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.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Delayed presentation and sub-optimal outcomes of pediatric patients with acute appendicitis during the COVID-19 pandemic

Claire D. Geralla, Jennifer R. DeFazio, Anastasia M. Kahan, Weijja Fan, Erica M. Fallon, William Middlesworth, Steven Stylianou, Angela V. Kadenhe-Chiweshe, Nitsana A. Spigland, Cornelia L. Griggs, Sandra K. Kabagama, Gabriel Apfel, Daniel B. Fenster, Vincent P. Duron

Division of Pediatric Surgery, Department of Surgery, Columbia University Vagelos College of Physicians and Surgeons / NewYork-Presbyterian Morgan Stanley Children's Hospital, 3959 Broadway CH2N, New York, NY 10032

Abstract

Objective: Early presentation and prompt diagnosis of acute appendicitis are necessary to prevent progression of disease leading to complicated appendicitis. We hypothesize that patients had a delayed presentation of acute appendicitis during the COVID-19 pandemic, which affected severity of disease on presentation and outcomes.

Patients and methods: We conducted a retrospective review of all patients who were treated for acute appendicitis at Morgan Stanley Children’s Hospital (MSCCH) between March 1, 2020 and May 31, 2020 when the COVID-19 pandemic was at its peak in New York City (NYC). For comparison, we reviewed patients treated from March 1, 2019 to May 31, 2019, prior to the pandemic. Demographics and baseline patient characteristics were analyzed for potential confounding variables. Outcomes were collected and grouped into those quantifying severity of illness on presentation to our ED, type of treatment, and associated post-treatment outcomes. Fisher’s Exact Test and Kruskal-Wallis Test were used for univariate analysis while cox regression with calculation of hazard ratios was used for multivariate analysis.

Results: A total of 89 patients were included in this study, 41 patients were treated for appendicitis from March 1 to May 31 of 2019 (non-pandemic) and 48 were treated during the same time period in 2020. Duration of symptoms prior to presentation to the ED was significantly longer in patients treated in 2020, with a median of 2 days compared to 1 day (p = 0.003). Additionally, these patients were more likely to present with reported fever (52.1% vs 24.4%, p = 0.009) and had a higher heart rate on presentation with a median of 101 beats per minute (bpm) compared to 91 bpm (p = 0.040). Findings of complicated appendicitis on radiographic imaging including suspicion of perforation (41.7% vs 9.8%, p < 0.001) and intra-abdominal abscess (27.1% vs 7.3%, p = 0.025) were higher in patients presenting in 2020. Patients treated during the pandemic had higher rates of non-operative treatment (25.0% vs 7.3%, p = 0.044) requiring increased antibiotic use and image-guided percutaneous drain placement. They also had longer hospital length of stay by a median of 1 day (p = 0.001) and longer duration until symptom resolution by a median of 1 day (p = 0.004). Type of treatment was not a predictor of LOS (HR = 0.565, 95% CI = 0.357–0.894, p = 0.015) or duration until symptom resolution (HR = 0.630, 95% CI = 0.405–0.979, p = 0.040).

Conclusion: Patients treated for acute appendicitis at our children’s hospital during the peak of the COVID-19 pandemic presented with more severe disease and experienced suboptimal outcomes compared to those who presented during the same time period in 2019.

Level of Evidence: III

Corresponding author at: Morgan Stanley Children’s Hospital of New York-Presbyterian, 3959 Broadway CH2N, New York, NY, 10032.

