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의학석사 학위논문

Changes in the epidemiology of
pediatric invasive bacterial
infections after the COVID-19
pandemic in Korea

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Changes in the epidemiology of pediatric invasive bacterial infections after the COVID-19 pandemic in Korea

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Abstract

Background: Invasive bacterial infection (IBI) remains a major burden of mortality and morbidity in children. As coronavirus disease 2019 (COVID-19) emerged, stringent non-pharmaceutical interventions (NPIs) were applied worldwide. This study aimed to evaluate the impact of NPIs on pediatric IBI in Korea.

Methods: From January 2018 to December 2020, surveillance for pediatric IBIs caused by nine pathogens (*S. pneumoniae*, *H. influenzae*, *N. meningitidis*, *S. agalactiae*, *S. pyogenes*, *S. aureus*, *Salmonella* species, *L. monocytogenes*, and *E. coli*) was performed at 22 hospitals throughout Korea. Annual incidence rates were compared before and after the COVID-19 pandemic.

Results: A total of 651 cases were identified and the annual incidence was 194.0 cases per 100,000 in-patients in 2018, 170.0 in 2019, and 172.4 in 2020. Most common pathogen by age group was *S. agalactiae* in infants < 3 months (n=129, 46.7%), *S. aureus* in 3 - <24 months (n=35, 37.2%), *Salmonella* spp. in 24 - <60 months (n=24, 34.8%), and *S. aureus* in children \geq 5 years (n=128, 60.7%). Compared to 2018-2019, the incidence rate in 2020 decreased by 57% for

invasive pneumococcal disease (26.6 vs. 11.5 per 100,000 in-patients, $p = 0.014$) and 59% for *Salmonella* spp. infection (22.8 vs. 9.4 per 100,000 in-patients, $p = 0.018$). In contrast, no significant changes were observed in invasive infections due to *S. aureus*, *S. agalactiae*, and *E. coli*.

Conclusions: The NPIs implemented during the COVID-19 pandemic reduced invasive diseases caused by *S. pneumoniae* and *Salmonella* spp., but not *S. aureus*, *S. agalactiae*, and *E. coli* in children.

Keyword: Children, COVID-19, Invasive bacterial infection, Non-pharmaceutical interventions, Pandemic

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Chapter 1. Introduction

Invasive bacterial infections (IBIs) are major causes of morbidity and mortality in children. Tracking epidemiological changes of serious IBIs is important for developing strategies to decrease the disease burden and proper management. Accordingly, multicenter, hospital-based surveillance systems for IBIs in Korean children have been maintained since 1996.¹
² The surveillance system can be used as an important tool to assess changes in epidemiology of IBIs during the coronavirus disease 2019 (COVID-19).

After the first COVID-19 case was diagnosed in January 2020 in South Korea, a subsequent regional, however large-scale outbreak occurred in February 2020, which prompted the health authorities to implement rigorous public health measures from March of 2020.^{3, 4} Following implementation of non-pharmaceutical interventions (NPIs) in attempt to control the COVID-19, a reduction in various infectious diseases including influenza, other respiratory viruses, and vaccine-preventable diseases has also been seen in South Korea.⁵⁻⁷ Reports from

other countries have also shown marked decline in acute respiratory viral infections including influenza and respiratory syncytial virus.^{8, 9}

Recent global studies found a significant reduction of IBIs due to *S. pneumoniae*, *H. influenzae* and *N. meningitidis* following the introduction of national COVID–19 containment in many countries.^{10, 11} An interesting study in children has also shown a dramatic reduction of common infectious diseases in Massachusetts between 2019 and 2020.¹² However, such reduction of infectious diseases can also be explained by decreased seeking of medical care in addition to implementation of NPIs.¹³ Given the severity of invasive infections in children, IBIs are less likely to be affected by healthcare utilization patterns. Only a few studies looked the change in the bacterial infections and, moreover, there has been little discussion on pediatric population. With this background, we investigated changes in the epidemiologic and etiologic distribution of IBIs caused by nine major pathogens among children before and during the implementation of NPIs to contain the COVID–19.

