

## HEALTH RELATED BEHAVIOURS

## Breast-feeding and risk of hospitalization for all causes and fever of unknown origin

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**Background:** Breast-feeding has shown to give a reduction in the risk of hospitalization due to respiratory tract infections and gastrointestinal conditions during the first two years of life. The association of breast-feeding with all admission causes and with fever of unknown origin (FUO) was analysed. **Methods:** A case-reference study in Cantabria (northern Spain) was carried out. Cases (n=336) were hospitalized children aged less than 24 months at University of Cantabria Hospital; the reference was a 1:1 matched (by time from delivery to admission) sample of children from mothers delivering at the same hospital. Information on breast-feeding, socioeconomic variables and employment were obtained. Odds ratios (ORs), their 95% confidence intervals (CIs), and mean length of breast-feeding were estimated after adjustment for confounding variables. **Results:** In the reference population, shorter duration of breast-feeding was associated with smoking, lower educational level, and less privileged social strata. The frequency of breast-feeding was higher in the reference than in the cases, 82.3% vs 75.6% (p=0.023). Significant negative trends were noted in univariate analyses between the length of breast-feeding and both all admission causes and FUO, although the statistical significance was lost after adjusting for confounding variables (educational level, social class, smoking, and use of incubator after delivery). The adjusted mean length of breast-feeding was shorter in hospitalized children ≤6 months old for both all admission causes (40.6 ± 5.4 vs 99.5 ± 5.4, p<0.001) and FUO (40.8 ± 12.4 vs 91.7 ± 12.4, p=0.006). **Conclusion:** Breast-feeding time is shorter in hospitalized children for both all admission causes and FUO.

**Keywords:** breast-feeding, fever of unknown origin, hospitalization

Breast-feeding is strongly recommended during the first months of life as it contains all the newborn's nutritional needs and provides immunological protection which it is thought to decrease the frequency of infections, mainly in the gastrointestinal and respiratory tracts.<sup>1,2</sup> However, the frequency of breast-feeding has varied over time, with a clear decline between 1950 and 1970.<sup>3-5</sup> The causes for the abandonment of this practice are multiple, including several misconceptions held by some women (e.g. aesthetic problems), the increase in the number of women entering the workforce, and the commercial pressure for the use of artificial milk.<sup>6,7</sup> Many advantages of breast-feeding for both maternal and child health are supported by strong evidence.<sup>8-10</sup> It decreases the risk of infections in children,<sup>11-18</sup> although some authors suggest that the effect of breast-feeding might be more important in decreasing the severity of infections (measured by the rate of hospitalization) than in reducing infection risk.<sup>19,20</sup> Furthermore, beyond benefits on child health, breast-feeding also provides wide social, psychological, economic, and environmental benefits.<sup>21</sup> The purpose of this study was to assess the relationships of breast-feeding with the risk of hospitalization of children aged up to 2 years, including fever of unknown origin (FUO). To our knowledge, FUO has not previously been reported as influenced by breast-feeding.

## METHODS

A case-reference study was conducted. The study period was from 1 April 1995 to 31 May 1996. The inclusion criteria were:

- the newborn was delivered at the University Hospital Marques de Valdecilla (Santander, Spain), and
- his/her mother belonged to the referral area of the hospital, and
- the newborn had to be discharged within the next week after delivery (to avoid diseased newborn who could not breast feed).

Newborns with congenital malformations were excluded. Cases were selected using 40% random sampling of all children up to 24 months old admitted to the hospital: a 40% random sample of days was generated with the EpiInfo 6.0 (CDC, Atlanta, USA) software and all admissions in those days were included. During the study period 342 cases were selected; one mother rejected participation and in another five mothers, a history of lactation could not be obtained, thus leaving 336 for the present report.

The reference population was obtained from mothers meeting the same inclusion criteria as cases during the study period. A 15% random sample of all mothers delivering at the hospital was drawn using a similar procedure to that used for cases. A total of 493 reference mothers were initially selected, of whom nine had also been selected as cases. Eight women rejected participation in the study, thus leaving 485 women in this group. The data on breast-feeding and other lifestyle habits (smoking, alcohol intake) in the reference population were obtained by phone and/or mail one year after recruitment. Ninety-two women did not respond to the follow-up. To avoid the bias of obtaining a longer history of breast-feeding in the reference group, controls were randomly 1:1 matched to cases, and the history of breast-feeding of each control was only considered up to the age at admission of its matched case.

