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【 ORIGINAL ARTICLE 】

A Reduction in the Number of Hospitalized Cases of Acute Meningitis during the COVID-19 Pandemic in Japan

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Abstract:

Objective

The changes in the prevalence of acute meningitis during the coronavirus disease 2019 (COVID-19) pandemic remain unclear. This study aimed to compare the prevalence of acute meningitis before and during the COVID-19 pandemic in Japan.

Methods

We retrospectively reviewed the Japanese nationwide administrative medical payment system database, Diagnosis Procedure Combination (DPC), from 2016 to 2022. A total of 547 hospitals consistently and seamlessly offered DPC data during this period. The study period was divided into the following three periods: April 2016 to March 2018 (fiscal years 2016-2017), April 2018-March 2020 (2018-2019), and April 2020-March 2022 (2020-2021).

Results Among the 28,161,806 patients hospitalized during the study period, 28,399 were hospitalized for acute meningitis: 16,678 for viral/aseptic type, 6,189 for bacterial type, 655 for fungal type, 429 for tuberculous, 2,310 for carcinomatous type, and 2,138 for other or unknown types of meningitis. A significant decrease during the pandemic was confirmed in viral (n=7,032, n=5,775, and n=3,871 in each period; p< 0.0001) and bacterial meningitis (n=2,291, n=2,239, and n=1,659; p<0.0001) cases. Meanwhile, no decrease was observed in fungal meningitis (n=212, n=246, and n=197; p=0.056) or carcinomatous meningitis (n=781, n=795, and n=734; p=0.27). The decrease in the number of tuberculous meningitis cases was equivocal (n= 166, n=146, and n=117; p=0.014). The decrease during the pandemic was more remarkable in younger populations aged <50 years than in older populations, both for viral and bacterial meningitis.

Conclusion

The number of hospitalized cases of acute meningitis clearly decreased during the COVID-19 pandemic, especially for viral and bacterial meningitis in younger populations aged <50 years.

Key words: Bacterial meningitis, COVID-19 pandemic, DPC database, prevalence, viral meningitis

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Introduction

Since the end of 2019, the world has faced a global pandemic of the coronavirus disease 2019 (COVID-19), and the World Health Organization declared it a global pandemic in March 2020 (1, 2). In Japan, the community spread of COVID-19 began in January 2020, and most people practiced strict infection prevention measures, including movement restrictions and wearing masks, until early 2023 (3). During this COVID-19 pandemic period, with adherent infection prevention measures, the spread of other droplet-associated infections, such as influenza virus, respiratory syncytial virus, *Mycoplasma pneumoniae*, and rubella, has been reported to have dramatically decreased (4-6). In parallel with the dramatic decrease in airborne and droplet-based community-acquired infections, it is reasonable to expect that the prevalence of infectious central nervous system diseases in the community would also decrease (7, 8), as many causative pathogens of meningitis are known to spread by the inhalation of pathogens (9). However, to date, there have only been a limited number of reports regarding the possible decrease in the number of patients with acute meningitis during the pandemic (8). Acute meningitis is a life-threatening disease that requires large amounts of medical resources (10-12). Elucidating the relationship between the performance of infection prevention and control measures during the pandemic and the incidence of acute meningitis is important. Therefore, this study evaluated the number of patients with acute meningitis and compared them before and during the COVID-19 pandemic using a large nationwide medical database to demonstrate the actual decrease in the prevalence of meningitis during the COVID-19 pandemic.

