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# Changes in the Incidence of Intussusception and Infectious Diseases After the COVID-19 Pandemic in Korea

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## ABSTRACT

**Background:** Intussusception refers to the invagination of a part of the intestine into itself. The exact cause for this condition is unknown in most cases. The active implementation of coronavirus disease 2019 (COVID-19) infection control guidelines has reduced the spread of COVID-19 and the incidence of other infectious diseases in children. The current study aimed to identify changes in pediatric intussusception and infectious diseases after the implementation of infection control guidelines and confirm the association between intussusception and contagious diseases.

**Methods:** We analyzed the electronic medical records of pediatric patients diagnosed with intussusception from seven hospitals in Korea between January 2017 and December 2020. We used open data from the Korea Disease Control and Prevention Agency to investigate changes in infectious diseases over the same period.

**Results:** Altogether, we evaluated 390 children with intussusception. There was a statistically significant decrease in the incidence of monthly visits with intussusception in the COVID-19 period group (9.0 vs. 3.5,  $P < 0.001$ ). When the monthly incidence of infectious diseases was compared between the pre-COVID-19 and the COVID-19 periods, a statistically significant decrease in respiratory viruses (7979.0 vs. 815.2,  $P < 0.001$ ), enterovirus infection (262.2 vs. 6.6,  $P < 0.001$ ), and viral enteritis (916.2 vs. 197.8,  $P < 0.001$ ) were confirmed in the COVID-19 period. Through interrupted time series analysis, it was confirmed that the incidence of intussusception and viral infectious diseases have drastically decreased since March 2020, when COVID-19 infection control guidelines were actively implemented.

**Conclusion:** We confirmed that implementing infection control guidelines during the COVID-19 pandemic resulted in a decrease in intussusception and viral infectious diseases. Through this result, it was possible to indirectly confirm the existing hypothesis that viral infections play a significant role in the pathophysiologic mechanism of intussusception.

**Keywords:** COVID-19; Intussusception; Viral infection, Social Distancing, Incidence Rate

## INTRODUCTION

Intussusception is the invagination of a part of the intestine into itself, and is the most common cause of acute intestinal obstruction in early childhood.<sup>1,2</sup> It is a clinically relevant

emergency disease as it can lead to ischemia, perforation, peritonitis, and even death in the absence of timely diagnosis and treatment.<sup>3</sup>

In some cases, anatomical lead points are the cause of intussusception. However, the exact cause is unknown in most cases.<sup>3-8</sup> One hypothesis is that infectious pathogens may be responsible for stimulating lymphatic tissue in the intestinal tract, resulting in hypertrophy of Peyer's patches in the lymphoid-rich terminal ileum.<sup>9</sup> This serves as a lead point for ileocolic intussusception. Consistent with this hypothesis, several studies have shown a statistically significant association between viral infections such as adenovirus, enterovirus, norovirus, or bacterial infection with intussusception.<sup>9-12</sup> Nonetheless, there is a shortage of information on the studies showing a clear association between intussusception and infection.

On March 11, 2020, the World Health Organization declared the coronavirus disease 2019 (COVID-19) outbreak a global pandemic.<sup>13</sup> Since then, many countries have initiated actions to prevent the spread of COVID-19.<sup>14</sup> In Korea, infection control policies such as social distancing, school closure, and enforcement of personal protection measures such as wearing masks in public, have been implemented during the COVID-19 pandemic.<sup>15</sup> These rapid lifestyle changes have reduced the spread of COVID-19 and had a great impact on the incidence of other pediatric infectious diseases, including respiratory viral infections and some non-infectious diseases, such as intussusception.<sup>16-19</sup>

Thus, the current study aimed to investigate the impact of the changing epidemiology of viral infections during the COVID-19 pandemic on the incidence of intussusception using data from seven hospitals and Korea Disease Control and Prevention Agency (KDCA) open data. And through this, we aimed to indirectly confirm the existing hypothesis that infectious diseases play an important role in the pathophysiologic mechanism relating to the occurrence of intussusception.

