BREASTFEEDING MEDICINE
Volume 15, Number 11, 2020

DOI: 10.1089/bfm.2020.0105

The Protective Effect of Breastfeeding on Febrile Seizures: A Case–Control Study

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Abstract

Objective: Our study was performed to analyze the interrelationship between breastfeeding for the first 6 months of life and the incidence of febrile seizures (FS).
Study Design: A case–control study was conducted in Renmin Hospital of Wuhan University. Three hundred thirty-six patients diagnosed with FS were enrolled as the case group, and 336 febrile children with matched age and gender were enrolled as the control group. Clinical information of all cases was collected from the Electronic Medical Record, including feeding patterns. The primary outcome was the difference of feeding modes between cases and controls, while the secondary outcome included the difference of feeding patterns between simple FS (SFS) and complex FS (CFS).
Results: The 336 patients with FS comprised 294 with SFS and 42 with CFS. The difference in feeding methods between the case group and the control group was statistically significant, and children who were breastfed exclusively had a lower risk of suffering from FS compared with formula feeding (odds ratio [OR], 0.504 and 95% confidence interval [CI], 0.303–0.841); although partial breastfeeding exhibited a slight protective effect against FS, the protective role was not statistically significant (OR, 1.016 and 95% CI, 0.560–1.846). In addition, our dates showed that feeding mode was not a risk factor in the occurrence of SFS or CFS ($p > 0.05$).
Conclusion: Our data confirm that exclusive breastfeeding is an independent protective factor that can reduce the occurrence of FS.

Keywords: interrelationship, breastfeeding, febrile seizures, Chinese children

Introductions

Febrile seizures (FS) usually occur in children 6–60 months of age, and undoubtedly, they are the most common form of convulsions in early childhood.[1,2] FS, a classic category of seizures, are always associated with fever, but show no evidence of central nervous system infection, metabolic abnormalities, or intoxication. According to published reports, the incidence of FS ranges from 2% to 5%,[2,3] with the peak incidence at one and a half years of age. FS can be further subdivided into two types, namely, simple FS (SFS) and complex FS (CFS). There is no convincing evidence regarding the increased mortality, hemiplegia, or mental retardation of children with FS.[4] Although FS are a sort of benign situation, because of their unique clinical manifestation, the experience of FS by parents of affected children may be frightening, and produce high degrees of anxiety.

Up to now, the etiology of FS is not fully understood; it is largely believed that FS may occur as a result of multiple factors affecting susceptible individuals, including genetic factors,[5,6] infectious factors,[7] and environmental factors.[8]

Breastfeeding, which is an alternative to manual and mixed feeding, is well known and scientifically supported in terms of its benefits to both infants and mothers. It is the most natural method of feeding, promotes maternal and infant health, and decreases feeding costs. Studies have shown a strong link between breastfeeding and early immune system development in infancy. It has been confirmed that breastfeeding reduces the incidences of many diseases, including infectious diseases[9,10] and metabolic diseases,[11,12] improves cognitive development,[13] and decreases the incidence of leukemia.[14] FS, just as the name suggests, are evoked by febrile diseases, and the main reason of fever is infection. Up to now, there is little date on the positive role of breastfeeding in FS,[15] especially among the children of developing countries.

Therefore, in this study, we analyzed the date of children hospitalized at Renmin Hospital of Wuhan University

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between January 2017 and August 2019 to determine the association between breastfeeding and FS.

Materials and Methods

Sample selection

After obtaining institutional research ethics board approval, we performed a hospital-based case–control study in Department of Pediatrics, Renmin Hospital of Wuhan University, Hubei, China, between January 2017 and August 2019. By searching for discharge diagnosis from Electronic Medical Record (EMR) of our hospital, 377 cases diagnosed with FS were picked out; simultaneously, we obtained the telephone numbers of the guardians of these children. Then we called them and offered full explanation of our project to them to acquire parental consent. Of these 377 cases, we excluded cases of those who were younger than 6 months or older than 60 months ($n=7$), whose EMR missed some important information, such as feeding patterns ($n=9$), whose guardians did not agree their children to participate in our study ($n=20$), and whose auxiliary examination could not completely rule out the possibility of central nervous system infections($n=5$). Finally, we got 336 effective cases. Accordingly, 336 age- and gender-matched children with fever, but without seizures were deemed as control group; these febrile diseases are primarily respiratory and digestive diseases, but not central nervous system infections (Fig. 1).