Methods

Study design

The Japanese nationwide administrative Diagnosis Procedure Combination (DPC) medical payment system database was retrospectively reviewed (13). The study period was from April 2016 to March 2022 and it was divided into the following three periods: April 2016 to March 2018 (fiscal years 2016-2017), April 2018-March 2020 (fiscal years 2018-2019), and April 2020-March 2022 (fiscal years 2020-2021). A total of 547 DPC-covered hospitals consistently offered medical records to the DPC database from April 2016 to March 2022, and agreed to its use for research purposes. Patients treated for acute meningitis at these 547 hospitals were enrolled in subsequent analyses. Meningitis was classified as viral (aseptic), bacterial, fungal, tuberculous, carcinomatous, or other/unknown. The disease name of "meningitis" was selected from the registered main disease names of hospitalization, which included the following three entries: [1] principal diagnosis, [2] disease as the primary reason of admission, and [3] disease that required the greatest amounts of medical resources (14, 15). We did not include any patients with suspected disease names without a confirmed diagnosis to obtain a reliable cohort with acute meningitis. Changes in the number of patients with acute meningitis were first evaluated for all patients and among those with each type of meningitis. The number of deceased cases during hospitalization was further compared among the three time periods. In meningitis cases with a significant decrease in the number of patients during the COVID-19 pandemic, changes in the number of patients were further evaluated after dividing the patients into 10-year age groups from 0 to 9 years to ≥90 years.

Statistical analyses

Changes in the prevalence of each type of meningitis among the three periods were evaluated by performing a goodness-of-fit test for each type of meningitis using the expected frequencies in each period with equal prevalence rates throughout the three periods. Because of the confirmatory nature of the analyses, the statistical significance was adjusted for the number of evaluated types of meningitis, and $p<0.01$ was considered to indicate statistical significance based on the Bonferroni correction method (16). Statistical analyses were performed using R Statistical Software program version 4.1.3 (R Foundation, Vienna, Austria).

Ethics

This study was approved by the Institutional Review Boards of the Tokyo Medical and Dental University (approval number: M2000-788) and Tohoku University Graduate School of Medicine (approval number: 2022-1-441). All procedures in this study were conducted in accordance with the latest version of the Declaration of Helsinki, revised in 2013.

Results

Of the 547 DPC-covered hospitals, 28,161,806 were hospitalized during the study period. Among them, 28,399 had acute meningitis. The types of meningitis were as follows: 16,678 (59%) viral/aseptic meningitis, 6,189 (22%) bacterial, 655 (2.3%) fungal, 429 (1.5%) tuberculous, 2,310 (8.1%) carcinomatous, and 2,138 (7.5%) other or unknown types. The number of patients with each type of meningitis during the three periods is shown in Table 1. The goodness-of-fit test revealed that the number of patients with viral and bacterial meningitis decreased significantly during the study period ($p<0.0001$ for both types), particularly during the COVID-19 pandemic from 2020 to 2021. The number of patients with fungal meningitis ($p=0.0557$) or carcinomatous meningitis ($p=0.2655$) did not change significantly during the study period. The significance level for tuberculous meningitis was equivocal ($p=0.0143$); however, the difference was not statistically significant ($p\geq0.01$). The total reduction in the number of cases during hospitalization with acute

Table 1. Number of Patients with Each Type of Meningitis in 2016-17, 2018-19, and 2020-21.

Type of meningitis	Time periods			χ^2 Statistics (df=2) *	*P**
	2016-2017	2018-2019	2020-2021		
Total hospitalized patients, n	9,485,065	9,744,580	8,932,161	36,684	<0.0001
With acute meningitis, n (%)	11,490 (0.121%)	9,875 (0.101%)	7,034 (0.079%)	1075.2	<0.0001
Hospitalized patients with each type of acute meningitis, n					
Viral/aseptic meningitis	7,032	5,775	3,871	911.2	<0.0001
Bacterial meningitis	2,291	2,239	1,659	119.3	<0.0001
Fungal meningitis	212	246	197	5.77	0.0557
Tuberculous meningitis	166	146	117	8.49	0.0143
Carcinomatous meningitis	781	795	734	2.65	0.2655
Others/unknown types	1,008	674	456	216.9	<0.0001
Demographics of the patients with acute meningitis					
Male, n (%)	6,378 (56%)	5,351 (54%)	3,709 (53%)	704.4	<0.0001
Female, n (%)	5,112 (44%)	4,524 (46%)	3,325 (47%)	384.0	<0.0001
Age, median and IQR (years)	34 (14-59)	40 (22-65)	50 (29-70)	NA	<0.0001†
Deceased, n (%) ‡	584 (5.1%)	663 (6.7%)	551 (7.8%)	11.05	0.0040

