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).*

Despite 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.[4] 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.[5] Although the vast majority of infants in low-income countries are breastfed for 12 months or more, over one-half of all infants initiate breastfeeding within 1 hour of birth.[6] Recommendations to initiate breastfeeding immediately after birth are based on evidence that early initiation promotes exclusive and prolonged breastfeeding[7] and is associated with a reduced risk of neonatal mortality.[8-10] 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.[9] 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
RR	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 HIV-uninfected 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

Table I. Maternal and child characteristics, stratified by time of breastfeeding initiation (n = 4203)

Characteristics	Early initiation (≤1 h) n = 3667 n (%)	Delayed initiation (2-96 h) n = 536 n (%)
Maternal age, y*		
<20	183 (5.1)	16 (3.1)
20-24	979 (27.1)	133 (25.4)
25-29	1312 (36.3)	184 (35.2)
30-34	845 (23.4)	130 (24.9)
≥35	293 (8.1)	60 (11.5)
Maternal education*		
None	153 (4.2)	21 (4.0)
Primary school	2643 (72.6)	383 (72.1)
Secondary school or more	846 (23.2)	127 (23.9)
Health facility delivery	3343 (91.2)	484 (90.3)
Delivered by cesarean	226 (6.2)	182 (34.0)
Male sex	1916 (52.3)	290 (54.1)
Low birth weight (<2500 g)	174 (4.8)	38 (7.1)

*Does not add to 100% due to missing data.

infection-specific mortality, ALRI mortality, malaria mortality, or diarrhea mortality (data not shown).

We found that delayed breastfeeding was associated with an increased risk of several common infectious morbidities in early infancy. 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 [RR] 1.11, 95% CI 1.02-1.21), a 49% increased risk of cough and other symptoms (RR 1.49, 95% CI 1.10-2.01), and a 48% increased risk of difficulty breathing (RR 1.48, 95% CI 1.09-2.01) during the first 6 months. Delayed initiation also was associated with a 13% increased risk of upper respiratory symptoms (RR 1.13, 95% CI 1.04-1.22) and 58% increased risk of vomiting (RR 1.58, 95% CI 1.10-2.26) 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 risk of any other morbidity during this time. Time of breastfeeding initiation was not associated with any morbidities from 12 to 24 months (**Table III**).

