

Impact of the COVID-19 pandemic on the incidence of intussusception: a systematic review

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Abstract. – OBJECTIVE: We aimed to assess the impact of the coronavirus disease 2019 (COVID-19) pandemic on the incidence of intussusception.

MATERIALS AND METHODS: Literature search of the PubMed and EMBASE databases was conducted for articles published in English until August 5, 2022.

RESULTS: Overall, 127 articles were retrieved, and five studies from South Korea (n=4) and the United States of America (n=1) containing clinical data from single-center medical records to nationwide databases were ultimately included in the systematic review. All the included studies reported that the incidence of intussusception decreased significantly during the pandemic period compared with the pre-pandemic period. The communicable disease incidence tended to decrease even as the incidence of non-communicable diseases did not significantly change. There was no significant difference in the time to diagnosis between the pre-pandemic and pandemic periods; however, the time to radiologic reduction was significantly longer or not depending on the study.

CONCLUSIONS: The COVID-19 pandemic significantly reduced the incidence of intussusception in children, supporting the hypothesis that infection plays a major role in the etiology of intussusception. Future studies in the late pandemic or post-pandemic era, which would represent the level of implementation of non-pharmaceutical interventions and social distancing as well as additional data from various countries will be needed.

Key Words:

Intussusception, COVID-19, Pandemic, Incidence, Epidemiology, Trend, Time-to-treatment, Time-to-diagnosis.

Introduction

Intussusception is the invagination of a proximal segment of the bowel into an adjacent dis-

tal segment and a common etiology of bowel obstruction and abdominal emergency in infant and early childhood^{1,3}. Approximately 60% of intussusceptions occur in children younger than 1 year⁴. The incidence of intussusception is reported to be 74 per 100,000 infant-years in those younger than 1 year of age, and the peak incidence is 5-7 months of age².

Early diagnosis and treatment of intussusception are crucial⁵. If untreated, intussusception can be fatal, resulting in bowel ischemia, bowel necrosis, and perforation^{1,2}. The imaging modality of choice is ultrasound (US) in children due to its high sensitivity and specificity as well as its noninvasive nature^{1,3}. Due to their low sensitivity, the role of abdominal radiographs in diagnosing intussusception is controversial^{1,6}. However, abdominal radiographs are recommended for patients with suspected intussusception as part of the initial evaluation to provide radiographic evidence of perforation with free air, which requires operative management⁷. The treatment modalities for intussusception depend on the type of intussusception: ileocolic intussusception requires US- or fluoroscopy-guided hydrostatic (liquid) or pneumatic (air) enema reduction³, whereas small bowel intussusception can usually be safely observed and will reduce spontaneously⁸. Surgery is indicated if the patient is hemodynamically unstable or when close observation or enema reduction has failed^{3,9}. In addition, patients who have evidence of bowel necrosis or perforation require surgery³.

The etiology of intussusception is most commonly idiopathic¹. In approximately 10% of cases, a pathological lesion (lead point) exists, including Meckel's diverticulum, a duplication cyst, Henoch-Schönlein purpura, a polyp, or lymphoma^{1,3,10}. However, several infectious pathogens are also reported to be associated with intussusception^{3,11-13}. Infection can stimulate intestinal lym-

phatic tissue, resulting in mesenteric lymphadenopathy or hypertrophy of Peyer's patches (serve as a lead point of intussusception)^{3,14}.

Recently, non-pharmaceutical interventions (NPIs) including social distancing, quarantine, lockdowns, travel restrictions, school closures, mask wearing, and frequent hand hygiene have been implemented to mitigate coronavirus disease 2019 (COVID-19) across the world¹⁵⁻¹⁸. As a result of such measures, the incidence of various infectious diseases including influenza^{19,20}, enveloped respiratory viruses (parainfluenza virus, respiratory syncytial virus, human metapneumovirus, human coronavirus)²¹, enteroviruses (such as polioviruses, coxsackie viruses, echoviruses)²², nontyphoidal *Salmonella*²³, and norovirus and rotavirus²⁴ has decreased^{17,18}.

