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Delayed Breastfeeding Initiation Increases Risk of Neonatal Mortality

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The authors have indicated that they have no relationships relevant to this article to disclose.

ABSTRACT

BACKGROUND. Breastfeeding promotion is a key child survival strategy. Although there is an extensive scientific basis for its impact on postneonatal mortality, evidence is sparse for its impact on neonatal mortality.

OBJECTIVES. We sought to assess the contribution of the timing of initiation of breastfeeding to any impact.

METHODS. This study took advantage of the 4-weekly surveillance system from a large ongoing maternal vitamin A supplementation trial in rural Ghana involving all women of childbearing age and their infants. It was designed to evaluate whether timing of initiation of breastfeeding and type (exclusive, predominant, or partial) are associated with risk of neonatal mortality. The analysis is based on 10 947 breastfed singleton infants born between July 2003 and June 2004 who survived to day 2 and whose mothers were visited in the neonatal period.

RESULTS. Breastfeeding was initiated within the first day of birth in 71% of infants and by the end of day 3 in all but 1.3% of them; 70% were exclusively breastfed during the neonatal period. The risk of neonatal death was fourfold higher in children given milk-based fluids or solids in addition to breast milk. There was a marked dose response of increasing risk of neonatal mortality with increasing delay in initiation of breastfeeding from 1 hour to day 7; overall late initiation (after day 1) was associated with a 2.4-fold increase in risk. The size of this effect was similar when the model was refitted excluding infants at high risk of death (unwell on the day of birth, congenital abnormalities, premature, unwell at the time of interview) or when deaths during the first week (days 2–7) were excluded.

CONCLUSIONS. Promotion of early initiation of breastfeeding has the potential to make a major contribution to the achievement of the child survival millennium development goal; 16% of neonatal deaths could be saved if all infants were breastfed from day 1 and 22% if breastfeeding started within the first hour. Breastfeeding-promotion programs should emphasize early initiation as well as exclusive breastfeeding. This has particular relevance for sub-Saharan Africa, where neonatal and infant mortality rates are high but most women already exclusively or predominantly breastfeed their infants.

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Dr Edmond conceived the idea for this study, took the lead role in its design, oversaw its conduct, conducted the statistical analysis, and wrote the first draft of the paper. She was responsible for the final version, together with Prof Kirkwood, who provided technical input to and was substantially involved in all aspects of the study. Mr Zandoh was head of fieldwork; Mr Amenga-Etego was responsible for the design and execution of the data management system; Dr Owusu-Agyei provided technical input to the design and conduct; and Ms Quigley provided technical input and contributed to the statistical analysis. All authors provided feedback on drafts of the article and approved the final version.

Key Words

breastfeeding, neonatal care, neonatal survival

Abbreviations

OR—odds ratio
aOR—adjusted odds ratio
PAF—population-attributable fraction
CI—confidence interval

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ALTHOUGH THE CHILD survival revolution of the 1980s led to dramatic reductions in overall child mortality, it had little impact on neonatal mortality.^{1,2} In 2002, ~4 million infants died during the first month of life, and neonatal deaths now account for 36% of deaths among children <5 years of age.^{1,2} Tackling neonatal mortality is essential if the millennium development goal for child mortality is to be met.^{3,4} Sub-Saharan Africa contributes a high proportion of neonatal deaths, yet its progress has been the slowest of any region in the world.^{2,3,5} Because the majority of neonatal deaths occur at home,¹ feasible interventions for home-based implementation are needed urgently.

The promotion of breastfeeding is a key component of child survival strategies.³ Furthermore, the recent *Lancet* neonatal survival series included breastfeeding in its recommended package of interventions to reduce neonatal mortality.⁶ International policy places emphasis on exclusive breastfeeding during the first 6 months of life, with some groups promoting early initiation of breastfeeding within 1 hour of birth.^{7,8} Although there is an extensive scientific basis for the impact of breastfeeding on postneonatal mortality,^{3,9,10} evidence is sparse for its impact on neonatal mortality^{1,6} and, to our knowledge, nonexistent for the contribution of the timing of initiation to any mortality impact.