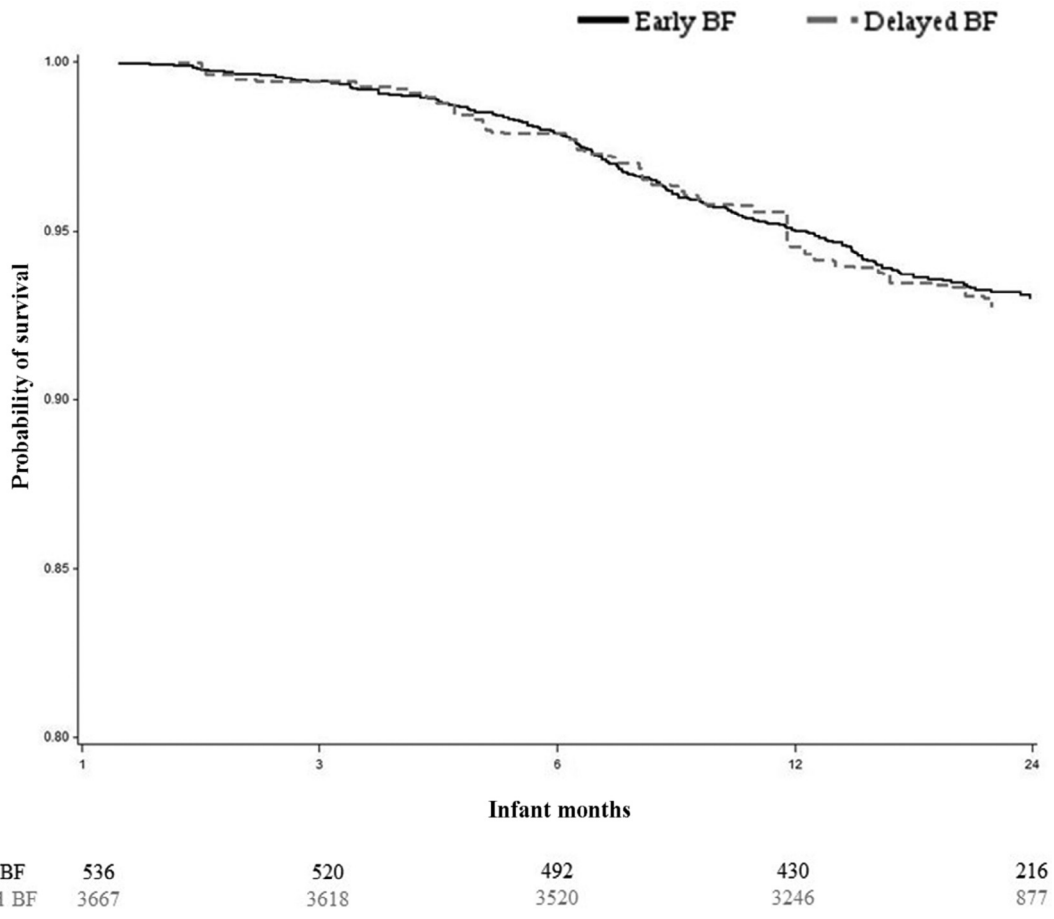

Figure 2. Adjusted survival curves comparing the probability of survival from 1 to 24 months, stratified by BF status, controlling for age mother, mother education, wealth tertile, birthweight, infant sex, cesarean delivery, health facility birth, and parent study (maternal HIV status). *BF*, breastfeeding.

Table III. Risk of common infectious morbidities associated with delayed breastfeeding initiation (n = 4203)

Infectious morbidities	0-6 mo Events*/visits†	0-6 mo RR (95% CI)‡	0-6 mo *P* value	6-12 mo Events*/visits†	6-12 mo RR (95% CI)‡	6-12 mo *P* value	12-24 mo Events*/visits†	12-24 mo RR (95% CI)‡	12-24 mo *P* value
Diarrhea	827/20 601	1.15 (0.95-1.40)	.16	996/18 274	1.00 (0.82-1.23)	.98	807/22 874	1.00 (0.79-1.26)	1.00
Cough	4827/20 568	1.11 (1.02-1.21)	**.01**	5408/18 236	1.00 (0.92-1.08)	1.00	6631/22 804	1.00 (0.93-1.09)	.93
Difficulty breathing	372/20 565	1.48 (1.09-2.01)	**.01**	217/18 232	1.66 (1.14-2.41)	**.008**	161/22 802	1.13 (0.72-1.78)	.59
Cough plus fever	965/20 568	1.17 (0.95-1.43)	.13	1390/18 236	1.03 (0.86-1.22)	.77	1475/22 804	1.03 (0.88-1.21)	.70
Cough +§	363/20 568	1.49 (1.10-2.01)	**.01**	471/18 236	1.13 (0.86-1.47)	.38	472/22 804	1.23 (0.93-1.62)	.15
Fever	1776/20 568	1.14 (0.98-1.33)	.08	2559/18 235	0.97 (0.85-1.10)	.61	2667/22 802	0.92 (0.81-1.05)	.21
Upper respiratory infection	5278/20 568	1.13 (1.04-1.22)	**.003**	4548/18 236	1.07 (0.98-1.16)	.15	5115/22 802	1.02 (0.92-1.12)	.75
Vomiting	252/20 566	1.58 (1.10-2.26)	**.01**	452/18 235	1.10 (0.82-1.48)	.53	373/22 802	0.94 (0.65-1.35)	.73
Refusal to eat	213/20 567	1.17 (0.78-1.76)	.44	694/18 232	1.01 (0.79-1.28)	.95	713/22 802	1.04 (0.80-1.34)	.78
Pus draining from ears	156/20 566	0.89 (0.52-1.51)	.66	145/18 232	0.82 (0.44-1.54)	.55	161/22 801	0.82 (0.38-1.80)	.63
Hospitalizations	97/20 471	0.70 (0.38-1.32)	.28	94/18 160	1.20 (0.70-2.04)	.51	79/22 778	1.28 (0.73-2.24)	.38
Unscheduled outpatient visits	359/20 425	1.05 (0.80-1.38)	.73	525/18 077	0.98 (0.75-1.28)	.91	647/22 431	1.19 (0.96-1.48)	.12

Bold values correspond to $P < 0.05$.
*Number of events based on maternal recall and diary of symptoms in the past 4 weeks.
†Number of visits is the number of nurse visits for all children.
‡RRs and corresponding 95% CIs were calculated by generalized estimating equations with binomial distribution, log link, and exchangeable covariance structure. Models control for age of mother; mother's education; wealth tertile; birth weight; infant sex; cesarean delivery; health facility birth; study assignment (maternal HIV status); randomized to multivitamins zinc, both, or placebo.
§Cough + is defined as cough plus at least one of the following: chest retractions, difficulty breathing, or refusal to eat.