Chapter 2. Methods

Multicenter surveillance for invasive bacterial infections

This multicenter surveillance for IBIs has been maintained in South Korea since 1996.^{1,2} From January 2018 to December 2020, 22 university–affiliated hospitals participated in this study: 13 hospitals located in the national capital and suburban region (Seoul St. Mary's Hospital, Seoul National University Children's Hospital, Severance Children's Hospital, Samsung Medical Center, Seoul Asan Medical Center, Nowon Eulji Medical Center, Ewha Womans University Medical Center, Inha University Hospital, Gachon University Gil Medical Center, Inje University Ilsan Paik Hospital, Korea University Ansan Hospital, Seoul National University Bundang Hospital, and CHA Bundang Medical Center), and 9 hospitals located in the regional central cities of provinces (Gangwon–do: Wonju Christian Hospital, Chungcheongbuk–do: Chungbuk National University Hospital, Chungcheongnam–do: Chungnam National University Hospital, Jeollabuk–do: Jeonbuk National University Hospital, Gwangju/Jeollanam–do: Chonnam National University Hospital, Daegu/Gyeongsangbuk–do: Keimyung University Dongsan Medical Center, Busan/Gyeongsangnam–do: Pusan National University Yangsan Hospital, Kosin University Gospel Hospital, and Jeju–do:

Jeju National University Hospital).

Data collection

IBI was defined as the isolation of bacterial organisms from a normally sterile site by using culture, antigen detection, or polymerase chain reaction. IBIs caused by nine bacterial organisms were collected: *S. pneumoniae*, *H. influenzae*, *N. meningitidis*, *S. agalactiae*, *S. pyogenes*, *S. aureus*, *Salmonella* species, *L. monocytogenes*, and *E. coli*. Infants over 37 weeks of gestation to adolescents under 19 years of age were included. Among cases, *E. coli* infections in children over 3 months of age and *S. aureus* infection in those with central catheters or immunocompromised conditions were excluded. Cases reported for invasive bacteria were retrospectively obtained on the annual basis (from January to December each year) for three years. All investigators submitted case information using a standard case report form that included age, sex, underlying medical conditions, isolated organism, and date of isolation.

Non-pharmaceutical interventions

During the COVID-19, various NPIs were introduced including social

distancing campaigns and enhanced personal hygiene such as mask wearing, hand washing, and cough etiquette. Especially, it was recommended mask be applied not only when having respiratory symptoms but in all close contact. Korea also pursued a school closure strategy by delaying the beginning of the school year from March 1 to April 6 when online learning proceeded. The government transitioned to stepwise on-site school reopening between May 20 and June 8. The off-line classes continued until July 31 when most public and private schools started summer break. The second semester gradually started from the mid-August with a hybrid school schedule by limiting attendance according to the grade, which maintained until winter vacation in January 2021.

Statistical analysis

The distribution of bacterial organisms was analyzed according to age and time. Age groups were stratified as follows: < 3 months of age, 3 to 23 months of age, 24 to 59 months of age, and \geq 5 years of age. Pearson's Chi-square was used to test annual difference of the proportion of age group, etiologic agents, and methicillin susceptibility of *S. aureus*. The weekly number of cases for each IBI was assessed in 2020 versus 2018–2019. The annual incidence of

IBIs except *S. agalactiae* and *E.coli* were calculated as the number of 100,000 new in-patients in the corresponding year. The annual incidence of IBIs due to *S. agalactiae* and *E.coli* were calculated per 10,000 newborns. The difference in annual cumulative incidences of IBIs by organism was compared by using a Poisson test. We performed statistical analyses using R version 4.0.5, and p-value < 0.05 was considered statistically significant.

Chapter 3. Results

Annual distribution of the causative organisms of IBIs

During the study period, a total of 362,581 new in-patients were identified in 22 hospitals; 134,544 cases in 2018, 132,330 in 2019, and 95,707 in 2020, respectively and the annual number of births was 20,110 babies in 2018, 20,067 in 2019, and 18,151 in 2020, respectively. The male to female ratio was 1.63:1 and the median age was 10.0 months (range, 0–226 months).

Among these, 651 cases with IBIs were identified in the participating hospitals; 261 cases in 2018, 225 in 2019, and 165 in 2020, respectively (Table 1). Overall, *S. aureus* was the most frequent cause of IBIs (n = 206, 31.6%), followed by *S. agalactiae* (n = 139, 21.4%), *E. coli* (n = 117, 18.0%), *S. pneumoniae* (n = 82, 12.6%), and *Salmonella* spp. (n = 70, 10.8%). There were few cases of *S. pyogenes* (n = 18, 2.8%) and *H. influenzae* (n = 15, 2.3%). In 2018–2019, more than 10% of IBIs were attributed to *S. pneumoniae* (13.0% in 2018 and 16.4% in 2019) and *Salmonella* spp. (13.8% in 2018 and 11.1% in 2019); however, only 6.7% and 5.5% were caused by *S. pneumoniae* and *Salmonella* spp. in 2020. Meanwhile, the proportion of *S. aureus*, *S. agalactiae*, *E. coli* infection did not show significant differences during the study period. The number of IBIs

caused by *S. pyogenes* and *H. influenzae* in 2020 decreased by 75.0% and 87.5%, respectively, compared to the previous years. Case of IBI due to *N. meningitidis* and *L. monocytogenes* was not observed in 2020. Among a total of 204 *S. aureus* isolates available for antibiotic susceptibility testing, 69.1% of cases were susceptible to methicillin and 30.9% were methicillin-resistant (Table 2). There was no significant difference in the proportion of methicillin susceptibility during the study period ($p = 0.560$).