The diagnostic criteria for FS were based on the guidelines formulated by the American Academy of Pediatrics (APP) in 2011. SFS are defined as primary generalized seizures with a duration of <15 minutes and no recurrence within 24 hours. CFS are defined as focal, persistent (≥15 minutes), and/or recurrent within 24 hours. In addition, FS in children with preexisting neurological disorders are also known as CFS.[4]

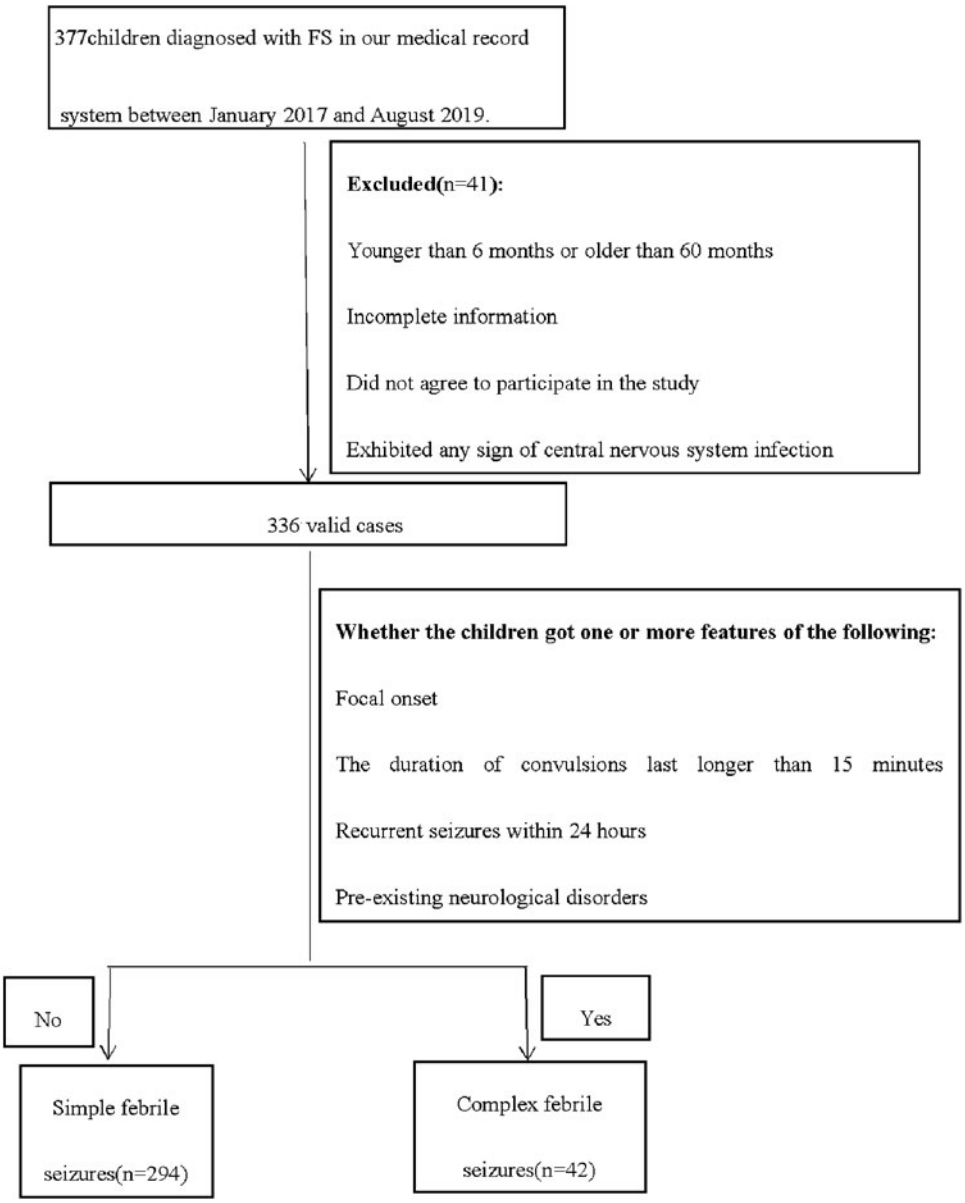

FIG. 1. Flowchart for selection of participants.

Date collection

We collated the basic information of these affected cases, including age of onset, gender, birth weight, whether the birth was preterm, mode of delivery, feeding patterns, temperature, pregnancy complication, previous history of FS, family history of FS, and family history of epilepsy. Especially, feeding modes were the most primary factors of our study. Due to the different feeding methods for the first 6 months after birth, we distinguished them into exclusive breastfeeding, partial breastfeeding, and formula feeding. Exclusive breastfeeding means those who only acquire breast milk, but without any solid or liquid supplement for the first 6 months (except water).

Besides, dates on the manifestation of convulsion, the duration of convulsion, and the number of convulsions during this course were also crucial information, and we used this information to further divide convulsions into SFS and CFS. Finally, we saved the date in excel files.

Statistical analyses

The dates were analyzed using Statistical Package for Social Science (SPSS, Inc., Version 21.0). The independent sample *t*-test was used to compare the means of continuous variables, such as age, while the chi-square test was used for analysis of qualitative variables. When the expected frequency of the data did not meet the conditions of the chi-square test, we applied continuity correction or Fisher's exact test. Simultaneously, after