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Timing of Breastfeeding Initiation and Exclusivity of Breastfeeding During the First Month of Life: Effects on Neonatal Mortality and Morbidity—A Systematic Review and Meta-analysis

Jehangir Khan · Linda Vesel · Rajiv Bahl · José Carlos Martines

Abstract The purpose of this study was to review the evidence on the effect of initiation of breastfeeding early after birth and of exclusive breastfeeding during the first month in reducing neonatal mortality and morbidity. We searched Cochrane and PubMed databases for all available papers addressing our review questions and identified eleven papers. Data were extracted using a standard abstraction form. Evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation system. Meta-analysis was done using STATA 11.0. Early initiation of breastfeeding was associated with a reduced risk of neonatal mortality. Initiating breastfeeding after the first hour doubled the risk of neonatal mortality. Exclusively breastfed neonates had a lower risk of mortality and infection-related deaths in the first month than partially breastfed neonates. Exclusively breastfed neonates also had a significantly lower risk of sepsis, diarrhea and respiratory infections compared with those partially breastfed. The pooled evidence indicates that substantial benefits in reducing neonatal mortality and morbidity can be achieved with effective promotion of early initiation of breastfeeding and exclusive breastfeeding during the first month of life.

Keywords Breastfeeding · Neonates · Mortality and morbidity

Introduction

Approximately 3 million newborns died worldwide in 2012 [1]. About 25–50 % of these deaths occurred on the first day and three quarters in the first week after birth [2, 3]. Although significant progress has been made in reducing newborn mortality over the past 20 years, with the neonatal mortality rate falling from 32 per 1,000 live births in 1990 to 21 per 1,000 live births in 2012 [1], this reduction has been slower than that in mortality of older children; newborn mortality now accounts for about 44 % of under-five deaths worldwide [1]. This proportion reaches more than 50 % in Eastern Asia and Latin America, where greater progress has been achieved in reducing overall child mortality [1]. Accelerating the reduction of newborn mortality is essential for countries to achieve Millennium Development Goal 4 (MDG4) of reducing under-five child deaths by two-thirds between 1990 and 2015 [4].

The identification of public health recommendations that are effective in reducing newborn mortality will assist countries in prioritizing their actions towards the achievement of MDG4. Interventions delivered early in the postnatal period have the highest potential for impacting mortality since they reach newborns when their risk of mortality is the highest. Early initiation of breastfeeding and exclusive breastfeeding in the first month of life is therefore two interventions which, if their impact on mortality is confirmed, can respond to this need.

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J. Khan (✉)
Faculty of Medicine, Lund University, Jan Waldenströms gata, 205 02 Malmo, Sweden
e-mail: doctorjkpk@yahoo.com

L. Vesel
Faculty of Epidemiology and Population Health, London School of Hygiene and Tropical Medicine, Keppel Street, London WC1E7HT, UK

R. Bahl · J. C. Martines
Maternal, Newborn, Child and Adolescent Health, World Health Organization, Avenue Appia 20, 202 Geneva, Switzerland

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Estimated rates of early initiation of breastfeeding, defined as initiation of breastfeeding within 1 h of birth, range from 42 % in Asia and Latin America to 49 % in Central and Eastern Europe and the Commonwealth of Independent States (CEE/CIS) [5].

Available data suggest that a high proportion of neonates are not exclusively breastfed during the first month of life. In India, for example, although breastfeeding is common at age 0–1 month, more than one-third of babies were given water or other supplements [6].

Although these behaviors are part of most intervention packages recommended for the reduction of newborn morbidity and mortality, no systematic review has been published to date on the effects of early initiation of breastfeeding and exclusive breastfeeding within the first month after birth on the risk for neonatal mortality and morbidity. We performed this review to examine the evidence on the prevention of newborn mortality and morbidity of two practices that are often promoted as part of essential newborn care: (1) early initiation of breastfeeding and (2) exclusive breastfeeding.