## METHODS

### Study definitions

In Korea, infection control policies such as social distancing, school closure, wearing masks in public, and encouraging frequent hand hygiene have been implemented since March 2020 due to the COVID-19 pandemic. Using this period as the reference point, the pre-COVID-19 and COVID-19 periods were divided. In our analysis, the 'pre-COVID-19 period' was defined as the time from January 2017 to February 2020, and the 'COVID-19 period' was defined as the time between March 2020 and December 2020.

### Subjects

We analyzed the electronic medical record data of pediatric patients diagnosed with intussusception from seven hospitals located in different regions of South Korea between January 2017 and December 2020: Seoul St. Mary's Hospital, Yeouido St. Mary's Hospital, Uijeongbu St. Mary's Hospital, Incheon St. Mary's Hospital, Bucheon St. Mary's Hospital, St. Vincent's Hospital, Eunpyeong St. Mary's Hospital. Three hospitals are located in the central region (Seoul), one hospital is located in the northern region (Uijeongbu), two hospitals are located in the western region (Incheon, Bucheon), and one hospital is located in the southwestern region (Suwon). Of the 7 hospitals, 4 hospitals are tertiary referral hospitals, 3 hospitals are secondary hospitals, and all have a pediatric emergency department

that is accessible at all hours. From 2017 to 2019, each hospital's pediatric emergency department had an estimated 2,000 to 6,000 annual visits. Due to the impact of the COVID-19 pandemic, the number of annual visits at each hospital had decreased from 1,000 to 4,000 in 2020. Emergency imaging tests for intussusception diagnosis were available at all times. All patients were diagnosed with intussusception through imaging tests, mostly through abdominal ultrasonography, and some through abdominal computed tomography. Patients were divided into a pre-COVID-19 period group and a COVID-19 period group, and demographic factors, clinical characteristics, and radiological findings of the patients were retrospectively analyzed.

Additionally, two different diseases (syncope and anaphylaxis) were selected that would have low relevance to infection control policies. We made these two selections based on the number of patients diagnosed with these diseases in the pediatric emergency room before and after the COVID-19 pandemic.

### Data extraction for the study of infectious diseases

The KDCA has been providing open data on various infectious diseases through its website since 2001.<sup>20</sup> KDCA provides monthly and yearly data on infectious diseases, including respiratory viruses, enteroviruses, and pathogens that cause gastroenteritis. The data were collected from 192 hospitals participating in sample surveillance through the National Infectious Disease Surveillance System. Data were for all age groups, and the total number of samples reported during the study period was 397,788.

We extracted data from January 2017 to December 2020 from the KDCA database. Respiratory viruses included adenovirus, human bocavirus, parainfluenza virus, respiratory syncytial virus, rhinovirus, human metapneumovirus, human coronavirus, and influenza virus. Besides, enteroviral ailments included diseases such as herpetic stomatitis, hand, foot, and mouth disease, acute hemorrhagic conjunctivitis, aseptic meningitis, encephalitis, myocarditis, pericarditis, and neonatal sepsis. Pathogens that cause gastroenteritis include rotavirus, astrovirus, enteric adenovirus, norovirus, sapovirus, *Salmonella enteritis*, *Vibrio cholerae* enterotoxigenic *Escherichia coli*, enteroinvasive *E. coli*, enteropathogenic *E. coli*, *Campylobacter sp.*, *Clostridium perfringens*, *Staphylococcus aureus*, *Bacillus cereus*, and *Yersinia enterocolica*. We compared changes in the number of patients monthly before and after the COVID-19 pandemic.

### Statistical analysis

Categorical variables were compared using the chi-squared test, and continuous variables were compared using the Mann-Whitney test. We performed an interrupted time-series analysis of disease incidence before and after the COVID-19 pandemic. In this study, the interrupted time series (ITS) model estimated the immediate change associated with the outbreak time point (change in level) and the change in slope from the baseline trend to the post-outbreak direction (change in trend). We used the Durbin-Watson test to detect autocorrelation. At the same time, we used SAS Proc AUTOREG with the BACKSTEP option to automatically select the correct order of the autoregressive model through backward elimination from an initial full model with order ( $k$ ) = 12. Model fit was assessed using visual plots (autocorrelation function, partial autocorrelation function white noise probabilities, and autocorrelation functions).

