Timing of initiation, patterns of breastfeeding, and infant survival: prospective analysis of pooled data from three randomised trials

*NEOVITA Study Group**

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Summary

Background Although the benefits of exclusive breastfeeding for child health and survival, particularly in the post-neonatal period, are established, the independent beneficial effect of early breastfeeding initiation remains unclear. We studied the association between timing of breastfeeding initiation and post-enrolment neonatal and post-neonatal mortality up to 6 months of age, as well as the associations between breastfeeding pattern and mortality.

Methods We examined associations between timing of breastfeeding initiation, post-enrolment neonatal mortality (enrolment 28 days), and post-neonatal mortality up to 6 months of age (29–180 days) in a large cohort from three neonatal vitamin A trials in Ghana, India, and Tanzania. Newborn babies were eligible for these trials if their mother reported that they were likely to stay in the study area for the next 6 months, they could feed orally, were aged less than 3 days, and the primary caregiver gave informed consent. We excluded infants who initiated breastfeeding after 96 h, did not initiate, or had missing initiation status. We pooled the data from both randomised groups of the three trials and then categorised time of breastfeeding initiation as: at ≤1 h, 2–23 h, and 24–96 h. We defined breastfeeding patterns as exclusive, predominant, or partial breastfeeding at 4 days, 1 month, and 3 months of age. We estimated relative risks using log binomial regression and Poisson regression with robust variances. Multivariate models controlled for site and potential confounders.

Findings Of 99 938 enrolled infants, 99 632 babies initiated breastfeeding by 96 h of age and were included in our prospective cohort. 56 981 (57·2%) initiated breastfeeding at ≤1 h, 38 043 (38·2%) at 2–23 h, and 4608 (4·6%) at 24–96 h. Compared with infants initiating breastfeeding within the first hour of life, neonatal mortality between enrolment and 28 days was higher in infants initiating at 2–23 h (adjusted relative risk 1·41 [95% CI 1·24–1·62], p<0·0001), and in those initiating at 24–96 h (1·79 [1·39–2·30], p<0·0001). These associations were similar when deaths in the first 4 days of life were excluded (1·32 [1·10–1·58], p=0·003, for breastfeeding initiation at 2–23 h, and 1·90 [1·38–2·62], p=0·0001, for initiation at 24–96 h). When data were stratified by exclusive breastfeeding status at 4 days of age (p value for interaction=0·690), these associations were also similar in magnitude but with wider confidence intervals for initiation at 2–23 h (1·41 [1·12–1·77], p=0·003) and for initiation at 24–96 h (1·51 [0·63–3·65], p=0·357). Exclusive breastfeeding was also associated with the lower mortality during the first 6 months of life (1–3 months mortality: exclusive *vs* partial breastfeeding at 1 month 1·83 [1·45–2·32], p<0·0001, and exclusive breastfeeding *vs* no breastfeeding at 1 month 10·88 [8·27–14·31], p<0·0001).

Interpretation Our findings suggest that early initiation of breastfeeding reduces neonatal and early infant mortality both through increasing rates of exclusive breastfeeding and by additional mechanisms. Both practices should be promoted by public health programmes and should be used in models to estimate lives saved.

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Introduction

Child mortality has decreased over the past decade, with an estimated 5·9 million deaths in children younger than 5 years reported in 2015 compared with 12·7 million in 1990.[1] The reduction in neonatal mortality has been much slower, with almost 2·7 million deaths occurring in 2015 (46% of all child deaths). Even a greater number of children are affected by serious consequences of prematurity, intrauterine growth retardation, and sepsis during the neonatal period, manifesting as poor physical and cognitive development and long-term effects on human capital.[2] Interventions that can be deployed at scale starting before birth and continuing throughout the postnatal

Research in context

Evidence before this study

We searched PubMed and the Cochrane Library for publications between 1963 and May, 2015, and identified four systematic reviews examining the effects of breastfeeding patterns or timing of breastfeeding initiation on risks of neonatal and early infant mortality. We found no relevant papers published beyond those identified in these reviews, using combinations of the following search terms: "breastfeeding", "breast feeding", "breast milk", "exclusive breastfeeding", "partial breastfeeding", "predominant breastfeeding", "initiation", "start", "begin", "neonatal mortality", "newborn mortality", "infant mortality".