E-mail address: vd2312@cumc.columbia.edu (V.P. Duron).
1. Patients and methods

1.1. Patient selection

Patients age 18 years and younger who were treated for acute appendicitis at Morgan Stanley Children's Hospital (MSCH) between March 1, 2020 and May 31, 2020 were compared to a cohort of appendicitis patients from March 1, 2019 and May 31, 2019. The first case of COVID-19 in NYC was diagnosed on March 1, 2020, with significant numbers of cases treated throughout May 2020. Presentation and outcomes of patients with acute appendicitis who were treated at our children’s hospital during the peak of the COVID-19 pandemic were compared to those of patients treated during corresponding months in 2019, when there was no pandemic. Patients who were confirmed positive for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) during their presentation for appendicitis were excluded from this study as treatment algorithms differ for this patient population and the extent of gastrointestinal effects of the virus remain unknown. Our standard protocol for treatment of acute appendicitis consists of operative treatment for all non-perforated and for perforated appendicitis without abscess formation. Patients with abscess identified on radiographic imaging are treated non-operatively with antibiotics in addition to image-guided drain placement when accessible. We continued to follow our established treatment protocol during the pandemic for patients who were COVID-19 negative, which is the patient population studied in this retrospective review.

During the COVID-19 pandemic, pediatric care centers in the NewYork-Presbyterian (NYP) hospital system redirected the care of many pediatric patients to MSCH including all patients who required acute surgery or hospital admission out of the necessity to redirect resource availability for adult patients with COVID-19. Therefore, the pediatric appendicitis patients treated at our institution during the pandemic consisted of all pediatric patients with appendicitis within the NYP hospital system. In comparison, those treated for appendicitis in 2019 were most often patients who presented to our hospital directly.

1.2. Patient variables and outcomes

Demographic data and baseline patient characteristics were collected from patient charts, including patient’s age, gender, race, body mass index (BMI), and other comorbidities. Collected outcomes were grouped into those quantifying severity of illness on presentation to our ED as well as type of treatment and associated post-treatment outcomes. Outcomes representing severity of illness on presentation include temperature, heart rate, mean arterial pressure (MAP), duration and type of symptoms before presentation, white blood cell count (WBC), suspected perforation, and diagnosis of intra-abdominal abscess on radiographic imaging. Treatment outcomes include type of treatment on initial presentation (operative vs non-operative), type of operative treatment (appendectomy only vs appendectomy and a course of antibiotics), and type of non-operative treatment (course of antibiotics only vs antibiotics and drain placement). Post-treatment outcomes consisted of diagnosis of perforation on pathology report, failure of non-operative treatment, post-operative complications, hospital length of stay (LOS) and number of days until symptom resolution. Non-operative failure and post-operative complications included return to the ED or need for readmission requiring antibiotics or drain placement on the subsequent presentation. Patients were grouped based on year of presentation and outcomes were compared between those treated in 2019 vs 2020.

1.3. Statistical analysis

Fisher’s Exact Test was used to compare categorical variables while Kruskal-Wallis Test was used to compare continuous variables between the two groups of patients. Categorical variables are reported as frequency and percentage and continuous variables are reported as median with first and third quartile as well as overall range. A Kaplan–Meier curve was used to visualize the distribution for time to event outcomes while the log rank test was used to compare between groups. Multivariate analysis with hazard ratios calculated by cox regression was also performed.

2. Results

A total of 93 patients were treated for acute appendicitis at our institution between March 1 and May 31 of 2019 and 2020. Four patients who presented in 2020 tested positive for SARS-CoV-2 and were
Table 2
Outcomes of pediatric patients presenting to Morgan Stanley Children’s Hospital (MSCH) for acute appendicitis between March 1 and May 31 of 2019 and 2020. Median with first and third quartile as well as range are reported for continuous variables. Frequency and percentage are reported for categorical variables. P-values from Fisher’s exact test are reported for categorical variables while p-values from Kruskal-Wallis test are reported for continuous variables.

