

Delayed Breastfeeding Initiation Is Associated with Infant Morbidity

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Objective To assess the relationship between breastfeeding initiation time and postneonatal mortality, morbidity, and growth through 24 months in a cohort of Tanzanian infants.

Study design We included 4203 infants from 2 trials of micronutrient supplementation. We used Cox proportional hazards models or general estimating equations to estimate relative risks.

Results A total of 13% of infants initiated breastfeeding >1 hour after birth (n = 536). There was no association between breastfeeding initiation time and risk of all-cause or cause-specific mortality, nor infant growth failure, from 6 weeks to 2 years of age. However, delayed breastfeeding was associated with an increased risk of several common infectious morbidities in early infancy, including upper respiratory infection symptoms and vomiting. Compared with those who initiated breastfeeding within the first hour of birth, delayed breastfeeding initiation was associated with an 11% increased risk of cough (relative risk 1.11, 95% CI 1.02-1.21) and a 48% increased risk of difficulty breathing (relative risk 1.48, 95% CI 1.09-2.01) during the first 6 months. Delayed initiation was associated with a greater risk of difficulty breathing from 6 to 12 months of age, but it was not associated with risk of any other morbidity during this time, nor any morbidity between 12 and 24 months.

Conclusion Delayed breastfeeding initiation is associated with an increased risk of infant morbidity during the first 6 months of life. Early breastfeeding initiation, along with exclusive and prolonged breastfeeding, should be prioritized and promoted in efforts to improve child health. (*J Pediatr 2017;191:57-62*).

espite a >50% reduction in child deaths since 1990, nearly 6 million children <5 years died in 2015.¹ The Sustainable Development Goals, launched in 2015, include targets of reducing under-5 mortality to <25 per 1000 livebirths and eliminating preventable child deaths by 2030.² Undernutrition is one of the leading causes of child mortality, and suboptimal breastfeeding practices are associated with >10% of all child deaths.³ Efforts to understand the epidemiology surrounding early infant nutrition and specific health outcomes are key to developing and targeting interventions to improve child health and survival.

Breastfeeding is associated with major reductions in morbidity, hospitalizations, and mortality due to diarrhea and pneumonia in children. Current recommendations regarding early infant feeding include breastfeeding initiation within 1 hour of birth, exclusive breastfeeding for 6 months, and continued breastfeeding (in conjunction with complementary foods) for 2 years or more. Although the vast majority of infants in low-income countries are breastfeed for 12 months or more, over one-half of all infants initiate breastfeeding within 1 hour of birth. Recommendations to initiate breastfeeding immediately after birth are based on evidence that early initiation promotes exclusive and prolonged breastfeeding and is associated with a reduced risk of neonatal mortality. Furthermore, early initiation of breastfeeding is associated with a reduced risk of postneonatal mortality

through 6 months, and the effect of early breastfeeding initiation operates in part through increasing rates of exclusive breastfeeding as well as through other mechanisms. Early exposure to maternal antibodies, lactoferrin, oligosaccharides, and other protective components in breast milk may improve neonatal and infant immune function. However, there is limited research regarding the relationship between breastfeeding initiation time and cause-specific mortality, infant morbidity, and growth. The objective of our study was to assess the association between delayed breastfeeding initiation and postneonatal mortality, infant morbidity, and growth failure in a cohort of infants in Tanzanian from 6 weeks to 2 years of age.

Methods

The prospective cohort was composed of infants who were enrolled in 2 randomized, double-blind clinical trials in Dar es Salaam, Tanzania, between August 2004

ALRI Acute lower respiratory infection

RB Relative risk

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and 2009. Dar es Salaam is the largest city in Tanzania. The first cohort was composed of infants born to HIV-infected women, and the second cohort included infants born to HIVuninfected women. The methods and main results of the primary trials have been published elsewhere. 11,12 To summarize, women who presented to labor wards or to antenatal care before 32 weeks' gestation were enrolled in the trials. Singleton infants were randomized between 5 and 7 weeks after birth if no congenital abnormality prevented feeding and the mother intended to stay in the study area. Mothers and children were asked to attend monthly clinic visits and participate in the study for 18-24 months following enrollment; care and treatment was consistent with the standard of care in the study area. In accordance with the Tanzanian standard of care at the time of the trial, mothers were counseled during antenatal care and delivery on both the risks (in the case of HIV-infected women) and benefits of exclusive breastfeeding, and those who chose to breastfeed were instructed not to provide any additional foods or fluids aside from medicines or oral rehydration solutions.

