Decreased Cases of Pediatric Intussusception During COVID-19

Jun Sung Park

Asan Medical Center

Young-Hoon Byun

CHA University School of Medicine

Seung Jun Choi

Asan Medical Center

Jong Seung Lee

Asan Medical Center

Jeong-Min Ryu

Asan Medical Center

Jeong-Yong Lee (✉ pedkorea@gmail.com)

Asan Medical Center

Research Article

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Abstract

Objectives: Coronavirus disease 2019 (COVID-19) changed the epidemiology of various diseases. The present study retrospectively investigated the epidemiologic and clinical changes of intussusception from before to after the COVID-19 outbreak, when communicable diseases other than COVID-19 have dramatically decreased due to social lockdown.

Methods: The incidence of intussusception and the total monthly visits, including communicable and non-communicable diseases, aged ≤ 7 years, were investigated from February 2019 to January 2021 in a single pediatric emergency department of a university-affiliated tertiary hospital. The relationship between the incidence of communicable disease and intussusception was analyzed. The clinical characteristics of patients with intussusception were compared for the one-year periods before (February 2019–January 2020) and after (February 2020–January 2021) social lockdown due to COVID-19.

Results: Incidence of communicable disease, non-communicable disease, and intussusception is decreased after COVID-19 outbreak (15,932 to 3,880 [24.4%], 12,994 to 8,050 [62.0%], and 87 to 27 [31.0%], respectively). The incidence of intussusception correlated significantly with the change in incidence of communicable diseases (Poisson log-linear regression, Odds ratio=2.15, 95% CI=1.08–4.26, $P=0.029$). Compared with non-pandemic period, patients of pandemic period showed higher proportions of pathologic leading point and hospitalization (14.8% vs. 2.3%, 18.5% vs. 4.6%, respectively), lower base excess (-4.8 mmol/L vs. -3.6 mmol/L), and higher lactate concentration (1.7 mmol/L vs. 1.5 mmol/L).

Conclusions: The incidence of pediatric intussusception decreased after the COVID-19 pandemic. This reduced incidence may be related to the reduced incidence of communicable diseases. However, the proportions of more severe disease and PLPs were higher after the COVID-19 pandemic.

Introduction

Coronavirus disease 2019 (COVID-19) is an acute respiratory disease caused by severe acute respiratory syndrome coronavirus 2 (1). It was declared a worldwide pandemic in March 2020, causing more than 100 million confirmed cases and more than 2 million deaths through January 2021 (2). Because more than 400,000 confirmed cases and 10,000 deaths per day, many countries have adopted quarantine strategies, such as wearing masks, social distancing, and lockdown, to reduce person-to-person contact and prevent further spread (3). Such responses during epidemics of other respiratory infections in the past, such as influenza H1N1 and Middle East respiratory syndrome, were found to reduce the incidence of other communicable diseases (4, 5). In Taiwan, these quarantine strategies during COVID-19 resulted in incidental reductions in infectious diseases, such as influenza and pneumococcal diseases (6).

Meanwhile, the possibility that the COVID-19 pandemic and its resultant quarantine strategies could have reduced the incidence of intussusception in pediatric patients is also suggested (7). Intussusception, the most frequent cause of intestinal obstruction in children aged 5 months to 3 years and the most common surgical abdomen in children younger than 2 years (8), is defined as the invagination of one segment of

the intestine within a more distal segment (9) but the etiology of intussusception remains poorly understood, with pathologic lead points (PLPs), such as lymphoproliferative diseases, and duplication cyst, seen in only 3% of patients, whereas 60–100% have idiopathic intussusception (9, 10). Several infectious factors, such as rotavirus vaccination, non-enteric type adenovirus, and human herpes virus-6, have been reported to contribute to the pathogenesis of intussusception (11–13). In addition, a seasonal variation of intussusception suggests that infectious or climatic conditions contribute to its pathogenesis (11, 13–15) as other surgical conditions do (16, 17). Likewise, epidemiologic and clinical changes of intussusception in the COVID-19 pandemic could provide a clue for its pathogenesis. However, there was no study conducted about epidemiologic and clinical changes of intussusception during the COVID-19 pandemic when communicable diseases other than COVID-19 have dramatically decreased due to social lockdown.

This study, therefore, evaluated changes in the incidence and clinical characteristics of intussusception between the pre-pandemic and pandemic period of COVID-19.

Materials And Methods

Study Design and Setting

This study retrospectively evaluated patients aged ≤ 7 years diagnosed with intussusception at the pediatric ED of a university-affiliated tertiary hospital between February 2019 and January 2021. The research institute's pediatric ED is available for pediatric specialists 24 hours a day, and about 40 thousand patients visit the hospital annually. Medical records showing patients' detailed demographic and clinical characteristics were reviewed, including age, gender, medical history, laboratory results, and hospital course. Recurrence of intussusception within 48 hours was considered the same episode, whereas recurrence after 48 hours was considered a separate episode. Patients with a history of abdominal surgery were excluded from this study. This study was approved by the Institutional Review Board for Human Research of Asan Medical Center (IRB No. 2021-0082).