The number of patients with each type of acute meningitis treated at the 547 Diagnosis Procedure Combination (DPC)-covered hospitals during each of the three study periods is shown.

df, degree of freedom; IQR, interquartile range; NA, not applicable

* χ^2 statistics and p-values for the number of hospitalized cases of acute meningitis were calculated by the goodness-of-fit test using the expected frequencies of the number of patients, based on an unchanged incidence (*i.e.*, uniform distribution) throughout the three periods.

† p value for age distribution was calculated using the Mann-Whitney U test.

‡ The number of deceased patients during hospitalization are shown. The percentage was calculated from the number of hospitalized cases of acute meningitis in each period.

meningitis was suggested to have decreased during the pandemic, but the mortality rate during hospitalization with acute meningitis did not decrease during the COVID-19 pandemic. Instead, the rate was found to slightly increase during the pandemic, in parallel with the decreased overall number of hospitalized cases of acute meningitis.

Number of patients by age groups and meningitis types

Based on the finding that a significant decrease in the number of patients during the COVID-19 pandemic was confirmed in viral and bacterial meningitis, further subgroup analyses after stratification by age at hospital admission were performed in all patients with meningitis and in those with these two types of meningitis. The results are presented in Table 2. For both viral and bacterial meningitis cases, the decrease in the number of patients with meningitis during the COVID-19 pandemic was more remarkable in younger populations aged <50 years than in older populations aged ≥ 50 years, which is known to have a higher mortality rate. In particular, the decrease during the COVID-19 pandemic was most remarkable in children aged 0-9 years (n=2,364, n= 1,403, and n=562 in the three periods, respectively). Changes in the number of patients with viral or bacterial meningitis in different age groups (0-19 years, 20-49 years, and ≥50 years) are shown in Figure. A clear discrepancy in the decrease in the number of patients with meningitis during the COVID-19 pandemic was observed between younger and older populations.

Based on the most remarkable decrease in the number of children with meningitis, the change in the number of patients with meningitis from 2016 to 2021 was further investigated after stratification by age, from 0 to 10 years (Table 3). A remarkable decrease in the number of patients with viral or bacterial meningitis among young children was consistently observed at all ages from 0 to 10 years.

Changes in the number of patients by the causative pathogens

Finally, to obtain deeper insight into the background of the decreased number of patients with meningitis during the COVID-19 pandemic, changes in the number of patients were further investigated for each specific type of viral and bacterial species (Table 4). A significant decrease in the number of patients with viral meningitis caused by the mumps virus during the COVID-19 pandemic was observed in both the 0-19 ($p<0.0001$) and 20-49 ($p<0.0001$) year age groups. A decrease in herpetic meningitis was observed in the 20-49 years age group ($p<0.0001$); however, the same phenomenon was not observed in older populations aged ≥ 50 years ($p=0.28$). For reference purposes, the number of children aged 0-9 years who were admitted to hospitals with herpetic meningitis during the three study periods was 18, 17, and 6, respectively. The number of children aged 0-9 years who were admitted to hospitals with mumps meningitis in the three study periods was 588, 57, and 5, respec-

Table 2. Age Group-stratified Numbers of Patients with Meningitis in the Three Study Periods between 2016 and 2021.