Table 1. Distribution of causative organisms for invasive bacterial infection in children by year (2018-2020)

Species of bacteria	No. of isolates by year (%)			Total (%)	P value*
	2018	2019	2020		
<i>S. aureus</i>	82 (31.4)	63 (28.0)	61 (37.0)	206 (31.6)	0.169
<i>S. agalactiae</i>	48 (18.4)	47 (20.9)	44 (26.7)	139 (21.4)	0.125
<i>E. coli</i>	44 (16.9)	36 (16.0)	37 (22.4)	117 (18.0)	0.220
<i>S. pneumoniae</i>	34 (13.0)	37 (16.4)	11 (6.7)	82 (12.6)	0.015
<i>Salmonella</i> spp.	36 (13.8)	25 (11.1)	9 (5.5)	70 (10.8)	0.025
<i>S. pyogenes</i>	8 (3.1)	8 (3.6)	2 (1.2)	18 (2.8)	-
<i>H. influenzae</i>	7 (2.7)	7 (3.1)	1 (0.6)	15 (2.3)	-
<i>L. monocytogenes</i>	2 (0.8)	2 (0.9)	(0.0)	4 (0.6)	-
<i>N. meningitidis</i>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-
Total	261 (100)	225 (100)	165 (100)	651 (100)	

* Indicates the comparison among 2018, 2019, and 2020

Table 2. Distribution of methicillin resistance among *S. aureus* isolates by year (2018-2020)

Methicillin resistance	No. of isolates by year (%)			Total (%)	P value*
	2018	2019	2020		
MSSA	55 (67.1)	42 (66.7)	44 (74.6)	141 (69.1)	0.560
MRSA	27 (32.9)	21 (33.3)	15 (25.4)	63 (30.9)	
Total	82 (100)	63 (100)	59 (100)	204 (100)	

* Indicates the comparison among 2018, 2019, and 2020

MSSA, Methicillin-susceptible *Staphylococcus aureus*; MRSA, Methicillin-resistant *Staphylococcus aureus*

Age proportion of IBIs by year

S. agalactiae was most predominant in infants younger than 3 months of age (n = 129, 46.7%), *S. aureus* in 3 – <24 months of age (n = 35, 37.2%), *Salmonella* spp. in 24 – <60 months of age (n = 24, 34.8%), *S. aureus* in children \geq 5 years of age (n = 128, 60.7%) (Figure 1A). During the three years, the frequency of IBIs was highest in the infants under 3 months of age group (42.5%), followed by 32.5% in 5–18 years old, 14.5% in 3–23 months old, and 10.6% in 24–59 months old. The age proportion of IBIs changed during the study period (Figure 2). In 2020, the proportion of IBIs in infants younger than 3 months of age was significantly greater than in the previous two years (38.7% in 2018 and 40.2% 2019 vs. 51.5% in 2020, $p = 0.008$) and the proportion of children aged 5–18 years tended to decrease (32.2% in 2018 and 37.1% in 2019 vs. 26.7% in 2020, $p = 0.084$).

The etiologic organisms of IBIs differed according to the age group. *S. agalactiae* (129/276, 46.7%) and *E.coli* (116/276, 42.0%) were responsible for the majority of IBIs in infants less than 3 months of age (Figure 1A and 1B). In children 3 months of age or older, *S. aureus* was the leading pathogen (47.9%, 179/374) followed by *S. pneumoniae* (21.9%, 82/374) and *Salmonella* spp. (18.5%, 69/374).

In children aged 3 – <60 months, *S. aureus* infection was the most common pathogen in 2020 (50.0%), while invasive pneumococcal disease was most prevalent in 2018–2019 (32.9% in 2018 and 39.2% in 2019). The proportion of *Salmonella* spp. infection in children under 2 years of age was 3.8% in 2018–2019 and 2.8% in 2020; however, in children aged 2–18 years, the proportion decreased from 23.0% in 2018–2019 to 10.3% in 2020 (Figure 3).

