İSTANBUL UNIVERSITY PRESS

Çocuk Dergisi - Journal of Child 2024;24(2):112-117
DOI: 10.26650/jchild.2024.1410612

RESEARCH ARTICLE

Febrile Seizures: The COVID-19 Pandemic and Beyond

Betül Diler Durgut[1], Emine Tekin[1], Cevriye Ceyda Kolaylı[2]

[1]Giresun University, Department of Child Neurology, Giresun, Türkiye
[2]Manisa Provincial Health Directorate, Public Health Services, Manisa, Türkiye

ORCID ID: B.D.D. 0000-0002-0322-2843; E.T. 0000-0002-5115-8890; C.C.K. 0000-0001-7734-8206

Citation: Diler Durgut B, Tekin E, Kolaylı CC. Febrile seizures: The COVID-19 pandemic and beyond. Çocuk Dergisi - Journal of Child2024;24(2):112-117. https://doi.org/10.26650/jchild.2024.1410612

ABSTRACT

Objective: Febrile seizures are common reasons for admission to paediatric emergency departments. There is evidence suggesting that the frequency, severity, and seasonal distribution of non-COVID infections have changed since the removal of measures during the COVID-19 pandemic. These changes may also impact febrile seizures, which are known to be triggered by infections.We aimed to reveal the frequency and seasonal distribution of febrile seizures during the COVID-19 pandemic and after the removal of social restrictions and measures.

Methods: Patients who presented to the emergency department with a febrile seizure were grouped as having first or recurrent febrile seizure, and demographic data were reported. The patients were then grouped according to the period of the pandemic as follows; the first year of the pandemic (Group 1), the second year (Group 2), and the period after the removal of measures (Group 3). The groups were compared in terms of the number of patients, seizure age, seizure duration, seizure frequency, season of admission, seizure type, seizure status at the time of admission to the emergency department (stopped or ongoing), and electroencephalography (EEG) findings.

Results: A total of 248 patients who presented with 272 febrile seizures were included. There were 34, 105, and 132 patients in Groups 1, 2, and 3, respectively. There were no significant differences among the three groups in terms of recurrent febrile seizures, continuation of seizures upon admission to the emergency department, duration of seizures, treatment requirement in the emergency department, or ratio of focal seizures ($p>0,05$). However, the number of febrile seizures increased in groups 2 and 3. There was seasonal variation in febrile seizures, with a decrease in autumn and an increase in winter. The majority of patients in all groups was under 3 years of age.

Conclusions: In this study, we attributed the decrease in the number of febrile seizures in the first year of the pandemic period and its increase in the subsequent years to the effects of the pandemic on the course of infections. The seasonal shift observed in febrile seizures after the removal of precautions may also reflect changes in the period of infection. Understanding that pandemics cause epidemiological changes in infections and related comorbidities is important for the early prediction and management of infections and their comorbidities.

Keywords: Febrile seizure, Covid-19, Pandemic, Child

INTRODUCTION

Febrile seizures are the most common seizure disorder of childhood and affect 2-5% of children (1,2). Febrile seizures are caused by genetic and environmental factors. Viral infections with fever are associated with febrile seizures. As viral infections increase seasonally, febrile seizures also increase. Therefore, changes in infections may affect the distribution and frequency of febrile seizures (3).

The first case of COVID-19 in our country was reported in March 2020, and the pandemic quickly spread nationwide. At the beginning of the pandemic, non-COVID infections and related emergency applications decreased significantly because of physical distancing measures, mandatory mask wearing, and travel precautions. After May 2022, pandemic measures were gradually lifted in our country. Following the removal of these measures, non-Covid infections increased. During this period, we observed an increase in the frequency, severity, and duration of infections compared with before the pandemic. This observation led to the hypothesis that these changes might affect emergency visits and fever-triggered seizures and that the lifting of measures would result in an increase in non-COVID infections and consequently an increase in febrile seizures. For this reason, we examined patients who presented to the emergency department with febrile seizures before and after the implementation of the pandemic measures.

Corresponding Author: Betül Diler Durgut **E-mail:** betudlr@hotmail.com

Submitted: 27.12.2023 • **Revision Requested:** 08.07.2024 • **Last Revision Received:** 09.07.2024 • **Accepted:** 29.07.2024

This work is licensed under Creative Commons Attribution-NonCommercial 4.0 International License

MATERIAL AND METHODS

The data of patients who presented to the emergency department with febrile seizures during and after the pandemic were retrospectively examined. During the 1-year period before the pandemic, the number of patients presenting with febrile seizures was determined, but detailed data could not be accessed.