Methods

Search Strategy

The Cochrane database was searched on 20/01/2012 for systematic reviews on breastfeeding. We also searched PubMed on 03/02/2012 using a predefined search strategy (see "Appendix 1"). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed in reporting the information in this systematic review [7].

Selection of Studies

The titles of the papers were examined independently by two reviewers, who decided whether each publication was eligible for inclusion in the systematic review. In addition, the bibliographies of relevant articles were reviewed in an effort to identify more papers for potential inclusion. If there was any disagreement, the reviewers consulted each other to reach a consensus on eligibility. The aim of the systematic review was to describe the effect of (1) early versus late initiation of breastfeeding and (2) exclusive breastfeeding versus other types of feeding on neonatal mortality and morbidity (sepsis, respiratory, and gastrointestinal infections) among a normal population of infants. This was defined as infants who did not suffer from severe acute morbidity, congenital malformation or a level of prematurity that might impair feeding. For the same reason, studies which included only special subgroups such as low birth weight or preterm infants were excluded. Neonatal mortality or morbidity was defined as deaths or illness reported to have taken place within the first month after birth. Both experimental and observational studies were accepted for inclusion in the review.

Statistical Analysis

The two reviewers independently assessed the methodological quality of the selected trials and extracted the data using a standardized data extraction form. The data extracted included the author's name, year of publication, year the study was conducted, setting, type of study, study population, risk of potential bias, loss to follow up, information on comparison groups, exposed and unexposed groups, and effect size for different outcomes with 95 % confidence interval. Additional relevant information for three of the studies was obtained after correspondence with the authors Edmond [8] and Mullany [9] who provided adjusted data on neonatal mortality related to early versus late initiation of breastfeeding, and Victora [10] who shared adjusted data on the effect of exclusive versus partial breastfeeding on infection-related neonatal mortality. The Grading of Recommendations Assessment, Development and Evaluation (GRADE) system was used for examining the quality of evidence for the set of included studies [11]. A meta-analysis was performed using Stata 11.0. Pooled estimates (relative risks with 95 % CI) of the outcome measures were calculated using the generic inverse variance method with the "metan" command in Stata. The natural logarithm converted values of the relative risks and their CIs from the individual studies (adjusted for cluster design effect) were used for computing the pooled estimates. The fixed effects model was used for pooling the results of the individual studies, unless there was evidence of a high degree of heterogeneity between studies.

Results

The search of the Cochrane library identified 70 systematic reviews addressing breastfeeding questions. Only one review approached our area of interest but its focus was on the introduction of early additional food and fluids for healthy breastfed full-term infants [12], and thus did not address our questions.

Our PubMed search generated 9951 titles. The review of the titles yielded 758 titles with potential relevance to this review. The abstracts for those titles were then read and 123 were identified as potentially relevant. After reading the full texts of these papers, we identified 11 papers that were eligible for inclusion in this systematic review. Figure 1 summarizes the results from the searches.

