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Full Breastfeeding and Hospitalization as a Result of Infections in the First Year of Life

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ABSTRACT

OBJECTIVE. Our objective was to assess the effect of breastfeeding on the probability of hospitalization as a result of infectious processes during the first year of life

METHODS. We followed 1385 infants from birth to age 1 year between 1996 and 1999. Recruitment and data collection were done at the 6-month well-infant visit under the National Child Health Program. Full breastfeeding, hospital admission, and other relevant variables related to the delivery, infant, mother, health services system, and sociologic aspects were recorded. The statistical analysis included Kaplan-Meier test, Cox regression to obtain the hazard ratio, and the adjusted attributable risk.

RESULTS. Full breastfeeding at discharge after delivery and at 3, 4, and 6 months of age were 85%, 52%, 41%, and 15%, respectively; 78 hospital admissions as a result of infections were recorded (38 respiratory tract, 16 gastrointestinal tract). Mean age at admission was 4.1 months. After estimating the attributable risk, it was found that 30% of hospital admissions would have been avoided for each additional month of full breastfeeding. Seemingly, 100% of full breastfeeding among 4-month-old infants would avoid 56% of hospital admissions in infants who are younger than 1 year.

CONCLUSIONS. On the basis of the present data, we conclude that full breastfeeding would lower the risk for hospital admission as a result of infections among infants who are younger than 1 year within an industrialized country.

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Key Words

full breastfeeding, hospitalization, infections, respiratory infections, gastroenteritis, Kaplan-Meier, Cox regression, hazard ratio, attributable risk

Abbreviations

FB—full breastfeeding
WHO—World Health Organization
OR—odds ratio
CI—confidence interval

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NUMEROUS STUDIES HAVE shown the benefits of breastfeeding for preventing morbidity from gastroenteritis¹⁻¹³ and respiratory infections,^{2,6,7,9-11,14-22} and the effects on decreasing hospitalization rates, health expenditure, and mortality as a result of these infections.^{1,12,13,16,22-26} These studies have been conducted in communities within poor and developing countries,* as well as industrialized nations.† The protection of breastfeeding against infection has been demonstrated in children who live under a wide variety of socioeconomic and sanitary conditions, even within the same country.¹⁰ There is controversy, however, in this regard. Some authors^{31,36-39} believe that the protection is overestimated, unfounded, or less evident and suggest that other public health measures, such as immunization, education, and food hygiene, are equally or more important. Furthermore, few original studies have demonstrated breastfeeding-related protection with regard to hospitalization as a result of infections.^{16,19,22-24,26,40-42}

In Spain, there are few reports on breastfeeding and infectious morbidity,^{34,38,39,43,44} with most of these studies finding little protective effect.^{38,39,43} Furthermore, decision-making health authorities still are reluctant to define risk-benefit-based policies to promote breastfeeding that are suitable for an industrialized nation.^{45,46} The objective of this study was to assess the effect of breastfeeding on the probability of hospitalization as a result of infectious processes during the first year of life.

METHODS

The study was conducted at a publicly funded, second-level referral hospital in the region of Marina Alta of Alicante, Spain, an area with a middle to upper-middle socioeconomic level and an unemployment rate almost half the national average. This hospital is the only center with pediatric admission within 100 km; it follows strict, consensus criteria for hospitalization, and computerized files are kept of pediatric patients and newborns who are admitted to the hospital.

A cohort of children who were born between January 1, 1996, and December 31, 1999, were followed during the first year of life. Eleven pediatricians from the primary care centers of the public health system in the region compiled data on all children who went for the 6-month well-child visit of the National Well-Child Program on the weekday with the lowest patient attendance, selecting all patients who were seen on this day. The data were collected from interviews with the mothers at the visits that were included in this program between age 5 days and 6 months, using a specific template that was created to obtain information on the incidence and duration of full breastfeeding (FB). The hospital records were checked later for admissions as a result of

infection during the first year of life by cross-referencing the patient history number, which is common for both the hospital and the primary care centers. The pediatricians at the primary care centers were unaware of the main purpose of the study and did not make decisions about admitting the children to the hospital.