Patients who presented with febrile seizures were included in the study. Patients diagnosed with central nervous system infection, symptomatic seizures, or fever-triggered epilepsy seizures were excluded.

The demographic data of the patients were examined by dividing them into two groups: patients with first febrile seizures and patients with recurrent febrile seizures. The groups were compared in terms of age, gender, seizure type, seizure onset type, number of patients with generalised tonic clonic (GTC) seizures, electroencephalography (EEG) findings, family history of febrile seizures and epilepsy, and presence of fever at first admission.

Patients who presented to the emergency department with febrile seizures after May 2020 were divided into three groups: Group I, patients admitted in the first year of the pandemic (1 May 2020–1 May 2021); Group II, patients admitted in the second year of the pandemic (1 May 2021–1 May 2022); and Group III, patients admitted in the period after the removal of pandemic measures (1 May 2022–1 May 2023). The groups were compared according to age, recurrent febrile seizures, seizure status upon admission, seizure duration, need for antiseizure treatment, and seasonal distribution.

Ethics Approval

This study was conducted in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Giresun University with register number 2023/01.

Statistics

Statistical analyses of the study were performed using the trial version of SPSS 22.0 (SPSS Inc., Chicago, IL) package software. Kolmogorov-Smirnov test was employed to examine whether the quantitative variables were suitable for normal distribution. Independent groups were compared using the Mann–Whitney U or Kruskal-Wallis H test for variables that were not normally distributed. The relationship between qualitative variables was examined using chi-square analysis. The descriptive statistics of the quantitative variables that conformed to the normal distribution are presented as mean ±standard deviation, and the descriptive statistics of the quantitative variables that were not normally distributed are presented as median (min-max) or mean ±standard deviation. Descriptive statistics for qualitative variables are expressed as frequency (%).

RESULTS

In total, 248 patients who presented with 272 febrile seizures were examined. Among these seizures, 140 occurred in girls and 132 in boys. The mean age was 32.8±27.8 months. A total of 19 patients experienced seizures that continued upon admission to the emergency department. The seizures of 5 patients lasted more than 15 min. Seizure onset was focal in 14 patients. Of the 14 patients, 175 presented with their first febrile seizure and 97 with recurrent febrile seizures. The mean age of patients with recurrent febrile seizures was significantly higher than that of patients with first febrile seizure ($p<0.001$). There were no significant differences between the groups in terms of sex distribution, seizure duration, seizure type, family history of epilepsy and febrile seizures, or presence of epileptic activity on EEG (Table 1). Similarly, the seasonal distribution of febrile seizures and recurrent febrile seizures showed no significant variation (Table 2). In the 1-year period before the pandemic (1 May 2019-1 May 2020), 65 patients presented to our emergency department with febrile seizures. The detailed data for these patients could not be accessed.

Table 1: Comparison of febrile and recurrent febrile seizure data

	FS n:272	First FS* n:175	Recurrent FS* n:97	p*
Age(mean ± SD) median (%)	32.8+27.8 24.5	28.91±21.85 21	40.05±35.23 29	**<0.001** **
Gender (M/F)	140/132	85/90	55/42	0.199
Ongoing seizure at admission	19 (7)	15 (8.6)	4 (4.1)	0254
Seizure duration of >15 m	5 (8.9)	5	0	0.145
Seizure duration of >10 m	10 (17.9)	9	1	0.072
Seizure duration of >5 m	18 (67.9)	15	3	0.137
Focal-onset seizures	14 (4.8)	9	5	1.00
GTC(%) seizure	80 (29.5)	52 (29.9)	28 (28.9)	0.609
Family history of epilepsy (%)	59 (21.8)	32 (18.4)	27 (27.8)	0.071
Family history of FS (%)	127 (46.9)	80 (46)	47 (48.5)	0.695
Epileptic activity in EEG (%)	20 (20.8)	13/49	7/47	0.249
Fever at admission(%)	216 (81.5)	137 (81.1)	79 (82.5)	0.934

*P= Comparison of Fs and RFs groups **Mann-Whitney U test. EEG:Electroencephalography F:Female FS:Febrile seizure m:minutes GTC:Generalised tonic clonic seizure M:Male

There were no differences between the groups in the frequency of first or recurrent febrile seizures, seizure status upon admission to the emergency department, seizure duration, treatment requirement, and focal onset frequency (Table 3).