We found similar results in a sensitivity analysis excluding HIV-infected children (**Table IV**; available at www.jpeds.com).

Compared with early initiation of breastfeeding, delayed breastfeeding initiation was not associated with any increased risk of stunting, wasting, or underweight, and the results were the same when we included exclusive breastfeeding status in the model (**Table V**). We also found similar results in a sensitivity analysis excluding HIV-infected children (**Table VI**; available at www.jpeds.com).

Discussion

We present findings from a cohort study to assess the relationship between delayed breastfeeding initiation and postneonatal mortality, morbidity, and growth. Although a number of studies have examined the relationship between breastfeeding initiation time and neonatal mortality,[8-10,16-22] postneonatal mortality has been examined in only one other cohort.[9] We found no association between delayed breastfeeding initiation and all-cause or cause-specific mortality from 6 weeks to 2 years of age. This finding is in contrast to a large cohort study of >100 000 infants in Ghana, India, and Tanzania that found that breastfeeding initiation delayed beyond the first hour of life was associated with an increased risk of death from any cause in the 1- to 3-month and 3- to 6-month periods.[9] However, our study had a significantly smaller sample size and lower postneonatal mortality than the previously published study, which may explain the lack of association. We also found no relationship between breastfeeding initiation time and infant growth. This finding is consistent with a cross-sectional assessment of 1-year-old children in eastern Uganda and another in Andhra Pradesh India; both studies found no significant relationship breastfeeding initiation time and stunting or wasting among 1-year-old children.[23,24] Notably, our study

Table V. Risk of growth failure at 6, 12, and 24 months associated with delayed breastfeeding initiation

Outcome	Events	Univariate* RR (95% CI)	Univariate* *P* value	Multivariate† RR (95% CI)	Multivariate† *P* value	Multivariate‡ RR (95% CI)	Multivariate‡ *P* value
I. Stunting (n = 4200)							
by 6 mo	758	1.12 (0.91-1.38)	.30	0.96 (0.77-1.20)	.73	0.96 (0.77-1.2)	.73
by 12 mo	1086	1.04 (0.87-1.25)	.64	0.95 (0.79-1.16)	.62	0.96 (0.79-1.17)	.71
by 24 mo	1416	0.99 (0.84-1.15)	.86	0.93 (0.79-1.1)	.38	0.94 (0.79-1.11)	.44
II. Wasting (n = 4199)							
by 6 mo	640	1.10 (0.88-1.37)	.39	1.15 (0.91-1.44)	.25	1.14 (0.91-1.44)	.26
by 12 mo	988	1.01 (0.84-1.21)	.94	1.04 (0.86-1.25)	.71	1.04 (0.86-1.26)	.68
by 24 mo	1194	0.98 (0.83-1.16)	.83	1.00 (0.84-1.19)	.99	1.00 (0.84-1.19)	.99
III. Underweight (n = 4200)							
by 6 mo	600	1.12 (0.90-1.39)	.32	0.99 (0.78-1.25)	.92	0.98 (0.78-1.24)	.87
by 12 mo	1086	1.04 (0.87-1.25)	.64	0.95 (0.79-1.16)	.62	0.96 (0.79-1.17)	.71
by 24 mo	1181	0.99 (0.84-1.17)	.90	0.89 (0.75-1.06)	.20	0.89 (0.75-1.06)	.21

*Estimated by Cox proportional hazards models included a fixed effect for parent study (maternal HIV status).
†Model 1: Estimated by Cox proportional hazards models controlling for age mother, mother education, wealth tertile, birth weight, infant sex, cesarean delivery, health facility birth, parent study (maternal HIV status).
‡Model 2: Model 1+ controlling for exclusive breastfeeding status at 6 weeks.

prospectively assessed the relationship between breastfeeding initiation time and infant growth through 2 years.

