

Infant feeding patterns and risks of death and hospitalization in the first half of infancy: multicentre cohort study

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Objective To determine the association of different feeding patterns for infants (exclusive breastfeeding, predominant breastfeeding, partial breastfeeding and no breastfeeding) with mortality and hospital admissions during the first half of infancy.

Methods This paper is based on a secondary analysis of data from a multicentre randomized controlled trial on immunization-linked vitamin A supplementation. Altogether, 9424 infants and their mothers (2919 in Ghana, 4000 in India and 2505 in Peru) were enrolled when infants were 18–42 days old in two urban slums in New Delhi, India, a periurban shanty town in Lima, Peru, and 37 villages in the Kintampo district of Ghana. Mother–infant pairs were visited at home every 4 weeks from the time the infant received the first dose of oral polio vaccine and diphtheria–pertussis–tetanus at the age of 6 weeks in Ghana and India and at the age of 10 weeks in Peru. At each visit, mothers were queried about what they had offered their infant to eat or drink during the past week. Information was also collected on hospital admissions and deaths occurring between the ages of 6 weeks and 6 months. The main outcome measures were all-cause mortality, diarrhoea-specific mortality, mortality caused by acute lower respiratory infections, and hospital admissions.

Findings There was no significant difference in the risk of death between children who were exclusively breastfed and those who were predominantly breastfed (adjusted hazard ratio (HR) = 1.46; 95% confidence interval (CI) = 0.75–2.86). Non-breastfed infants had a higher risk of dying when compared with those who had been predominantly breastfed (HR = 10.5; 95% CI = 5.0–22.0; $P < 0.001$) as did partially breastfed infants (HR = 2.46; 95% CI = 1.44–4.18; $P = 0.001$).

Conclusion There are two major implications of these findings. First, the extremely high risks of infant mortality associated with not being breastfed need to be taken into account when informing HIV-infected mothers about options for feeding their infants. Second, our finding that the risks of death are similar for infants who are predominantly breastfed and those who are exclusively breastfed suggests that in settings where rates of predominant breastfeeding are already high, promotion efforts should focus on sustaining these high rates rather than on attempting to achieve a shift from predominant breastfeeding to exclusive breastfeeding.

Keywords Infant nutrition; Feeding behavior; Breast feeding; Infant mortality; Cause of death; Diarrhea/mortality; Respiratory tract infections/mortality; Hospitalization; Infant; Cohort studies; Multicenter studies; Ghana; India; Peru (*source: MeSH, NLM*).

Mots clés Nutrition nourrisson; Comportement alimentaire; Allaitement au sein; Mortalité nourrisson; Cause décès; Diarrhée/mortalité; Voies aériennes supérieures, Infection/mortalité; Hospitalisation; Nourrisson; Etude cohorte; Etude multicentrique, Ghana; Inde; Pérou (*source: MeSH, INSERM*).

Palabras clave Nutrición infantil; Alimentos infantiles; Conducta alimentaria; Lactancia materna; Mortalidad infantil; Causa de muerte; Diarrea/mortalidad; Infecciones del tracto respiratorio/mortalidad; Hospitalización; Lactante; Estudios de cohortes; Estudios multicéntricos; Ghana; India; Perú (*fuentes: DeCS, BIREME*).

الكلمات المفتاحية: تغذية الرضع، سلوك التغذية، الرضاعة من الثدي، معدل وفيات الرضع، أسباب الوفيات، الإسهال، معدلات الوفيات بسبب الإسهال، التهاب الطرق التنفسية، معدل الوفيات بسبب التهابات الطرق التنفسية، الإدخال في المستشفى، الرضيع، دراسة الأتراب، دراسة متعددة المراكز، غانا، الهند، بيرو. (المصدر: رؤوس الموضوعات الطبية، المكتب الإقليمي لشرق المتوسط)

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Introduction

The recognition that human immunodeficiency virus (HIV) is transmitted through breast milk has resulted in the need to inform all women infected with HIV about this risk and to recommend that they avoid breastfeeding if replacement feeding is

acceptable, feasible, affordable, safe and sustainable; alternatively, they should be advised to breastfeed exclusively but to stop as early as possible (1). The advice to breastfeed exclusively is based on the finding that infants who are exclusively or predominantly breastfed have a lower risk of dying from

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common childhood infections than those who are partially or completely weaned (2) and that exclusive breastfeeding may carry a lower risk of HIV transmission than partial breastfeeding (3, 4). The most important elements of the information given to HIV-infected mothers in order to help them make an informed decision on infant feeding concern the risk of HIV transmission through breastfeeding and the risk of mortality and severe morbidity caused by infectious diseases that is associated with avoidance of all breastfeeding.

A pooled analysis of data from six developing countries has quantified the effect of an infant never being breastfed on the risk of mortality caused by infectious disease (5). An important limitation of this pooled analysis was that most of the studies did not supply sufficient information on patterns of breastfeeding, such as whether a child was exclusively breastfed, predominantly breastfed or partially breastfed. For our purposes, exclusive breastfeeding means that a child is fed only breast milk; predominant breastfeeding means that the infant may also be given some non-breast-milk liquids but not animal milk, formula or solids; partial breastfeeding means that the infant may be given animal milk, formula or solids in addition to breast milk. In the absence of this information, the pooled analysis could not compare the effect of no breastfeeding with different breastfeeding patterns, particularly with exclusive breastfeeding, which is the recommendation for the first 6 months of life (6). A subsequent study in Bangladesh attempted to address this issue but included only a small number of non-breastfed infants and consequently grouped them with those who had been partially breastfed (7).