The outcome variable was hospitalization as a result of an episode of infection in the first year of life, excluding infections of perinatal cause but not other infections that occurred within 2 weeks after birth. Infections were considered to exist when the main diagnosis listed on the discharge report had 1 of the following codes of the *International Classification of Diseases, Ninth Revision, Clinical Modification*: 001 to 139, 320, 326, 381 to 383, 464 to 487, 590, 595, 680 to 686, 711, 730, or 780.6. In the 7 children who were hospitalized more than once in the first year of life (5 on 1 additional occasion, 2 an additional 2 times), we counted only 1 hospitalization that was attributable to infection, or when they were hospitalized more than once per infection, the first hospitalization that was attributable to infection. During the study period, the Spanish vaccination schedule was similar to the U.S. schedule except for pneumococcal vaccine, and immunization rates were >97%.

The independent explanatory variable was time of breastfeeding received (measured in months, with precision of 1 week). Data were collected on FB, as defined by the World Health Organization (WHO) recommendations: "Full breastfeeding is defined as exclusive (no other liquid or solid is given to the infant) or almost exclusive (vitamins, mineral water, juice, or ritualistic feeds are given infrequently in addition to breastfeeds)."^{47,48} All pediatricians were instructed to collect FB according to this definition at all pediatric visits as part of normal practice.

Other explanatory variables were gender, birth weight, prematurity, twin status, birth month, mother's age, educational level, employment, smoking habit, number of children, economic level, unemployment rate, and distance to hospital from the place of residence. Except for hospitalization, all variables were collected from the pediatric office records.

No procedures other than the usual follow-up were conducted, the files that were sent for the study contained no personal identifying data, and the computerized files were compiled in accordance with the legal regulations regarding data privacy. The study was approved by the institutional review board at the hospital, and the study was conducted in accordance with the Declaration of Helsinki guidelines for good clinical practice.

Statistical Analyses

To assess the representativeness of the study cohort, we compared the distribution of the values for the variables with that of the equivalent variables that were taken from the newborn records in the maternity ward and for

* Refs 2, 3, 9, 11-13, 15, 16, 20, 25, and 27-32.

† Refs 1, 4-7, 10, 14, 18, 19, 21-23, 26, and 33-35.

hospitalized children, using the χ^2 test or Student's *t* test, according to the type of variable analyze. A univariate analysis was done on the frequency of hospitalization as a result of infections compared with the duration of FB and the remaining variables. The statistical analyses consisted of χ^2 and odds ratio (OR) and its Cornfield 95% confidence interval (CI), as well as the χ^2 for trends on hospital admissions according to length of FB.

The Kaplan-Meier survival analysis was performed for hospitalizations that were attributable to infection according to 3 periods of breastfeeding received (FB for 0 months, FB for <4 months, and FB for \geq 4 months) and analyzed graphically and by the log-rank (Mantel-Haenszel) test for survival curves. Cox regression was used for the multivariate analysis. A descriptive model was constructed with the dependent variable days of life until hospitalization as a result of infection, and the independent variable FB (grouped in 3 categories) was introduced into the model, as well as all secondary covariables that were significant in the univariate analysis or epidemiologically relevant and that preceded hospitalization. The Wald backward stepwise method was used for the analysis.

The models selected were shown to meet the suppositions of proportionality and log-linear ratio. The same Cox regression procedure was used by introducing the main explanatory variable in months of FB. The hazard ratio that was obtained in the Cox regression then was used to calculate the adjusted population attributable at risk. The statistical package Epi Info 5, version 5.01 (Centers for Disease Control and Prevention, Atlanta, GA; WHO, Geneva, Switzerland) was used for the data compilation, descriptive study, and univariate analysis, and the SPSS for Windows version 10.0.5 (SPSS, Inc, Chicago, IL) was used for the multivariate analysis.