ALRI and diarrhea are the leading cause of postneonatal death globally.[1] We found that delaying breastfeeding beyond the first hour after birth was associated consistently with an increased risk of respiratory infection symptoms, including cough, difficulty breathing, and symptoms of upper respiratory infection during early infancy. Although there is strong evidence that any breastfeeding protects against pneumonia morbidity and mortality,[4] there is only 1 other study that has examined the association between breastfeeding initiation time and respiratory infections. A cross-sectional, household survey in Vietnam of infants aged 0-6 months found that those initiating breastfeeding within 1 hour of birth were less likely to have cough or cold symptoms with fever (aOR 0.91, 95% CI 0.80-1.03).[25] We also found that delayed breastfeeding was associated with nearly 60% increased risk of vomiting in the first 6 months of infancy, although interestingly there was no significant relationship between time of initiation and diarrhea. A small, prospective cohort study in rural Egypt found that breastfeeding initiation within 3 days of birth was associated with a significantly reduced risk of diarrhea during the first 6 months, although any apparent protection in early infancy did not extend to the 6- to 12-month period.[26] Another study in Vietnamese children found that those initiating breastfeeding within 1 hour of birth had 26% reduced odds of diarrhea among a group of infants aged less than 6 months.[25] The present study is the first to assess and find a relationship between breastfeeding initiation time and vomiting.

Exposure to breast milk protects against morbidity and mortality in part due to infant acquisition of maternal antibodies (eg, secretory IgA), lactoferrin, oligosaccharides, and other protective components from breast milk consumption.[27,28] There are a number of specific biological mechanisms through which breast milk components might protect infants from morbidity; for example, oligosaccharides in breast milk prevent *Haemophilus influenzae* and pneumococci attachment to pharyngeal epithelial cells.[29] However, it is not clear why the time of exposure to these breast milk components might be important given that colostrum is produced for the first several days; we hypothesize that early exposure to colostrum might induce epigenetic changes in the newborn immune system, metabolism, or microbiome. The makeup of breast milk, including composition of the milk microbiome and the total IgA level, has been shown to change over the first days and months postpartum.[30,31] However, there is limited evidence regarding changes in breast milk composition in the first hours after birth. Delayed breastfeeding also is associated with prelacteal feeding. For example, in our cohort, 30% of infants who delayed breastfeeding beyond 24 hours had prelacteal feeds compared with only 1% of infants who initiated feeding within the first hour. Further research is needed to understand the mechanisms through which early breastfeeding initiation might affect infant health.

There are several limitations of this study. Although this cohort includes high-quality, prospective data about infant morbidity and growth, the study was underpowered to assess all-cause and cause-specific mortality. In addition, the time of breastfeeding initiation was assessed at 6 weeks postpartum, and exclusive breastfeeding was assessed each month using 7-day recall, which may have resulted in some measurement error. However, data regarding the exposure of interest were measured before the assessment of the outcomes; any misclassification is thus likely nondifferential and would attenuate any effects we found. Our cohort assessed health outcomes beginning at 6 weeks, and infants who died or possibly those who were ill during the neonatal period were excluded from this cohort, which would also attenuate any effects of delayed breastfeeding initiation. Also, the vast majority of infants in our study initiated breastfeeding within 1 hour of birth, and we could not evaluate a potential dose-response relationship between time of initiation and each outcome. Our cohort is composed of urban infants who were largely born in health facilities, and one-half of the infants were born to HIV-infected women. Furthermore, we observed postneonatal mortality in this study that was much lower than the national average in Tanzania, and infants had unusually high contact with the health system due to regular study visits. Our findings may not be generalizable to the general population in Tanzania or sub-Saharan Africa, and this study should be replicated in other cohorts from low- and middle-income countries.