Exclusive breastfeeding during the first 6 months of life has been identified as one of the key interventions for reducing childhood deaths in a group of articles on child survival published in the *Lancet* (8). Although 90% infants in the 42 countries that accounted for 90% of childhood deaths worldwide in 2000 are estimated to be breastfed up until the age of 12 months, demographic surveys show that only 39% of infants aged < 6 months are exclusively breastfed (range = 1–84%) (8). Studies conducted with more rigour report even lower prevalences of exclusive breastfeeding, probably because many infants who are predominantly breastfed have been classified as exclusively breastfed during demographic surveys (7, 9–13). Randomized trials in different parts of the world have demonstrated the feasibility of improving breastfeeding rates through community-based interventions (9–11). While the interventions resulted in some infants shifting from partial breastfeeding to exclusive breastfeeding, the largest move to exclusive breastfeeding probably occurred among those infants who had been predominantly breastfed (9–11). In India, for example, 31% more infants were exclusively breastfed at 3 months of age in the intervention group when compared with the control group. Correspondingly, when compared with the control group 21% fewer infants in the intervention group were predominantly breastfed, 9% fewer infants were partially breastfed, and 1% fewer infants were not breastfed (9). These studies were, however, too small to assess the effect of the intervention on mortality. Estimates of the proportion of deaths that can be prevented by such programmes require ascertainment of the effect of exclusive breastfeeding on the overall risk of mortality and the cause-specific risk of mortality from infectious disease when compared with predominant breastfeeding and partial breastfeeding.

Two questions therefore remain. First, among children who are not breastfed, what is the excess risk of overall mortality, cause-specific mortality and severe morbidity during the first 6 months of life compared with children who are exclusively or predominantly breastfed? Second, what is the effect of partial breastfeeding on the same outcomes when compared with exclusive or predominant breastfeeding?

To answer these questions we performed a secondary analysis of data from a multicentre randomized controlled trial on immunization-linked vitamin A supplementation; the results related to vitamin A supplementation have been published earlier (14). The findings of this secondary analysis are presented in this paper.

Methods

A detailed description of the study sites and methods has been published earlier (14). Methods relating to secondary analysis of the association between infant feeding patterns and the risk of overall mortality, cause-specific mortality and severe morbidity are described here.

Setting

The study took place in Ghana, India and Peru. Participants were enrolled from two urban slums in New Delhi, a periurban shanty town in Lima and from 37 villages in the Kintampo district of Ghana. Initiation of breastfeeding was almost universal within the first few days after birth; and in all regions more than 94% of the infants were receiving breast milk after the age of 9 months. All study sites were characterized by high rates of infant morbidity, especially from diarrhoea and respiratory infections. In Kintampo, malaria was also common. Stunting (defined as length for age < -2 z scores) and wasting (weight for length < -2 z scores) at 12 months of age were common in New Delhi (42% of children classed as stunted and 6% as having wasting) and Kintampo (32% classed as stunted and 4% as having wasting), but less so in Lima (10% classed as stunted and 0.7% as having wasting).

Between January 1995 and June 1997, 9424 mother–infant pairs were enrolled when the infants were 18–24 days old; there were 2919 pairs in Ghana, 4000 in India and 2505 in Peru. Follow-up lasted until the infant was 12 months old, except among the last 806 pairs in Ghana and 522 in Lima whose follow-up was stopped some time after 6 months old in order to adhere to the study's timeline. This truncation does not affect the results presented in this paper, since the period of interest is from enrolment to the age of 6 months.

Data collection

At the time of enrolment, information was collected from each mother–infant pair on socioeconomic and environmental variables, such as the mother's educational level, place of defecation, where the household got its water, the number of family members, amount of household sleeping space (that is, the total number of family members who had slept in the house the previous night and the number of rooms available for sleeping), and the type of house. Information was also collected on maternal age and the infant's sex and birth order. All infants were also weighed.

Beginning from the age when the infant was given the first dose of oral polio vaccine and diphtheria–pertussis–tetanus vaccine (at 6 weeks in Ghana and India and 10 weeks in Peru),

each enrolled pair was visited at home by a trained field worker every 4 weeks. At each visit, mothers were queried about what they had offered their child to eat or drink during the past week. After the mother's unprompted response was recorded, she was asked whether she had offered her own breast milk, breast milk from a wet nurse, animal milk, infant formula, other fluids or solid foods at any time during the week.

Information was also collected on hospital admissions and deaths. The primary cause of death was ascertained from hospital records or verbal autopsy using forms developed by Johns Hopkins University, the London School of Hygiene and Tropical Medicine, and the WHO Verbal Autopsy Validation Collaborative Group. Verbal autopsies were conducted within 6 weeks of an infant's death through interviews with caregivers at their home. Three paediatricians at each study site independently reviewed the verbal autopsy forms to ascertain the primary cause of death; any differences of opinion were discussed, and agreement was reached through consensus. The primary causes of hospitalizations were determined from hospital records or discharge papers.

Statistical analysis and definitions

Exclusive breastfeeding was defined as an infant being fed only breast milk and nothing else, not even water, with the exception of vitamin supplements and prescribed medicines. Predominant breastfeeding was defined as an infant being fed breast milk along with some other non-breast-milk fluids but not animal milk, infant formula or solids. Infants who were offered breast milk and animal milk, infant formula or solids were considered to be partially breastfed. These definitions are consistent with WHO definitions for breastfeeding patterns (6).