RESULTS

Description of the Sample

A total of 1385 records were obtained for the 4-year period (1996–1999), accounting for 31.8% of the 4356 births that occurred during this period. The mean distance to the hospital was 17.1 km (SD: 10.37; range: 2.9–36.2 km), for a mean of 16.9 minutes by car (SD: 9.6; range: 3–31 minutes).

Mean maternal age was 30 years (SD: 4; range: 16–48), and 47% of the mothers worked outside the home, 58% had completed primary studies, 7% had finished university studies, and 30% were smokers (mean of 10 cigarettes a day; SD: 7; range: 1–40); 70% of the deliveries were performed in the public hospital, and 18% were by cesarean section. The infant was the first child in 50% of the cases, mean birth weight was 3280 g (SD: 500; range: 760–4980), 4% were twins, and 3% were premature. No significant differences were found between the distribution of values for variables in the study

cohort and that of the equivalent values that were taken from the newborn records in the maternity ward and hospitalized children who were younger than 1 year in the pediatrics ward.

Breastfeeding

Among the 1385 children in the register, 84.5% initially received FB, followed by 68.4% at 1 month, 60% at 2 months, 51.7% at 3 months, 41.1% at 4 months, 32.4% at 5 months, and 14.6% at 6 months. The mean duration of FB in infants in the register was 2.79 months (SD: 2.25 months).

Hospitalizations for Infection

Seventy-eight hospitalization episodes for nonperinatal infection were recorded in the first year of life (5.6% of the total), 38 of them for respiratory infections (31 lower respiratory tract: 2 pneumonias and 29 bronchiolitis; 18 caused by respiratory syncytial virus), 16 for gastrointestinal infections, and 24 for other types (9 febrile syndromes possibly caused by viral infections, 6 pyelonephritis, 3 viral rashes, 2 pneumococcal meningitis, 1 lymphocytic meningitis, 1 septicemia, and 1 cellulitis). A total of 367 hospital days were recorded, with a mean stay of 4.7 days. Most hospitalizations (35) occurred in the first 3 months of life, 23 between 4 and 6 months, 15 between 7 and 9 months, and only 5 children between 10 and 12 months of age (mean age at admission: 4.1 months).

Univariate Analysis

A statistically significant inverse relationship was observed between FB according to month and hospitalizations for infections (Fig 1). Table 1 provides the results of the univariate analysis with significant relationship of the distribution of the variables according to infants who

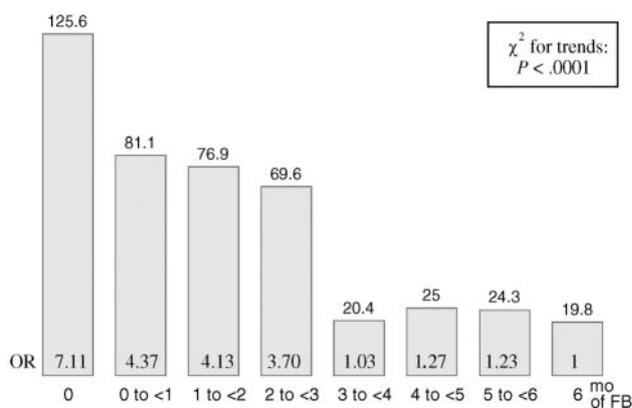


FIGURE 1 Hospitalizations for infection, according to months of FB OR and relative frequency per thousand children of age 1 year. Hospitalizations as a result of infectious cause are according to months of FB. Data are OR and relative frequency per 1000 infants younger than 1 year. Regional Lactation Registry of Marina Alta (1996–1999). $P < .0001$, χ^2 for trends.