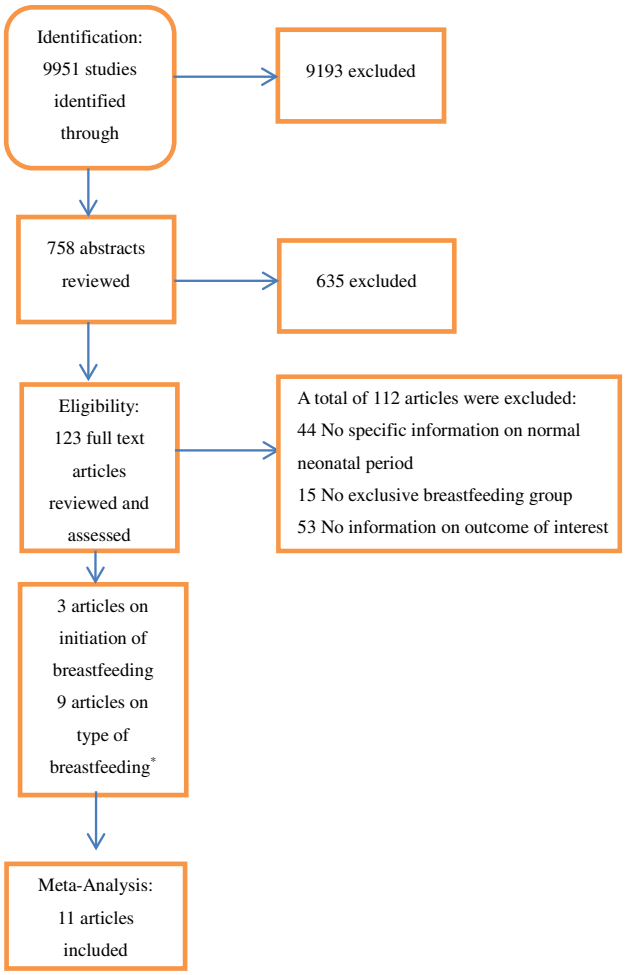

Fig. 1 Flow diagram of article selection in the systematic review of early initiation and type of breastfeeding on mortality and morbidity in neonates. *Edmond [9] presented information on both early initiation and type of breastfeeding

Three papers presented information on the effects of timing of initiation of breastfeeding on newborn morbidity and mortality, and nine papers examined the effects of type of breastfeeding in the first month on the risk of newborn mortality or morbidity. One paper by Edmond et al. [8] presented information on both timing of initiation and type of breastfeeding. All of the studies were observational and were published between 1982 and 2011. The 11 papers presented information from a total number of 10 studies—five conducted in Asia, four in America and one in Africa. India and the United States each contributed 2 studies. Four of the studies were conducted in community settings, four in settings that included health facilities and communities and two only in health facilities. Six studies reported on neonatal mortality as an outcome, two on sepsis and other infections, four on acute respiratory infection (ARI) and three on gastrointestinal infections.

The effects of timing of breastfeeding initiation on neonatal mortality are presented in Tables 1 and 2. Two studies [8, 9] examined the effect of initiation of breastfeeding within the first hour on neonatal mortality while three studies [8, 9, 16] examined the effect of initiation of breastfeeding within 24 h of birth on the same outcome. The overall quality of evidence was considered to be moderate as it was generated from well-conducted observational studies.

The methodological strengths of these studies are that they are large cohort studies with a very low loss to follow up. They had low risk of selection or measurement bias and most of the studies excluded multiple birth and very low birth weight or premature infants, aiming to reduce their possible confounding effect. Almost all studies included measures to adjust for confounding. All studies also included measures to reduce the risk of reverse causality—i.e., the risk that a pre-existing severe illness of the newborn delayed or prevented breastfeeding. The risk of reverse causality was significantly reduced by the exclusion from the studies of infants who were severely ill in early life. Most of the studies examining the risks of mortality went further in avoiding reverse-causality by also excluding newborns who died early—the timing of exclusion ranging from those who died within 2 days to those dying within 8 days of birth.

The pooled effect is presented in Table 1. It indicates that neonates who started to breastfeed after the first hour of life had twice (pooled OR 2.02, 95 % CI 1.40–2.93) the risk of dying in the first month of life compared to those breastfed within first hour. The meta-analysis also showed that neonates who were first breastfed after 24 h of birth were at a higher risk of mortality compared to those breastfed within the first 24 h (pooled OR 1.73, 95 % CI 1.42–2.11) (Table 2).

The effect of exclusive breastfeeding on neonatal mortality and morbidity is presented in Table 3. Two studies [8, 17] conducted in developing countries evaluated the effect of exclusive breastfeeding in the first month of life on the risk for neonatal mortality. The quality of evidence was graded as moderate as the studies were well-conducted observational studies. Mortality rates were significantly higher among partially breastfed neonates compared with those who were exclusively breastfed (pooled OR 3.67, 95 % CI 2.04–6.61). There was no significant difference in the effect of exclusive versus predominant breastfeeding on neonatal mortality (pooled OR 1.37, 95 % CI 0.96–1.96).