| Outcomes                  | 2019 (N = 41) | 2020 (N = 48) | p-Value |
|---------------------------|---------------|---------------|---------|
| **Reported symptoms**     |               |               |         |
| Abdominal pain            |               |               |         |
| -Yes                      | 41 (100.0%)   | 48 (100.0%)   | 1.000   |
| -No                       | 31 (75.6%)    | 23 (47.9%)    | 0.009   |
| -Yes                      | 10 (24.4%)    | 25 (52.1%)    |         |
| Fever                     |               |               |         |
| -No                       | 17 (41.5%)    | 14 (29.2%)    | 0.268   |
| -Yes                      | 24 (58.5%)    | 34 (70.8%)    |         |
| Nausea                    |               |               |         |
| -No                       | 30 (73.2%)    | 38 (79.2%)    | 0.618   |
| -Yes                      | 11 (26.8%)    | 10 (20.8%)    |         |
| Vomiting                  |               |               |         |
| -No                       | 29 (70.7%)    | 27 (56.2%)    | 0.190   |
| -Yes                      | 12 (29.3%)    | 21 (43.8%)    |         |
| Duration of symptoms before presentation (Days) | | | |
| -Median (Q1, Q3)          | 1.00          | 2.00          | 0.003   |
| -Range                    | 0.50–10.00    | 0.50–14.00    |         |
| **Findings on presentation** |             |               |         |
| Temperature               |               |               |         |
| -Median (Q1, Q3)          | 37.15         | 37.20         | 0.959   |
| -Range                    | 36.30–39.10   | 36.00–39.40   |         |
| Heart rate                |               |               |         |
| -Median (Q1, Q3)          | 91.00         | 101.00        | 0.040   |
| -Range                    | 79.50–107.75  | 91.00–113.50  |         |
| MAP                       |               |               |         |
| -Median (Q1, Q3)          | 82.00         | 80.50         | 0.752   |
| -Range                    | 77.00–87.50   | 76.00–87.75   |         |
| WBC                       |               |               |         |
| -Median (Q1, Q3)          | 15.01         | 17.79         | 0.099   |
| -Range                    | 11.20–18.87   | 12.83–20.45   |         |
| Suspicion for perforation on imaging | | | |
| -No                       | 37 (90.2%)    | 28 (58.3%)    | < 0.001 |
| -Yes                      | 4 (9.8%)      | 20 (41.7%)    |         |
| Abscess on imaging        |               |               |         |
| -No                       | 38 (92.7%)    | 35 (72.9%)    | 0.025   |
| -Yes                      | 3 (7.3%)      | 13 (27.1%)    |         |
| Treatment                 |               |               |         |
| Treatment on initial presentation | | | |
| -Operative                | 38 (92.7%)    | 36 (75.0%)    | 0.044   |
| -Non-operative            | 3 (7.3%)      | 12 (25.0%)    |         |
| Type of non-operative treatment |         |               | 0.505   |
| -Antibiotics              | 3 (100.0%)    | 7 (58.3%)     |         |
| -Antibiotics and drain placement |      | 0 (0.0%)      |         |
| Type of operative treatment |           |               | 0.013   |
| -Appendectomy             | 33 (89.2%)    | 23 (63.9%)    |         |
| -Appendectomy and antibiotic course | 4 (10.8%) | 13 (36.1%)    |         |
| Post-treatment            |               |               |         |
| Failure of non-op treatment |           |               | 1.000   |
| -No                       | 2 (66.7%)     | 6 (50.0%)     |         |
| -Yes                      | 1 (33.3%)     | 6 (50.0%)     |         |
| Perforation on pathology  |               |               | 0.332   |
| -No                       | 36 (90.0%)    | 29 (80.6%)    |         |
| -Yes                      | 4 (10.0%)     | 7 (19.4%)     |         |
| Per-operative complications |           |               | 0.670   |
| -No                       | 36 (94.7%)    | 33 (91.7%)    |         |