To analyze epidemiologic changes of the overall ED visits, we collected information of all the patients under age 7 who visited the research ED during the same study period. None was excluded. Basic demographic characteristics and diagnoses of these patients were recorded. Diagnoses were coded according to the International Statistical Classification of Diseases and Related Health Problems, tenth Revision version 2019 (ICD-10 ver. 2019) by ED physicians who were specialists in pediatrics or emergency medicine and had experience using ICD-10 codes over 7 years. The diagnostic codes were classified into two groups: communicable and non-communicable diseases. Communicable diseases included all codes of groups A and B, corresponding to certain infectious and parasitic diseases, and codes of infectious diseases for each system (e.g., G03, meningitis in the nervous system; H66, acute otitis media in the ear and mastoid process; and J18, pneumonia in the respiratory system). To include all possible infectious diseases, the specific codes of group R, corresponding to the symptoms, signs, and abnormal clinical and laboratory findings not otherwise classified, were included: fever, cough, sputum,

rhinorrhea, vomiting, and diarrhea. All diagnoses that did not correspond to these descriptions were classified as non-communicable diseases.

The time point for dividing the pre-pandemic from the pandemic period was defined as February 2020, the time of the first COVID-19 outbreak and lockdown of public facilities, schools, and kindergartens (supplementary figure 1). The pre-pandemic period was defined as the 1-year period from February 2019 to January 2020, and the pandemic period was the 1-year period from February 2020 to January 2021. The local COVID-19 epidemiology and lockdown status of the research institution was determined from press releases by the government institutions (18).

Measures and Outcomes

The primary outcome was the incidence of intussusception before and after the outbreak of the COVID-19 pandemic. The secondary outcome was the correlation between epidemiological changes in communicable diseases and the incidence of intussusceptions. The last outcome was the differences in the clinical characteristics of patients with intussusception before and after the outbreak of COVID-19.

Data Analyses

Descriptive data on the COVID-19 outbreak and ED visits were recorded and expressed using a graph and table, as determined by Excel 365 (Microsoft Corp., Redmond, WA). Continuous variables before and after the pandemic outbreak were compared using the Mann-Whitney *U* test, and categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. Correlations between the incidence of intussusception and disease categories were determined by Poisson log-linear regression analyses. All statistical analyses were performed using PASW Statistics for Windows Version 18.0 (SPSS Inc., Chicago, Ill), with *P* values < 0.05 considered statistically significant.

Results

Incidence of intussusception and its association with monthly ED visits

Epidemiological information of the COVID-19 outbreak in the local research institution is presented in supplementary figure 1. Three outbreaks of COVID-19 occurred in 2020, in February, August, and December. Limited use or lockdown of all public facilities, schools, and daycare centers was implemented immediately after the first outbreak and was continued due to repeated outbreaks.

Figure 1 shows monthly ED visits by patients aged ≤ 7 years during the 1-year pre-pandemic period from February 2019 to January 2020 and during the 1-year pandemic period from February 2020 to January 2021. There were 28,018 ED visits by patients in this age group during the pre-pandemic period, but after the outbreak, all kinds of visits decreased dramatically, and there were only 11,800 (42.1%) of the overall visits (figure 1A). ED visits for communicable diseases decreased from 15,912 to 3,880 (24.4%), and the proportions also decreased from 56.9% to 32.9% during the pandemic period compared to the pre-

pandemic period (figure 1B). On the other hand, although visits for non-communicable diseases decreased from 12,994 to 5,080 (62%), the proportion increased from 46.4% to 68.2% during the pandemic compared to the pre-pandemic period.

During the 2-year study period, 114 patients were diagnosed with intussusceptions. Of these 114 patients, 87 were diagnosed with intussusception during the pre-pandemic year, whereas 27 (31% of those with the pre-pandemic period) were diagnosed after the outbreak of COVID-19 (figure 1C). Poisson log-linear regression analysis showed that only monthly visits for communicable diseases significantly correlated with the incidence of intussusception (Odds ratio=2.15, 95% CI=1.08–4.26, $P=0.029$, supplementary figure 2).