Three studies [10, 18, 19] from developing country settings examined the effect of exclusive compared with partial breastfeeding on infection-related neonatal mortality; the quality of evidence was graded as moderate as the studies were well-conducted observational studies. Partially breastfed neonates had a significantly higher risk of infection-related mortality than did exclusively breastfed neonates (pooled OR 3.81, 95 % CI 2.19–6.64).

The quality of evidence for all morbidity outcomes described below was considered to be low. The most

Table 1 Initiation of breastfeeding in the first hour after birth and risk of mortality in neonates: detailed GRADE table

Outcome	No. of studies	Design	Limitations of studies				Precision	Consistency	Generalizability/ directness	Overall Quality of evidence	Pooled effect size (95 % CI) OR Range of effect sizes (where pooled effect size not possible to ascertain)
			Allocation concealment (the two groups comparable and low risk of reverse causality)	Blinding or other approaches to reduce measurement bias	Loss to follow-up (<20 %)	Analysis intention to treat; cluster adjusted if applicable (adjusted for confounding)					
Mortality (Neonatal)	2 Edmond,Mullany	Observational	Comparable baseline and low risk reverse causality	Objective outcome, data on feeding initiation collected before outcome	<5 %	Yes	CI does not include null and CI limits indicate meaningful benefits	Both in the same direction as pooled effect but only 2 studies	Evidence from studies in population of interest in developing countries (Africa and Asia)	MODERATE	OR 2.02 (1.40–2.93)

Population: all neonates

Intervention (exposed in observational studies): initiation of breastfeeding within the first hour of life

Control (unexposed in observational studies): initiation of breastfeeding after the first hour of life

Table 2 Initiation of breastfeeding in the first 24 h after birth and risk of mortality in neonates

Outcome	No. of studies	Design	Limitations of studies				Precision	Consistency	Generalizability/ directness	Overall quality of Evidence	Pooled effect size (95 % CI) OR Range of effect sizes (where pooled effect size not possible to ascertain)
			Allocation concealment (the two groups comparable and low risk of reverse causality)	Blinding or other approaches to reduce measurement bias	Loss to follow-up (<20 %)	Analysis intention to treat; cluster adjusted if applicable (adjusted for confounding)					
Mortality (Neonatal)	3 Edmond, Mullany, Garcia	Observational	Comparable baseline and low risk reverse causality	Objective outcome, data on feeding initiation collected before outcome	<5 %	Yes in all studies	CI does not include null and CI limits indicate meaningful benefits	All evidence in same direction as the pooled effect	All studies from developing country settings (2 Asia, 1 Africa)	MODERATE	Fixed effect OR 1.73 (1.42–2.11)

Population: all neonates

Intervention (exposed in observational studies): initiation of breastfeeding within the first 24 h of life

Control (unexposed in observational studies): initiation of breastfeeding after the first 24 h of life

Table 3 Type of breastfeeding in the first month and risk of mortality and morbidity in neonates: detailed GRADE table