TABLE 1 Univariate Analysis of Absolute Frequency of Hospitalizations Among Infants Who Were Younger Than 1 Year for Infectious Disease and Cumulative Incidence Per 1000 According to Variables Related to the Mother, Delivery, Child, and Social–Health Care Conditions

| | Cases With Hlnf | Cases Without Hlnf | CI–Hlnf | OR | 95% CI | P |
|----------------------------|-----------------|--------------------|---------|------|-----------|-------|
| Maternal variables | | | | | | |
| >1 child | | | | | | |
| Yes | 55 | 635 | 79.7 | 2.52 | 1.49–4.30 | .0002 |
| No | 23 | 669 | 33.2 | | | |
| Smoker | | | | | | |
| Yes | 32 | 379 | 77.9 | 1.83 | 1.1–3.3 | .012 |
| No | 42 | 910 | 44.1 | | | |
| Cigarettes per day | | | | | | |
| 0 | 42 | 910 | 44.1 | 1 | | .008 |
| 1–5 | 6 | 120 | 47.6 | 1.08 | | |
| ≥6 | 26 | 259 | 91.2 | 2.18 | | |
| Delivery–related variables | | | | | | |
| Hospital | | | | | | |
| Public | 68 | 963 | 66.0 | 2.81 | 1.10–9.17 | .04 |
| Private | 4 | 159 | 24.5 | | | |
| Infant–related variables | | | | | | |
| Gender | | | | | | |
| Male | 47 | 660 | 66.5 | 1.49 | 0.91–2.45 | .094 |
| Female | 31 | 647 | 45.7 | | | |
| Premature | | | | | | |
| Yes | 5 | 29 | 147.1 | 2.74 | 0.92–6.93 | .053 |
| No | 71 | 1129 | 59.2 | | | |
| Birth weight | | | | | | |
| <3000 g | 27 | 228 | 105.9 | 2.06 | 1.19–7.55 | .004 |
| ≥3000 g | 42 | 731 | 54.3 | | | |

Variables with $P > .1$: Mother: educational level and work; delivery: season of the year, cesarean/vaginal termination; infant: twin status; social–health care: distance from hospital, family economic status. Hlnf indicates hospitalizations as a result of infection in infants younger than 1 year; CI–Hlnf, cumulative incidence of Hlnf per 1000 infants younger than 1 year.

were admitted or not as a result of infectious disease in the first year of life. No significant relationship was found between hospitalization that was attributable to infections and other variables such as remunerated work or education level of the mother, vaginal or cesarian birth, season in which the child was born, gender, twin status, distance to the hospital, or family economic status.

Among the 78 children who were admitted, 27 had never been breastfed, 38 had received FB for <4 months, and 13 had received FB for 4 months or more. At the time of hospitalization, 67 children had not been receiving FB for a mean of 3.5 months (SD: 2.4; 95% CI: 2.9–4.1 months) before admission (including those who never received FB). The remaining 11 continued to receive FB for a mean of 2.7 months after admission (SD: 1.8; 95% CI: 1.6–3.9 months)

Comparison of Cumulative Survival Curves

Figure 2 contains the survival curves for hospitalizations that were attributable to infection among the study cohort according to the 3 categories of FB (0 months, <4 months, and 6 months). The different rate at which the curves decrease indicates increasing risk for hospitalization in the groups with shorter lactation times; significant differences were confirmed with the log-rank test for comparing the survival curves.

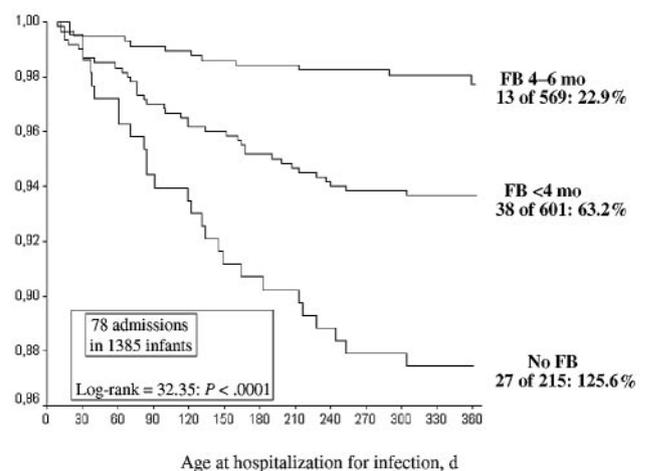


FIGURE 2 Cumulative survival curves of hospitalizations for infection according to FB categories. Regional Lactation Registry of Marina Alta (1996–1999). $P < .0001$; log rank = 32.35.