Two reviews by Lamberti and colleagues indicated that there was moderate quality evidence that exclusive breastfeeding was associated with reduced neonatal and 0–5 month mortality. Two reviews (Debes and colleagues, and Khan and colleagues) suggested that early breastfeeding initiation was associated with reduced neonatal mortality. Early initiation of breastfeeding was not proposed as an independent intervention in the *Lancet* 2013 Nutrition Series, in the expectation that it might only operate through effects on exclusive breastfeeding.

Added value of this study

This is the first study to examine the association between early breastfeeding initiation and post-neonatal mortality. Our findings from almost 100 000 infants substantially strengthen the evidence base showing that both early initiation and exclusive breastfeeding are associated with reduced neonatal and infant mortality.

Importantly, our analysis gives the first epidemiological evidence that early initiation has both a direct and indirect effect on reducing mortality. This finding concurs with research on the complex role of breastmilk in terms of immunology, epigenetics, the microbiome, and stem cells that strengthens the plausibility that early exposure to breastmilk has beneficial effects that go above and beyond a mere increase in the duration of exclusive breastfeeding.

Implications of all the available evidence

Our findings emphasise the crucial importance of prioritising the promotion of early breastfeeding initiation both to mothers and to the health workers who assist and support them. Although this promotion is already part of WHO recommendations for newborn care, it is not a universal practice with only half of newborn babies in the world being breastfed in the first hour of life.

Second, our findings strengthen the scientific basis for including early initiation in addition to exclusive breastfeeding in models, such as the LiST tool, that estimate survival benefits of scaling up key interventions to end preventable child deaths. Early initiation is currently omitted because it has been assumed that this only works through its influence on exclusive breastfeeding. Our findings challenge this assumption and suggest that the total number of deaths that could be saved if both breastfeeding best practices (early initiation and exclusivity) were adopted are currently being underestimated.

period are therefore needed to address neonatal mortality and morbidity.

Exclusive breastfeeding for the first months of life is one such intervention, which has been recommended in view of established benefits of reducing the risks of morbidity and mortality in the first 6 months of life.[3,4] However, there is little evidence about the effects of exclusive breastfeeding on neonatal mortality.[3,4]

Another intervention reported to be associated with improved newborn survival is early initiation of breastfeeding.[5–8] However, it has not been elucidated whether the benefits of early initiation are only mediated through increased exclusive breastfeeding, or are also through independent mechanisms such as earlier and more frequent exposure to colostrum, improved thermal status conferred through contact with the mother, strengthened gastrointestinal barrier resulting in decreased risk of microbial translocation, or improved nutritional or immunological status.[9–11]

Currently, only 50% of infants in the world are breastfed during the first hour of life.[12] Barriers to early initiation include facility practices leading to separation of mother and infant in the early hours after birth, tiredness after lengthy labour, caesarean sections, and cultural norms that lead mothers to discard colostrum and give other traditional foods and fluids. Concerted programmatic action is required to address this situation. A strong evidence base for the survival benefits of early initiation, with a better understanding of whether these benefits include independent effects beyond those conferred by improvements in exclusive breastfeeding, is necessary to increase investment in this intervention.

Data from randomised trials are not and will not be available since it would not be ethical to randomly assign infants to a delayed initiation of breastfeeding. Analyses of well designed cohort studies would greatly advance our understanding of the magnitude and extent of the protective effects of early initiation of breastfeeding.[9] We used data from a large cohort of mothers and infants who participated in three large neonatal vitamin A trials[13–15] in Ghana, India, and Tanzania for such analyses. We aimed to study the association between timing of breastfeeding initiation and post-enrolment neonatal and post-neonatal mortality up to 6 months of age. Our secondary objectives were to assess the relation between breastfeeding patterns and mortality, and whether the association between early initiation and mortality was modified by exclusive breastfeeding status.