Outcome	No. of studies	Design	Limitations of studies				Precision	Consistency	Generalizability/ directness	Overall quality of evidence	Pooled effect size (95 % CI) OR Range of effect sizes (where pooled effect size not possible to ascertain)
			Allocation concealment (the two groups comparable and low risk of reverse causality)	Blinding or other approaches to reduce measurement bias	Loss to follow-up (<20 %)	Analysis intention to treat; cluster adjusted if applicable (adjusted for confounding)					
Mortality (Neonatal)	2	Observational	Low risk reverse causality	Objective outcome, data on feeding initiation collected before outcome data	<12 %	Yes	For partial breastfeeding, CI does not include null and limits of CI indicate substantial benefit	Both in the same direction as pooled effect for partial breastfeeding	Evidence from studies in developing countries—Africa and Asia.	MODERATE	Predominant versus exclusive OR 1.37 (0.96–1.96) Partial versus exclusive OR 3.67 (2.04–6.61)
Mortality by infections (Neonatal)	3	Observational	Groups comparable and low risk reverse causality [2]	Yes	<5 %	Yes (2/3)	CI does not include null and limits of CI indicate substantial benefit	Evidence from 3 studies in the same direction as the pooled effect	All 3 studies from developing country settings (Africa, Americas and Asia). Direct but one in <2 m	MODERATE	OR 3.81 (2.19-6.64)
Morbidity Sepsis and other infections	2	Observational	Groups comparable	Yes	<13 %	Not adjusted for confounding	CI does not include null and limits of CI indicate substantial benefit	Studies in the same direction as the pooled effect but only 2	2 studies from Asia, direct	LOW	OR3.46 (2.41–4.98)
Morbidity ARI	4	Observational	Differences in baseline [2], no data [2]	Yes	>20 % [1], 13 % [2], 1 % [1]	Yes (only in 2)	CI does not include null and limits of CI indicate substantial benefit	4 studies in the same direction as the pooled effect	2 in US, 1 Latin America, 1 Asia, 3 direct	LOW	Random effects ($I^{2=}$86 %) OR 1.69 (1.08–2.63)

Table 3 continued

Outcome	No. of studies	Design	Limitations of studies				Precision	Consistency	Generalizability/ directness	Overall quality of evidence	Pooled effect size (95 % CI) OR Range of effect sizes (where pooled effect size not possible to ascertain)
			Allocation concealment (the two groups comparable and low risk of reverse causality)	Blinding or other approaches to reduce measurement bias	Loss to follow-up (<20 %)	Analysis intention to treat; cluster adjusted if applicable (adjusted for confounding)					
Morbidity—Diarrhoea	3	Observational	Comparable at baseline [2], data not shown [1]	Yes	<13 %	Not adjusted for confounding	CI does not include null and limits of CI indicate substantial benefit	All 3 studies in same direction as the pooled effect	2 Asia, 1 LA, direct	LOW	Random effects ($I^2 = 88$ %) OR 2.97 (1.38–6.41)

Population: all neonates

Intervention (exposed in observational studies): exclusive breastfeeding in the first month of life

Control (unexposed in observational studies): predominant or partial breastfeeding in the first month of life

common flaw in the methodology, in addition to the absence of information generated from studies with an experimental design, was that some of the studies did not adjust for confounding despite baseline differences.

Two studies [18, 20] conducted in developing countries evaluated the effect of exclusive breastfeeding compared with partial breastfeeding on morbidity due to sepsis or other infections. Partially breastfed neonates had a significantly higher risk of sepsis or other infections compared with those who were exclusively breastfed (pooled RR 3.46, 95 % CI 2.41–4.98).

Four studies [13–15, 20], two of which were conducted in developing country settings [14, 21], examined the effect of partial versus exclusive breastfeeding on the risk of respiratory infections. Partially breastfed neonates had a significantly higher risk of suffering from ARI (pooled RR 1.69, 95 % CI 1.08–2.63, random effects model).

Three studies [13, 18, 20], all from developing countries, evaluated the effect of partial versus exclusive breastfeeding on diarrhea morbidity. Partially breastfed neonates had a significantly higher risk of having diarrhea (pooled RR 2.97, 95 % CI 1.38–6.41, random effects model).

Discussion

This systematic review consistently shows that delayed initiation of breastfeeding beyond the first hour of life is associated with an increased risk of neonatal mortality. It also shows that neonates who are partially breastfed are at greater risk of all-cause mortality and infection-related mortality in the first month of life compared with those who are exclusively breastfed. They are also at greater risk of sepsis, acute respiratory and gastrointestinal infections. The evidence available is too limited to allow the comparison of predominant versus exclusive breastfeeding in relation to morbidity and mortality in the first month of life.

We found no evidence of harm related to initiation of breastfeeding in the first hour and exclusive breastfeeding in the first month of life. On the other hand, the evidence of substantial benefits indicates that the effective promotion of these practices could lead to a major reduction in neonatal mortality, given the current low coverage rates. It has been estimated that one-fifth of all neonatal deaths could be prevented through early initiation of breastfeeding within the first hour after birth [21].