adjustments were made for gender, age, whether the birth was preterm, temperature, previous history of FS, family history of FS, and family history of epilepsy, binary logistic regression analysis was used to assess the risk of feeding pattern on the occurrence of convulsion. $p < 0.05$ was taken to indicate statistical significance.

Results

Our results showed that there were no statistically significant differences in the two groups regarding age, gender, birth weight, temperature, pregnancy complication, or family history of epilepsy ($p > 0.05$); however, feeding patterns, previous history of FS, and family history of FS were strongly associated with the occurrence of FS, and there were statistically significant differences between the two groups regarding these factors ($p < 0.05$) (Table 1).

Table 1. Comparison of Risk Factors Between 336 Cases and 336 Controls

	Cases (n = *336*)	*Controls* (n = *336*)	p
Age (months) ($\bar{x} + s$)	27.63 ± 13.64	27.43 ± 16.48	0.862
Gender			0.095
Male	219 (65.2)	198 (58.9)	
Female	117 (34.8)	138 (41.1)	
Birth weight (g)			0.121
<2,500	6 (1.8)	15 (4.4)	
2,500–4,000	319 (94.9)	308 (91.7)	
>4,000	11 (3.3)	13 (3.9)	
Preterm or not			0.311
Yes	6 (1.8)	10 (3.0)	
No	330 (98.2)	326 (97.0)	
Mode of delivery			0.699
Vaginal	157 (46.7)	152 (45.2)	
Cesarean	179 (53.3)	184 (54.8)	
Feeding patterns (within 6 months after birth)			0.019
Exclusive breastfeeding	122 (36.3)	150 (44.6)	
Partial breastfeeding	158 (47.0)	151 (44.9)	
Formula feeding	56 (16.7)	35 (10.4)	
Temperature (°C)			0.700
38–39	162 (48.2)	167 (49.7)	
>39	174 (51.8)	169 (50.3)	
Maternal complication			0.686
Yes	4 (1.2)	2 (0.6)	
No	332 (98.8)	334 (99.4)	
Previous history of FS			0.000
Yes	76 (22.6)	8 (2.4)	
No	260 (77.4)	328 (97.6)	
Family history of FS			0.000
Yes	27 (8.0)	0 (0.0)	
No	309 (92.0)	336 (100.0)	
Family history of epilepsy			0.499
Yes	2 (0.6)	0 (0.0)	
No	334 (99.4)	336 (100.0)	

FS, febrile seizures.