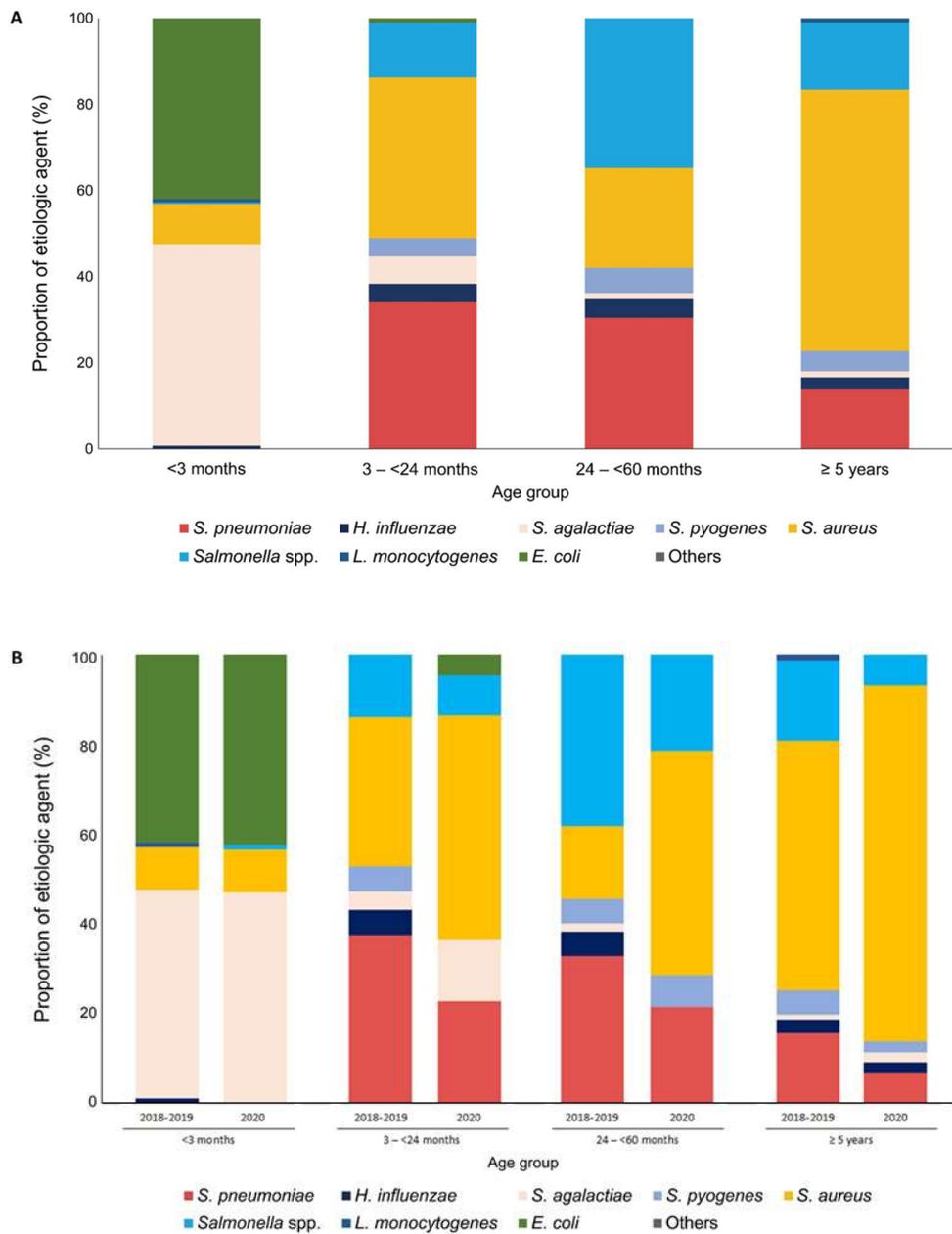


Figure 1. Proportion of etiologic agent by age group. A, Proportion of etiologic agent by age group from 2018 to 2020. B, Proportion of etiologic agent by age group in 2018-2019 and 2020.