(continued on next page)
Appendicitis is a common indication for surgery in pediatric patients, with a lifetime risk of approximately 9% in males and 7% in females [12]. It is a time-sensitive condition with delayed diagnosis often leading to more severe disease including increased rates of perforation and intra-abdominal abscess formation [6,13]. Appendiceal perforation is associated with higher morbidity, increased postsurgical complications, as well as longer hospital LOS and higher rates of readmission. Additionally, roughly 20% of children with perforated appendicitis will develop a post-operative abscess compared to only 0.8% in those patients without perforation [14]. Delay in treatment due to misdiagnosis or delayed presentation increases the risk of perforation, with younger patients affected at higher rates due to the inability to adequately describe their pain as well as a higher incidence of generalized associated clinical symptoms which mimic nonsurgical diagnoses [15–19]. Socioeconomic factors also play a role in delayed presentation of pediatric patients as seeking medical care is dependent upon parents’ knowledge of illness, availability of transportation, insurance status, and financial state [20,21].

During the peak of the pandemic, there were multiple additional sources of delay leading to more complicated presentations of acute appendicitis in pediatric patients of all ages. We hypothesize that the most significant source of delay was the fear of contracting COVID-19 in the hospital setting, resulting in parents delaying presentation to the ED. As discussed previously, several studies have described a fear that parents and patients have of presenting to the hospital during the COVID-19 pandemic, which may delay their time course to seek medical care. Lazzerini et al. found that pediatric emergency department (ED) visits in Italy were decreased during the peak of their COVID-19 outbreak by as much as 88% when compared to visits within the same time period in 2018 and 2019 [10]. Pediatric patients who presented to the ED during Italy’s peak were noted to have overall worse outcomes while parents reported avoiding hospital care secondary to fear of infection with SARS-CoV-2. Additionally, Snapiri et al. reported on the experience of delayed diagnosis of acute appendicitis in pediatric patients in Israel during the pandemic, noting a complication rate twice as high [22% vs 11%] when compared to the same time period in 2019, with complications defined as perforation and abscess formation [11]. Although fear of contracting COVID-19 likely played a role, the delay in presentation is multifactorial. An increased reliance on outpatient care during a time when many clinics were not seeing patients most likely contributed to delays. Furthermore, as hospital systems were reaching capacity, a delay in presentation was created due to the need for transfer from one healthcare center to another.

At our institution, year of presentation correlated with increased severity of disease on presentation and higher rates of perforation and intra-abdominal abscess formation. Additionally, we noted increased use of antibiotics, longer LOS during initial admission, more frequent treatment failure or complications and longer duration until symptom resolution for patients treated during the pandemic. Our findings are consistent with current literature suggesting that delayed diagnosis is associated with higher incidence of complications [11,16–19]. As noted by Pham et al., pediatric patients with symptoms greater than 24 h were over five times more likely to have complicated appendicitis when compared to those with symptoms for 24 h or less [22]. Our data supports this as the median duration of symptoms before presentation for patients in 2019 was 1 day compared to 2 days in 2020, with 36.6% of patients in 2019 presenting after 24 h compared to 64.6% in 2020.

We suspect that delayed presentation during the pandemic affected the severity of disease on presentation, rates of non-operative management, and overall outcomes, which is supported by the recently published results from Italy, Israel and Colombia [10,11,23]. Although reported duration of symptoms before presentation is a subjective measure, our objective data shows that patients presented during the pandemic with more advanced disease, likely a result of delayed presentation to the ED. Post-operative outcomes including LOS and duration until symptom resolution may also be affected by type of treatment, with both outcomes often longer in patients treated non-operatively. For this reason, we excluded COVID positive patients from our analysis specifically to avoid confounding our results as our institutional practice was to treat COVID positive patients non-operatively. Although the management algorithm of acute appendicitis for COVID-negative patients was identical in 2020 to that provided in 2019, we suspect that surgeons may have been more inclined to treat appendicitis non-operatively during the pandemic - even in COVID-negative patients - independent of disease severity given the risk of false negative testing and viral transmission to healthcare workers in the operating room as well as to minimize hospital resource utilization. To take this into account, we performed a multivariate analysis adjusting for mode of treatment. LOS and number of days until symptom resolution remained significantly longer during the pandemic, further suggesting that the severity of disease patients presented with correlated with outcomes.