Infants were classified by the exposure variable (breastfeeding status) as exclusively breastfed, predominantly breastfed, partially breastfed or not breastfed at the 6 week, 10 week, 14 week, 18 week and 22 week follow-up visits. If breastfeeding status was recorded as missing at a particular visit it was inferred to be the same as that at the immediately preceding visit. If breastfeeding status had also been recorded as missing at the preceding visit, then no further extrapolation was carried out. Periods of time during which breastfeeding status was missing were omitted from all analyses.

The outcome variables were all-cause deaths, deaths due to acute lower respiratory tract infections (ALRI), diarrhoea-specific deaths, all-cause hospitalizations, ALRI-specific hospitalizations and diarrhoea-specific hospitalizations occurring between the ages of 6 weeks and 26 weeks.

All analyses were carried out using Stata software, version 8.2. Breastfeeding status at each follow-up visit was related to mortality in the following period using Cox's models with time-dependent covariates stratified by country. Such models allow hazard ratios to be estimated while also allowing the underlying risk of death to vary during the follow-up period. Breastfeeding status at each follow-up visit was also related to the risk of hospitalization in the following period using Poisson models with (log) length of period as an offset. Such models allow incidence ratios to be estimated. The models included the period and site and their interactions as covariates in order to allow for changes in risk over time by site. They were fitted using a generalized estimating equation framework in order to allow for potential non-independence of hospital admissions in cases in which children were admitted more than once; robust standard errors are reported.

We included as covariates those potential confounders that have been previously reported to be associated with risk of mortality and morbidity and possibly with infant feeding patterns. These potential confounders were the infant's sex, twin status, birth order and weight at enrolment (as a marker of birth weight), mother's educational level, place of defecation and household water supply. Randomization to receive vitamin A supplementation or placebo was not considered to be a confounder because it was neither associated with mortality or hospitalization between the ages of 6 weeks and 26 weeks nor with patterns of feeding.

The primary comparisons were made between being exclusively breastfed and predominantly breastfed, between not being breastfed and being predominantly breastfed, and between being partially breastfed and predominantly breastfed. The group of infants who had been predominantly breastfed was considered to be the reference group because it was substantially larger than the exclusive breastfeeding group and therefore was likely to yield more robust results.

The study was approved by the appropriate ethics review committees of all participating institutions and the WHO Ethics Review Board.

Findings

Of the 9424 infants enrolled in the study, 9200 infants (2870 in Ghana, 3921 in India and 2409 in Peru) received their first dose of vitamin A or placebo and their first diphtheria–pertussis–tetanus and polio vaccinations; these were given at the age of 6 weeks in India and Ghana and 10 weeks in Peru (12). Among these 9200 infants, 206 (2.2%) were not available at the 26-week visit, and 118 had died between the age of 6 weeks and 6 months.

Among the same 9200 infants, information on infant feeding practices was available for 94.1% at the 6-week visit (for Ghana and India only); information was available for 97.4% of infants at the 10-week visit, 96.2% at the 14-week visit, 94.3% at the 18-week visit and 92.1% at the 22-week visit. Information on feeding at either of the two visits immediately preceding death was not available for 14 of the 118 infants who died.

Feeding patterns

In Ghana and India the prevalence of exclusive breastfeeding was about 21% (568/2649 in Ghana; 788/3738 in India) at 6 weeks; this fell to about 3–4% (73/2603 in Ghana; 138/3557 in India) at the 22-week visit. The prevalence of exclusive breastfeeding was higher in Peru; it was about 44% (1022/2315) at the 10-week visit and 33% (766/2311) at the 22-week visit.

The most common feeding pattern in Ghana was predominant breastfeeding from the age of 6 weeks to the age of 6 months. In India the most common pattern at 6 weeks was predominant breastfeeding, but partial breastfeeding became the most prevalent pattern after the age of 14 weeks. In Peru exclusive breastfeeding was the most common feeding pattern from the ages of 10 weeks to 18 weeks, but partial breastfeeding had become the most prevalent pattern by the age of 22 weeks (Table 1).

Overall, of the 3264 infant–years of follow-up between the age of 6 weeks and 26 weeks, predominant breastfeeding was the most common feeding pattern (48.6% of total follow-up), followed by partial breastfeeding (31.0%), exclusive breastfeeding (18.5%) and no breastfeeding (1.9%).

Causes of death

Table 2 and Table 3 show the distribution of deaths by age and cause of death. Overall, infectious diseases accounted for about three-quarters of all deaths occurring between the ages of 6 weeks and 26 weeks, with the most common causes being diarrhoea (accounting for 42% (40/95) of all deaths with known cause) and ALRIs (accounting for 20% (19/95) of all deaths with known cause). However, in Peru there were no diarrhoeal deaths: acute respiratory infections, sepsis and meningitis accounted for more than half the deaths with known causes (5/9) (Table 2 and Table 3).

Mortality

There was no significant difference in the risk of death between infants who had been predominantly breastfed and those who had been exclusively breastfed (Table 4). Non-breastfed infants were at a substantially higher risk of dying compared with those who had been predominantly breastfed (adjusted hazard ratio (HR) = 10.5; 95% confidence interval (CI) = 5.0–22.0; $P < 0.001$). Partially breastfed infants were also at a significantly higher risk of death compared with those who had been predominantly breastfed (HR = 2.46; 95% CI = 1.44–4.18; $P = 0.001$, Table 4).