Our prospective study documented that 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. ■

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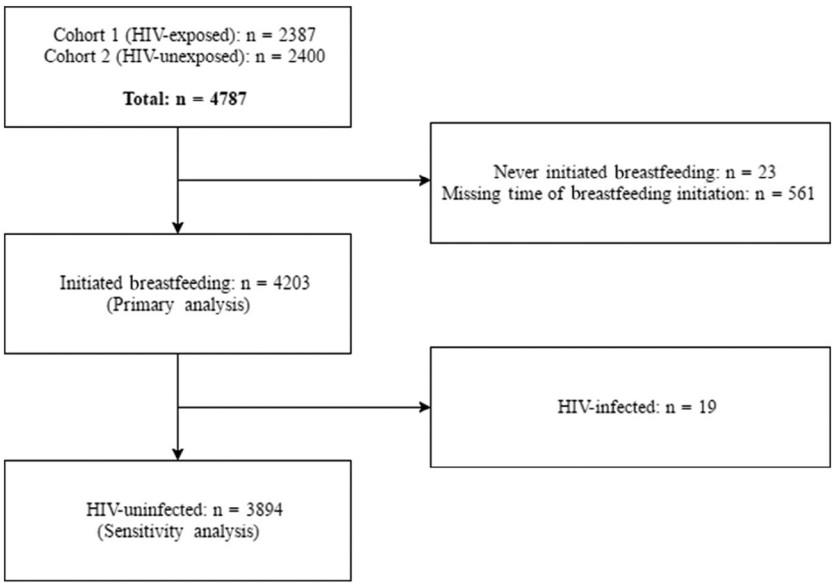

Figure 1. Study flowchart.

Table II. Mortality risk at 3, 6, 12, and 24 months by hour of breastfeeding initiation (n = 4203)

			Pooled (study as fixed effect)					
			Univariate*		Multivariate†		Multivariate‡	
Mortality	Events	Newborns	RR (95% CI)	*P* value	RR (95% CI)	*P* value	RR (95% CI)	*P* value
I. Mortality (3 mo)								
Initiation ≤1 h	20	3667	Ref.		Ref.		Ref.	
Initiation >1 h	5	536	1.00 (0.37-2.69)	.99	0.97 (0.34-2.78)	.95	0.94 (0.32-2.75)	.91
II. Mortality (6 mo)								
Initiation ≤1 h	65	3667	Ref.		Ref.		Ref.	
Initiation >1 h	18	536	1.10 (0.65-1.86)	.71	0.99 (0.56-1.75)	.98	0.98 (0.56-1.74)	.95
III. Mortality (12 mo)								
Initiation ≤1 h	160	3667	Ref.		Ref.		Ref.	
Initiation >1 h	42	536	1.11 (0.79-1.57)	.54	1.01 (0.70-1.46)	.97	1.00 (0.69-1.45)	.99
IV. Mortality (24 mo)								
Initiation ≤1 h	215	3667	Ref.		Ref.		Ref.	
Initiation >1 h	55	536	1.11 (0.82-1.49)	.51	1.02 (0.74-1.41)	.89	1.03 (0.74-1.41)	.88

*Estimated by Cox proportional hazards models included a fixed effect for parent study (maternal HIV status).
†Model 1: Estimated by Cox proportional hazards models controlling for age mother, mother education, wealth tertile, birth weight, infant sex, cesarean delivery, health facility birth, parent study (maternal HIV status).
‡Model 2: Model 1+ controlling for exclusive breastfeeding status at 6 weeks.

Table IV. Risk of common infectious morbidities associated with delayed breastfeeding initiation, excluding HIV-infected infants (n = 3894)