All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA) and R software version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria). A two-sided  $P$  value  $< 0.05$  was considered statistically significant.

### Ethics statement

The study was approved by the Institutional Review Board (IRB) of Seoul St. Mary's Hospital (IRB No. XC21WIDI0015). Informed consent from the study participants and their guardians was waived.

## RESULTS

### Baseline characteristics of patients with intussusception

In this study, we studied 390 children with intussusception. The median age of the patients was 24 months (interquartile range, 15.0–34.0 months), and 70.5% were male. None of the patients had COVID-19 infection before or at the time of intussusception diagnosis.

### Changes in the incidence of intussusception and other pediatric emergency diseases after the COVID-19 pandemic

We compared the monthly number of patients with intussusception, anaphylaxis, and syncope in the pediatric emergency departments of seven hospitals in the pre-COVID-19 and COVID-19 periods. A statistically significant decrease in the number of patients with intussusception ( $P < 0.001$ ) was confirmed, while the number of patients with anaphylaxis ( $P = 0.547$ ) and syncope ( $P = 0.493$ ) did not change significantly, as shown in **Table 1**.

### Changes in the incidence of infectious diseases after the COVID-19 pandemic

We analyzed the sample surveillance data from KDCA between January 2017 and December 2020 to ascertain the monthly incidence of infectious diseases in the pre-COVID-19 and COVID-19 periods. When the average monthly incidence of diseases in the pre-COVID-19 and COVID-19 periods was compared, a sharp decrease in respiratory viruses ( $P < 0.001$ ), enterovirus infection ( $P < 0.001$ ), and viral enteritis ( $P < 0.001$ ) were observed. There was no statistically significant change in the incidence of bacterial enteritis ( $P = 0.542$ ) (**Table 2**).

**Table 1.** Comparison of the monthly incidence of emergency pediatric diseases before and after COVID-19 in seven hospitals

Diseases	Pre-COVID-19 period	COVID-19 period	$P$ value
Intussusception	9.0 (6.0–11.0)	3.5 (2.0–5.0)	$< 0.001$
Anaphylaxis	6.0 (4.0–8.0)	5.5 (5.0–7.0)	0.547
Syncope	28.0 (20.0–37.0)	32.5 (23.0–41.0)	0.493

Data are presented as median (interquartile range).

COVID-19 = coronavirus disease 2019.

**Table 2.** Comparison of the monthly incidence of infectious diseases before and after COVID-19; confirmed as per the open data obtained from the Korea Disease Control and Prevention Agency