In order to address reverse causality — that is, the possibility of breastfeeding patterns changing because of a serious illness that led to death — we repeated the above analysis excluding those deaths that occurred within 7 days of an assessment of feeding practices. In this analysis, the effect sizes remained unchanged (for non-breastfed infants HR = 10.7; 95% CI = 4.54–25.1; $P < 0.001$, and for partially breastfed infants HR = 2.42; 95% CI = 1.31–4.49; $P = 0.005$).

Table 4 also shows that non-breastfed infants were at a substantially greater risk of death when compared with predominantly breastfed infants, from both diarrhoea (HR = 8.96; 95% CI = 2.56–31.4; $P = 0.001$) and ALRI (HR = 32.7; 95% CI = 6.82–157.2; $P < 0.001$). Partially breastfed infants also had a greater risk of dying from both these causes, although

the 95% confidence interval for the hazard ratio for ALRI just includes 1 ($P = 0.004$ for diarrhoea-specific mortality and $P = 0.063$ for ALRI-specific mortality).

Feeding patterns and hospital admissions

Table 5 shows that there were no significant differences in the risk of hospitalization between infants who were exclusively breastfed and those who were predominantly breastfed or between those who were partially breastfed and those who were predominantly breastfed. However, non-breastfed infants were at a substantially higher risk of all-cause hospitalization (incidence rate ratio (IRR) = 3.39; 95% CI = 1.74–6.61; $P < 0.001$) and diarrhoea-specific hospitalization (IRR = 5.59; 95% CI = 2.17–14.4; $P < 0.001$) when compared with infants who had been predominantly breastfed. The risk of ALRI-specific hospitalization was also higher but was not statistically significant at the 5% level (IRR = 2.50; 95% CI = 0.93–6.74; $P = 0.069$).

Discussion

Principal findings

The two main findings are, first, that the risks of death or hospitalization associated with being predominantly breastfed were not significantly different from those associated with being exclusively breastfed. Second, infants who had not been breastfed had a 10-fold higher risk of dying of any cause and a 3-fold higher risk of being hospitalized for any cause when compared with those who had been predominantly breastfed.

Strengths of the study and comparison with other studies

This paper presents the findings on overall mortality and cause-specific risks of mortality and hospitalization associated with infant feeding patterns among children aged from 6 weeks to 6 months; these results came from a large multicentre study that followed more than 9400 infants in three sites in Africa, Asia and Latin America. Previously published mortality risks associated with not being breastfed have mostly been based on a comparison with any breastfeeding.

Table 1. Infant feeding patterns at age 6, 10, 14, 18 and 22 weeks, by site in Ghana, India and Peru. Values are number (%) of visits to infants

| Age at visit (weeks) | Ghana | | | | India | | | | Peru | | | |
|----------------------|------------------------------------|-------------------------|---------------------|---------------|-----------------------|-------------------------|---------------------|---------------|-----------------------|-------------------------|---------------------|---------------|
| | Exclusively breastfed ^a | Predominantly breastfed | Partially breastfed | Not breastfed | Exclusively breastfed | Predominantly breastfed | Partially breastfed | Not breastfed | Exclusively breastfed | Predominantly breastfed | Partially breastfed | Not breastfed |
| 6 | 568 (21.4) | 1984 (74.9) | 94 (3.5) | 3 (0.1) | 788 (21.1) | 1852 (49.5) | 1054 (28.2) | 44 (1.2) | NA ^b | NA | NA | NA |
| 10 | 419 (15.0) | 2291 (81.9) | 84 (3.0) | 3 (0.1) | 577 (15.0) | 1815 (47.1) | 1382 (35.9) | 78 (2.0) | 1022 (44.1) | 491 (21.2) | 775 (33.5) | 27 (1.2) |
| 14 | 303 (11.0) | 2327 (84.7) | 114 (4.1) | 3 (0.1) | 381 (10.2) | 1609 (43.2) | 1631 (43.8) | 106 (2.8) | 1187 (50.0) | 425 (17.9) | 728 (30.6) | 36 (1.5) |
| 18 | 163 (6.1) | 2391 (89.6) | 112 (4.2) | 3 (0.1) | 225 (6.1) | 1221 (33.3) | 2083 (56.9) | 133 (3.6) | 1029 (43.9) | 411 (17.5) | 850 (36.2) | 55 (2.3) |
| 22 | 73 (2.8) | 2340 (89.9) | 185 (7.1) | 5 (0.2) | 138 (3.9) | 786 (22.1) | 2446 (68.8) | 187 (5.3) | 766 (33.1) | 417 (18.0) | 1046 (45.3) | 82 (3.5) |

^a A full explanation of the feeding categories can be found in the text.

^b NA = not available.

Table 2. Distribution of deaths occurring between 6 weeks and 26 weeks of age in Ghana, India and Peru by feeding pattern

| Age (weeks) | Ghana | | | | India | | | | Peru | | | |
|--------------------------|-------------------------------------|-------------------------|----------------------|----------------|------------------------|-------------------------|----------------------|----------------|------------------------|-------------------------|----------------------|----------------|
| | Exclusively breast-fed ^a | Predominantly breastfed | Partially breast-fed | Not breast-fed | Exclusively breast-fed | Predominantly breastfed | Partially breast-fed | Not breast-fed | Exclusively breast-fed | Predominantly breastfed | Partially breast-fed | Not breast-fed |
| 6–10 | 1 | 5 | 0 | 0 | 1 | 5 | 9 | 0 | NA ^b | NA | NA | NA |
| 10–14 | 1 | 4 | 0 | 1 | 2 | 2 | 11 | 3 | 4 | 0 | 3 | 0 |
| 14–18 | 1 | 4 | 0 | 1 | 0 | 2 | 5 | 3 | 0 | 0 | 1 | 0 |
| 18–22 | 0 | 3 | 0 | 1 | 1 | 1 | 3 | 2 | 0 | 1 | 2 | 0 |
| 22–26 | 1 | 10 | 1 | 0 | 0 | 1 | 5 | 1 | 1 | 0 | 1 | 0 |
| Total^c | 4 | 26 | 1 | 3 | 4 | 11 | 33 | 9 | 5 | 1 | 7 | 0 |

^a A full explanation of the feeding categories can be found in the text.