Maternal colostrum, produced during the first days after delivery, has long been thought to confer additional protection because of its immune and nonimmune properties.¹¹ However, epidemiologic data indicate that a high proportion of neonatal deaths are a result of obstetric complications,^{1,12} and these are unlikely to be affected by colostrum, transitional breast milk, or mature breast milk. Elucidating the role of timing of initiation of breastfeeding is particularly relevant for sub-Saharan Africa, where neonatal and infant mortality rates are high but most women already exclusively or predominantly breastfeed their infants.²

A surveillance system from a large trial in rural Ghana of the impact of weekly vitamin A supplementation to women of childbearing age on maternal and infant mortality (ObaapaVitA trial) afforded the opportunity to evaluate the association between early breastfeeding practices and deaths in breastfed neonates. Our primary objective was to evaluate the association between the timing of initiation of breastfeeding and neonatal mortality. The secondary objective was to assess whether the different types of breastfeeding (exclusive, predominant, and partial breastfeeding) were associated with substantially different risks of neonatal death.

METHODS

Setting and Participants

The ObaapaVitA trial is an ongoing community-based, cluster-randomized, double-blind, placebo-controlled

trial to assess the impact of weekly vitamin A supplementation on maternal mortality. It involves all women of childbearing age who live in 4 rural contiguous districts (Kintampo, Wenchi, Techiman, and Nkoranza) in the forest-savanna transitional ecological zone in the Brong Ahafo region of central Ghana. It covers ~12 000 km², and ~80% of the study population live in remote and rural villages.

All of the singleton infants born to mothers in the ObaapaVitA trial between July 1, 2003, and June 30, 2004, who initiated breastfeeding, survived to day 2, and whose mothers were visited in the neonatal period were included in the present study. Both the ObaapaVitA trial and this nested study were approved by the ethics committees of Ghana Health Service and London School of Hygiene and Tropical Medicine.

Data Collection

Women were visited once every 4 weeks by a network of trained village-based fieldworkers to distribute vitamin A capsules and collect data on morbidity and mortality. When a birth was reported, the fieldworker administered a "birth" questionnaire, which included birth outcome, birth weight (if taken within 48 hours of birth at a health facility), gestational age, details of the delivery, health care during pregnancy, health of the mother, socioeconomic and environmental characteristics, and home-based neonatal care practices, including early breastfeeding practices. The mother was asked when she initiated breastfeeding and was prompted for the exact timing (within 1 hour, after 1 hour but first day, day 2, day 3, day 4–7, or after day 7). She was then asked what she offered her child to eat or drink in the 24 hours before the interview. After noting the unprompted response, the mother was asked if she offered her own breast milk, breast milk from a wet nurse, animal milk, infant formula, milk-based fluids, water-based fluids, or solid foods. The mother was also asked about the infant's health on the day of birth and in the previous 24 hours. At the next 4-week visit, an "infant" questionnaire was administered to obtain additional outcome data (infant morbidity and mortality) and information about infant feeding practices. Infants were followed up at subsequent visits every 4 weeks until they reached 12 months of age.

Study Definitions and Statistical Analysis

An infant was considered to be breastfed if breast milk constituted any portion of their diet. Infants were classified according to the timing of breastfeeding initiation (first hour, after first hour but day 1, day 2, day 3, and after day 3). "Early initiation" of breastfeeding referred to breastfeeding that started on the first day of life. "Late initiation" indicated breastfeeding that began after the first day of life. "Established breastfeeding" referred to the reported breastfeeding pattern in the 24 hours before

the first interview (median: 14 days postpartum; interquartile range: 7–21 days). “Exclusive breastfeeding” was defined as feeding of only breast milk and nothing else, not even water, with the exception of vitamin supplements and prescribed medicines. “Predominant breastfeeding” was defined as feeding of breast milk along with other nonmilk fluids. Infants who were offered breast milk and animal milk, infant formula, or solids were considered to be “partially breastfed.” These definitions are consistent with the current World Health Organization definitions for breastfeeding patterns.⁸

The primary comparisons were made between early and late initiation of breastfeeding and between the types of established breastfeeding patterns (exclusive, predominant, and partial). To reduce problems with reverse causality (ie, the possibility of the breastfeeding pattern being affected by serious illnesses that lead to death), only infants who survived to day 2 and who were breastfed successfully were included in the primary analyses. Multiple births, noninitiators, and those who were interviewed outside the neonatal period were also excluded. The primary outcome variable was calculated as the number of breastfed singleton infants who died during ages 2 to 28 days per 1000 singleton births surviving to day 2. Early neonatal deaths were infants who died from days 2 to 7, and late neonatal deaths were infants who died from 8 to 28 days of age.