In this paper, we aim to determine whether the incidence of intussusception changed between the pre-pandemic and pandemic periods to elucidate the impact of NPIs due to the COVID-19 pandemic on the incidence of intussusception.

Materials and Methods

We conducted and reported this systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement²⁵.

Search Strategy, Inclusion and Exclusion Criteria, and Data Extraction

Two authors (SE and SHY) searched the PubMed and EMBASE databases for articles published in English until August 5, 2022, using the following terms: ("COVID-19" OR "COVID-19 pandemic" OR "coronavirus disease 2019" OR "SARS-CoV-2" OR "severe acute respiratory syndrome coronavirus 2" OR "novel coronavirus") AND ("intussusception"). We included studies that evaluated the incidence of intussusception between the pre-pandemic and COVID-19 pandemic periods. If reported in the included studies, we also investigated the impact of the COVID-19 pandemic as it pertains to the diagnosis and treatment process of intussusception. Reviews, case reports, commentaries, editorials, and laboratory experiments were excluded. The following data from included studies were extracted: publication year, first author, country, clinical setting, data sources, inclusion and exclusion criteria, patient characteristics including age, gender, and concomitant COVID-19 status,

changes between the pre-pandemic period vs. pandemic period including the incidence, time to diagnosis, time to reduction of intussusception; and incidence of communicable (infectious) and non-communicable (non-infectious) diseases, if reported. We included studies in which intussusception was diagnosed with imaging studies (US or computed tomography) and/or either non-operative radiologic reduction (pneumatic or hydrostatic pressure by enema) or surgery.

Quality Assessment

The quality of each study was evaluated by two reviewers (C.H. Han and S.H. Yoon) using a modified version of the risk of bias tool (Table I)^{26,27}. The score range is 0-8, and studies were categorized into three groups based on the total score: low risk of bias (scores 0-2), moderate risk of bias (scores 3-4), and high risk of bias (scores ≥ 5)²⁶. We defined an adequate length of the shortest study period as one month. Disagreements were arbitrated by discussion.

Results

The literature search yielded 127 articles. Of these, after removing 43 duplicates, 84 articles were screened, and 70 articles were excluded based on the inclusion criteria (Figure 1). From the 14 full-text reviews, the following nine studies were excluded: three studies did not assess the incidence of intussusception, and six studies reported insufficient diagnostic criteria. Therefore, the remaining five studies²⁸⁻³² were finally included in this systematic review.

Characteristics of the Included Studies

The majority of studies were performed in South Korea (n=4)^{28,29,31,32}, and only one study was performed in the United State of America (n=1)³⁰. Two studies were single-center studies^{28,30} (one from a pediatric emergency department (ED) of a tertiary hospital and one from a tertiary children's hospital), and three studies were multicenter studies^{29,31,32}. One study²⁹ used data from the Healthcare Bigdata Hub from the single-payer health insurance system in South Korea. One study³¹ used the National Emergency Department Information System (NEDIS) database, which includes administrative and clinical information for all patients who have visited EDs across the country (403 EDs in 2020). Finally, one study³² used medical records from seven hospitals including

Table 1. Risk of bias items for assessing the included studies.

	Low risk of bias	High risk of bias
Study setting		
Population	0	
Hospital		1
Study design		
Prospective cohort	0	
Retrospective cohort		1
Intussusception type		
Specified such as ileocolic or ileo-ileal	0	
Unspecified		1
Diagnosis of Intussusception		
US, fluoroscopy, or CT scan	0	
Non-operative reduction and/or surgical reduction	0	
Plain abdominal film		1
Sex subgroups		
Reported	0	
Not reported		1
Presence of a pathological lead point		
Reported*	0	
Not reported		1
Age distribution		
Reported	0	
Not reported		1
Was the length of the shortest study period appropriate?		
Yes [†]	0	
No		1

CT, computed tomography; US, ultrasound. *If authors initially excluded cases with pathological lead points, we considered it to be reported. [†]We defined an adequate length of the shortest study period as one month.