As hospitals and emergency departments were overwhelmed with COVID-19 patients and orders to stay at home were established, parents were understandably reluctant to seek medical care due to concern of contracting the virus in the hospital setting. Additionally, many outpatient clinics were temporarily closed to prevent spread of the virus as well as to better allocate resources to the hospitals, resulting in decreased ability to be evaluated by a primary care physician. Telemedicine has quickly been instituted as a means for providing healthcare while limiting exposure during the pandemic [24]. Although performing a physical exam is more challenging with telemedicine, as our comfort with virtual patient care continues to evolve, we will be able to better integrate telemedicine into our triage of patients. Fear of contracting COVID-19 and decreased access to outpatient clinics secondary to reallocation of resources experienced during the pandemic must be balanced with parent education of non-specific symptoms and the importance of seeking early medical care. Additionally, practitioners need to continue integrating a heightened awareness of this delay in presentation in their evaluation of children presenting with common symptoms that may be the forerunner of serious illness.

It is likely that COVID-19 will remain with us for some time and become a long-term presence that pervades all aspects of our patient care. We need to start thinking of strategies to quell patients’ fear of healthcare institutions. This starts in the doctor’s office or on the office’s answering service, with evidence-based messages outlining the risks of contracting COVID in different hospital and non-hospital settings. As our understanding of the virus and its mode of transmission has improved, hospitals have instituted infection control measures and rapid testing that have shown to prevent nosocomial transmission of SARS-CoV-2 [25]. Systems-based strategies, with broad testing programs have already been implemented and will continue to support frontline hospital administration. Local, state and federal government involvement will continue to be crucial, through the use of informative public service...
announcements, efforts to improve access to care and funding for wide
spread testing and contact tracing.

Limitations of our study include those inherent to a retrospective
review. In addition, although we do not believe that COVID-19 testing
led to significant delays in time to OR, we cannot verify that it did not impact
timeliness. Initial COVID-19 testing took up to 8–12 h to result, however our institution quickly acquired rapid tests
that would result within 1–2 h, which we do not believe contributed to
any delays in treatment or time to operation. Furthermore, even
during the time of early testing, the inherent delay associated with
waiting for OR availability was likely more significant than the delay
caused by testing. Another limitation of the study is that the follow up
time for patients treated in 2020 is notably shorter than that of patients
treated in 2019. Post-operative complications and non-operative failure
rates in patients treated in 2019 have been collected over several
months. However, data collected on patients treated between March
and May of 2020 was collected in June, resulting in limited follow up
time to obtain data on post-treatment outcomes with known readmis
sion of patients treated during the pandemic since data collection
ended. As previously mentioned, the NYP hospital system redirected
the care of all of its pediatric patients to our institution during the
pandemic. Although similar studies noted decreased total ED visits
and diagnosis of common conditions during the pandemic, we are
unable to compare the total number of patients diagnosed with appendicitis
during the pandemic to those diagnosed during a similar time
period in 2019 before the pandemic as we were unable to obtain patient
data from each pediatric hospital during 2019. As a result, the total
number of patients diagnosed in 2019 primarily represents those
patients who would otherwise present directly to our institution,
whereas the patient population in 2020 represents patients from all
children’s hospitals in the NYP system, contributing to the increased
number of patients diagnosed with appendicitis in the designated
timeframe in 2020. Finally, in order to compare two patient populations
with similar baseline characteristics and similar type of treatment, we
excluded COVID positive patients from the study. Although including
COVID positive patients may reflect a more real world experience, we
considered that their inclusion would introduce confounding variables
into the statistical analysis and make it less rigorous. For this reason,
we excluded these patients who received different treatment and may
also have GI side effects from COVID itself.