The data on sociodemographic characteristics (race, education level, type of job, family income, and social class according to the Black Report<sup>22</sup>), lifestyle (tobacco and alcohol consumption) and breast-feeding (for the present report at least once a day every day) were obtained by personal interview during hospital stay in cases. The interview was carried out within three

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days after delivery in the reference population and by phone and/or mail one year after delivery. An infant was considered to be breast-fed if she/he received it at least once every day. Causes of admission were coded according to the International Classification of Diseases, 9<sup>th</sup> revision.<sup>23</sup> FUIO was defined according to established criteria.<sup>24</sup>

In statistical analyses, matched odds ratios (ORs) and their 95% confidence intervals (CIs) were estimated.<sup>25</sup> Multiple conditional logistic regression was applied to adjust for confounding variables.<sup>26</sup> The variables controlled for by multivariate analysis were those changing the coefficient of lactation by more than 10%.<sup>27</sup> The adjusted mean duration of lactation in cases and controls was estimated by analysis of covariance. All the analyses were carried out with the Stata 7-SE statistical package (Stata Corp., College Station, Texas, USA).

## RESULTS

The description of both the study population and the reference mothers not responding to follow-up is summarized in *table 1*. There were no differences in maternal age between the hospitalized children and the reference ( $29.2 \pm 4.8$  (SD) years versus  $29.0 \pm 5.2$ ,  $p=0.43$ ). Among hospitalized children there were significantly more gypsies, parents with a lower educational level, families more frequently belonging to the lowest social class, mothers smoked more frequently, and family income was lower. Reference women with missing data on breast-feeding were more similar to mothers of cases than other reference women; the exceptions were maternal job out of the home and smoking, which were much lower in non-participating reference women. Breast-feeding was associated with factors related to lifestyle and sociodemographic characteristics (*table 2*). Longer duration of breast-feeding was observed in mothers who did not smoke, those who belonged to a higher socio-economic status, those who obtained a college degree, and those with an age between 21 and 35 years. Non-significant differences were found regarding other variables (maternal employment and ethnic background). The overall results for the relationship between breast-feeding and risk of hospital admission are shown in *table 3*. In univariate analyses, a significant and negative trend was found between the length of breast-feeding and the risk of hospital admission, overall and after stratifying by age (up to six months and older). These associations disappeared after adjusting for social class, education level, maternal smoking and use of incubator during the first week of life. The risk of hospital admission due to FUIO is also shown in *table 3* with similar results to those for all admissions; the results have not been stratified by age as the numbers were small.

**Table 1** Description of the study population

Variable	Hospitalized children n=336 %	Reference Data on breast-feeding		p-value <sup>a</sup>
		Yes n=336 %	No n=92 %	
Breast-feeding	75.6	82.8	—	0.023
Single mother	11.0	7.7	16.3	0.010
Ethnic gipsy	8.1	3.6	8.1	0.019
Maternal education lower than high school	14.5	6.5	12.0	0.002
Paternal education lower than high school	13.2	5.1	9.6	0.001
Lowest social class (level V)	23.2	13.1	22.8	0.003
Mother's job out of home	31.5	36.6	14.1	<0.001
Maternal smoking	47.3	37.2	13.0	<0.001
Income <\$700/month <sup>b</sup>	31.0	17.6	29.2	<0.001

a: Pearson chi-squared test.

b: 20 mothers did not answer this question.

Breast-feeding was dichotomized according to different cut-off levels (*figure 1*). The maximum protection (minimum odds ratio) for all causes was obtained for breast-feeding longer than two months and stronger for children up to six months of age than for older infants. For FUIO the lowest ORs were for durations of breast-feeding longer than 120 days, although these figures were not statistically significant.

The length of breast-feeding was also analysed (*table 4*). Overall, it was significantly shorter in cases, and this was found in

**Table 2** Duration of breast-feeding (days) according to several variables

Variable	Duration of breast-feeding	
	Mean $\pm$ SEM	p-value <sup>a</sup>
Maternal smoking		
Yes	72.0 $\pm$ 7.0	<0.001
No	114.3 $\pm$ 6.4	
Social class		
I-II	120.8 $\pm$ 9.8	0.064
III	113.1 $\pm$ 12.7	
IV	89.1 $\pm$ 6.8	
V	107.6 $\pm$ 14.5	
Education		
Primary school	88.7 $\pm$ 21.4	0.004
Secondary school	97.1 $\pm$ 3.4	
University	113.1 $\pm$ 5.1	
Ethnic		
Caucasian	101.4 $\pm$ 4.9	0.396
Gipsy	80.6 $\pm$ 29.6	
Maternal age (years)		
<21	74.8 $\pm$ 20.3	0.010
21-35	104.2 $\pm$ 5.4	
>35	78.2 $\pm$ 11.4	
Maternal employment		
Yes	103.1 $\pm$ 7.6	0.693
No	99.1 $\pm$ 6.3	