Logistic regression was used to calculate crude and adjusted odds ratios (aORs) for mortality associated with the breastfeeding-exposure variables. Potential confounders relating to the mother (health, parity, age, educational level, and cash income), household (water supply and place of defecation), health system (number of antenatal visits, place of birth, and birth attendant), and the infant (gender, birth size, gestational age, presence of a congenital anomaly, health on the day of birth, and health at the time of interview) were included a priori in the models. ObaapaVitA trial group (maternal vitamin A supplementation or placebo) was not included; it was not a confounder, because it was not associated with infant feeding patterns.

Only 3264 infants had their weight measured within 48 hours of birth, but perceived birth size was available from all of the mothers. Mothers’ perception of an infant

as “very tiny” or “smaller than average” gave a sensitivity of 80% and specificity of 95% in detecting a birth weight of <2.0 kg (Table 1). Thus, the mother’s perception of birth size was used in the logistic-regression models as a proxy for birth weight.

To further reduce problems with reverse causality, analyses were repeated excluding infants at high risk of death and ill health (congenital anomalies, premature, unwell on the day of birth, and unwell at the time of interview) and early neonatal deaths. All of the analyses were conducted in Stata 8.2 (Stata Corp, College Station, TX). aORs and 95% confidence intervals (CIs) are presented. Because neonatal mortality is a relatively rare event, these ORs closely approximate relative risks and are referred to as such in the text. To elucidate the public health importance of improving early breastfeeding patterns, the proportions of all neonatal deaths that would be avoided if all infants initiated breastfeeding during the first hour or during the first day of life (the population-attributable fractions [PAFs]) were calculated also.

RESULTS

There were 14 403 live births in the ObaapaVitA trial area from July 1, 2003, to June 30, 2004, and 433 neonatal deaths, giving a neonatal mortality rate of 30.1 per 1000 live births. Data were captured for 11 316 (82%) of the 13 860 singleton births within 28 days of delivery (median: 14 days postpartum; interquartile range: 7–21 days). This included 268 neonatal deaths, 109 (41%) of which occurred within the first day of birth. We excluded 106 (0.9%) of the day-2 singleton survivors who either did not initiate breastfeeding or started then stopped, plus 154 (1.4%) whose mothers moved out of the study area before the second infant interview. This analysis is based on the remaining 10 947 infants, among whom there were 145 neonatal deaths from days 2 to 28.

Breastfeeding Patterns and All-Cause Neonatal Mortality

Breastfeeding was initiated within the first day of birth in 71% of the infants and by the end of day 3 in all but 1.3% of them (Table 2); 70% of the infants were exclusively breastfed during the neonatal period (Table 3). There was a marked dose response of increasing risk of

TABLE 1 Validation of Mother’s Perception of Birth Size

Perception of Birth Size	Birth Weight, kg ^a				Total, N	Mean (SD) Birthweight, kg
	<2.00	2.00–2.49	2.50–3.49	≥3.50		
Very tiny	8 (35)	6 (26)	8 (35)	1 (4.4)	23	2.23 (0.70)
Smaller than average	10 (6.0)	57 (34)	97 (58)	3 (1.8)	167	2.50 (0.45)
Average size	5 (0.3)	134 (7.5)	1389 (78)	261 (15)	1789	2.95 (0.43)
Larger than average	0	21 (3.2)	388 (59)	248 (38)	657	3.30 (0.46)
Very big baby	0	0	326 (52)	302 (48)	628	3.45 (0.46)
Total	23 (0.7)	218 (6.7)	2208 (68)	815 (25)	3264	3.09 (0.51)

^a Values are n (%).