Considering the distribution of febrile seizures, no significant seasonal differences were observed between the first and second years of the pandemic. However, after these measures were implemented, the number of patients with febrile seizures decreased in autumn and increased in winter, although there was no statistical difference between the groups (Table 3). The expected peak of febrile seizures in autumn did not occur, shifting to winter months (Figure 1). There was no difference in the rate of recurrent febrile seizures between the pandemic period and after the measures were lifted (comparing the

Table 2: Seasonsal distribution of febrile seizures.

	Spring	Summer	Autumn	Winter	Total	p
First FS	34 (19.4)	51 (29.1)	35 (20)	55 (31.4)	175	0,225
Rekpurrent FS	26 (26.8)	19 (19.6)	17 (17.5)	35(36.1)	97	
Total	60(22.1)	70(25.7)	52(19.1)	90(33.2)	272	

FS:Febrile seizure

Table 3: Distribution of febrile seizures by age

	Pandemic-1st Year n:34 (Group1)	Pandemic-2nd Year n:105 (Group 2)	After lifting social isolation measures are lifted n:132 (Group 3)	p
Age (mean ± SD) median	26±19.64 18	29.04±17.61 25	37.78±34.8 27	0.49
Age<3 (%)	29 (85.2)	80 (76.2)	78 (60.4)	0,02
FS	24 (70,6)	70 (66,7)	81 (60,9)	0,47
Recurrent FS	10 (29,4)	35 (33,3)	52 (39,1)	
Emergency admission				
Ongoing seizure	4 (11,8)	9 (8,6)	6 (4,5)	0,246
Without seizure	30 (88,2)	96 (91,4)	126 (95,5)	
Seizure duration				
>5 m	3 (8,8)	4 (3,8)	11 (8,3)	0,334
<5 m	31 (91,2)	101 (96,2)	122 (91,7)	
Seizure stopped without				
medication	25 (73,5)	76 (72,4)	95 (71,4)	0,96
with medication	9 (26,5)	29 (27,6)	38 (28,6)	
Focal	1 (2,9)	4 (3,8)	9 (6,8)	0,487
Generalise	33 (97,1)	101 (96,2)	124 (93,2)	
Spring	7 (20,6)	17 (16,2)	36 (27,1)	
Summer	8 (23,5)	27 (25,7)	35 (26,3)	0,254
Autumn	9 (26,5)	25 (23,8)	18 (13,5)	
Winter	10 (29,4)	36 (34,3)	44 (33,1)	

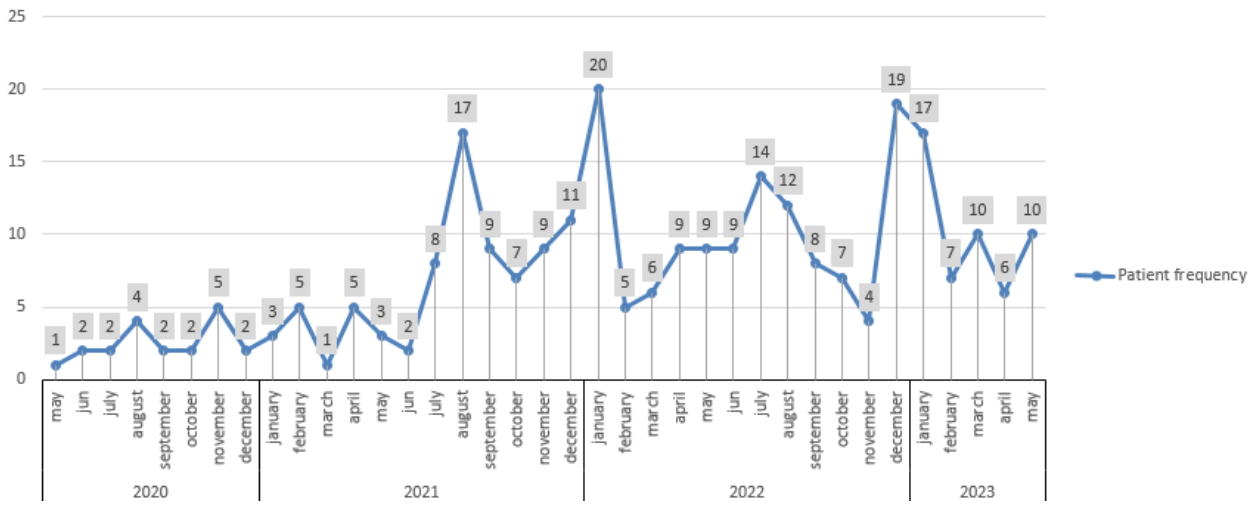

Figure 1: Patient distribution by months.