	0-6 mo			6-12 mo			12-24 mo		
Infectious morbidities	Events*/ visits†	RR (95% CI)‡	*P* value	Events*/ visits†	RR (95% CI)‡	*P* value	Events*/ visits†	RR (95% CI)‡	*P* value
Diarrhea	732/19 210	1.05 (0.85-1.30)	.63	919/17 158	1.08 (0.87-1.33)	.48	750/21 147	1.05 (0.82-1.33)	.71
Cough	4399/19 181	1.10 (1.00-1.21)	**.04**	4948/17 121	0.97 (0.89-1.06)	.53	6031/21 085	0.99 (0.91-1.08)	.85
Difficulty breathing	317/19 178	1.53 (1.08-2.15)	**.02**	176/17 117	1.72 (1.13-2.63)	**.01**	145/21 083	1.19 (0.74-1.93)	.48
Cough plus fever	825/19 181	1.21 (0.97-1.50)	.09	1214/17 121	0.99 (0.82-1.20)	.91	1318/21 085	1.03 (0.86-1.22)	.78
Cough +§	306/19 181	1.46 (1.04-2.04)	**.03**	407/17 121	1.11 (0.83-1.50)	.48	427/21 085	1.26 (0.94-1.70)	.12
Fever	1539/19 181	1.16 (0.98-1.36)	.08	2288/17 120	0.95 (0.83-1.09)	.48	2410/21 083	0.93 (0.81-1.07)	.32
Upper respiratory infection	4830/19 181	1.13 (1.04-1.23)	**.006**	4186/17 121	1.05 (0.96-1.15)	.30	4703/21 083	1.00 (0.90-1.10)	.96
Vomiting	220/19 179	1.55 (1.05-2.30)	**.03**	413/17 120	1.16 (0.85-1.60)	.35	345/21 083	0.96 (0.65-1.41)	.82
Refusal to eat	189/19 180	1.05 (0.67-1.67)	.82	635/17 117	1.02 (0.79-1.32)	.89	653/21 083	1.02 (0.77-1.34)	.89
Pus draining from ears	129/19 179	1.05 (0.67-1.67)	.82	113/17 117	0.50 (0.25-1.02)	.06	89/21 082	0.68 (0.33-1.40)	.29
Hospitalizations	72/19 080	0.72 (0.35-1.51)	.39	68/17 044	1.27 (0.70-2.30)	.42	66/21 051	1.49 (0.82-2.69)	.19
Unscheduled outpatient visits	310/19 034	1.17 (0.87-1.56)	.31	467/16 961	1.06 (0.80-1.40)	.68	595/20 704	1.22 (0.97-1.53)	.09

*Number of events based on maternal recall and diary of symptoms in the past 4 weeks.
†Number of visits is the number of nurse visits for all children.
‡RR and corresponding 95% CIs were calculated by generalized estimating equations with binomial distribution, log link, and exchangeable covariance structure. Models control for age of mother; mother's education; wealth tertile; birth weight; infant sex; cesarean delivery; health facility birth; study assignment (maternal HIV status); randomized to multivitamins zinc, both, or placebo.
§Cough + is defined as cough plus at least one of the following: chest retractions, difficulty breathing, or refusal to eat.

Table VI. Risk of growth failure at 6, 12, and 24 months associated with delayed breastfeeding initiation

		Univariate*		Multivariate†		Multivariate‡	
Outcome	Events	RR (95% CI)	*P* value	RR (95% CI)	*P* value	RR (95% CI)	*P* value
I. Stunting							
by 6 mo	655	1.11 (0.89-1.4)	.35	0.94 (0.73-1.21)	.65	0.94 (0.73-1.21)	.65
by 12 mo	950	0.99 (0.81-1.2)	.92	0.94 (0.76-1.16)	.56	0.95 (0.76-1.18)	.63
by 24 mo	1238	0.96 (0.81-1.13)	.60	0.92 (0.77-1.11)	.40	0.93 (0.77-1.12)	.46
II. Wasting							
by 6 mo	549	1.22 (0.96-1.56)	.10	1.11 (0.86-1.44)	.43	1.11 (0.86-1.44)	.43
by 12 mo	849	1.11 (0.91-1.36)	.29	0.98 (0.79-1.22)	.86	0.98 (0.79-1.22)	.86
by 24 mo	1031	1.1 (0.92-1.32)	.30	0.97 (0.80-1.17)	.73	0.97 (0.80-1.17)	.73
III. Underweight							
by 6 mo	482	1.31 (1.02-1.69)	.03	0.88 (0.67-1.16)	.36	0.87 (0.66-1.15)	.33
by 12 mo	950	0.99 (0.81-1.2)	.92	0.94 (0.76-1.16)	.56	0.95 (0.76-1.18)	.63
by 24 mo	989	1.1 (0.91-1.32)	.32	0.84 (0.68-1.02)	.08	0.84 (0.69-1.02)	.08

*Estimated by Cox proportional hazards models including a fixed effect for parent study (maternal HIV status).
†Model 1: Estimated by Cox proportional hazards models controlling for age mother, mother education, wealth tertile, birth weight, infant sex, cesarean delivery, health facility birth, parent study (maternal HIV status).
‡Model 2: Model 1+ controlling for exclusive breastfeeding status at 6 weeks.