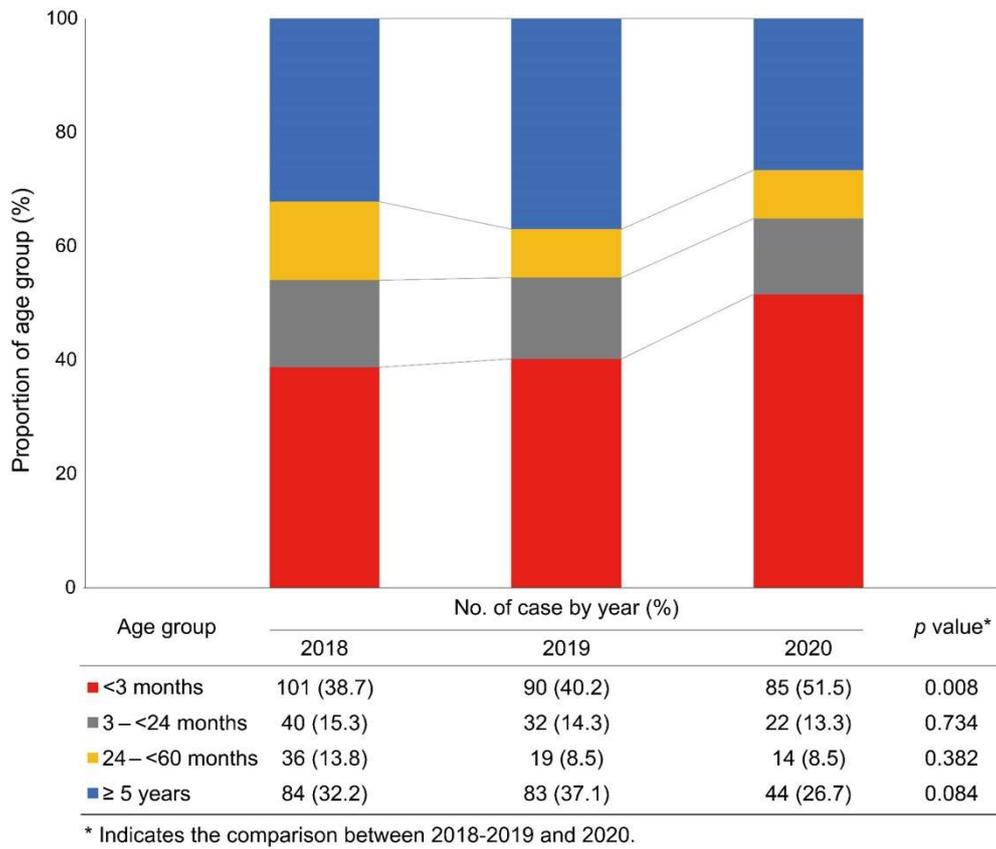


Figure 2. Age proportion of invasive bacterial infection by year (2018-2020)

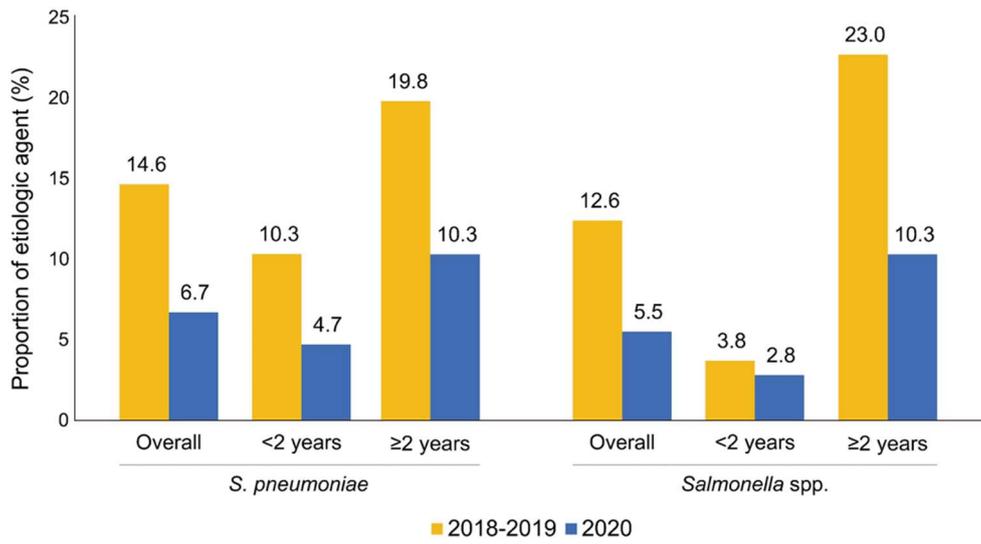


Figure 3. The proportion of *S. pneumoniae* and *Salmonella* spp. infection in children < 2 and ≥ 2 years of age.

Annual trend of cumulative cases and incidence of each causative organism of IBIs

The annual trend in the number of weekly count for IBIs by each organism was shown in Figure 4A. There were significant reductions in the cumulative cases of *S. pneumoniae* and *Salmonella* spp. in 2020 compared to 2018–2019. The cumulative case number of *S. pneumoniae* was similar to that of the previous two years until March 2020, while thereafter, the case number did not rise. A sharp rising pattern in late autumn and early winter detected in 2018–2019 was not seen in 2020. Among *Salmonella* spp. infection, 21 and 17 cases were detected from June to September in 2018 and 2019, respectively while 6 cases were identified during the same period in 2020. In contrast, the cumulative curve patterns of *S. agalactiae*, *S. aureus*, and *E. coli* were similar throughout the study period. Figure 4B showed the annual incidence of IBIs by each organism from 2018 to 2020. Consistent with the results of the cumulative weekly count, a substantial reduction in the incidence of *S. pneumoniae* and *Salmonella* spp. infection in 2020 was observed, compared to 2018–2019.