Clinical characteristics of intussusception before and during the COVID-19 pandemic

Table 1 summarizes the demographic and clinical characteristics of pediatric patients diagnosed with intussusception in the pre-pandemic and the pandemic period. Age at onset, sex, previous history of intussusception, rate of rotavirus vaccination, concomitant gastrointestinal tract infection, symptoms of upper respiratory tract infection, duration of illness, and initial presentations did not differ between the two periods (all $P \geq 0.05$). Time to air enema reduction was significantly longer during the pandemic period than during the pre-pandemic period (3.1 hours vs. 2.6 hours, $P < 0.001$), but there were no differences in the final rates of successful reduction ($P = 0.139$). However, hospital admission rate (18.5% vs. 4.6%, $P = 0.03$) and proportion of underlying PLP (14.8% vs. 2.3%, $P = 0.03$) were higher during the pandemic than during the pre-pandemic period. Laboratory testing showed that base excess (BE) was lower (-4.8 mmol/L vs. -3.6 mmol/L, $P = 0.03$) and serum lactate concentration higher (1.7 mmol/L vs. 1.5 mmol/L, $P = 0.02$) after the outbreak of COVID-19.

Discussion

The present study showed that the incidences of both ED visits and intussusception were lower during the pandemic period compared to the pre-pandemic period of COVID-19. The decrease in ED visits for communicable diseases was more pronounced than the decrease in visits for non-communicable diseases, with the former significantly correlating with the incidence of intussusception. This suggests that communicable diseases may participate in the pathogenesis of intussusception. In addition, intussusceptions following the COVID-19 outbreak had a higher proportion of PLPs and showed more deteriorated laboratory tests than intussusceptions before the pandemic.

Epidemiological studies have attempted to determine the correlation between intussusception and communicable diseases (14, 15, 19, 20). Because these studies are oriented to seasonal or epidemiological changes in gastroenteritis and climate, the variables can confound each other. To our knowledge, the present study is the first to report that a marked reduction in the incidence of communicable diseases correlated with a reduction in the incidence of intussusception during the same period of 12 months, covering the same season and climate. Because the incidence of intussusception due to PLP rather increased between two study periods, the change in the incidence of intussusception

would be mainly due to a reduction in communicable diseases. Mesenteric lymphoid tissue swelling or bowel wall thickening may partially explain the relationship between non-specific communicable diseases and intussusception (12). Enteric viruses, including astroviruses, enteroviruses, noroviruses, and caliciviruses, are frequently asymptomatic or undetected but may be a trigger or predisposing factor for developing of intussusception (6, 21–23). In addition, COVID-19 associated intussusception may result from the widespread immune activation occurring in COVID-19 (24). Although none of the patients in this study were confirmed as having COVID-19, non-specific communicable diseases other than gastrointestinal tract infection might activate the immune system, resulting in hypertrophy of intestinal Peyer's patches and inducing intussusception.

Although basic demographic and clinical characteristics did not differ in patients who visited the ED before and after the outbreak of COVID-19, PLPs were more frequent during the pandemic period. Compared with idiopathic intussusception, intussusceptions due to PLP have been associated with poorer outcomes and may not be amenable to standard treatment owing to differences in intussusception locations (25, 26). Indeed, there were differences in serum lactate levels and base excess, possible markers of organ failure, in patients assessed before and after the COVID-19 outbreak. In particular, high serum lactate levels have been associated with poor outcomes of intussusception (27). Although air enema reduction was delayed for about 0.5 hours in patients who visited during the pandemic period, the duration of illness in these patients was similar to that in patients who visited during the pre-pandemic period. Patients underwent laboratory tests immediately after diagnosis of intussusception indicating that organ failure had already progressed rather than delayed treatment. The differences in patient characteristics before and after the outbreak of COVID-19 indicate that patients with intussusception during the COVID-19 outbreak may require more careful efforts to identify the PLP and undergo rapid resuscitation.

This study had several limitations. First, the decrease in ED visits for intussusception indicates a decrease in its actual incidence because intussusception is hard to be reduced spontaneously and requires immediate reduction; otherwise, it can be fatal (28). Second, although the dramatic reduction in ED visits for communicable diseases observed after the COVID-19 outbreak is consistent with global trends (6, 21–23), changes in ED visits for communicable diseases may not reflect actual changes in their incidence. The patients with relatively mild symptoms could be reluctant to visit ED and underestimated due to the fear of contact with COVID-19 and limited medical resources (24). Third, considering it was a retrospective study using the previously recorded ICD-10 codes and not all the patients underwent diagnostic tests to identify a specific pathogen, there is a possibility to misclassify the patients because the codes, especially the R code without a discrete diagnosis of disease, did not completely describe the affected system or specific pathogen. However, we used the final diagnosed code of an episode in the overall follow-up period, including all the ED, admission, and outpatient clinic visits, to minimize misclassification. Forth, the statistical power of this study was likely reduced due to the small number of patients with intussusception. Therefore, further large-scale, multi-center studies are needed to validate our results, because of the dramatically decreased incidence of intussusception in a single center. Finally, it is important to understand the epidemiological peculiarities of South Korea with a

smaller population geographically than countries in Europe and the USA and sufficient medical infrastructure than developing countries.