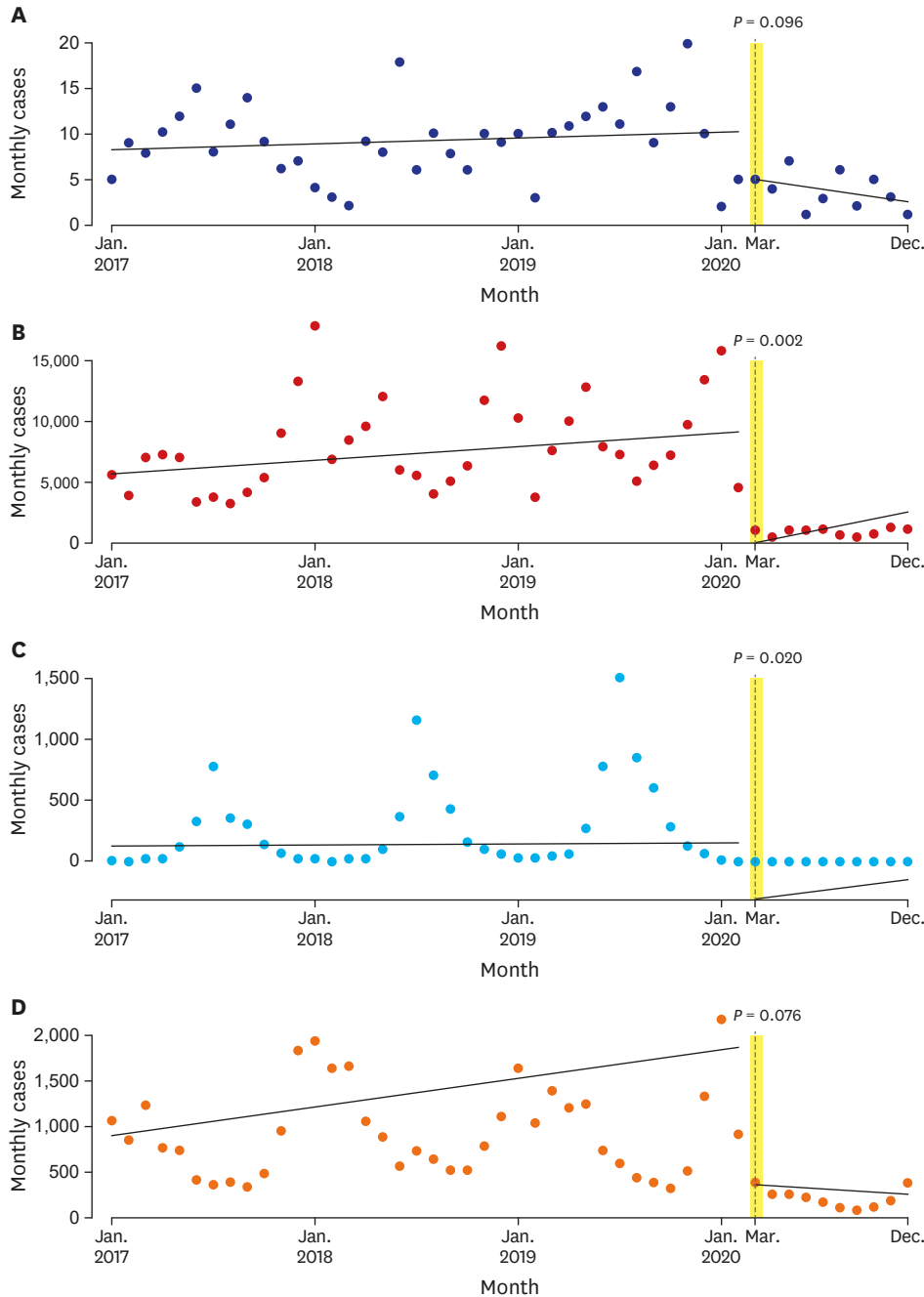
Diseases	Pre-COVID-19 period	COVID-19 period	$P$ value
Respiratory viruses	7,979.0 $\pm$ 3,850.8	815.2 $\pm$ 309.4	$< 0.001$
Enteroviruses	262.2 $\pm$ 353.6	6.6 $\pm$ 3.8	$< 0.001$
Viral gastroenteritis	916.2 $\pm$ 495.7	197.8 $\pm$ 105.2	$< 0.001$
Bacterial gastroenteritis	686.3 $\pm$ 334.0	776.3 $\pm$ 407.4	0.542

Data are presented as mean  $\pm$  standard deviation.

COVID-19 = coronavirus disease 2019.

**Impact of strong infection control policies on the occurrence of intussusception and viral infections**

An ITS analysis was performed using March 2020 as a time point, and a decrease in the monthly number of patients with intussusception ( $P = 0.096$ ) after the time point was confirmed. Although the  $P$  value was greater than 0.05, it was less than 0.1, indicating a marginally significant result. In the ITS analysis of respiratory viruses ( $P = 0.002$ ), enteroviruses ( $P = 0.02$ ), and viral enteritis ( $P = 0.076$ ), a decrease in the number of monthly patients was confirmed after March 2020, as shown in **Fig. 1**. Unlike ‘change in intercept,’



**Fig. 1.** Interrupted time series regression analysis of monthly cases by diseases. Horizontal lines depict interventions. The significance of intervention is shown in the center of the lines. (A) Intussusception. (B) Respiratory viruses. (C) Enteroviruses. (D) Viral enteritis.