	Patients with acute meningitis in 2016-17 / 2018-19 / 2020-21, n (Deceased cases in 2016-17 / 2018-19 / 2020-21, n)		
	Total	Viral meningitis	Bacterial meningitis
0-9 years old (Deceased)	2,364 / 1,403 / 562 (5 / 4 / 2)	1,713 / 854 / 229 (0 / 0 / 0)	478 / 452 / 299 (5 / 4 / 2)
10-19 years old (Deceased)	1,092 / 742 / 425 (5 / 1 / 4)	938 / 655 / 361 (1 / 1 / 1)	74 / 47 / 43 (3 / 0 / 0)
20-29 years old (Deceased)	1,544 / 1,353 / 801 (6 / 2 / 7)	1,238 / 1,146 / 675 (1 / 0 / 1)	138 / 109 / 63 (1 / 0 / 3)
30-39 years old (Deceased)	1,658 / 1,400 / 809 (12 / 11 / 5)	1,289 / 1,111 / 662 (0 / 1 / 0)	162 / 154 / 70 (2 / 3 / 0)
40-49 years old (Deceased)	1,171 / 1,078 / 826 (47 / 44 / 34)	738 / 728 / 562 (1 / 0 / 1)	207 / 166 / 113 (12 / 16 / 4)
50-59 years old (Deceased)	880 / 879 / 836 (71 / 73 / 70)	394 / 392 / 434 (1 / 3 / 2)	196 / 226 / 177 (18 / 16 / 12)
60-69 years old (Deceased)	1,089 / 1,026 / 908 (137 / 142 / 113)	307 / 323 / 337 (1 / 6 / 4)	336 / 304 / 227 (23 / 25 / 30)
70-79 years old (Deceased)	1,001 / 1,187 / 1,108 (161 / 215 / 178)	234 / 334 / 343 (5 / 12 / 12)	391 / 437 / 350 (62 / 77 / 47)
80-89 years old (Deceased)	603 / 710 / 643 (118 / 145 / 109)	158 / 199 / 232 (8 / 11 / 18)	271 / 297 / 262 (47 / 77 / 47)
≥90 years old (Deceased)	88 / 97 / 116 (22 / 26 / 29)	23 / 33 / 36 (2 / 6 / 5)	38 / 47 / 55 (13 / 13 / 13)
All age groups (Deceased)	11,490 / 9,875 / 7,034 (584 / 663 / 551)	7,032 / 5,775 / 3,871 (20 / 40 / 44)	2,291 / 2,239 / 1,659 (186 / 231 / 158)

The 547 DPC-covered hospitals consistently provided patient data during the study period, between April 2016 and March 2022. A remarkable decrease in the number of patients with meningitis was observed during the COVID-19 pandemic between 2020 and 2021, particularly in the younger population aged<50 years.