In 2020, there was a 57% reduction in the incidence rate of invasive pneumococcal disease compared to that of 2018–2019 (26.6 per

100,000 in-patients in 2018–2019 vs. 11.5 per 100,000 in-patients in 2020, rate ratio of 0.43; 95% CI 0.22–0.86; $p = 0.014$, Table 3). Likewise, the incidence rate of invasive disease due to *Salmonella* spp. in 2020 showed 59% decrease compared with the average incidence over the past two years (22.8 per 100,000 in-patients in 2018–2019 vs. 9.4 per 100,000 in-patients in 2020, rate ratio of 0.41; 95% CI 0.19–0.88; $p = 0.018$, Table 3). The cumulative incidences of *S. aureus*, *S. agalactiae*, and *E.coli* infection did not change significantly over three years (Table 3).

Table 3. Comparison of cumulative incidence between 2018-2019 and 2020

Species of bacteria	Cumulative incidence (per 100,000 in-patients/year)*		Rate ratio (95% CI)	P value
	2018-2019	2020		
<i>S. aureus</i>	54.3	63.7	1.17 (0.82-1.68)	0.387
<i>S. agalactiae</i>	23.6	24.2	1.03 (0.58-1.81)	0.931
<i>S. pneumoniae</i>	26.6	11.5	0.43 (0.22-0.86)	0.014
<i>Salmonella</i> spp.	22.8	9.4	0.41 (0.19-0.88)	0.018
<i>S. pyogenes</i>	6.0	2.1	0.35 (0.07-1.68)	0.171
<i>H. influenzae</i>	5.2	1.0	0.19 (0.23-1.63)	0.092
<i>E. coli</i>	19.9	20.4	1.03 (0.55-1.90)	0.937
Total	183.6	172.4	0.94 (0.76-1.16)	0.553

*For *E. coli* and *S. agalactiae*, incidence rates were calculated with annual birth number and divided by 10,000.

CI, Confidence interval

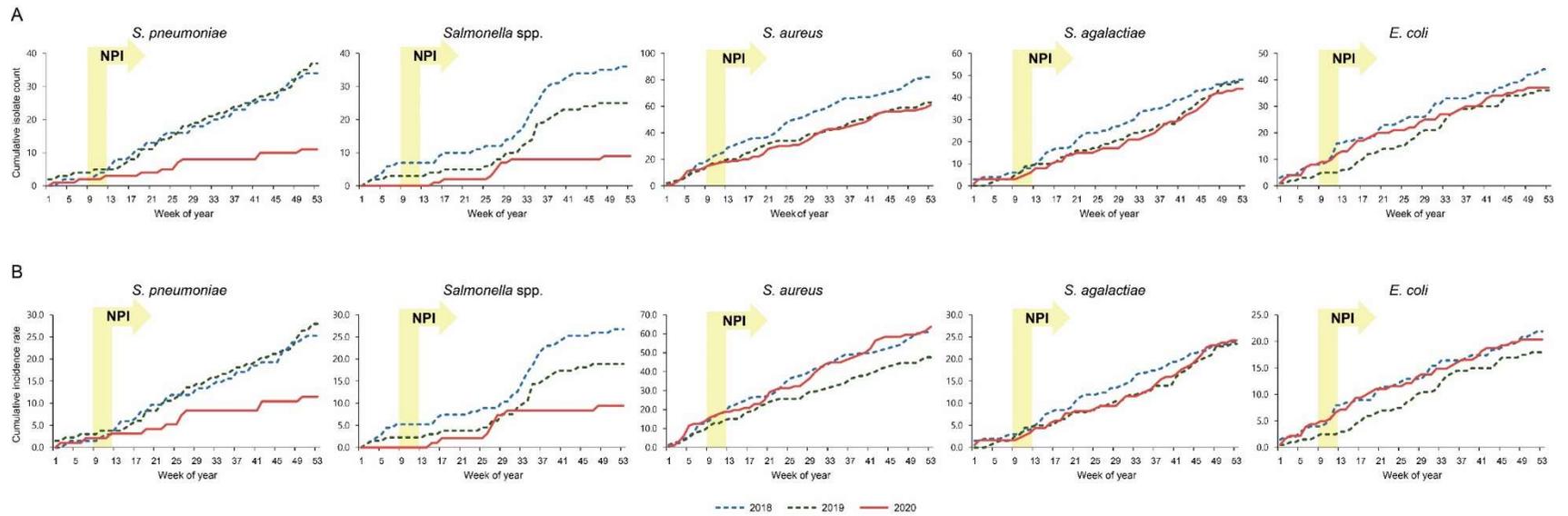


Figure 4. Annual trend in the number of weekly count for invasive bacterial infection by etiologic agent. A, Annual cumulative isolate count of invasive bacterial infection by etiologic organism from 2018 to 2020. B, Annual cumulative incidence of invasive bacterial infection in children by etiologic organism from 2018 to 2020.