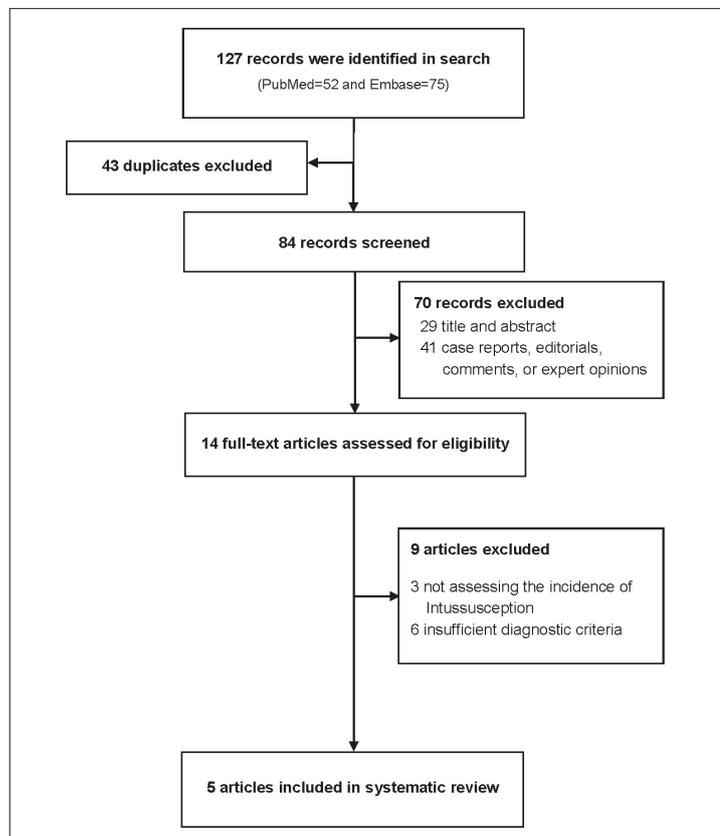


Figure 1. Flow chart of the study selection process.

four tertiary referral hospitals and three secondary hospitals that all had pediatric EDs. Only pediatric patients were included in the studies. All of the included studies were published between 2021 and 2022. The case ascertainment criteria and exclusion criteria of each study are described in Table II. Regarding quality assessment, two studies were classified to have low (score 2) risk of bias, and the other three studies were classified to have moderate (score 3-4) risk of bias (Table II and [Supplementary Table I](#)).

Change In Intussusception Incidence

All the included studies reported that the incidence of intussusception significantly declined during the pandemic period compared with the pre-pandemic period (Table III). Park et al²⁸ reported that the number of intussusception cases decreased by 69% relative to the pre-pandemic incidence. In particular, increased proportions of pathologic lead points were noted during the pandemic period. Handa et al³⁰ reported that the monthly number of intussusceptions decreased by 72% (95% confidence interval [CI]=49-85%; $p<0.001$). Choe et al²⁹ showed that the net risk ratio of intussusception incidence in 2020 compared with that from 2010-2019 was 0.53 (95% CI=0.43-0.64) for boys and 0.56 (95% CI=0.44-0.71) for girls ($p=0.017$). Lee et al³¹ also reported that the incidence rates were significantly lower in the pandemic period (4.19 per 100,000 person-half-years) than in two separate pre-pandemic periods (7.85 and 11.30 per 100,000 person-half-years) ($p<0.05$). Yoo et al³² also reported that the monthly number of intussusceptions decreased from 9.0 to 3.5 ($p<0.001$). The timing of regional NPI initiation in each study and the patient age and gender characteristics in the pre-pandemic and post-pandemic groups are described in [Supplementary Table II](#).

Change in Communicable and Non-Communicable Disease Incidence

Although a few studies presented the incidence of communicable diseases with that of intussusception together during the same study period, Park et al²⁸ reported that ED visits for communicable diseases during the pandemic period declined to 24.4% compared with the pre-pandemic period, and their proportions over the total ED visits also declined from 56.9% to 32.9%. The incidence of intussusception and change in the incidence of communicable diseases was significantly correlated (odds ratio=2.15,

95% CI=1.08-4.26, and $p=0.029$). However, ED visits for non-communicable diseases declined to 62%, but their proportions over the total ED visits increased from 46.4% to 68.2%. Yoo et al³² also reported that there was a sharp decrease in the average monthly incidence of communicable diseases including respiratory viruses ($p<0.001$), enterovirus infection ($p<0.001$), and viral enteritis ($p<0.001$) during the pandemic period. In contrast, the monthly incidence of bacterial enteritis ($p=0.542$), anaphylaxis ($p=0.547$), and syncope ($p=0.493$) did not significantly change during the pandemic period³². These two studies^{28,32} also reported that there was no patient who was concomitantly affected by both intussusception and COVID-19. Handa et al³⁰ reported that only one (1 of 11) patient had an intussusception and active COVID-19 infection (Table IV).