Conclusions

The incidence of pediatric intussusception was decreased after the COVID-19 pandemic. This reduced incidence may be related to the reduced incidence of communicable diseases. However, the proportions of more severe disease and PLPs were higher after the COVID-19 pandemic.

Declarations

Ethics approval and consent to participate: This study was approved by the institutional review board of the Asan Medical Center, Seoul, Korea (IRB number: 2021-0082). Waiver of informed consent was granted because there was minimal risk to subjects as A) this study retrospectively reviewed data collected from patients as part of established or routine standard of care B) no diagnostic or therapeutic interventions were performed. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication: Not applicable

Availability of data and materials: The datasets generated and analyzed during the current study are not publicly available due that IRB of the Asan Medical Center (IRB No. 2021-0082) did not allow to share with out-of-hospital facility because of ethical consideration but are available from the corresponding author on reasonable request after permission of the institutional review board and de-identification of data.

Competing interests: The authors declare that they have no competing interests

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Authors' contributions: All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Jun Sung Park, Young-Hoon Byun, Seung Jun Choi, Jong Seung Lee, Jeong-Min Ryu, and Jeong-Yong Lee. The first draft of the manuscript was written by Jun Sung Park and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1. Clinical characteristics of patients with intussusception before and after the COVID-19 outbreak

Variables	Non-pandemic N=87	Pandemic N=27	Total N=114	<i>P</i> value
Age, month	25 (16–37)	24 (14–31)	24.5 (16–36)	0.582
Sex, male	63 (72.4)	23 (85.2)	86 (75.4)	0.210
Past history of intussusception	9 (10.3)	6 (22.2)	15 (13.2)	0.188
Rotavirus vaccination	78 (89.7)	24 (88.9)	102 (89.5)	1.000
Concomitant GITI	21 (24.1)	6 (22.2)	27 (23.7)	1.000
Concomitant URTI	13 (14.9)	4 (14.8)	17 (14.9)	1.000
Duration of illness	13 (4–48)	9 (4–24)	12 (4–24)	0.140
Symptoms				
Abdominal pain	83 (95.4)	25 (92.6)	108 (94.7)	0.626
Cyclic irritability	74 (85.1)	22 (81.5)	96 (84.2)	0.763
Vomit	31 (35.6)	11 (40.7)	42 (36.8)	0.653
Hematochezia	14 (16.1)	8 (29.6)	22 (19.3)	0.161
EDLOS, h	9.5 (7.9–11.4)	9.2 (7.7–11.5)	9.4 (7.8–11.4)	0.886
ED course				
Time to diagnosis	0.6 (0.3–1)	0.8 (0.4–1.6)	0.6 (0.4–1.1)	0.063
Time to air reduction	2.6 (1.8–3.6)	3.1 (2.5–4.5)	2.9 (2.0–3.7)	0.000
Success to air reduction	86 (98.9)	25 (92.6)	111 (97.4)	0.139
Admission	4 (4.6)	5 (18.5)	9 (7.9)	0.033
Pathologic leading point	2 (2.3)	4 (14.8)	6 (5.3)	0.027
Laboratory test				
WBC, $\times 10^3/\mu\text{L}$	10 (7.6–12.9)	10.5 (8–15.6)	10.3 (7.9–13.2)	0.437
CRP, mg/dL	0.2 (0.1–0.6)	0.3 (0.1–0.7)	0.2 (0.1–0.6)	0.839
Bicarbonate, mmol/L	19.6 (18.4–21.1)	19.2 (17.7–20.9)	19.6 (18.3–21.1)	0.454
BE, mmol/L	-3.6 (-4.9–2.3)	-4.8 (-5.5–3.7)	-4 (-5.1–2.6)	0.030
lactate, mmol/L	1.5 (1.1–1.8)	1.7 (1.4–2.4)	1.5 (1.2–1.9)	0.016
COVID-19 confirmed	0 (0)	0 (0)	0 (0)	NA

Abbreviations: COVID-19, coronavirus disease 2019; GITI, gastrointestinal tract infection; URTI, upper respiratory tract infection; EDLOS, length of ED stay; ED, emergency department; WBC, white blood cell; CRP, c-reactive protein; BE, base excess; NA, not applicable.

Results are presented as number (%) or median (interquartile range).

Figures

Figure 1

Trends of ED visits and prevalence of childhood intussusception along COVID-19 outbreak. A: Monthly ED visits during overall study period. B: Monthly proportion of communicable and non-communicable diseases over total ED visits. C: Monthly number of patients with intussusception. Vertical dotted line: COVID-19 outbreak and closure of public facilities including kindergarten

Supplementary Files

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