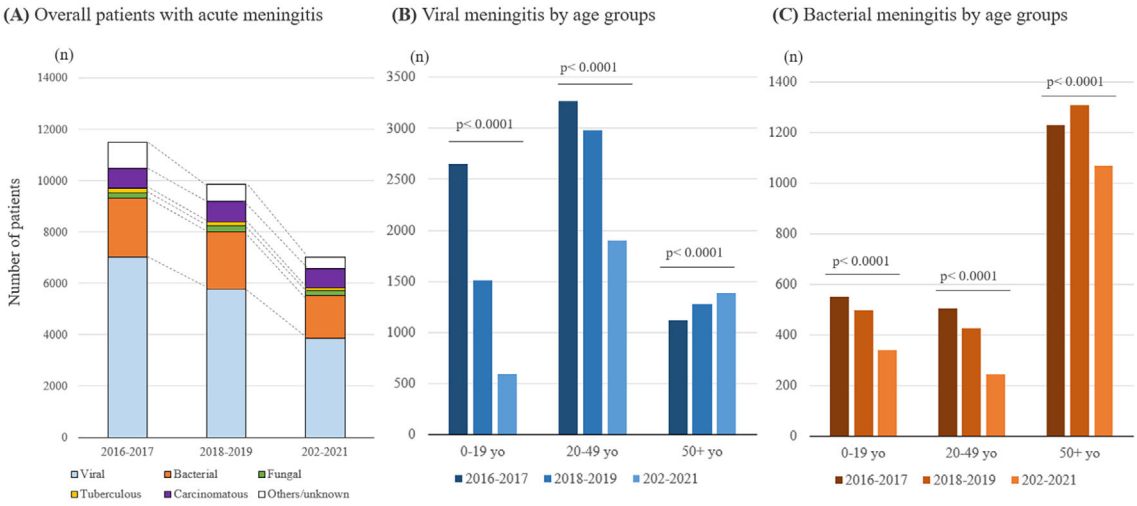

Figure. The decrease in the number of patients with acute meningitis in younger populations during the coronavirus disease 2019 (COVID-19) pandemic. The number of patients with acute meningitis admitted to 547 Diagnosis Procedure Combination (DPC)-covered hospitals during each of the three study periods (April 2016-March 2018, April 2018-March 2020, and April 2020-March 2022) is shown. (A) The overall number of patients with acute meningitis decreased remarkably from 2016 to 2021, particularly during the COVID-19 pandemic in 2020-2021. (B) Changes in the number of patients with viral meningitis by age group showed that a decrease in the number of patients was observed in younger populations aged <50 years but not in older populations aged ≥50 years. (C) Changes in the number of patients with bacterial meningitis during the COVID-19 pandemic were not as remarkable as those in patients with viral meningitis; however, changes were observed in all age groups, especially in younger populations aged <50 years. The p-values were calculated by the goodness-of-fit test using the expected frequencies of the number of patients, based on an equal prevalence throughout the three periods.

tively. The number of cases of viral meningitis caused by the varicella zoster virus did not decrease during the COVID-19 pandemic in any age group. Instead, the incidence of viral meningitis with varicella zoster virus among adults gradually increased during the study period, and the resultant mortality appears to have also increased in older people aged ≥50 years.

A decrease in bacterial meningitis with non-pneumococcal streptococci was absent in all the age groups. A decrease in bacterial meningitis with *Streptococcus pneumoniae* was confirmed in the 0-19 (p=0.0012), 20-49 (p<0.0001), and ≥ 50 (p<0.0001) age groups. A decrease in tuberculous menin-

Table 3. the Age-stratified Number of Patients with Meningitis in the Three Study Periods among Children Aged 0-10 Years.

	Number of patients with meningitis in 2016-17 / 2018-19 / 2020-21, n (Reduction in the number of cases in 2016-17 / 2018-19 / 2020-21, n)		
	Total	Viral meningitis	Bacterial meningitis
0 years old (Deceased)	941 / 767 / 369 (5 / 2 / 2)	495 / 356 / 104 (0 / 0 / 0)	351 / 349 / 240 (5 / 2 / 2)
1 years old (Deceased)	89 / 67 / 50 (0 / 1 / 0)	45 / 31 / 24 (0 / 0 / 0)	35 / 30 / 25 (0 / 1 / 0)
2 years old (Deceased)	58 / 32 / 11 (0 / 0 / 0)	36 / 16 / 2 (0 / 0 / 0)	19 / 11 / 6 (0 / 0 / 0)
3 years old (Deceased)	112 / 52 / 19 (0 / 0 / 0)	79 / 36 / 11 (0 / 0 / 0)	24 / 14 / 8 (0 / 0 / 0)
4 years old (Deceased)	174 / 82 / 21 (0 / 0 / 0)	152 / 66 / 13 (0 / 0 / 0)	11 / 13 / 6 (0 / 0 / 0)
5 years old (Deceased)	237 / 98 / 24 (0 / 0 / 0)	215 / 85 / 22 (0 / 0 / 0)	7 / 9 / 2 (0 / 0 / 0)
6 years old (Deceased)	198 / 87 / 18 (0 / 1 / 0)	178 / 76 / 14 (0 / 0 / 0)	7 / 8 / 3 (0 / 1 / 0)
7 years old (Deceased)	203 / 80 / 18 (0 / 0 / 0)	188 / 71 / 13 (0 / 0 / 0)	10 / 8 / 4 (0 / 0 / 0)
8 years old (Deceased)	199 / 74 / 12 (0 / 0 / 0)	184 / 62 / 8 (0 / 0 / 0)	9 / 7 / 3 (0 / 0 / 0)
9 years old (Deceased)	153 / 64 / 20 (0 / 0 / 0)	141 / 55 / 18 (0 / 0 / 0)	5 / 3 / 2 (0 / 0 / 0)
10 years old (Deceased)	114 / 53 / 20 (0 / 0 / 0)	105 / 48 / 18 (0 / 0 / 0)	6 / 5 / 2 (0 / 0 / 0)

The age-stratified number of children with meningitis treated at the evaluated 547 DPC-covered hospitals during each of the three study periods are shown. A remarkable decrease in the number of children with meningitis was observed for all ages, from 0 to 10 years.