Unfortunately, the number of patients included in our study was too
small to examine the impact of socioeconomic background on time to
presentation and outcomes. We suspect that patients with poorer access
to healthcare, including virtual healthcare, were disproportionally
affected a more real world experience, we
considered that their inclusion would introduce confounding variables
into the statistical analysis and make it less rigorous. For this reason,
we excluded these patients who received different treatment and may
also have GI side effects from COVID itself.

Unfortunately, the number of patients included in our study was too
small to examine the impact of socioeconomic background on time to
presentation and outcomes. We suspect that patients with poorer access
to healthcare, including virtual healthcare, were disproportionally
affected a more real world experience, we
considered that their inclusion would introduce confounding variables
into the statistical analysis and make it less rigorous. For this reason,
we excluded these patients who received different treatment and may
also have GI side effects from COVID itself.

4. Conclusion

Pediatric patients who presented to the ED at our institution with
appendicitis during the peak of the COVID–19 pandemic had higher
rates of delayed presentation, more severe illness and worse outcomes
when compared to patients presenting during the same months in
2019. We hypothesize that the fear of contracting COVID–19 in the
hospital setting primarily led to our observed outcomes. Additionally,
decreased access to outpatient care and increased need for transfer
between healthcare centers likely also contributed to delayed presenta-
tion and treatment. The continued COVID-19 outbreak poses many
challenges with trying to mitigate viral transmission while continuing
to provide care for patients with other illnesses. Integrating telemedici-
ene as an avenue for outpatient screening of patients for conditions
requiring timely treatment may help decrease delay in presentation
during a pandemic. Additionally, creating public service announce-
ments guiding parents on the symptoms of appendicitis as well as the
importance of contacting an established medical hotline or virtual
provider for triage provides another resource for preventing delays.
We must continue to advocate for our patients and create an environ-
ment in which they feel safe seeking medical care.

Declarations of competing interest

None.

Funding

None.

References

[1] Van den Bogaard V, Euser S, Van der Ploeg T, et al. Diagnosed perforated appendicitis
in pediatric patients: a new model. J Pediatr Surg. 2016;51(3):444–8. https://doi.org/
10.1016/j.jpedsurg.2015.10.054.

[2] Singh M, Kadian Y, Rattan K, et al. Complicated appendicitis: analysis of risk factors
in children. Afr J Paediatr Surg. 2014;11(2):109–13.

[3] Williams R, Blakely M, Fischer P, et al. Diagnosing ruptured appendicitis preopera-
tively in pediatric patients. J Am Coll Surg. 2009;208(5):819–25. https://doi.org/10.
1016/j.jamcollsurg.2009.01.029.

[4] Bekele A, Mekasha A. Clinical profile and risk factors for perforation of acute appen-
dicitis in children. East Afr Med J. 2006;83(8):434–9. https://doi.org/10.4314/eamj.
2006.83.8.457.

[5] Ashcraft KW, Holcomb III GW, Murphy JP. Ashcraft’s Paediatric surgery. 5th ed.
Philadelphia: Elsevier; 2010.

[6] Papandria D, Goldstein S, Rhee D, et al. Risk of perforation increases with delay in
recognition and surgery for acute appendicitis. J Surg Res. 2013;184(2):723–9.
https://doi.org/10.1016/j.jss.2012.12.008.

[7] Cappendijk V, Hazebroek F. The impact of diagnostic delay on the course of acute
appendicitis. Arch Dis Child. 2000;83(1):64–6. https://doi.org/10.1136/adc.83.1.64.

[8] Broeker M, van Lieshout E, van der Elst M, et al. Discriminating between simple and
perforated appendicitis. J Surg Res. 2012;176(1):79–83. https://doi.org/10.1016/j.
jss.2011.09.049.

[9] Oliak D, Yamin D, Udani V, et al. Can perforated appendicitis be diagnosed
preoperatively based on admission factors? J Gastrointest Surg. 2000;4(5):470–4.
https://doi.org/10.1016/S1091-255X(00)80088-8.