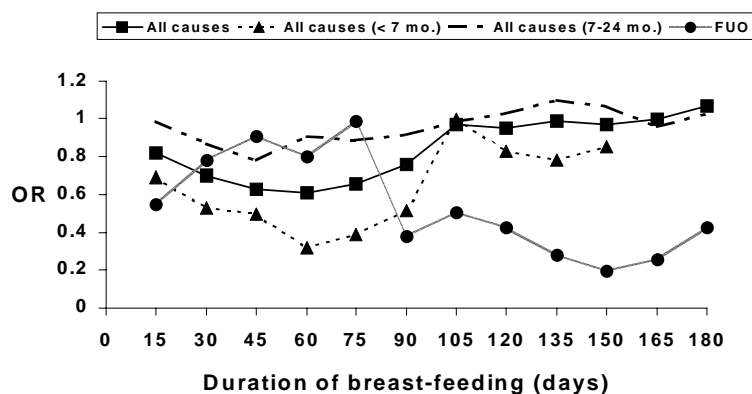
SEM: standard error of the mean.

a: Student *t*-test or one-way ANOVA.

admissions of children up to 6 months of age, but not for older children. The same was observed for FUO. If the analysis is restricted to children with FUO between 3 and 12 months of age, a significant difference was still observed ( $69 \pm 19$  days in cases vs.  $139 \pm 21$ ,  $p=0.018$ ).

**DISCUSSION**

With a matched design, taking into account the history of breast-feeding of the control group up to the age of admission of cases, it is believed that the influence of breast-feeding on risk of hospital admission is not over-estimated. Level and type of breast-feeding (complete, partial, artificial) were not analysed because of lack of variability: most women (95%) after the third month used partial



**Figure 1** Risk of admission according to different cut-off levels of duration of breast-feeding

**Table 3** Breast-feeding and risk of hospital admission

Breast-feeding	Cases	Reference	Univariate OR (95% CI)	Adjusted OR <sup>a</sup> (95% CI)
<b>All admission causes</b>				
No	82	58	1 (reference)	1 (reference)
Yes	254	278	0.66 (0.45–0.95)	1.14 (0.72–1.79)
1–45 days	117	88	0.95 (0.53–1.72)	1.63 (0.97–2.76)
46–90	67	92	0.72 (0.35–1.47)	0.86 (0.49–1.49)
91–180	51	76	0.42 (0.20–0.94)	0.80 (0.44–1.45)
≥181	19	22	0.25 (0.05–1.18)	1.06 (0.44–2.55)
Test for trend			$p=0.031$	$p=0.591$
<b>All admission causes among children 1–6 months old</b>				
No	47	31	1 (reference)	1 (reference)
Yes	132	148	0.60 (0.36–0.99)	0.90 (0.50–1.63)
1–45 days	80	65	0.83 (0.42–1.65)	1.19 (0.62–2.27)
46–90	33	51	0.38 (0.14–1.08)	0.61 (0.28–1.34)
≥91	19	32	0.44 (0.14–1.44)	0.46 (0.18–1.19)
Test for trend			$p<0.010$	$p=0.188$
<b>All admission causes among children 7–24 months old</b>				
No	35	27	1 (reference)	1 (reference)
Yes	122	130	0.73 (0.42–1.27)	1.60 (0.77–3.34)
1–45 days	37	23	1.40 (0.44–4.41)	2.79 (1.11–7.01)
46–90	34	41	1.60 (0.52–4.89)	1.29 (0.56–2.94)
91–180	33	44	0.50 (0.19–1.33)	1.44 (0.67–3.36)
≥181	18	22	0.13 (0.02–0.99)	1.60 (0.55–4.70)
Test for trend			$p=0.012$	$p=0.975$
<b>All admissions due to fever of unknown origin</b>				
No	11	10	1 (reference)	1 (reference)
Yes	41	42	0.89 (0.34–2.30)	1.05 (0.34–3.22)
1–45 days	14	11	0.80 (0.21–2.98)	1.03 (0.31–3.49)
46–90	19	16	3.00 (0.31–28.8)	1.66 (0.40–6.82)
91–180	6	10	0.50 (0.04–5.51)	0.54 (0.10–2.84)
≥181	2	5	0.00 <sup>b</sup>	<sup>b</sup>
Test for trend			$p=0.077$	$p=0.191$

a: Adjusted for socio-economic status (5 categories), educational level (5 categories), smoking (non-smokers, 1–10 cig/d, ≥11 cig/d), and use of incubator after delivery.

b: Not estimable as there were no discordant pairs.

natural lactation, and less than 10% of women used partial lactation before. This was due to paediatricians' recommendations. Women from the control group who did not respond to follow-up to give information on breast-feeding were different from those participating. We have tried to overcome this bias by adjusting for the main variables that showed baseline differences (smoking, social class, and educational level).