Table 2. Multivariable Analysis of Feeding Patterns Associated with Febrile Seizures

	Multivariate		
Feeding patterns	*OR*[a]	*95% CI*	p
Exclusive breastfeeding	0.504	0.303–0.841	0.009
Partial breastfeeding	1.016	0.560–1.846	0.957
Formula feeding	*Ref*		

[a]Adjusted for gender, age, whether the birth was preterm, temperature, previous history of FS, family history of FS, and family history of epilepsy.

CI, confidence interval; FS, febrile seizures; OR, odds ratio; *Ref*, reference.

The results of binary logistic regression analysis suggested that children who breastfed exclusively had a lower risk of suffering from FS than those who were formula fed (odds ratio [OR], 0.504 and 95% confidence interval [CI], 0.303–0.841). Although partial breastfeeding performed a slight protective effect against FS, the protective role was not statistically significant (OR, 1.016 and 95% CI, 0.560–1.846) (Table 2).

Since FS were divided into SFS and CFS in accordance with the guidelines issued by the APP in 2011, after confirming that exclusive breastfeeding played a protective role against FS, we further wanted to determine whether it had a stronger inhibitory effect on SFS or CSF. A total of 294 SFS cases and 42 CFS cases were obtained, respectively. However, we did not find any statistically significant risk factor among the SFS group and CFS group, covering feeding patterns($p > 0.05$) (Table 3).

Discussion

The results of our case–control study indicated that exclusive breastfeeding was a positive factor against the happening of FS. The major protective effect of breastfeeding on FS did not change significantly due to a series of confounding factors. For SFS and CFS, the difference in feeding patterns was not at a high level of significance.

The nutritional properties of breast milk have been known for hundreds of years. In many societies, breastfeeding is considered one of the most important measures toward improving a child's health; moreover, breast milk is even considered a therapeutic agent that can be used in combination

Table 3. Comparison of Risk Factors Between 294 Simple Febrile Seizures and 42 Complex Febrile Seizures

	SFS (n = 294)	*CFS (n = 42)*	p
Age (months) ($\bar{x} + s$)	27.86 ± 13.76	26.05 ± 12.76	0.42
Gender			0.299
Male	195 (66.3)	24 (57.1)	
Female	99 (33.7)	18 (42.9)	
Birth weight (g)			0.696
<2,500	6 (2.0)	0 (0.0)	
2,500–4,000	279 (94.9)	40 (95.2)	
>4,000	9 (3.1)	2 (4.8)	
Preterm or not			1.000
Yes	6 (2.0)	0 (0.0)	
No	288 (98.0)	42 (100.0)	
Mode of delivery			0.623
Vaginal	139 (47.3)	18 (42.9)	
Cesarean	155 (52.7)	24 (57.1)	
Feeding patterns (within 6 months after birth)			0.406
Exclusive breastfeeding	106 (36.1)	16 (38.1)	
Partial breastfeeding	136 (46.3)	22 (52.4)	
Formula feeding	52 (17.7)	4 (9.5)	
Temperature (°C)			0.622
38–39	140 (47.6)	22 (52.4)	
>39	154 (52.4)	20 (47.6)	
Maternal complication			1.000
Yes	4 (1.4)	0 (0.0)	
No	290 (98.6)	42 (100.0)	
Previous history of FS			1.000
Yes	67 (22.8)	9 (21.4)	
No	227 (77.2)	33 (78.6)	
Family history of FS			0.595
Yes	25 (8.5)	2 (4.8)	
No	269 (91.5)	40 (95.2)	
Family history of epilepsy			1.000
Yes	2 (0.7)	0 (0.0)	
No	292 (99.3)	42 (100.0)	

CFS, complex FS; FS, febrile seizures; SFS, simple FS.