^b NA = not available.

^c Of the 118 deaths that occurred during this period, information on feeding could not be characterized for 14 infants (5 in Ghana, 7 India and 2 in Peru).

An earlier pooled analysis, by the WHO Collaborative Study Team on the Role of Breastfeeding on the Prevention of Infant Mortality, found point estimates of odds ratios for an increased risk of death ranging from 2.5 to 4.2 at different ages for children who had not been breastfed when compared with those who had had any breastfeeding (5). The studies included in the pooled analysis did not have sufficient information to examine the excess risk of death associated with not breastfeeding when compared with exclusive or predominant breastfeeding. Our study revealed that the risks associated with not being breastfed when compared with being predominantly (or exclusively) breastfed are considerably higher: the hazard ratio was 10.5 with a 95% confidence interval ranging from 5.0 to 22.0.

Furthermore, these results are likely to be an underestimate of the true protective effect of exclusive or predominant

breastfeeding during the first half of infancy: the design of this study did not permit us to examine the effect of feeding patterns during the first 6 weeks of life. The analysis by the WHO Collaborative Study Team reported a higher protective effect for any breastfeeding in the first 2 months of life when compared with the effect of breastfeeding among older infants (5).

The effect on diarrhoeal deaths among infants not being breastfed was almost as strong as the effect on all-cause mortality; the effect on ALRI was even stronger. These findings are in contrast to those of previous studies, which have reported stronger negative effects of not being breastfed on deaths due to diarrhoea than those due to ALRI when compared with any breastfeeding (2, 5, 15, 16). In this study, not being breastfed was associated with a higher risk of hospitalization due to diarrhoea than to ALRI.

Table 3. Distribution of deaths occurring between 6 weeks and 26 weeks of age in Ghana, India and Peru for which information about the preceding visit's feeding category was available, by infant feeding pattern and primary cause of death^a

| Primary cause of death | Ghana | | | | India | | | | Peru | | | |
|---|-------------------------------------|-------------------------|----------------------|----------------|------------------------|-------------------------|----------------------|----------------|------------------------|-------------------------|----------------------|----------------|
| | Exclusively breast-fed ^b | Predominantly breastfed | Partially breast-fed | Not breast-fed | Exclusively breast-fed | Predominantly breastfed | Partially breast-fed | Not breast-fed | Exclusively breast-fed | Predominantly breastfed | Partially breast-fed | Not breast-fed |
| Diarrhoea | 1 | 9 | 0 | 1 | 2 | 4 | 20 | 3 | 0 | 0 | 0 | 0 |
| Acute lower respiratory tract infection | 0 | 7 | 0 | 1 | 0 | 1 | 5 | 3 | 0 | 0 | 2 | 0 |
| Sepsis or meningitis | 2 | 2 | 0 | 0 | 0 | 1 | 1 | 0 | 1 | 0 | 2 | 0 |
| Malaria | 0 | 3 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Others | 1 | 4 | 1 | 1 | 2 | 4 | 5 | 2 | 2 | 0 | 2 | 0 |
| Unknown ^c | 0 | 1 | 0 | 0 | 0 | 1 | 2 | 1 | 2 | 1 | 1 | 0 |
| Total | 4 | 26 | 1 | 3 | 4 | 11 | 33 | 9 | 5 | 1 | 7 | 0 |

^a Of the 118 deaths that occurred during this period, information on feeding could not be characterized for 14 infants (5 in Ghana, 7 India and 2 in Peru).

^b A full explanation of the feeding categories can be found in the text.

^c Verbal autopsies to ascertain the cause of death could not be done for 3 deaths in India and 4 deaths in Peru. The cause of 1 death in Ghana and 1 in India was classified as uncertain.

Table 4. Effect of feeding pattern on risk of all-cause mortality, diarrhoea-specific mortality and acute lower respiratory infection-specific mortality among infants aged 6–26 weeks in Ghana, India and Peru. All analyses stratified by site

| Feeding pattern | Infant–years of follow up | All-cause mortality | | | Diarrhoea-specific mortality | | | ALRI-specific mortality ^a | | |
|------------------------------------|---------------------------|---------------------|--------------------------------------|------------------------------------|------------------------------|-------------------------|------------------------------------|--------------------------------------|-------------------------|------------------------------------|
| | | No. of deaths | Unadjusted hazard ratio ^b | Adjusted hazard ratio ^c | No. of deaths | Unadjusted hazard ratio | Adjusted hazard ratio ^c | No. of deaths | Unadjusted hazard ratio | Adjusted hazard ratio ^c |
| Exclusively breastfed ^d | 603.7 | 13 | 1.37 (0.70–2.68) | 1.46 (0.75–2.86) | 3 | 1.32 (0.36–4.84) | 1.36 (0.37–5.03) | 0 | – | – |
| Predominantly breastfed | 1587.2 | 38 | 1.0 | 1.0 | 13 | 1.0 | 1.0 | 8 | 1.0 | 1.0 |
| Partially breastfed | 1011.1 | 41 | 2.86 (1.69–4.85) | 2.46 (1.44–4.18) | 20 | 4.01 (1.77–9.09) | 3.37 (1.46–7.75) | 7 | 3.64 (0.97–13.6) | 3.57 (0.93–13.7) |
| Not breastfed | 61.5 | 12 | 15.5 (7.51–32.2) | 10.5 (5.0–22.0) | 4 | 14.6 (4.28–49.5) | 8.96 (2.56–31.4) | 4 | 38.9 (8.37–180.4) | 32.7 (6.82–157.2) |