In addition to the benefits on newborn morbidity and mortality explored in this review, early initiation of breastfeeding has been reported to have other benefits for both mothers and infants including improved mother–child bonding and reduction in the risk of postpartum hemorrhage and infection, as it aids in the release of oxytocin,

increasing uterine activity and breast milk stimulation [22–24].

No experimental study could be identified addressing this topic. The meta-analysis relied on data collected in the context of large cohort studies that had many methodological strengths, such as the measures taken to reduce the risk of reverse causality and controlling for confounding. In doing so, newborns who were more vulnerable (very premature, low birth weight, severely ill, twins) were excluded. We believe that it is unlikely that the exclusions would lead to an over-estimate of breastfeeding's survival benefit. On the contrary, the available evidence suggests that the benefits of breastfeeding would have been even greater in the excluded infants [25].

The lack of experimental data on the issues addressed by this review is an important gap. We recommend that the effects of timing of breastfeeding initiation and exclusive breastfeeding in the first month of life be addressed in a randomized controlled trial. This can be ethically achieved through designs such as used by the Kramer et al. in Belarus [26] with intensive promotion of early initiation and exclusive breastfeeding in the intervention group compared with standard promotion. Even observational studies were few. We recommend that data from other cohorts be analyzed following the approach used by Edmond and Mullany [8, 9]. This would add significantly to the strength of the evidence and the robustness of estimates in future reviews.

The World Health Organization (WHO) and UNICEF recommend that breastfeeding be initiated within the first hour after birth (step 4) and newborns be given no other foods or liquids (step 6) as two of the "ten steps to successful breastfeeding" [27] that are at the core of the Baby Friendly Hospital Initiative [28]. The findings of this review support these recommendations and highlight the significant contribution that widespread adoption of these two practices could make to the achievement of MDG4.

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Conflict of interest None.

Appendix 1: PubMed Search

Systematic Review PICO Questions

1. In all newborn infants (P), does initiation of breastfeeding within the first hour after birth (I) compared with later initiation of breastfeeding (C) reduce the risk of mortality and morbidity during the neonatal period (O)?
2. In all newborn infants (P), does exclusive breastfeeding during the first month of life (I) compared with predominant (C) or partial breastfeeding (C) reduce the risk of mortality and morbidity during the neonatal period (O)?

Search Criteria

("breast feeding"[MeSH Terms] OR ("breast feeding"[MeSH Terms] OR ("breast"[All Fields] AND "feeding"[All Fields]) OR "breast feeding"[All Fields] OR "breastfeeding"[All Fields]) OR ("breast feeding"[MeSH Terms] OR ("breast"[All Fields] AND "feeding"[All Fields]) OR "breast feeding"[All Fields]) OR ("breast feeding"[MeSH Terms] OR ("breast"[All Fields] AND "feeding"[All Fields]) OR "breast feeding"[All Fields]) OR breastfed[All Fields] OR ("breast feeding"[MeSH Terms] OR ("breast"[All Fields] AND "feeding"[All Fields]) OR "breast feeding"[All Fields] OR ("breast"[All Fields] AND "fed"[All Fields]) OR "breast fed"[All Fields]) OR ("breast feeding"[MeSH Terms] OR ("breast"[All Fields] AND "feeding"[All Fields]) OR "breast feeding"[All Fields] OR ("breast"[All Fields] AND "fed"[All Fields]) OR "breast fed"[All Fields]) OR "colostrum"[MeSH Terms] OR ("colostrum"[MeSH Terms] OR "colostrum"[All Fields]) OR ("colostrum"[MeSH Terms] OR "colostrum"[All Fields] OR "colostrums"[All Fields])))