Table 4. Changes in the Number of Patients with Meningitis according to the Causative Pathogens.

Type of meningitis	Number of patients, n (deceased, n)			χ^2 Statistics (df=2) *	p *
	2016-2017	2018-2019	2020-2021		
Viral meningitis with mumps virus, n (deceased, n)					
0 - 19 years old	752 (0)	67 (0)	9 (0)	1237.5	<0.0001
20 - 49 years old	158 (0)	17 (0)	2 (0)	251.1	<0.0001
≥50 years old	4 (0)	3 (0)	0 (0)	3.714	0.1561
Viral meningitis with herpes simplex virus, n (deceased, n)					
0 - 19 years old	48 (0)	45 (0)	24 (0)	8.769	0.0125
20 - 49 years old	271 (0)	241 (0)	160 (0)	29.44	<0.0001
≥50 years old	138 (5)	113 (2)	123 (6)	2.540	0.2808
Viral meningitis with varicella zoster virus, n (deceased, n)					
0 - 19 years old	36 (0)	42 (0)	33 (0)	1.135	0.5669
20 - 49 years old	129 (1)	196 (0)	210 (1)	21.02	<0.0001
≥50 years old	160 (5)	281 (4)	354 (10)	72.46	<0.0001
Bacterial meningitis with nonpneumococcal Streptococci, n (deceased, n)					
0 - 19 years old	90 (3)	76 (0)	72 (1)	2.252	0.3243
20 - 49 years old	7 (0)	18 (2)	13 (0)	4.790	0.0912
≥50 years old	39 (4)	55 (4)	67 (3)	7.354	0.0253
Bacterial meningitis with *Streptococcus pneumoniae*, n (deceased, n)					
0 - 19 years old	66 (0)	53 (1)	30 (0)	13.38	0.0012
20 - 49 years old	63 (5)	61 (3)	23 (0)	20.73	<0.0001
≥50 years old	219 (24)	218 (35)	97 (16)	55.29	<0.0001
Tuberculous meningitis (*Mycobacterium tuberculosis*), n (deceased, n)					
0 - 19 years old	3 (0)	4 (0)	1 (0)	1.750	0.4169
20 - 49 years old	51 (2)	34 (1)	22 (1)	11.91	0.0026
≥50 years old	112 (15)	108 (12)	94 (16)	1.707	0.4259

* χ^2 statistics and p-values for the number of hospitalized cases of acute meningitis were calculated by the goodness-of-fit test using the expected frequencies of the number of patients, based on an unchanged incidence (*i.e.*, uniform distribution) throughout the three periods.

gitis was observed in the 20-49 years age group (p=0.0026); however, the same decrease was not observed in older populations aged ≥50 years (p=0.43).

Discussion

This study demonstrated a remarkable decrease in the number of patients with acute meningitis in Japan during the COVID-19 pandemic from 2020 to 2021. A decrease in viral and bacterial meningitis was observed; however, a similar decrease was not observed in fungal and carcinomatous meningitis. Prevention of droplet and airborne transmission during the pandemic could have suppressed the occurrence of viral or bacterial meningitis caused by culprits primarily transmitted through respiratory droplets or aerosols. Based on age group-stratified subgroup analyses, a decrease in viral and bacterial meningitis was seen in younger populations aged <50 years, especially in children aged 0-9 years; however, such a decrease was not seen in older populations aged ≥50 years. Considering that the number of patients in the older population did not change during the study period, a possible selection bias with an underdiagnosis of acute meningitis caused by a possible refrain from visiting hospitals among the patients seems to be less likely to be the primary cause of the observed decrease. The observed remarkable decrease in viral or bacterial meningitis was most likely due to a significant reduction in the droplet- or airborne-based spread of the causative pathogens among younger populations resulting from the practice of infection prevention measures during the pandemic. Cumulatively, the findings of this study implied that nearly half of the cases of viral or bacterial meningitis in younger populations aged <50 years were caused by community spread of the causative pathogens, which could have been prevented by practicing basic infection prevention measures during the COVID-19 pandemic.