Time to Diagnosis, Non-Operative Reduction, and Surgical Reduction

When comparing between the pre-pandemic and pandemic periods, Park et al²⁸ reported that the time to diagnosis ($p=0.063$) and rate of successful non-operative reduction (air enema; $p=0.139$) were not significantly different, but the time to non-operative reduction was significantly longer ($p<0.001$) in a pediatric ED of a tertiary hospital during the pandemic period. However, Lee et al³¹ reported that there were no differences in the time to diagnosis [from the ED visit to US ($p=0.575$)], time to non-operative reduction (p -value was not available), and time to surgical reduction ($p=0.904$) in nationwide data (Table IV).

Discussion

In this review, a significant decrease in the incidence of intussusception was reported during the pandemic period compared with the pre-pandemic period in all the included studies. Periods set as the pandemic period in the included studies were mostly after the introduction of regional NPIs; thus, these results support the hypothesis that communicable infection can be an important etiology of intussusception. Specifically, the up to 70% decrease in the incidence during the pandemic period indicates that infection is a major contributor to cases of intussusception^{28,30}. In addition, although the microbiological data of individual patients were not investigated, two studies^{28,32} showed that the incidence of commu-

Table II. Summary characteristics of the included studies.

Reference	Country	Center	Clinical setting	Data sources	Age	Case ascertainment criteria	Exclusion criteria	Quality scores
Park et al ²⁸ 2021	South Korea	Single center	Pediatric ED of a tertiary hospital	Medical records	Age ≤ 7 years	US*	1) History of abdominal surgery 2) Intra-abdominal anomaly 3) Other medical conditions having a risk of intussusception (i.e., Peutz-Jeghers syndrome, Henoch-Schönlein purpura)	3
Choe et al ²⁹ 2022	South Korea	Multicenter	N/A	Based on national level data (Healthcare Big data Hub) [†]	Age < 5 years	ICD-10 code (K561) + either RR or SR [‡]	N/A	4
Handa et al ³⁰ 2022	USA	Single center	Tertiary children's hospital	Medical records	Age ≤ 18 years	Ileocolic intussusception diagnosed by RR (air contrast enema)	1) Previous air contrast enema within the past year 2) Surgically proven pathological lead point as the cause of intussusception 3) Intussusception that did not involve the colon	2
Lee et al ³¹ 2022	South Korea	Multicenter	Emergency healthcare facilities	Based on national level data (NEDIS) [§]	Age < 18 years	ICD code (K561) + either RR or SR [¶]	1) Participants with missing demographic information 2) Participants who were missing US time, RR or SR time 3) Patients with a documented time of US, RR or SR prior to their arrival time at the ED (time error) 4) Patients who did not undergo US, RR, or SR	3
Yoo et al ³² 2022	South Korea	Multicenter	4 tertiary referral hospitals and 3 secondary hospitals (all with pediatric ED)	Medical records	N/A	Imaging tests (mostly US, and some APCT)	N/A	2

APCT, abdominal computed tomography; ED, emergency department; ICD, International Classification of Disease; N/A, not available; NEDIS, National Emergency Department Information System; RR, radiologic reduction; SR, surgical reduction; US, ultrasound; USA, United States of America. *Radiologist-performed ultrasound; the authors considered a recurrence of intussusception within 48 hours as the same case. [†]From the single-payer health insurance system in South Korea. [‡]Only the first examination result of each patient was included. [§]An emergency patient information database operated by the Ministry of Health and Welfare in South Korea. [¶]The authors considered recurrent intussusceptions after hospital discharge as a new case.