AND

(("infant, newborn"[MeSH Terms] OR ("infant"[MeSH Terms] OR "infant"[All Fields]) OR ("infant, newborn"[MeSH Terms] OR ("infant"[All Fields] AND "newborn"[All Fields]) OR "newborn infant"[All Fields] OR "newborn"[All Fields]) OR ("infant, newborn"[MeSH Terms] OR ("infant"[All Fields] AND "newborn"[All Fields]) OR "newborn infant"[All Fields] OR "newborns"[All Fields]) OR ("infant, newborn"[MeSH Terms] OR ("infant"[All Fields] AND "newborn"[All Fields]) OR "newborn infant"[All Fields] OR "neonate"[All Fields]) OR ("infant, newborn"[MeSH Terms] OR ("infant"[All Fields] AND "newborn"[All Fields]) OR "newborn infant"[All Fields] OR "neonates"[All Fields]) OR neonatal[All Fields] OR ("infant, newborn"[MeSH Terms] OR ("infant"[All Fields] AND "newborn"[All Fields]) OR "newborn infant"[All Fields] OR "baby"[All Fields] OR "infant"[MeSH Terms] OR "infant"[All Fields]) OR ("infant"[MeSH Terms] OR "infant"[All Fields] OR "babies"[All Fields]) OR "infant, newborn"[MeSH Terms])

AND

("breast feeding"[MeSH Terms] OR ("breast feeding"[MeSH Terms] OR ("breast"[All Fields] AND "feeding"[All Fields]) OR "breast feeding"[All Fields] OR ("breast"[All Fields] AND "feeding"[All Fields] AND "exclusive"[All Fields])) OR "breast feeding"[MeSH Terms] OR ("breast feeding"[MeSH Terms] OR ("breast"[All Fields] AND "feeding"[All Fields]) OR "breast feeding"[All Fields] OR ("breastfeeding"[All Fields] AND "exclusive"[All Fields])) OR "breast feeding"[MeSH Terms] OR ("breast feeding"[MeSH Terms] OR ("breast"[All Fields] AND "feeding"[All Fields]) OR "breast feeding"[All Fields] OR ("exclusive"[All Fields] AND "breast"[All Fields] AND "feeding"[All Fields]) OR "exclusive breast feeding"[All Fields]) OR "breast feeding"[MeSH Terms] OR ("breast feeding"[MeSH Terms] OR ("breast"[All Fields] AND "feeding"[All Fields]) OR "breast feeding"[All Fields] OR ("exclusive"[All Fields] AND "breastfeeding"[All Fields]) OR "exclusive breastfeeding"[All Fields]) OR initiate[All Fields] OR initiation[All Fields] OR begin[All Fields] OR beginning[All Fields] OR start[All Fields] OR starting[All Fields] OR started[All Fields] OR initiated[All Fields] OR begun[All Fields] OR initiating[All Fields])

NOT "addresses"[Publication Type] NOT "autobiography"[Publication Type] NOT "bibliography"[Publication Type] NOT "biography"[Publication Type] NOT "case reports"[Publication Type] NOT "clinical conference"[Publication Type] NOT "collected works"[Publication Type] NOT "comment"[Publication Type] NOT "congresses"[Publication Type] NOT "consensus development conference"[Publication Type] NOT "consensus development conference, nih"[Publication Type] NOT "dictionary"[Publication Type] NOT "directory"[Publication Type] NOT "editorial"[Publication Type] NOT "electronic supplementary materials"[Publication Type] NOT "ephemera"[Publication Type] NOT "festschrift"[Publication Type] NOT "guideline"[Publication Type] NOT "historical article"[Publication Type] NOT "in vitro"[Publication Type] NOT "interactive tutorial"[Publication Type] NOT "interview"[Publication Type] NOT "lectures"[Publication Type] NOT "legal cases"[Publication Type] NOT "legislation"[Publication Type] NOT "letter"[Publication Type] NOT "news"[Publication Type] NOT "newspaper article"[Publication Type] NOT "practice guideline"[Publication Type] NOT "review"[Publication Type]

Limits applied: humans, new born: birth-1 month.