1st Year of the pandemic and after the measures were lifted p=0.398, comparing the 2nd Year of the pandemic and after the measures were lifted p=0.435, comparing the 1st and 2nd Year of the pandemic p=0.831).

DISCUSSION

Febrile seizures are one of the most common conditions in paediatric neurology practise. COVID-19-related febrile seizures have been reported at rates ranging from 0.5% to 5.7% in the literature (4, 5, 6). In a case–control study by Hanlon et al. focusing on COVID-19 infection, febrile seizures were observed in 2.7% of patients with COVID-19. The study concluded that there was no increased risk of febrile seizures associated with COVID-19 (4).

The COVID-19 pandemic encompassed three distinct periods: closure (group 1, first year), ease of measures (group 2, second year), and removal of measures (group 3). In the present study on the course of febrile seizures during the pandemic period, we did not find any statistically significant differences in the frequency of first febrile or recurrent febrile seizures, seizure status at admission to the emergency department, seizure duration, treatment requirement, or focal onset frequency between the first year of the pandemic, the second year, or the 1-year period after the measures were lifted. However, there was an increase in the number of febrile seizures during the second and third years after implementation of the measures, and a seasonal shift was observed in febrile seizures.

In this study, the number of patients was significantly lower in group 1. Due to the widespread use of masks and social distancing, there was likely a decrease in respiratory virus infections, which was indirectly reflected in the reduced number of febrile seizures triggered by infection and fever. There was a rapid increase in the number of cases in the second year of the pandemic (group 2), and the number rose further in the third year when the measures were lifted. This led us to hypothesise that compliance with measures decreased from the second year of the pandemic onwards, and non-covid infections increased following the removal of measures. Additionally, we detected a seasonal shift in the occurrence of febrile seizures. We hypothesised that this might be related to the shift in infection periods. The literature contains studies from various countries on the course of infections during and after the pandemic. According to a study conducted by Agha et al. in New York, it was observed that the RSV (Respiratory Syncytial Virus) peak, which is usually observed between September and February in the years 2016-2019, was not observed in 2020. Instead, there was a shift of RSV infection to the spring months of 2021, specifically from March to May. (7). Similarly, New York health surveillance data showed that the RSV peak occurred later and remained at a lower level in 2020-2021, but peaked earlier and was higher than expected in 2022-2023. The same findings are also applicable to influenza infection (8). In a similar study conducted in Australia, it was shown that although the RSV epidemic typically started in April before the pandemic, it began in late September 2020 (9). In Park et al. in Korea, the pre-pandemic period (March 2016-February 2020) was compared with the pandemic period (March 2020-February 2022). The incidence of febrile seizures increased dramatically in autumn during the pandemic and decreased significantly in spring. The same study reported a decrease in influenza and an increase in parainfluenza virus throughout the pandemic. Although the pathogens and epidemic periods vary, seasonal shifts are common in these studies. In this study, we observed a seasonal shift in infection-related febrile seizures, which is consistent with the literature (Figure 1).

In the 1-year period before the pandemic (1 May 2019-1 May 2020), 65 patients presented to our emergency department with febrile seizures. During the first year of the pandemic, there was a significant decrease in febrile seizures (n: 34). However, we observed an increase in the number of patients presenting with febrile seizures during the second year of the pandemic (n: 105) and further in the third year (n: 132) when the measures were lifted. This increase coincided with a noticeable increase in the severity and frequency of non-COVID infections in our daily practise compared to previous years, contributing to the expected increase in febrile seizures. Studies in the literature have also indicated a post-pandemic increase in infections. A study from China reported increases of 70.9% in Mycoplasma infections, 259.5% in influenza, 9.8% in parainfluenza, 174.3% in RSV, and 35% in bocavirus infections (10). A review from Germany highlighted that pandemic measures initially reduced infections, but their cessation increased invasive group A streptococcal infections. The study also noted, similar to our findings, a shift in the timing of infections outside the usual period (11). In Italy, following the lifting of restrictions, a study observed changes in the epidemiology of respiratory syncytial virus (RSV), leading to increased hospitalisation rates (12).