^a ALRI = acute lower respiratory infection.

^b Values in parentheses are 95% confidence intervals.

^c Adjusted for infant's weight at enrolment, sex, twin status, birth order, and mother's educational level, place of defecation, and household water supply.

^d A full explanation of the feeding categories can be found in the text.

The increased risks of hospitalization associated with partial breastfeeding and non-breastfeeding (compared with predominant breastfeeding) were considerably lower than the associated increased risks of dying; for partial breastfeeding the increased risk of hospitalization was moderate and non-significant. It should be noted that these are additional risks on top of the risks associated with death. This suggests that the more severe the outcome the more protective predominant breastfeeding will be.

Limitations

Observational studies of breastfeeding and infant health may be affected by a number of methodological problems including self-selection, reverse causality and confounding; these have been described elsewhere (17–20). In this analysis, we addressed confounding by adjusting for most of the important characteristics of the infants and maternal and household characteristics known to be associated with infant mortality and morbidity or with breastfeeding. We conducted an analysis that excluded all deaths occurring within 7 days of any assessment of feeding in order to examine the issue of reverse causality. Our analysis showed that excluding these deaths did not alter the size of the effects. Therefore, we found no evidence of reverse causality in our dataset and have presented the overall analysis including all deaths and hospitalizations.

The difference in the risks between different causes should be interpreted with caution because all sites had a relatively small proportion of non-breastfed infants, and Ghana and India had small proportions of exclusively breastfed infants. The former resulted in an imprecise estimation of the mortality risk of non-breastfed infants (CI = 5 to 22 times), and the latter may have made it difficult to assess the difference in risk between exclusive breastfeeding and predominant breastfeeding.

Implications

Our findings have two important implications for child health programmes and policies. First, the extremely high risks of mortality and morbidity associated with infants who are not breastfed compared with those who are predominantly or exclusively

breastfed need to be taken into account when informing HIV-infected mothers of the risks and benefits of breastfeeding. The high risk of infant mortality associated with partial breastfeeding (compared with predominant or exclusive breastfeeding) coupled with an earlier report of an increased risk of HIV transmission among children who are partially breastfed (compared with those who are exclusively breastfed) (3, 4) reinforces the need to discourage partial breastfeeding by both HIV-infected mothers and uninfected mothers.

Second, our finding that the risks of death are similar among infants who have been predominantly breastfed and those who have been exclusively breastfed implies that promotion programmes aimed at encouraging exclusive breastfeeding would have little impact on child survival in settings where rates of predominant breastfeeding are already high, such as in rural Ghana. However, a large impact could be achieved in areas where partial breastfeeding and not breastfeeding are common, such as in urban India and Peru. The potential impact of programmes to promote exclusive breastfeeding on child survival therefore needs to be refined, taking into account the prevalence of exclusive breastfeeding plus predominant breastfeeding as well as the prevalence of partial breastfeeding. The common practice has been to calculate impact estimates by applying the risks associated with non-breastfeeding to the prevalence of non-exclusive breastfeeding (8). ■

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Table 5. Effect of feeding pattern on risk of all-cause hospitalization, diarrhoea-specific hospitalization and acute lower respiratory infection-specific hospitalization among infants aged 6–26 weeks in Ghana, India and Peru. All analyses adjusted for by site, period of follow-up and their interactions

| Feeding pattern | Infant-years of follow-up | All-cause hospitalization | | | Diarrhoea-specific hospitalization | | | ALRI-specific hospitalization ^a | | |
|------------------------------------|---------------------------|---------------------------|------------------------------------|----------------------------------|------------------------------------|-----------------------|----------------------------------|--|-----------------------|----------------------------------|
| | | No. of events | Unadjusted rate ratio ^b | Adjusted rate ratio ^c | No. of events | Unadjusted rate ratio | Adjusted rate ratio ^c | No. of events | Unadjusted rate ratio | Adjusted rate ratio ^c |
| Exclusively breastfed ^d | 603.7 | 21 | 0.72 (0.44–1.18) | 0.77 (0.47–1.25) | 4 | 0.61 (0.20–1.81) | 0.67 (0.23–2.01) | 12 | 0.81 (0.42–1.54) | 0.86 (0.45–1.64) |
| Predominantly breastfed | 1587.2 | 109 | 1.0 | 1.0 | 24 | 1.0 | 1.0 | 47 | 1.0 | 1.0 |
| Partially breastfed | 1011.1 | 66 | 1.15 (0.79–1.66) | 1.12 (0.78–1.62) | 33 | 1.61 (0.85–3.06) | 1.57 (0.83–2.96) | 31 | 1.02 (0.61–1.71) | 1.03 (0.61–1.73) |
| Not breastfed | 61.5 | 13 | 3.77 (1.99–7.14) | 3.39 (1.74–6.61) | 8 | 6.26 (2.56–15.3) | 5.59 (2.17–14.4) | 5 | 2.75 (1.06–7.10) | 2.50 (0.93–6.74) |

^a ALRI = acute lower respiratory infection.