Table III. Change in intussusception incidence.

Reference	Pre-pandemic period		Pandemic period		Summary of results
	Follow-up	Incidence	Follow-up	Incidence	
Park et al ²⁸ 2021	Feb 2019-Jan 2020 (12 months)	Total number of intussusceptions per total ED visits: 87/28,018	Feb 2020-Jan 2021 (12 months)	Total number of intussusceptions per total ED visits: 27/11,800	Relative to the pre-pandemic period, 69% reduction.
Choe et al ²⁹ 2022	2010-2019 (120 months)	Monthly incidence rate; In boys: 17-30 per 100,000 In girls: 12-19 per 100,000	2020 (12 months)	Monthly incidence rate; In boys: 8-17 per 100,000 In girls: 8-15 per 100,000	The net risk ratio of intussusception incidence for 2020 compared with 2010-2019 was 0.53 for boys and 0.56 for girls ($p = 0.017$).
Handa et al ³⁰ 2022	Mar 2010-Feb 2020 (120 months)	Monthly number of cases (mean): 3.3	Apr 2020-Mar 2021 (12 months)	Monthly number of cases (mean): 0.9	The mean monthly number of ileocolic intussusceptions was decreased by 72% ($p < 0.001$).
Lee et al ³¹ 2022	Jan-Jun 2019 (Control group 1; 6 months) Jul-Dec 2019 (Control group 2; 6 months)	Jan-Jun 2019: 7.85 per 100,000 person-half-years Jul-Dec 2019: 11.30 per 100,000 person-half-years	Jan-Jun 2020 (Study group; 6 months)	4.19 per 100,000 person-half-years	The incidence rates were significantly lower in the study group than in control groups 1 and 2 ($p < 0.05$).
Yoo et al ³² 2022	Jan 2017-Feb 2020 (38 months)	Monthly number of cases (median): 9.0	Mar 2020-Dec 2020 (10 months)	Monthly number of cases (median): 3.5	The number of intussusceptions were significantly decreased in the pandemic period ($p < 0.001$).

nicable diseases also simultaneously decreased with the incidence of intussusception, whereas the incidence of non-communicable diseases did not significantly change or their proportions over total ED visits were increased. A significant correlation between the incidence of intussusception and the change in the incidence of communicable diseases was also reported²⁸.

In addition, Handa et al³⁰ reported that the incidence of hypertrophic pyloric stenosis did not differ between the pre-pandemic and pandemic period, which can be used as a negative control for intussusception. The clinical characteristics of hypertrophic pyloric stenosis are similar to those of intussusception, but infection has not been suspected as an etiology of hypertrophic pyloric stenosis³³. Regarding COVID-19 as a cause

of intussusception, several intussusception cases that were likely associated with SARS-CoV-2 infection have been published³⁴⁻³⁷. However, among our included studies, Handa et al³⁰ reported that only one (1 of 11) patient had a concomitant intussusception and an active COVID-19 infection. Two other studies^{28,32} reported that no patients experienced both intussusception and an active COVID-19 infection. Thus, it can be presumed that other infectious pathogens other than severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) play major causative roles³⁰.

Unlike adult cases, pediatric intussusception has a male predominance^{3,4}. Interestingly, Choe et al²⁹ reported that a greater decrease in the incidence of intussusception occurred in boys than in girls. The connection between gender and the

Table IV. Changes between the pre-pandemic and pandemic periods.