Multivariate Analysis: Cox Regression for Hospitalization for Infection

Siblings and birth weight <3 kg were risk factors for hospitalization as a result of infection in the first year of life. In contrast, FB showed a protective role, with the risk for admission for infection in the first year of life

4.91 times higher among infants who never received FB and 2.45 times higher among those who received FB for <4 months, when compared with infants who were breastfed for 4 months or more (Table 2).

When the breastfeeding variable (grouped according to months) was introduced into the original model, Cox regression selected the same variables, and the B coefficients for the variables birth weight <3 kg and siblings showed no significant changes with respect to those presented. In this model, for every month without FB, the risk for hospitalization for infection in the first year of life was multiplied by 1.43 (95% CI: 1.27-1.59; $P < .0001$). FB showed a statistically significant protection against both respiratory infections and gastrointestinal infections when considered separately.

Adjusted Measures of Epidemiologic Impact

Every additional month of FB would prevent 30.1% of hospitalizations as a result of infection in children who had not received FB that month. Among the total population of children who were younger than 1 year, FB for 4 months or more would have prevented 56.4% (95% CI: 30.9%–69.4%) of hospital admissions for non-perinatal infection.

DISCUSSION

After adjustment for the variables that could confound or change the effect of the relationship in this study, as well as previous studies, multivariate analysis showed a protective effect against hospitalization as a result of infection by 3 factors: FB, birth weight of 3 kg or more, and no siblings. The adjusted population attributable at risk, as a measure of epidemiologic impact, clearly demonstrates the importance of breastfeeding in the prevention of hospitalization for infection, a finding that is consistent with previously published series, in which lower birth weight (particularly <2500 g) increased the risk for death as a result of infections,²⁵ the frequency of pneumonia,⁴⁹ and the incidence of hospitalizations as a result of bronchiolitis.⁴² For prevention of overestimation of the benefits of breastfeeding for preventing infection, birth weight always must be included as a variable in this kind of study because it is related to the

frequency and the duration of lactation and, therefore, is a potential confounding factor.^{50,51} Having siblings also has been identified as a risk factor for infection by most series that analyze this relationship.^{2,11,20,22,44}

In our study, the relationship between maternal smoking and hospitalization for infection that was observed in the univariate analysis was not found in the multivariate analysis, however. Several reports have shown that maternal and family smoking increases the frequency of respiratory tract infections and hospitalizations for this reason,^{11,42,44,52,53} although the relationship is not entirely clear: some studies have not found an association,^{15,21,54} another found it only in the univariate analysis,⁵⁵ and another found it in a multivariate analysis, in which relevant variables such as birth weight, gender, and presence of siblings were missing.⁵² The economic level, unemployment rate, and distance to the hospital, described in other studies,^{42,56–58} were not shown to be predisposing factors for infection or hospitalizations for infection among infants in this study, perhaps because of a low variability of these parameters in our health area and because free universal access to medical care is available through a primary health care network.⁵⁹

We found a protective effect of breastfeeding on hospitalization as a result of infections, consistent with other series^{19,22,23,41} as well as with a meta-analysis that was performed by Bachrach²⁶ of studies that were conducted in industrialized countries. Only 2 studies in industrialized nations report no breastfeeding protection against hospitalizations as a result of infection, whether caused by gastroenteritis²⁴ or infections in general.⁸ In another study, Chen et al²⁴ showed breastfeeding protection against hospitalizations that were caused by nongastrointestinal infections but did not report the same effect for hospitalizations for gastroenteritis, perhaps because of a lengthy follow-up of 18 months of life, late data collection (questionnaire at 18 months, possibly encouraging a memory bias), and the contrast between formula-feeding and any type of breastfeeding, without using the WHO definitions.