In a study from Israel, social restrictions led to a significant decrease in infectious disease morbidity, but non-SARS-CoV viruses resurged in the months following the easing of measures, particularly affecting children under the age of 3 (13). Early-life exposure to microorganisms is linked to the development of robust immunity (14). Precautionary measures and lockdowns during the pandemic may have prevented infants, especially those in their early years and without prior exposure to microorganisms, from developing strong immune systems. This could explain the increased susceptibility observed in children aged 3 years. In our study, most patients in all three groups were under 3 years old (85.2%, 76.2%, and 60% respectively by year). In group 3, the proportion of patients aged 3 years was the lowest ($p<0.05$).

In a study conducted in our country in 2011, the clinical findings of 1385 patients with febrile seizures were recorded, with a mean age of 22.2±1.24 months (15). In the current study, the mean age was 28.91±21.85 (median 21) in the group experiencing their first febrile seizure during the first year of the pandemic, and 26±19.64 (median 18) in the first year of the pandemic. The median age of all groups was 36 months (Table

1, 3). Our study included patients aged under 5 years, which is consistent with the literature, as this age group is most affected by infections that increased following the lifting of restrictions.

In a study examining RSV and non-RSV bronchiolitis in Italy, there was a significant decrease in bronchiolitis and other respiratory infections during the SARS-CoV-2 quarantines (2020-2021), followed by a general increase in cases in the subsequent season, 2021-2022. It was observed that patients in 2021-2022 required more intensive care than children in the previous four seasons (16). Based on these findings, it can be inferred that reduced exposure to infections in 2020-2021 led to decreased immunity and more severe infections in 2022.

In this study, we hypothesised that the number of febrile seizures decreased in the first year of the pandemic and increased in subsequent years because of the pandemic's impact on infection patterns. The increase in febrile seizures and their seasonal distribution, mirroring infection trends, suggest similar fluctuations in our country as well.

Limitations of the study

This study was constrained by its retrospective design and the absence of specific infectious agents.

In conclusion, our study supported the hypothesis that the frequency and seasonal distribution of febrile seizures may vary during pandemic periods. Recognising that pandemics induce epidemiological shifts in infections and associated comorbidities is crucial for the early prediction and management of these conditions.

Ethics Committee Approval: This study was approved by the ethics committee of Giresun University with register number 2023/01.

Informed Consent: Written consent was obtained from the participants.

Peer Review: Externally peer-reviewed.

Author Contributions: Conception/Design of Study- B.D.D., E.T., C.C.K.; Data Acquisition- B.D.D., E.T.; Data Analysis/Interpretation- B.D.D., C.C.K.; Drafting Manuscript- B.D.D.; Critical Revision of Manuscript- E.T., C.C.K.; Final Approval and Accountability- B.D.D., E.T., C.C.K.

Conflict of Interest: Authors declared no conflict of interest.

Financial Disclosure: Authors declared no financial support.