An apparent decrease in the number of patients with viral meningitis in younger populations aged 0-9 and 10-19 years was observed between 2016 and 2017, and 2018 and 2019, both before the COVID-19 pandemic. This could be explained by the outbreak of mumps virus infection in children during the period from 2016-2017 (17). Based on an annual sentinel surveillance report, the number of children with mumps infection peaked in 2016 and dramatically decreased by approximately 90% during the COVID-19 pandemic. This could be why a significant decrease in the number of children with viral meningitis was already observed before the COVID-19 pandemic (i.e., 2016-17 vs. 2018-2019). A further decrease of mumps meningitis during the COVID-19 pandemic (i.e., 2018-19 vs. 2020-21) could have been brought by the prevention measures of droplet and airborne transmission during the pandemic.

Another possible explanation for the decreased prevalence of bacterial meningitis in younger populations is the routine vaccination of children against *Streptococcus pneumoniae* and *Haemophilus Influenzae* type b, both of which have been routinely immunized with the costs covered by local governments since 2013 in Japan (18, 19). However, considering that a decrease in the number of patients with bacterial meningitis during the COVID-19 pandemic was also observed in older populations aged ≥20 years, the decrease in the number of patients with bacterial meningitis during the COVID-19 pandemic could be due to both the effect of routine immunization and the decreased spread of causative bacteria in the community. Another conceivable theory is an underdiagnosis among the younger population due to refraining from visiting hospitals during the pandemic, especially among those with mild and self-remitting symptoms of viral meningitis. An underdiagnosis of cases of acute meningitis, if present, could thus be considered to be a negative aspect associated with the pandemic, as a delayed lumbar puncture was shown to be associated with increased medical costs and higher mortality rates (20, 21). Therefore, both the actual decrease in the prevalence of acute meningitis and possible underdiagnosis due to refraining from visiting hospitals among mild cases could have contributed to the dramatic decrease in the number of hospitalized cases of acute meningitis during the pandemic.

This study is associated with several limitations. First, the DPC database covers >70% of all annual hospitalizations in Japan; however, the remaining 30% are not included in the DPC database (22). Therefore, the enrolled patients with meningitis in this study may not accurately represent all the patients with meningitis in Japan. Another limitation is that the practice of infection prevention measures during the COVID-19 pandemic differed significantly among countries worldwide, and whether the findings of this study can be generalized to other countries with different races and ethnicities remains uncertain. During the COVID-19 pandemic, especially during the early 2020-2021 pandemic, most adults and children aged ≥3 years wore masks properly (23). Therefore, the decrease in the number of patients with viral or bacterial meningitis during the pandemic might have been less pronounced in other countries.

In summary, this study demonstrated a remarkable decrease in the number of patients hospitalized for viral or bacterial meningitis during the COVID-19 pandemic in Japan. Particularly in younger populations aged 0-9 years, the decrease in the number of patients with viral meningitis was conspicuous, with a >70% decrease from 2018 to 2019. This decrease in the number of patients with meningitis was absent or less remarkable in older populations aged ≥50 years. These findings strongly suggest that the majority of cases of viral meningitis among younger populations are caused by droplet- or airborne-based community spread, which was dramatically suppressed by the infection prevention measures implemented during the COVID-19 pandemic.

The authors state that they have no Conflict of Interest (COI).

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Data availability statement

Individual-level data were not available because of the agreement with the contributing hospitals and approval condition of the institutional review boards that approved this study. An additional anonymized summary of data supporting the present study and the detailed study protocol are available from the corresponding author upon reasonable request.

Competing interests

The authors declare no conflicts of interest in association with this study.

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