Reference	Communicable disease	Non-communicable disease	Time to diagnosis	Time to non-operative reduction	Time to surgical reduction	Success to non-operative reduction	Concomitant COVID-19
Park ²⁸ 2021	ED visits for communicable diseases: pre-pandemic (n = 15,932, 56.9% of total ED visits) vs. pandemic (n = 3,880, 32.9% of total ED visits)	ED visits for non-communicable diseases: pre-pandemic (n = 12,994, 46.4% of total ED visits) vs. pandemic (n = 8,050, 68.2% of total ED visits)	Pre-pandemic vs. pandemic: 0.6h vs. 0.8h ($p = 0.063$)	Pre-pandemic vs. pandemic: 2.6h vs. 3.1h ($p < 0.001$)*	N/A	Pre-pandemic vs. pandemic: 98.9% vs. 92.6% ($p = 0.139$)*	None
Handa et al ³⁰ 2022	N/A	No significant change in the mean monthly number of cases with HPS: pre-pandemic (4.4) vs. pandemic (3.6) ($p = 0.19$)	N/A	N/A	N/A	N/A	One of 11 cases with intussusception had active COVID-19 infection during the pandemic period
Lee et al ³¹ 2022	N/A	N/A	No differences (ED visit to US; $p = 0.575$)	No differences (ED visit to RR)	No differences (ED visit to SR; $p = 0.904$)	N/A	N/A
Yoo et al ³² 2022	Sharp decrease in the monthly incidence of respiratory viruses, enterovirus infection, and viral enteritis ($p < 0.001$); no significant change in the incidence of bacterial enteritis ($p = 0.542$) in the pandemic period [‡]	No significant change in the monthly number of cases with anaphylaxis ($p = 0.547$) and syncope ($p = 0.493$).	N/A	N/A	N/A	N/A	None

ED, emergency department; HPS, hypertrophic pyloric stenosis; N/A, not available; RR, radiologic reduction; SR, surgical reduction. *Air reduction; † p -value is not available. ‡From the Korea Disease Control and Prevention Agency database.

development of intussusception has not yet been elucidated. Thus, future studies will be needed on the relationship between gender factors and infections causing intussusception.

The COVID-19 pandemic has caused a 70-80% decrease pediatric ED visits possibly due to the fear of COVID-19 or of the lockdown itself³⁸⁻⁴⁰. Delaying an ED visit can delay timely management of surgical emergencies and worsen the clinical course^{41,42}. Regarding intussusception, a delay in diagnosis and radiologic reduction can increase the risks of surgical intervention and even death^{2,43,44}. Our results did not show a significant difference in the time to intussusception diagnosis between the pre-pandemic and pandemic periods, but a significantly longer time to radiologic reduction was noted during the pandemic period in a pediatric ED of a tertiary hospital²⁸, whereas another study using nationwide ED data showed no difference³¹. Referral bias may have affected these results, and overall, trained professionals are usually aware of the risks in delaying the diagnosis of intussusception; thus, this may have affected the time to diagnosis and reduction during the pandemic period. However, healthcare systems or resources vary considerably both across and within countries. Therefore, detailed and extensive investigations are needed in various countries to determine how much lockdown has affected diagnostic delays and the outcomes of intussusception.

One of the strengths of our study is that it is the first systematic review to assess the impact of the COVID-19 pandemic on the incidence of intussusception through various clinical data from single-center medical records to nationwide databases. However, our study also has several limitations. First, all of the included studies were retrospective, and three of five (60%) studies had a moderate risk of bias. Second, most studies did not provide microbiological testing results or antecedent illnesses of each patient, which would explain a direct causal relationship between intussusception and infectious diseases. Third, restrictions to healthcare access during the COVID-19 pandemic may have prevented identification of the true incidence of diseases. However, we estimate that the effect of this factor is somewhat low because patients with intussusception suffer from acute and severe pain, their parents or guardians may be more likely to take them to the ED despite the lockdown. Fourth, a limited number of studies were included, and most studies were conducted in South Korea. This may not reflect

the current situation of the COVID-19 pandemic in various countries. Finally, it was hard to define the source population for the hospital-based studies thus we could not calculate the incidence rate through a meta-analysis.

Conclusions

The COVID-19 pandemic significantly reduced the incidence of intussusception in children, supporting the hypothesis that infection (especially communicable diseases) is a major cause of intussusception. To strengthen our results, future studies in the late pandemic or post-pandemic era, which could account for the level of NPI implementation and social distancing, will be necessary to determine whether the incidence of intussusception has increased or not. In addition, further research is needed on the status of healthcare access among patients with intussusception in various countries to establish current and post-pandemic preparedness plans.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Neither financial support nor any sort of sponsorship was received for this study.

Data Availability

All data generated or analyzed during this systematic review are included in this article.

Informed Consent

Not applicable.

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