^b Values in parentheses are 95% confidence intervals.

^c Adjusted for infant's weight at enrolment, sex, twin status, birth order, and mother's educational level, place of defecation, and household water supply.

^d A full explanation of the feeding categories can be found in the text.

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Résumé

Alimentation du nourrisson et risques de décès et d'hospitalisation dans les six premiers mois : étude de cohorte multicentrique

Objectif Déterminer l'association entre différents modes d'alimentation des nourrissons (allaitement maternel exclusif, allaitement maternel prédominant, allaitement maternel partiel et absence d'allaitement maternel) et la mortalité et les hospitalisations pendant les six premiers mois.

Méthodes Le présent document s'appuie sur une analyse secondaire des données provenant d'un essai contrôlé randomisé multicentrique sur la supplémentation en vitamine A associée à la vaccination. Au total, 9424 enfants et leurs mères (2919 au Ghana, 4000 en Inde et 2505 au Pérou) ont été inclus dans l'essai alors que les nourrissons avaient entre 18 et 42 jours dans deux taudis urbains de New Delhi (Inde), un bidonville périurbain de Lima (Pérou) et 37 villages du district de Kintampo (Ghana). Des visites au domicile des couples mère-enfant ont été effectuées à des intervalles de 4 semaines à compter de l'administration au nourrisson de la première dose de vaccin antipoliomyélique b uccal et de vaccin antidiphthérique-anticoquelucheux-antitétanique, à 6 semaines au Ghana et en Inde et à 10 semaines au Pérou. A chaque visite, les mères devaient dire ce qu'elles avaient proposé à boire ou à manger à leur nourrisson au cours de la semaine écoulée. Des données ont aussi été recueillies sur les hospitalisations et les décès de nourrissons entre 6 semaines et 6 mois. Les principaux critères de jugement utilisés étaient la

mortalité toutes causes confondues, la mortalité par diarrhée, la mortalité due à des infections aiguës des voies respiratoires inférieures et les hospitalisations.

Résultats Le risque de décès ne variait pas sensiblement selon que les enfants étaient nourris au sein exclusivement ou de façon prédominante (rapport des risques ajustés (RR) = 1,46 ; intervalle de confiance à 95% (IC) = 0,75-2,86). Le risque de décès était plus élevé pour les enfants n'étant pas nourris au sein que pour les enfants nourris au sein de façon prédominante (RR = 10,5 ; IC à 95% = 5,0-22,0 ; $p < 0,001$), ce qui était également le cas des enfants nourris partiellement au sein (RR = 2,46 ; IC à 95% = 1,44-4,18 ; $p = 0,001$).

Conclusion Ces résultats ont deux incidences majeures. Premièrement, le risque de mortalité infantile extrêmement élevé associé à l'absence d'allaitement au sein doit être pris en compte dans les options proposées aux mères infectées par le VIH concernant l'alimentation de leur nourrisson. Deuxièmement, compte tenu des risques de décès similaires pour les nourrissons nourris au sein de façon prédominante et pour ceux qui sont nourris au sein exclusivement, les mesures de promotion, là où les taux d'allaitement au sein prédominant sont déjà élevés, devraient viser à maintenir ces taux élevés et non à tenter de substituer l'alimentation au sein exclusive à l'alimentation au sein prédominante.

Resumen

Pautas de alimentación del lactante y riesgos de defunción y hospitalización en la primera mitad de la lactancia: estudio multicéntrico de cohortes

Objetivo Determinar la relación existente entre diferentes pautas de alimentación de los lactantes (lactancia materna como alimentación exclusiva, predominante, parcial o nula) y la mortalidad y los ingresos hospitalarios durante la primera mitad de la lactancia.

Métodos Este artículo se basa en un análisis secundario de los datos aportados por un ensayo controlado aleatorizado multicéntrico sobre la administración de suplementos de vitamina A vinculada a la inmunización. En total, 9424 pares de madre y lactante (2919 en Ghana, 4000 en la India y 2505 en el Perú) entraron a participar en este estudio cuando los lactantes tenían 18–42 días en dos barrios pobres urbanos de Nueva Delhi, India, un poblado periurbano de chabolas de Lima, Perú, y 37 aldeas del distrito de Kintampo en Ghana. Cada madre y lactante fueron visitados en su vivienda a intervalos de 4 semanas desde el momento en que el niño recibió la primera dosis de vacuna antipoliomielítica oral y de difteria-tétanos-tos ferina, a la edad de 6 semanas en Ghana y la India, y de 10 semanas en el Perú. En cada visita se preguntaba a las madres qué habían dado de comer y beber al niño durante la última semana. También se recogía información sobre los ingresos hospitalarios y las defunciones que se hubieran producido entre las 6 semanas y los 6 meses. Las principales medidas de resultado fueron la mortalidad por todas las causas, la mortalidad específica por diarrea, la mortalidad

por infecciones agudas de las vías respiratorias inferiores y los ingresos en hospitales.