The frequency of breast-feeding has oscillated in the past, with a massive abandonment between the 1950s and 1970s, and progressive recovery from then up to date. At the end of the 1980s in Spain the prevalence of breast-feeding varied between 62 and 90%.<sup>28</sup> More than 85% of mothers in the reference group breast-fed their children, whereas almost a 25% of hospitalized children had not been breast-fed. These results are consistent with those from previous studies.<sup>29</sup> The average duration of breast-feeding in the reference group was similar to that found in another Spanish study.<sup>29</sup> In our study breast-feeding was more frequent and longer in mothers with higher educational level and belonging to higher social classes, in agreement with other studies.<sup>30,31</sup>

Among the numerous advantages of breast-feeding, the most important one might be the decreased risk of infection, mainly in the respiratory and gastrointestinal tracts,<sup>32</sup> although some controversy exists as to whether this really protects in Western countries where the frequency and severity of infections is lower. This controversy also includes uncertainty about the degree of protection.<sup>2</sup> In several studies, and after stratifying by the severity of illness, it has been found that breast-feeding decreases the risk of hospitalization due to infection (severe infections) rather than the risk of infection not requiring hospital admission.<sup>19,32</sup> In our study this distinction could not be made as infections not requiring hospitalization were not monitored. We could not assess the protection of breast-feeding on either recurrent otitis, found in other reports,<sup>12</sup> or severity of respiratory tract infections.<sup>33</sup>

After adjusting for differences in socio-demographic variables, related to both risk of hospitalization and breast-feeding,<sup>2,34,35</sup> the duration of breast-feeding was unrelated to the overall risk of hospitalization, although certain trends can be observed.

Other studies have found the opposite results.<sup>36</sup> Chen *et al.*<sup>1</sup> found that, after adjusting for several confounding variables, a twofold increase in the risk of hospitalization for respiratory diseases was observed in children smaller than 18 months who were not breast-fed. Our results on the average length of breast-feeding yielded significant differences, not explained by confounding factors, in children up to 6 months. To reconcile these apparent contradictory results with those based on OR estimation, it should be emphasized that analyses with continuous variables usually have more statistical power than those based on categories.

Studies *in vitro* have shown the beneficial immunological properties of maternal milk,<sup>37,38</sup> thus explaining the epidemiological evidence on protection against infection. F.U.O. is very frequent among children under 2 years of age,<sup>39</sup> and these patients, in whom no source is observed at clinical examination and routine laboratory tests, are frequently hospitalized for observation.<sup>40,41</sup> It is important to remember that the criteria for F.U.O. were established for children aged more than 3 months, and we have used the same criteria for younger children; this can introduce a bias. If we restrict analysis to children with F.U.O. between 3 and 12 months of age, a significant difference is still noted. No previous report has been found relating breast-feeding to a decreased risk of F.U.O.

In conclusion, these results confirm that breast-feeding is for a shorter time in hospitalized children, even for F.U.O. This reduction is observed in children aged 6 months or less, but not at older ages.

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**Table 4** Length of breast-feeding (days) in cases and controls

	Crude mean $\pm$ SEM	p-value	Adjusted mean $\pm$ SEM	p-value
All admission causes				
Cases	59.2 $\pm$ 4.0	<0.001	64.8 $\pm$ 4.4	<0.001
Controls	100.5 $\pm$ 4.8		97.0 $\pm$ 4.4	
All admission causes $\leq$ 6 months				
Cases	37.4 $\pm$ 3.2	<0.001	40.6 $\pm$ 5.4	<0.001
Controls	100.5 $\pm$ 6.8		99.5 $\pm$ 5.4	
All admissions 7-24 months				
Cases	84.0 $\pm$ 7.2	0.100	93.4 $\pm$ 6.7	0.991
Controls	100.6 $\pm$ 6.9		93.5 $\pm$ 6.8	
Admissions due to F.U.O.				
Cases	59.5 $\pm$ 8.3	0.006	62.5 $\pm$ 10.9	0.011
Controls	102.9 $\pm$ 12.9		102.5 $\pm$ 10.9	
Admissions due to F.U.O. $\leq$ 6 months				
Cases	38.3 $\pm$ 7.3	0.003	40.8 $\pm$ 12.4	0.006
Controls	90.8 $\pm$ 15.5		91.7 $\pm$ 12.4	
Admissions due to F.U.O. 7-24 months				
Cases	88.5 $\pm$ 14.9	0.248	96.8 $\pm$ 18.3	0.598
Controls	119.5 $\pm$ 21.9		111.1 $\pm$ 18.3	

SEM: standard error of the mean.

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