Chapter 4. Discussion

In this nationwide multicenter retrospective study, we demonstrated a significant reduction in invasive bacterial disease due to *S. pneumoniae* and *Salmonella* spp. during the COVID-19 outbreak, in comparison with the previous two years of 2018-2019. However, there was no significant difference in the incidence of invasive disease due to *S. aureus*, *S. agalactiae*, and *E. coli* during the same period.

Most noteworthy was the observation that IBIs caused by *S. pneumoniae* and *Salmonella* spp. markedly decreased. Although there was no statistical significance due to the small number, *S. pyogenes* and *H. influenzae* also declined. The most possible explanation for the differential impact of COVID-19 NPIs on the epidemiology of pediatric IBIs is the difference in the transmission route by organism. *S. pneumoniae*, *S. pyogenes*, and *H. influenzae* reside in the respiratory tracts and are mainly transmitted person-to-person through the inhalation of respiratory droplets or close contact.^{14, 15} Day care attendance and crowding are well-known risk factors for invasive pneumococcal disease in children by facilitating the person-to-person transmission and nasopharyngeal carriage.^{16, 17} It is likely that school closure, avoiding attendance to daycare center,

mandatory use of facial masks, and enhanced personal hygiene applied during the COVID-19 pandemic led to substantial decrease in pneumococcal transmission. Studies from England described the association of reduction in invasive pneumococcal disease with lockdown during the COVID-19 pandemic.^{18, 19} A report from a single center found significant declines in 2020 compared with 2018 to 2019 in invasive infections due to *S. pyogenes* and *S. pneumoniae* but not *S. aureus*.²⁰ Brueggemann et al. reported worldwide reduction in invasive disease caused by *S. pneumoniae* and *H. influenzae* in early 2020 along with the implementation of public large-scale containment measures.¹⁰

Another remarkable finding was a reduction in the incidence of *Salmonella* spp. infection in 2020. *Salmonella* infection is a food-borne illness and it peaks during the summer months on north hemisphere, which is probably associated with rapid replication in warm temperature and frequent eating out in summer.²¹ Approximately 95% of salmonellosis in humans occurs through contaminated food, in particular, eggs, raw meat, dairy products, and fresh vegetables.²² International travel is also a major source in *Salmonella* infection, comprising 4–9% of traveler' s diarrhea.²³ In a study for imported infectious diseases in South Korea, salmonellosis

was associated with international travel during summer season, and imported cases comprised of 15.3% of salmonellosis with increasing trend.²⁴ Hand hygiene procedures are already known as an effective tool to lower the incidence of *Salmonella* infection.²⁵ The mandatory 14-day quarantine policy for all overseas travelers introduced from April 2020 in South Korea and worldwide lockdown led to decrease in domestic and international travel. Enhanced public hygiene and food handling processes, changes in eating behavior, and decreased international travel may have contributed to a reduction in *Salmonella* infection.

Additional plausible explanation for decrease in IBIs may be related to decrease in various respiratory viral infections affected by NPIs. Secondary bacterial infections are commonly seen after respiratory infection.²⁶ Respiratory viral infections have an effect on mucosal/epithelial barrier, immunologic dysregulation, and microbiota residing on both respiratory and gastrointestinal tract, which might increase a susceptibility to secondary bacterial infections.^{27, 28} During the COVID-19 pandemic, a remarkable reduction in respiratory viral infections have been reported in many countries including South Korea.^{29, 30} Decline in viral respiratory tract infections may have affected a decrease in pneumococcal infection. However, a decline in

Salmonella spp. infection, a non-respiratory pathogen, is more likely a direct result of NPIs itself through reinforcement of personal hygiene and interruption of movement and person-to-person contact.