TABLE 2 Risks of Neonatal Mortality According to Timing of Initiation of Breastfeeding in Singletons Who Initiated Breastfeeding and Survived to Day 2

Initiation of Breastfeeding	No. (%) of Infants	No. of Deaths (% risk) ^a	aOR 1 (95% CI) ^b	aOR 2 (95% CI) ^c
Within 1 h	4763 (43)	34 (0.7)	1	1
From 1 h to end of day 1	3105 (28)	36 (1.2)	1.45 (0.90 to 2.35)	1.43 (0.88 to 2.31)
Day 2	2138 (20)	48 (2.3)	2.70 (1.70 to 4.30)	2.52 (1.58 to 4.02) ^d
Day 3	797 (7.3)	21 (2.6)	3.01 (1.70 to 5.38)	2.84 (1.59 to 5.06) ^d
After day 3	144 (1.3)	6 (4.2)	4.42 (1.76 to 11.09)	3.64 (1.43 to 9.30) ^d
Total	10 947 (100)	145 (1.3)		
			<i>P</i> LRT < .0001	<i>P</i> LRT = .0001
			<i>P</i> trend < .0001	<i>P</i> trend < .0001

LRT indicates likelihood ratio test.

^a % risk = no. of deaths/no. of infants in exposure category.

^b Adjusted for gender, birth size, gestational age, presence of a congenital anomaly, health on the day of birth, health at the time of interview, mother's health at the time of delivery, age of mother, parity, educational level of mother, mother having cash income, household water supply, place of defecation, number of antenatal visits, place of birth, and birth attendant.

^c Adjusted for all factors mentioned previously plus established breastfeeding pattern.

^d The combined aOR for initiation of breastfeeding after 1 d was 2.88 (95% CI: 1.87 to 4.42).

TABLE 3 Risks of Neonatal Mortality According to Established Breastfeeding Pattern in Singletons Who Initiated Breastfeeding and Survived to Day 2

Established Neonatal Breastfeeding Pattern	No. (%) of Infants	No. of Deaths (% risk) ^a	aOR 1 (95% CI) ^b	aOR 2 (95% CI) ^c
Exclusive	7680 (70)	84 (1.1)	1	1
Predominant	3034 (27)	48 (1.6)	1.41 (0.97 to 2.03)	1.30 (0.90 to 1.87)
Partial	233 (2.1)	13 (5.6)	4.51 (2.38 to 8.55)	3.82 (1.99 to 7.34)
Total	10 947 (100)	145 (1.3)		
			<i>P</i> LRT < .0001	<i>P</i> LRT = .0001
			<i>P</i> trend < .0001	<i>P</i> trend < .0001

Median age of ascertainment of established breastfeeding patterns was 14 days (interquartile age, 7–21 days). LRT indicates likelihood ratio test.

^a % risk = no. of deaths/no. of infants in exposure category.

^b Adjusted for gender, birth size, gestational age, presence of a congenital anomaly, health on the day of birth, health at the time of interview, mother's health at the time of delivery, age of mother, parity, educational level of mother, mother having cash income, household water supply, place of defecation, number of antenatal visits, place of birth, and birth attendant.

^c Adjusted for all factors mentioned previously plus timing of initiation of breastfeeding.

neonatal mortality with increasing delay in initiation of breastfeeding from 1 hour to day 7 (Table 2); overall late initiation (after day 1) was associated with a 2.4-fold increase in the risk of neonatal mortality (Table 4).

The size of this effect was similar (aOR: 2.44; 95% CI: 1.60 to 3.74; *P* < .0001) when the model was refitted to exclude infants at high risk of death (unwell on the day of birth, congenital abnormalities, premature, and unwell at the time of interview) or when deaths during the first week (days 2–7) were excluded (aOR: 2.36; 95% CI:

1.44 to 3.87]; *P* = .001). Furthermore, the trend with late initiation was still significant after adjusting for the type of breastfeeding (Table 2), and the increased risk associated with late initiation was similar within each breastfeeding category (Table 4). Infants who were given prelacteal feeds (any food or fluids before breastfeeding was established) on day 1 also had a high neonatal mortality risk (aOR: 1.63; 95% CI: 1.09 to 2.45; *P* = .017).