**Table 3.** Interrupted time series regression analysis of monthly cases by diseases

Diseases	Change in intercept			Change in slope		
	Coefficient	Standard error	P value	Coefficient	Standard error	P value
Intussusception	-5.01	2.95	0.096	-0.34	0.43	0.440
Respiratory viruses	-7,748.74	2,405.84	0.002	-226.22	365.76	0.540
Enteroviruses	-452.4	186.73	0.020	-4.8	29.31	0.871
Viral enteritis	-621.69	341.94	0.076	-8.27	56.19	0.884

which shows changes in disease incidence, ‘change in slope,’ which shows trends in disease occurrence, did not show a statistically significant change in any disease, as shown in **Table 3**.

**Comparison of clinical characteristics of patients with intussusception before and after COVID-19**

The demographic and clinical characteristics of patients in the pre-COVID-19 and COVID-19 periods are summarized in **Table 4**. There was no difference between the two periods concerning the patient's age at the time of diagnosis, sex, intussusception type, and reduction method, and there were no other differences in clinical symptoms except for the occurrence of bloody or currant jelly stool ( $P = 0.002$ ) and fever ( $P = 0.049$ ). Laboratory examination showed no statistically significant difference in platelet count ( $P = 0.011$ ).

**Table 4.** Comparison of clinical characteristics of patients with intussusception before and after COVID-19

Variables	Pre-COVID-19 period (n = 346)	COVID-19 period (n = 44)	P value
Age at the time of diagnosis, mon	24 (15.0–35.0)	18.5 (10.5–31.8)	0.100
Male	245 (70.8)	30 (68.2)	0.719
The methods of reduction			0.211
Non-operative reduction	324 (93.6)	39 (88.6)	
Operation	22 (6.4)	5 (11.4)	
Intussusception type			1.000
Ileocolic type	16 (28.6)	6 (31.6)	
Ileoileal type or colocolic type	7 (2.0)	1 (2.3)	
Clinical symptom			
Abdominal pain or irritability	303 (87.6)	37 (84.1)	0.515
Vomiting	115 (33.2)	16 (36.4)	0.679
Bloody or currant jelly stool	69 (19.9)	18 (40.9)	0.002
Diarrhea	30 (8.7)	4 (9.1)	0.926
Fever	42 (12.1)	1 (2.3)	0.049
Upper respiratory symptoms	28 (8.1)	2 (4.5)	0.556
Past history of intussusception	36 (10.4)	6 (13.6)	0.604
Recurrent intussusception within 72 hr	44 (12.7)	6 (13.6)	0.864
Confirmation of leading points	2 (0.6)	1 (2.3)	0.302
Laboratory examination			
WBC	10,995 (8,617–13,777)	11,400 (10,060–14,340)	0.149
Eosinophil, %	0.5 (0.1–1.3)	0.3 (0.1–1.1)	0.196
Hb	12.3 (11.7–12.8)	12.4 (11.6–13.0)	0.838
Platelet	305,500 (259,500–369,750)	340,000 (302,000–425,000)	0.011
CRP	0.3 (0.1–0.9)	0.3 (0.1–1.0)	0.606
Glucose	103 (91–116)	102 (91–113)	0.639
Total protein	6.7 (6.4–6.9)	6.7 (6.4–7.0)	0.229
Albumin	4.4 (4.2–4.6)	4.5 (4.3–4.6)	0.207
AST	36 (31–41)	37 (32–40)	0.255
ALT	15 (13–20)	15 (12–21)	0.647
Sodium	139 (137–140)	138 (135–140)	0.047
Potassium	4.3 (4.1–4.6)	4.3 (4.2–4.6)	0.585
Chloride	104 (103–106)	104 (103–106)	0.275

Data are presented as median (interquartile range) or number (%). COVID-19 = coronavirus disease 2019, WBC = white blood cell, Hb = hemoglobin, CRP = C-reactive protein, AST = aspartate transaminase, ALT = alanine transaminase.