REFERENCES

1. Capovilla G, Mastrangelo M, Romeo A, Vigevano F. Recommendations for the management of "febrile seizures": Ad Hoc Task Force of LICE Guidelines Commission. Epilepsia. 2009 Jan;50 Suppl 1:2-6. doi: 10.1111/j.1528-1167.2008.01963.x. PMID: 19125841.
2. Subcommittee on Febrile Seizures; American Academy of Paediatrics. Neurodiagnostic evaluation of the child with a simple febrile seizure. Paediatrics. 2011 Feb;127(2):389-94. doi: 10.1542/peds.2010-3318. PMID: 21285335.
3. Park EG, Kim JM, Suh W, Han JY, Han SB. Impact of COVID-19 on the incidence of respiratory viral infections and clinical characteristics of associated febrile seizures. Transl Pediatr. 2023 Apr 29;12(4):528-537. doi: 10.21037/tp-22-406. Epub on Mar. 31, 2023. PMID: 37181019; PMCID: PMC10167401.
4. Hanlon SM, Sim D, Schneider JG, Yang Z, Thompson SM. The Association Between COVID-19 and Febrile Seizure: A Retrospective Case-Control Study. *Pediatr Emerg Care*. 2023;39(5):360-363. doi:10.1097/PEC.0000000000002935
5. Cadet K, Boegner J, Ceneviva GD, Thomas NJ, Krawiec C. Evaluation of Febrile Seizure Diagnoses Associated With COVID-19. J Child Neurol. 2022 Apr;37(5):410-415. doi: 10.1177/08830738221086863. Epub on March 14, 2022. PMID: 35286175; PMCID: PMC9086105.
6. Mohamed ZA, Tang C, Thokerunga E, Deng Y, Fan J. Paediatric infection with the Omicron variant increases the risk of febrile seizures among COVID-19 infected children. Front Pediatr. 2023 Aug 17;11:1226403. doi: 10.3389/fped.2023.1226403. PMID: 37664550; PMCID: PMC10469930.
7. Agha R, Avner JR. Delayed Seasonal RSV Surge Observed During the COVID-19 Pandemic. Paediatrics. 2021;148(3):e2021052089
8. New York City Department of Health and Mental Hygiene. Influenza surveillance report: Week ending on April 17, 2021 (week 15). Available online: https://www1.nyc.gov/assets/doh/downloads/pdf/hcp/weeklysurveillance04172021.pdf (accessed on April 26, 2021
9. Foley DA, Yeoh DK, Minney-Smith CA, Martin AC, Mace AO, Sikazwe CT, et al. Interseasonal Resurgence of Respiratory Syncytial Virus in Australian Children Following the Reduction of Coronavirus Disease 2019-Related Public Health Measures. Clin Infect Dis. 2021 Nov 2;73(9):e2829-e2830. doi: 10.1093/cid/ciaa1906. PMID: 33594407; PMCID: PMC7929151.
10. Xu Y, Yang C, Sun P, Zeng F, Wang Q, Wu J, et al. Epidemic features and metagenomic analysis of childhood *Mycoplasma pneumoniae* following the COVID-19 pandemic: a 6-year study in southern China. Emerg Microbes Infect. 2024 Dec;13(1):2353298. doi: 10.1080/22221751.2024.2353298. Epub 2024 Jun 27. PMID: 38721691; PMCID: PMC11212572.
11. Goldberg-Bockhorn E, Hagemann B, Furitsch M, Hoffmann TK. Invasive Group A Streptococcal Infections During the COVID-19 Pandemic. Dtsch Arztebl Int. 2024 Oct 4;(Forthcoming):arztebl.m2024.0127. doi: 10.3238/arztebl.m2024.0127. Epub ahead of print. PMID: 38961826.
12. Pierangeli A, Midulla F, Piralla A, Ferrari G, Nenna R, Pitrolo AMG, et al. Sequence analysis of respiratory syncytial virus cases reveals a novel subgroup B strain in northern-central Italy after pandemic restrictions. J Clin Virol. 2024 Aug;173:105681. doi: 10.1016/j.jcv.2024.105681. Epub 2024 May 10. PMID: 38733664.
13. Amar S, Avni YS, O'Rourke N, Michael T. Prevalence of Common Infectious Diseases After COVID-19 Vaccination and Easing of Pandemic Restrictions in Israel. JAMA Netw Open. 2022 Feb 1;5(2):e2146175. doi: 10.1001/jamanetworkopen.2021.46175. PMID: 35103792; PMCID: PMC8808334.
14. Simon AK, Hollander GA, McMichael A. Evolution of the immune system in humans from infancy to old age. Proc Biol Sci. 2015;282(1821):20143085. doi:10.1098/rspb.2014.3085

15. Özaydın E, Yaşar MZ, Güven A, Değerliyurt A, Vidinlisan S, Köse G. Clinical characteristics and risk factors of 1385 cases with febrile convulsion. Turkish Journal of Paediatric Disease. 2011;5(1):11-8.
16. Faraguna MC, Lepri I, Clavenna A, Bonati M, Vimercati C, Sala D et al. The bronchiolitis epidemic in 2021-2022 during the SARS-CoV-2 pandemic: experience of a third-level centre in Northern Italy. Ital J Pediatr. 2023;49(1):26. Published 2023 Feb 21. doi:10.1186/s13052-023-01425-8.