Kramer et al,⁸ in a study that compared 2 large cohorts from different regions of Belarus, found that

TABLE 2 Cox Regression by Wald Backward Stepwise Method: Variables That Were Selected in the Final Model for the Risk for Hospitalization for Infections in the First Year of Life

| | HR | 95% CI of HR | B | EE | Wald | P |
|----------------------|------|--------------|-------|-------|-------|------|
| FB | | | | | | |
| 0 mo | 4.91 | 2.41–9.99 | 1.591 | 0.36 | 19.26 | .000 |
| Up to 4 mo | 2.45 | 1.28–4.66 | 0.894 | 0.33 | 7.36 | .007 |
| ≥4 mo | 1 | | | | | |
| Siblings | 2.04 | 1.19–3.49 | 0.711 | 0.275 | 6.69 | .010 |
| Birth weight <3000 g | 1.87 | 1.13–3.08 | 0.624 | 0.256 | 5.94 | .015 |

HR indicates hazard ratio, interpretable as relative risk. –2 log likelihood: 852.5, overall χ^2 : 44.79; $P < .0001$. Model variables: (1) FB, (2) siblings, (3) gender, (4) birth weight <3000 g, (5) prematurity, (6) smoking mother, and (7) birth at public hospital; and interactions: (1 × 2), (1 × 4), and (1 × 6).

breastfeeding provided protection during the first year of life against gastroenteritis but not respiratory infections or otitis and not for hospitalizations as a result of infection. This study performed an ecological assignment of the main explanatory variable, percentage breastfeeding of population, although the spatial and cultural distances, probably large, between the 2 cohorts did not seem to have been reflected in the statistical adjustment.

One limitation of our study could be that the detection bias was not completely eliminated: the knowledge that we obtained regarding the protective role of breastfeeding or the differing confidence (breastfed infants are less likely to be admitted) that we had in the mother's caregiver skills according to type of lactation could influence hospitalization. Nevertheless, the protection may have been underestimated, because it is observed despite the low level of hospitalization found. Although the type of follow-up used could have hidden unsuspected biases, the distribution of the cohort was consistent with those observed in the 2 other files that were available to us: 1 for hospitalized patients and another for infants who were born in the hospital.

Child care attendance is a known factor for higher risk for infections in the early years of childhood,^{41,60,61} although it does not always appear¹⁵ or appears in association with poverty conditions.⁶⁰ This variable was not controlled in this study because only 2 of the children admitted were attending a child care center.

For prevention of most of the supposed methodologic problems of lactation studies,⁶² all potential confounding and interaction variables that were mentioned in the literature were controlled and statistical methods that were considered appropriate for survival time analysis were used. In addition, the WHO criteria were followed for the main independent variable (FB), the outcome measure was defined precisely, and the dose-response effect was measured by introducing FB time as a continuous variable (expressed in months), making it possible to determine of risk ratio of hospitalization that was attributable to infection per unit time of FB. Finally, the independence of lactation time was checked with respect to hospitalization as a result of an infectious cause because the hospitalization did not affect the duration of breastfeeding. Possible memory biases were avoided by careful collection of data on the main variables. Advanced techniques for survival studies were used in the statistical analysis, in particular, Cox regression, a method first used by Arifeen et al²⁵ to analyze the ratio between breastfeeding and mortality from respiratory and gastrointestinal infections.

CONCLUSIONS

This study is the first that was conducted in Spain and 1 of the few conducted in industrialized nations to study the relationship between breastfeeding and hospitalization as a result of infection among an extensive cohort

(1385 children) using multivariate Cox regression. The results are consistent with early studies and add to the body of evidence confirming the hypothesis that FB lowers the risk for hospitalization as a result of infectious diseases during the first year of life in a developed country.

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