with medication for some condition.[16,17] As a matter of fact, the associations between breast milk and diseases have been studied for a long time, and unsurprisingly, the results have indicated that breast milk is protective against diseases. Although the benefits of breastfeeding have been demonstrated in the context of many diseases, it is worth nothing that studies addressing the association between breastfeeding and FS are not very common. In 2010, Iranian scholars focused on the risk factors of first FS, and their findings emphasized the intimate relationship between the breastfeeding duration and FS. The shorter the duration of breastfeeding was, the higher the incidence of FS would be.[18] In 2019, some Japanese researchers confirmed this conclusion. They performed a large sample date study, and their results revealed that breastfeeding did have a protective effect, in that, it reduced the incidence of FS in the first year of life.[15] In this study, we arrived at a similar conclusion. The number of children in the case group who breastfed exclusively was significantly lower than that in the control group. This result strongly affirmed that breastfeeding was positively correlated with reducing the incidence of FS. In addition, we also verified this conclusion by excluding confounding factors, and our results again showed that the protective effect of breast milk was independent of many possible confounding factors, such as gender, birth weight, mode of delivery, and so on. When we further tried to demonstrate the association between feeding patterns and the type of convulsions, unfortunately, our results yielded no evidence supporting the interrelationship between feeding mode and specific types of convulsions. This may have something to do with the small sample size of CFS patients. In the near future, we will continue to collect cases for further study.

Breast milk is the nutrition that a baby is given during the first few months after birth, which is a key period for the development of the immune system and the programming of metabolic and endocrine functions. The World Health Organization (WHO) specifically recommends that all children be exclusively breastfed for 6 months. In this study, we confirmed that breast milk played an active role against FS. There are several possible mechanisms. First, breast milk contains natural taurine long-chain polyunsaturated fatty acids and lactose, which promote the growth of white matter and the formation of nerve myelin. Second, breast milk is rich in immunoglobulin A,[19] which enhances the child's resistance to infectious diseases, thus reducing the chance of fever and in turn alleviating the chance of convulsions. Third, n-3 long-chain polyunsaturated fatty acids, which are active ingredients in breast milk, have been suggested to exert the important effect of reducing neuronal excitability and preventing convulsions.[14]. Although FS have a certain chance of transforming into epilepsy, breastfeeding did not appear to have a positive effect on epilepsy.[20]

There are several advantages to our study. First, to the best of our knowledge, this is the first study to evaluate the strong association between breastfeeding and FS in our city and in China; additionally, the protective role of human breast milk against FS is independent of other potential confounding factors. Furthermore, our study evaluated the crucial role of family history in FS, which was not observed in other researches before.[15] However, there are some limitations in our study. First, several confounding factors are involved in the occurrence of FS, and in this study, it is impossible to cover them all. Some other significant confounding factors have not been taken into account in this study, such as socioeconomic status or size of family, which may also contribute to the occurrence of FS. Second, as this is a retrospective case–control study, recall biases are the inevitable drawbacks of such studies. Finally, due to the large land area and population in China, although our hospital is a large general hospital, the selection bias of our date is inevitable. Prospective studies and population-based national surveys are needed in the future to further address this important issue.

Conclusion

Convulsions are common pediatric emergency, and parents often feel anxiety about the sudden onset of convulsions in their children. Our findings show that exclusive breastfeeding plays a positive role against FS. Thus, breast milk is an effective factor that can reduce the incidence of FS. This study provides another piece of convincing evidence that helps us recommend breastfeeding.

Authors' Contributions

X.P. contributed to the study design, experiment implement, data analysis, and article writing; B.Y. contributed to study design and experiment implement; S.W. and S.Y. contributed to data analysis and article writing; and C.F. and Y.X. called for informed consent. All authors approved the final version of this article.

Consent and Ethical Approval

This study was approved by the Ethics Committee of Renmin Hospital of Wuhan University. Informed consent was obtained from the guardians of all individual participants.

Disclosure Statement

No competing financial interests exist.

Funding Information

Our study was supported by the Medical Science Advancement Program of Wuhan University (no. TFLC 2018001).

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