The type of breastfeeding was also found to be asso-

TABLE 4 Neonatal Mortality Risk by Time of Initiation of Breastfeeding and Established Diet

Established Neonatal Breastfeeding Pattern	Initiation of Breastfeeding		Late vs Early Initiation	
	Early (first day) No. of Deaths (% risk) ^a	Late (After 1 d) No. of Deaths (% risk) ^a	aOR (95% CI) ^b	<i>P</i>
Exclusive	48/5767 (0.8)	36/1913 (1.9)	2.19 (1.38 to 3.49)	.001
Predominant	18/1968 (0.9)	30/1066 (2.8)	2.55 (1.38 to 4.71)	.003
Partial	4/133 (3.0)	9/100 (9.0)	2.63 (0.60 to 11.63)	.202
Overall	70/7868 (0.9)	75/3079 (2.4)	2.40 (1.69 to 3.40)	<.0001

^a % risk = no. of deaths/no. of infants in exposure category.

^b Late vs early initiation, adjusted for gender, birth size, gestational age, presence of a congenital anomaly, health on the day of birth, health at the time of interview, mother's health at the time of delivery, age of mother, parity, educational level of mother, mother having cash income, household water supply, place of defecation, number of antenatal visits, place of birth, and birth attendant.

ciated with mortality risk. Both predominantly (aOR: 1.41; 95% CI: 0.97 to 2.03) and partially (aOR, 4.51; 95% CI, 2.38 to 8.55) breastfed infants had higher risks of neonatal death than exclusively breastfed infants, although the risk was much higher and only statistically significant in the partially breastfed group (Table 3). The pattern was unchanged after adjustment for timing of initiation of breastfeeding; the size of the ORs was only slightly reduced (Table 3).

These findings indicate that both timing of initiation and type of breastfeeding pattern exert independent influences on neonatal mortality. Furthermore, there was no evidence of any interaction between the sizes of these effects and birth weight or gestational age.

PAFs

The percentage of neonatal deaths from 2 to 28 days of life that could be prevented if all of the infants in the study population initiated breastfeeding in the first hour of life was 41.3% (Table 5, PAF). This is equivalent to preventing 22.3% of all neonatal deaths if it is assumed that breastfeeding has no impact on deaths during the first day of life. The equivalent PAFs associated with initiating breastfeeding on the first day (rather than the first hour) are 30.2% of neonatal deaths saved from days 2 to 28 or 16.3% of all neonatal deaths.

DISCUSSION

Statement of Principal Findings

Interventions to improve early infant feeding practices can result in considerable reductions in neonatal mortality. All-cause neonatal mortality could be reduced by 16.3% if all infants initiated breastfeeding on day 1 of life and by 22.3% if initiation took place within the first hour. The risk of neonatal death is increased approximately fourfold if milk-based fluids or solids are provided to breastfed neonates.

Strengths and Relation to Other Studies

This article presents the risks of neonatal mortality that are associated with early breastfeeding practices from a large cohort study of >10 000 infants in rural Ghana. The protective relationship between early initiation of

breastfeeding and neonatal mortality risk was demonstrated after controlling for factors that are known to be associated with earlier onset of breastfeeding,^{13,14} lower rates of perinatal and infant mortality,^{3,6} and established breastfeeding practices.^{15,16} The prevalence of HIV infection is relatively low in the Brong Ahafo region of Ghana (4% prevalence in women of reproductive age)^{17,18} and, thus, is unlikely to have influenced the promotion of breastfeeding by health care providers in the region.

To our knowledge, this is the first study that has examined the impact of initiation of breastfeeding on mortality during the neonatal period. A Guinea-Bissau study found no effect of early initiation (day 1) on postneonatal mortality (in infants aged 29 days to 3 years).¹⁹ However, the World Health Organization Collaborative Study Team¹⁰ reported a higher protective effect against mortality of any breastfeeding in the first 2 months compared with later ages, and 3 studies found early initiation of breastfeeding (days 1–3) to be suggestively²⁰ or significantly^{13,21} associated with a lower rate of diarrhea during infancy. Two of these studies adjusted for confounding factors,^{13,20} but only 1 adjusted for later breastfeeding patterns.¹³

Data showing the impact of postinitiation breastfeeding patterns on neonatal mortality are also sparse. The only study identified examined infants in Bangladesh and reported no significant differences between exclusive and predominant breastfeeding on neonatal or postneonatal mortality (excluding infants who died within <3 days) after adjusting for confounding factors.¹⁵ This study grouped together partially breastfed and non-breastfed neonates and presented a combined hazard ratio of 1.17 (95% CI: 0.26 to 5.38) for not exclusively breastfeeding.