## DISCUSSION

In this study, we were able to confirm that the incidence of intussusception and viral infections in children after the COVID-19 pandemic was significantly reduced. To the best of our knowledge, there have been no such studies thus far, except for one study on the COVID-19 pandemic and changes in pediatric emergency diseases, including intussusception.<sup>21</sup> This is significant as it is the first study to reveal the impact of infection control measures during the COVID-19 pandemic on the incidence of intussusception.

During the COVID-19 pandemic, there have been many changes in the behavior of patients, especially pediatric patients in hospitals. There were more cases wherein hospital visits were avoided because of the fear of exposure to hospital-acquired COVID-19 infection. Besides, there were instances where it was difficult to visit the hospital due to each hospital's infection control guidelines. Since intussusception rarely improves on its own and there is gradual worsening of symptoms in the absence of proper treatment, it was thought that it would be relatively less affected by these changes than other pediatric diseases.<sup>3</sup> In addition, we attempted to increase the reliability of this study by analyzing data from seven hospitals across different regions and comparing it with other emergency pediatric diseases. Our analysis indicated that the incidence of other pediatric emergency diseases did not decrease even after the COVID-19 pandemic. When data from the seven hospitals were combined, there were no statistically significant differences in the incidences of other pediatric emergency diseases, however, only the incidence of intussusception was significantly reduced, despite the fact that all diseases included were medical emergencies. Therefore, it can be concluded that the incidence of intussusception decreased after the COVID-19 pandemic.

After the robust implementation of COVID-19 infection control policies, reduction of other pediatric infectious diseases was an expected consequence in clinical practice. We confirmed a statistically significant decrease in viral infections after the COVID-19 pandemic using the KDCA open data. Bacterial enteritis did not decrease during the period as food-mediated transmission is the leading cause of such infections.<sup>17</sup>

ITS analysis was performed to confirm how the implementation of a firm infection control policy directly affected the occurrence of intussusception and viral infections, and we investigated the relationship between intussusception and viral infection. Through ITS analysis, both intussusception and viral infections showed a decrease in the monthly number of patients after March 2020. Intussusception is not an infectious disease. Nevertheless, intussusception significantly decreased after implementation of the infection control policy, which is a result that can reinstate the existing hypothesis that viral infections play an important role in the pathophysiologic mechanism of intussusception.

When the basic demographic and clinical characteristics of patients were compared in cases of intussusception in the pre-COVID period group and the COVID period group, no difference was observed in most factors. There were statistically significant differences only in the occurrence of bloody or currant jelly stool, fever, and platelet count. Due to the limitations of the retrospective study, the time from the onset of symptoms to diagnosis in the emergency room could not be confirmed. However, due to the COVID-19 pandemic, it can be estimated that the time from intussusception to diagnosis is longer, and as a result, the number of patients with bloody or currant jelly stool and patients with elevated platelet counts has increased. The decrease in the number of patients with fever at the time of

diagnosis of intussusception was presumed to be related to a decrease in the incidence of intussusception associated with viral infection.

This study has several limitations. First, since the data of patients with intussusception is not large-scale data like that of the patients with infectious diseases and the hospitals participating in the study were concentrated in a specific area of Korea, there is a limit to the conclusions being representative of all patients in Korea. In addition, the ITS analysis did not show a strong statistical significance owing to the lack of the number of patients with intussusception. Nevertheless, we believe that since data were collected from multiple centers rather than a single hospital, it strengthens the findings of the study. Second, as mentioned earlier, factors other than viral infection may have influenced the reduction of intussusception. However, because intussusception is an emergency disease requiring treatment, and since changes in other emergency diseases were compared, the analysis for the different effects would not be significant.

In conclusion, after implementing infection control policies during the COVID-19 pandemic, the incidence of pediatric viral infections decreased sharply, along with the decrease in the incidence of intussusception. Through this, it was possible to indirectly confirm the existing hypothesis that viral infections play a significant role in the pathophysiologic mechanism relating to the occurrence of intussusception.

## ACKNOWLEDGMENTS

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