Meanwhile, there was no significant difference in the incidences of *S. agalactiae* and *E. coli* over the three years. In line with earlier studies,^{1,2} *S. agalactiae* and *E. coli* remained main contributors to IBIs of the infants group. Since *S. agalactiae* and *E. coli* are usually acquired and colonizes during the perinatal period, it is assumed that these organisms were minimally affected by NPIs in 2020.³¹ This implicates *S. agalactiae* and *E. coli* are unlikely to be preventable by NPIs, especially in neonates and young infants. *S. aureus* remained the leading cause of pediatric IBI without a significant difference in incidence throughout the study period, especially in children aged \geq 5 years. This may be due to the fact that *S. aureus* is a human commensal residing on the skin and anterior nares.³²

In this study, an increase in the proportion of cases under 3 months of age was observed in concordance with the reduction of cases among preschool and school-aged children in 2020. Taking into consideration of the major pathogens of this age group (*S. agalactiae* and *E. coli*) and route of acquisition of these pathogens this may be

explained. The relative increase in proportion of infants under 3 months of age is also related to the decrease of infections in older children, who were more physically and socially active before COVID-19. Low adherence to personal hygiene and limitations in mask use might have a role in the preserved proportion of children under 5 years old.

There are several limitations in our study. First, the decline of IBI cases might result from reduced healthcare-seeking behaviors during the COVID-19 pandemic. To avoid the underestimation of IBI, we calculated the incidence with annual number of pediatric admission and birth number. Since most of IBIs manifest with a fever and lethargic feature, it is less likely to be missed. In fact, the number of infections caused by *S. agalactiae* and *E.coli* in young infants did not decrease, demonstrating that this surveillance system had not been disrupted by the COVID-19. Second, because this is an observational study, it is difficult to figure out exactly which of the various NPIs primarily contributed to the change in epidemiology of IBIs in children. Third, it is not possible to determine whether the decrease in IBIs is the result of reduced bacterial transmission and acquisition or the reduction in various viral respiratory tract infections. Changes in antibiotic prescriptions can have affected the

epidemiology of IBIs.³³ Lastly, serotypes were not determined for *H. influenzae* and *S. pneumoniae* in this surveillance.

Despite these limitations, through comparison of incidence rate of IBIs due to nine bacterial pathogens before and after stringent implementation of various NPIs, we found distinct differences in changes in epidemiology according to pathogen and different age groups in children. These findings give insights into factors associated with the development of IBIs in children.

Chapter 5. Conclusion

In summary, among nine major pathogens of IBIs in children, the incidences of *S. pneumoniae* and *Salmonella* spp. decreased significantly in 2020, when NPIs came into effect, compared to in 2018 and 2019. This finding suggests that public health measures may attribute to prevention of some IBIs in the pediatric population.

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요약 (국문초록)

연구배경: 침습성 세균 감염은 소아청소년의 사망률과 이환율의 주요 원인이다. 코로나바이러스감염증-19 팬데믹으로 비약물적 중재요법이 전세계적으로 도입되었다. 본 연구는 비약물적 중재요법이 국내 소아청소년의 침습성 세균 감염에 미치는 영향을 평가하고자 하였다.

연구방법: 2018년 1월부터 2020년 12월까지 전국 22개 병원에서 9개 병원체(*S. pneumoniae*, *H. influenzae*, *N. meningitidis*, *S. agalactiae*, *S. pyogenes*, *S. aureus*, *Salmonella* spp., *L. monocytogenes*, *E. coli*)에 의한 침습성 세균 감염 사례 감시 연구를 수행하였다. 코로나바이러스감염증-19 팬데믹 전후의 연간 발병률을 비교하였다.

연구결과: 총 651건의 사례를 수집하였고, 연간 발생률은 입원환자 10만 명당 2018년 194.0건, 2019년 170.0건, 2020년 172.4건이었다. 연령별 가장 흔한 병원체는 3개월 미만 영아에서 *S. agalactiae*(n = 129, 46.7%), 3- <24개월에서 *S. aureus*(n = 35, 37.2%), 24- <60개월에서 *Salmonella* spp.(n = 24, 34.8%), 5세 이상의 소아에서 *S. aureus*(n = 128, 60.7%)였다. 2020년 연간발생률을 2018-2019년의 평균 연간발생률과 비교하였을 때 침습성 폐구균 질환의 경우 57%(입원 환자 10만 명당 26.6 대 11.5, $p = 0.014$), 살모넬라 감염증의 경우 59% 감소를 보였다(입원 환자 10만명당 22.8 대 9.4, $p = 0.018$). 반면 *S. aureus*, *S. agalactiae*, *E. coli* 감염의 경우 유의한 변화가 관찰되지 않았다.

결론: 코로나바이러스감염증-19 팬데믹으로 도입된 비약물적 중재요법은 *S. pneumoniae* 및 *Salmonella* spp.에 의한 침습성 감염을 감소시켰지만 *S. aureus*, *S. agalactiae* 및 *E. coli*에 의한 감염에는 유의한 영향을 미치지 않았다.

주요어 : 침습성 세균감염, 소아, 코로나19, 비약물적 개입, 팬데믹

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