Potential Limitations

Observational studies of breastfeeding and infant health may be affected by a number of methodologic problems including self-selection, reverse causality, confounding, and misclassification.^{22–24} However, we analyzed data for the entire study population of singleton births and addressed reverse causality by excluding all deaths before day 2, excluding infants who either did not start or

TABLE 5 PAFs for Initiation of Breastfeeding in Breastfed Singletons Who Survived to Day 2

	No. (%) of Deaths	aOR ^a (95% CI)	PAF, ^b % (95% CI)
Within 1 h	34 (23.4)	1	—
After 1 h to end of day 1	36 (24.8)	1.45 (0.90 to 2.35)	7.7 (–2.8 to 13)
Day 2	48 (33.1)	2.70 (1.70 to 4.30)	20.8 (10 to 19)
Day 3	21 (14.4)	3.01 (1.70 to 5.38)	9.6 (5.9 to 12)
After day 3	6 (4.1)	4.42 (1.76 to 11.09)	3.2 (1.8 to 3.7)
Total	145 (100)		41.3

^a Adjusted for gender, birth size, gestational age, presence of a congenital anomaly, health on the day of birth, health at the time of interview, mother's health at the time of delivery, age of mother, parity, educational level of mother, mother having cash income, household water supply, place of defecation, number of antenatal visits, place of birth, and birth attendant.

^b PAF indicates proportion of deaths exposed (aOR – 1)/aOR.

started and stopped breastfeeding, controlling for high-risk infants, and repeating analyses excluding all deaths before day 8 and high-risk infants (which did not alter effect estimates). We also adjusted for many potential confounding variables, although residual confounding cannot be discounted. Finally, any differential misclassification of type of breastfeeding would have tended to underestimate rather than overestimate effect sizes.

Potential Mechanisms

Early initiation of breastfeeding could affect neonatal mortality risk by ≥ 4 mechanisms. First, the lower rate of mortality in early initiators may have occurred because mothers who suckle their offspring shortly after birth have a greater chance of successfully establishing and sustaining breastfeeding throughout infancy²⁵ and because breastfeeding during infancy is related protectively to mortality.¹⁰ However, the effect of early initiation persisted after controlling for established neonatal breastfeeding patterns and was stronger than the effect of established exclusive breastfeeding in our multivariate models. Second, prelacteal feeding with nonhuman milk antigens may disrupt normal physiologic gut priming.^{11,26} Third, early human milk is rich in a variety of immune and nonimmune components that may accelerate intestinal maturation, resistance to infection, and epithelial recovery from infection.^{11,27,28} Total protein and immunoglobulin levels also decrease markedly over the first days of life (concentrations are highest on day 1, halve by day 2, and slowly decrease thereafter).^{11,29} This process could explain the dose response seen in our study. Finally, promotion of warmth and protection may reduce the risk of death from hypothermia during day 1 (especially in preterm infants).³⁰ Our planned analysis of associations with cause-specific neonatal mortality (using verbal postmortem data) may help to explain these mechanisms.

Implications for Policy and Research

Tackling neonatal mortality is essential if the millennium development goal for child mortality is to be met. Our findings indicate that promotion of early initiation of breastfeeding has the potential to make a major contribution; 16% of neonatal deaths could be saved if all infants were breastfed from day 1 and 22% if breastfeeding were started within the first hour after birth.

These findings have important implications for neonatal health programs and policy. They suggest that breastfeeding-promotion programs in less-developed settings should place considerable emphasis on early initiation of breastfeeding, as well as promoting exclusive breastfeeding. This is particularly relevant for sub-Saharan Africa, where neonatal and infant mortality rates are high, most women already exclusively or predominantly breastfeed their infants, and delay of initiation of breastfeeding beyond the first day of life is common.

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