Resultados No se observó ninguna diferencia importante entre el riesgo de defunción de los niños que fueron amamantados como alimentación exclusiva y los alimentados predominantemente al pecho (razón de riesgo (RR) ajustada = 1,46; intervalo de confianza (IC) del 95% = 0,75–2,86). Los lactantes no amamantados presentaron un mayor riesgo de morir que los predominantemente amamantados (RR = 10,5; IC95% = 5,0–22,0; P < 0,001), y lo mismo ocurrió con los alimentados al pecho de forma parcial (RR = 2,46; IC95% = 1,44–4,18; P = 0,001).

Conclusión Estos resultados tienen dos implicaciones muy importantes. Primero, a la hora de informar a las madres infectadas por el VIH acerca de las opciones para alimentar a sus lactantes, hay que tener en cuenta el riesgo extremadamente alto de mortalidad infantil asociado a la ausencia de lactancia natural. Segundo, nuestro hallazgo de un riesgo de defunción semejante para los lactantes que sólo recibieron leche materna y los que se alimentaron predominantemente de ese modo lleva a pensar que, en los entornos donde las tasas de lactancia natural predominante son ya elevadas, las actividades de promoción deben centrarse en mantener esas tasas altas, antes que en intentar forzar un cambio de lactancia materna predominante a lactancia materna exclusiva.

ملخص

أنماط تغذية الرضع واحتمال تعرّضهم لخطر الموت والإدخال للمستشفى في النصف الأول من فترة الرضاعة: دراسة متعددة المراكز للأتراب

الموجودات: لم يكن هناك فارق كبير في احتمال خطر التعرّض للموت بين الأطفال الذين اقتصر تغذيتهم على الرضاعة من الثدي والذين غلبت على تغذيتهم الرضاعة من الثدي، فقد كانت النسبة المصحّحة للمخاطر 1.46 وفاصلة الثقة 95% إذ تراوحت النسبة المصحّحة للمخاطر بين 0.75 و 2.86. فيما تعرض الأطفال الذين حرّموا من الرضاعة من الثدي لخطر أكبر للموت بالمقارنة بأولئك الذين غلبت على تغذيتهم الرضاعة من الثدي، فقد كانت النسبة المصحّحة للمخاطر 10.5 وفاصلة الثقة 95% إذ تراوحت النسبة المصحّحة للمخاطر بين 5.0 و 22.0 وكانت قيمة الاحتمال أقل من 0.001، وانطبق ذلك أيضاً على الرضع الذين كانت رضاعتهم من الثدي جزئية، فقد كانت النسبة المصحّحة للمخاطر لديهم 2.46 وفاصلة الثقة 95% إذ تراوحت النسبة المصحّحة للمخاطر بين 1.44 و 4.18 وقيمة الاحتمال 0.001.

الاستنتاج: تشير الموجودات إلى أمرين هامين، أولهما الارتفاع الشديد جداً في احتمال خطر تعرّض الرضع للموت إذا لم يرضعوا من الثدي، وهو أمر ينبغي أخذه بالحسبان عند إبلاغ الأمهات المصابات بالعدوى بفيروس العوز المناعي البشري حول الاختيارات المتاحة لهن حول تغذية أطفالهن، وثانيهما أن احتمالات خطر تعرض الأطفال للموت تتشابه لدى من يغلب لديهم الإرضاع من الثدي والذين تقتصر تغذيتهم على الإرضاع من الثدي، مما يشير إلى وجوب تركيز جهود الدعوة في المناطق التي يغلب فيها الرضاعة من الثدي بمعدلات عالية على الاستمرار على هذه المعدلات العالية بدلاً من محاولة تحويلهم إلى الاقتصاص على الرضاعة من الثدي.

الهدف: التعرّف على الترابط بين أنماط مختلفة لتغذية الرضع (الاقتصار على الرضاعة من الثدي، غلبة الرضاعة من الثدي، والإقلال من الرضاعة من الثدي، وعدم الرضاعة من الثدي) ومعدل الوفيات والإدخال في المستشفى في النصف الأول من فترة الرضاعة.

الطريقة: ارتكزت هذه الورقة على تحليل ثانوي للمعطيات المستمدة من دراسة متعددة المراكز ومعشاة ومضبوطة بالشواهد حول التكميل بإعطاء الفيتامين A المصاحب للتمنيع. وقد شملت الدراسة 9424 زوجاً من الأطفال وأمهم (2919 من غانا و 4000 من الهند و 2505 من بيرو) حيث كان عمر الرضع يتراوح بين 18 و 42 يوماً في اثنين من الأحياء الفقيرة بمدينة نيودلهي في الهند ومنطقة عشوائية بمدينة ليمبا في بيرو، و 37 قرية في مقاطعة كينتامبو في غانا. وتمت زيارة الأمهات وأطفالهن في بيوتهم كل 4 أسابيع بدءاً من الوقت الذي تلقى فيه الرضع الجرعة الأولى من لقاح شلل الأطفال الفموي واللقاح الثلاثي للخناق (الدفترية) والشاهوق (السعال الديكي) والكزاز (التتانوس) عند عمر 6 أسابيع في كل من غانا والهند و 10 أسابيع في بيرو. وفي كل زيارة توجه الأسئلة للأمهات حول ما قدموا لأطفالهم من طعام وشراب أثناء الأسبوع المنصرم. كما جمعت المعلومات حول الإدخال في المستشفى وحول الوفيات في الفترة بين 6 أسابيع و 6 أشهر. وكانت حصيلة الدراسة معدل الوفيات التي تعود لجمع الأسباب ومعدل الوفيات بسبب الإسهال ومعدل الوفيات الناجمة عن التهاب الطرق التنفسية السفلية ومعدلات الإدخال بالمستشفى.

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