[10] Lazzarini M, Barbi E, Apicella A, et al. Delayed access or provision of care in Italy
resulting from fear of COVID-19. Lancet Child Adolesc Health. 2020;4(5):E10–1.
https://doi.org/10.1016/S2325-4647(20)30108-5.

[11] Snapir O, Danziiger C, Krauze I, et al. Delayed diagnosis of paediatric appendicitis
during the COVID-19 pandemic. Acta Paediatr. 2020. https://doi.org/10.1111/apa.
15376.

[12] Howell E, Dubina E, Lee S. Perforation risk in pediatric appendicitis: assessment
and management. Pediatric Health Med Ther. 2018;9:135–45. https://doi.org/10.2147/PHMT.S153302.

[13] Williams N, Bello M. Perforation rate relates to delayed presentation in childhood
acute appendicitis. J R Coll Surg Edinb. 1998;43(2):101–2.

[14] St Peter S, Sharp S, Holcomb B, et al. An evidence-based definition for perforated
appendicitis derived from a prospective randomized trial. J Pediatr Surg. 2008;43(12):
2242–5. https://doi.org/10.1016/j.jpedsurg.2008.08.051.

[15] England R, Crabbe D. Delayed diagnosis of appendicitis in children treated with
antibiotics. Pediatr Surg Int. 2006 Jun;22(6):541–5. https://doi.org/10.1007/s00383-
005-1625-0.

[16] Rothrock S, Skeoch G, Rush J, et al. Clinical features of misdiagnosed appendicitis
in children. Ann Emerg Med. 1991;20(1):45–50. https://doi.org/10.1016/s0196-0644
(05)81117-5.

[17] Wilson D, McCallion W. Diagnostic delay in appendicitis. Br J Gen Pract. 1995;45
(395):326.

[18] Horowitz J, Gursoy M, Jaksic T, et al. Importance of diarrhea as a presenting
symptom of appendicitis in very young children. Am J Surg. 1997;173(2):80–2. https://doi.
org/10.1016/S0002-9610(96)90417-5.

[19] Choi J, Ryyo E, Jo J, et al. Risk factors of delayed diagnosis of acute appendicitis in
children: for early detection of acute appendicitis. Korean J Pediatr. 2016;59(9):
368–73. https://doi.org/10.3345/kjp.2016.59.9.368.

[20] O’Toole S, Karamanoukian H, Allen J, et al. Insurance-related differences in the prese-
ntation of pediatric appendicitis. J Pediatr Surg. 1996;31(8):1032–4. https://doi.org/
10.1016/S0022-3468(96)90079-2.

[21] Smink D, Fishman S, Kleinman K, et al. Effects of race, insurance status and hospital
volume on perforated appendicitis in children. Pediatrics. 2005;115(4):920–5.
https://doi.org/10.1542/peds.2004-1363.
[22] Pham XB, Sullins V, Kim D, et al. Factors predictive of complicated appendicitis in children. J Surg Res. 2016;206(1):62–6. https://doi.org/10.1016/j.jss.2016.07.023.

[23] Romero J, Valencia S, Guerrero A. Acute appendicitis during coronavirus disease 2019 (COVID-19): changes in clinical presentation and CT findings. J Am Coll Radiol. 2020. https://doi.org/10.1016/j.jacr.2020.06.002.

[24] Keesara S, Jonas A, Schulman K. Covid-19 and health care’s digital revolution. NEJM. 2020. https://doi.org/10.1056/nejmp2005835 Epub ahead of print.

[25] Cheng V, Wong S, Chen J, et al. Escalating infection control response to the rapidly evolving epidemiology of the coronavirus disease 2019 (COVID-19) due to SARS-CoV-2 in Hong Kong. Infect Control Hosp Epidemiol. 2020;41(5):493–8. https://doi.org/10.1017/ice.2020.58.