-6.
32. Halpin DMG, Faner R, Sibila O, Badia JR, Agusti A. Do chronic respiratory diseases or their treatment affect the risk of SARS-CoV-2 infection? Lancet Respir Med 2020;8:436-8.
33. Yang J, Zheng Y, Gou X, Pu K, Chen Z, Guo Q, et al. Prevalence of comorbidities and its effects in patients infected with SARS-CoV-2: a systematic review and meta-analysis. Int J Infect Dis 2020;94:91-5.
34. Halpin DMG, Singh D, Hadfield RM. Inhaled corticosteroids and COVID-19: a systematic review and clinical perspective. Eur Respir J 2020;55:2001009.
35. Chugh H, Awasthi A, Agarwal Y, Gaur RK, Dhawan G, Chandra R. A comprehensive review on potential therapeutics interventions for COVID-19. Eur J Pharmacol 2021;890:173741.
36. Matsuyama S, Kawase M, Nao N, Shirato K, Ujike M, Kamitani W, et al. The Inhaled steroid ciclesonide blocks SARS-CoV-2 RNA replication by targeting the viral replication-transcription complex in cultured cells. J Virol 2020;95:e01648-016420.
37. Yamaya M, Nishimura H, Deng X, Sugawara M, Watanabe O, Nomura K, et al. Inhibitory effects of glycopyrronium, formoterol, and budesonide on coronavirus HCoV-229E replication and cytokine production by primary cultures of human nasal and tracheal epithelial cells. Respir Investig 2020;58:155-68.
38. Festic E, Carr GE, Cartin-Ceba R, Hinds RF, Banner-Goodspeed V, Bansal V, et al. Randomized clinical trial of a combination of an inhaled corticosteroid and beta agonist in patients at risk of developing the acute respiratory distress syndrome. Crit Care Med 2017;45:798-805.
39. Artigas A, Camprubí-Rimblas M, Tantinyà N, Bringué J, Guillamat-Prats R, Matthay MA. Inhalation therapies in acute respiratory distress syndrome. Ann Transl Med 2017;5:293.
40. McKeever T, Harrison TW, Hubbard R, Shaw D. Inhaled corticosteroids and the risk of pneumonia in people with asthma: a case–control study. Chest 2013;144:1788-94.
41. Davies JM, Carroll ML, Li H, Poh AM, Kirkegard D, Towers M, et al. Budesonide and formoterol reduce early innate anti-viral immune responses in vitro. PLoS One 2011;6:e27898.
42. Simpson JL, Carroll M, Yang IA, Reynolds PN, Hodge S, James AL, et al. Reduced antiviral interferon production in poorly controlled asthma is associated with neutrophilic inflammation and high-dose inhaled corticosteroids. Chest 2016;149:704-13.
43. Singanayagam A, Glanville N, Girkin JL, Ching YM, Marcellini A, Porter JD, et al. Corticosteroid suppression of antiviral immunity increases bacterial loads and mucus production in COPD exacerbations. Nat Commun 2018;9:2229.
44. Southworth T, Pattwell C, Khan N, Mowbray SF, Strieter RM, Erpenbeck VJ, et al. Increased type 2 inflammation post rhinovirus infection in patients with moderate asthma. Cytokine 2020;125:154857.
45. Vila-Córcoles A, Ochoa-Gondar O, Satué-Gracia EM, Torrente-Fraga C, Gomez-Bertomeu F, Vila-Rovira A, et al. Influence of prior comorbidities and chronic medications use on the risk of COVID-19 in adults: a population-based cohort study in Tarragona, Spain. BMJ Open 2020;10:e041577.
46. Choi JC, Jung S-Y, Yoon UA, You S-H, Kim M-S, Baek MS, et al. Inhaled corticosteroids and COVID-19 risk and mortality: a nationwide cohort study. J Clin Med 2020;9:E3406.
47. Kow CS, Hasan SS. Preadmission use of inhaled corticosteroids and risk of fatal or severe COVID-19: a meta-analysis. J Asthma 2021:1-4. https://doi.org/10.1080/02770903.2021.1878531

Table II. Association of COVID-19 positivity with medication use before and during quarantine (n = 202)

All (n = 202)	COVID-19+/ Med + before n/n (%)	COVID-19+/ Med–Before n/n (%)	*P* value*	COVID-19+/ Med + During n/n (%)	COVID-19+/ Med–During n/n (%)	*P* value*
H2 antagonist	2/32 (6.3)	2/170 (1.2)	.12	1/30 (3.3)	3/172 (1.7)	.48
PPI	3/55 (5.5)	1/147 (0.68)	.06	**4/61 (6.6)**	**0/141 (0.0)**	**.01**
Inhaled steroid	2/55 (3.6)	2/147 (1.4)	.30	**3/46 (6.5)**	**1/156 (0.6)**	**.04**
Swallowed steroid	0/17 (0.0)	4/185 (2.2)	.70	1/21 (4.7)	3/181 (1.7)	.36
Antihistamines	2/53 (3.8)	2/149 (1.3)	.28	2/60 (3.3)	2/142 (1.4)	.34
Montelukast	0/15 (0.0)	4/187 (2.1)	.73	0/16 (0.0)	4/186 (2.2)	.72
Cromolyn	0/1 (0.0)	4/201 (2.0)	.98	0/1 (0.0)	4/201 (2.0)	.98
Prokinetics	2/33 (6.0)	2/169 (1.1)	.13	2/34 (5.9)	2/168 (1.2)	.13
Albuterol	2/46 (4.3)	2/156 (1.3)	.22	2/38 (5.3)	2/164 (1.2)	.16
Antibiotics	2/53 (3.8)	2/149 (1.3)	.28	2/47 (4.3)	2/155 (1.3)	.23

COVID+, COVID-19 positive; *Med+*, patient on medication before/during quarantine; *Med–*, patient note on medication before/during quarantine.
Statistically significant values ($P < .05$) are shown in bold.
*Fisher exact test.