At enrollment (5-7 weeks' postpartum), the mother was asked how many hours after birth she first breastfed the newborn. We defined "early breastfeeding initiation" as initiation ≤1 hour and "delayed breastfeeding initiation" as initiation >1 hour. Because of the relatively small proportion of infant initiation beyond 1 hour, we did not further categorize delayed breastfeeding. Breastfeeding was assessed at enrollment and longitudinally by the mother's report during monthly clinic visits. Specifically, the mother was asked if the child consumed any foods from a specified list of 17 items (breast milk, water, cow's milk, formula, juice, etc) during the previous week. Infants were categorized as exclusively breastfeeding at 6 weeks if they consumed only breast milk (although oral rehydration solution, vitamin, or medicines were also allowed) at their 6-week visit or later.

Outcomes of interest included time to death, morbidity, and growth failure. All-cause mortality was defined as death from any cause, and cause-specific mortality was categorized as infection-specific, acute lower respiratory infection (ALRI), malaria, or diarrhea according to physician-coded verbal autopsies. We assessed the risk of death at 3, 6, 12, and 24 months. Morbidities were defined as specific symptoms assessed by nurses at monthly clinic visits by reviewing illustrated daily diaries kept by caregivers: diarrhea; cough; difficulty breathing; fever; refusal to eat, drink, or breastfeed; pus draining from ears; and vomiting. We also considered maternal reports of hospitalizations and unscheduled outpatient visits as indicators of all-cause morbidity. Growth failure was defined as <2 SDs below the mean height-for-age (stunting), weight-for-age (underweight), or weight-for-height (wasting) z score according to World Health Organization growth standards. 13 We longitudinally assessed time to first instance of growth failure from 6 weeks up to 6, 12, and 24 months.

Statistical Analyses

The cohort was characterized with baseline data regarding household, maternal, and infant characteristics by means or proportions for continuous and categorical data, respectively. To examine the relationship between delayed breastfeeding and time to death or growth failure, we used Cox proportional hazard models. We used inverse probability weights to create an adjusted survival curve. 14 We assessed the association between delayed breastfeeding and morbidity using generalized estimating equation models with binomial distribution, log link, and exchangeable covariance structure to account for repeated observations. We a priori stratified time into 3 categories: 0-6, >6-12, and >12-24 months. The parent study was included as a fixed effect in all models, and treatment (ie, zinc or multivitamins) was included in the morbidity models based on the results of the parent trials.¹¹ Potential confounders included in the multivariate models were woman's age (≥20 years, <20 years), woman's education (<2 years, ≥2 years), wealth tertile, birth weight of recent delivery (continuously), infant sex (male, female), cesarean delivery (yes, no), and health facility delivery (yes, no). Because ongoing breastfeeding may be a confounder, or possibly a mediator, of the relationship between early breastfeeding initiation and infant health, we included exclusive breastfeeding (yes, no) at 6 weeks in models as a sensitivity analysis. In a second sensitivity analysis, we also excluded HIV-infected children from the analysis. The missing indicator method was used for any missing confounders.¹⁵ Analyses were performed with SAS software version 9.2 (SAS Institute Inc, Cary, North Carolina).

Written informed consent was obtained from all women participating in the parent trials. The trial protocols were approved by the institutional review boards of the Harvard T.H. Chan School of Public Health, Muhimbili University of Health and Allied Sciences, Tanzania Food and Drug Authority, and the Tanzania National Institute of Medical Research.

Results

We included 4203 infants who initiated breastfeeding and had information about the time of breastfeeding initiation in the primary analysis (**Figure 1**; available at www.jpeds.com). We compared those excluded from the analysis (never initiated breastfeeding or missing time of breastfeeding initiation) with those included in our cohort; we found that the 2 groups were similar across all baseline characteristics, except excluded women were more likely to have had a cesarean delivery (14% compared with 10%). The mean age of women in the cohort was 27 years, and more than 23% attended school beyond primary school. Nearly 13% of infants initiated breastfeeding more than 1 hour after birth (n = 536). Infants who delayed breastfeeding were more likely to be low birthweight or to have been delivered by cesarean delivery than infants who initiated breastfeeding within 1 hour (**Table I**).

There was no association between delayed breastfeeding initiation and risk of mortality from 6 weeks to 2 years of age (Figure 2). The results were the same when we included exclusive breastfeeding at 6 weeks in the model (Table II; available at www.jpeds.com). We found similar results in a sensitivity analysis excluding HIV-infected children. Similarly, we found no relationship between delayed breastfeeding initiation and

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