Characteristics of the Included Studies

Arifeen 2001

Methods	Cohort study
Participants	1,677 singleton births included into the study born to a cohort of mothers resident in 5 sub-districts of Dhaka city, Bangladesh between November 1993 and June 1995
	Loss to follow up: <12 %
Intervention	Type of breastfeeding: [1] exclusively breastfed, [2] predominantly breastfed and [3] partial or not breastfed
Outcome	Neonatal mortality was attributed to all causes, ARI and diarrhea

Risk of bias

Items	Author's judgment	Description
Confounding	Differences in height and education	Controlled

Cushing 1997

Methods	Cohort study
Participants	1,202 babies born between January 1, 1988 and June 30, 1990 in Albuquerque, New Mexico, United States
	Inclusion criteria: Mother's age above 18 years, English speaking non-smoker and with access to telephone at home
	Exclusion criteria: If parents plan to put the infants in the full time day care and if the family plans to move from Albuquerque within the next 18 months
	Loss to follow up: 13 %
Intervention	Type of breastfeeding: [1] fully breastfed, [3] partially breastfed and [3] not breastfed
Outcome	Lower, upper and all respiratory illness

Risk of Bias

Item	Author's judgment	Description
Confounding	Differences in income and maternal education	Controlled
Misclassification	Mild	Possible due to recall (telephone interviews) and errors in mother's filling of the diaries

Clavano 1982

Methods	Cohort study
Participants	9,886 charts reviewed from babies delivered between January 1973 and April 1977 in a hospital in the Philippines Inclusion criteria: Newborns Exclusion criteria: No feeding record available, newborns deaths due to different causes like those acutely ill at birth, immature and having congenital abnormalities Loss to follow up: <3 %
Intervention	Type of breastfeeding: [1] breastfed, [2] mixed fed and [3] formula fed
Outcomes	Neonatal mortality and morbidity attributed to diarrhea, sepsis and oral thrush

Risk of bias

Item	Author's judgment	Description
Confounding	Groups reported as comparable	Data was not provided

Garcia 2011

Methods	Cohort study as part of randomized, placebo controlled trial for Vitamin A
Participants	10,464 newborns in a rural village in Tamil Nadu, India Inclusion criteria: Newborns between 2 and 28 days old and breastfeeding initiation time could be determined Exclusion criteria: Women delivered 20 km or more outside the study area, first visit >7 days after birth Loss to follow up: <1 %
Intervention	Breastfeeding initiation time: [1] <12 h after birth, [2] 12–24 h after birth and [3] >24 h after birth
Outcome	Neonatal mortality

Risk of bias

Item	Author's judgment	Description
Reverse causation bias	Mild	Risk reduced as deaths in the first 48 h excluded
Recall bias	Low	Only infants with visits done in the first 7 days after birth included
Confounding	Birth weight, sex, care at birth, vitamin A status, household head's occupation	Controlled

Edmond 2006

Methods	Cohort study as part of a large Vitamin A trial
Participants	10,947 newborns in rural Ghana Inclusion criteria: Infants surviving to day 2 and who were breastfed successfully Exclusion criteria: Multiple births, non-initiators and those interviewed outside the neonatal period Loss to follow up: 4.4 %
Intervention	Initiation of breastfeeding: [1] Early versus [2] late Type of breastfeeding: [1] Exclusive, [2] partial and [3] predominant
Outcome	Neonatal mortality

Risk of bias

Item	Author's judgment	Description
Reverse causality	Mild	Risk was reduced as all deaths in the 1st 2 days were excluded
Misclassification	Moderate	24 h recall for feeding status at 1 month, but 4 weeks recall for timing of initiation
Confounding	Gender, birth size, gestational age, congenital anomaly, health on day of birth, health at time of interview, mother's health at delivery, mother's age, parity, education, cash income, household water supply, place of defecation, antenatal visits, place of birth and presence of birth attendant	Controlled

Edmond 2007

Methods	Cohort study as part of a large Vitamin A trial
Participants	10,942 newborns in rural Ghana Inclusion criteria: Infants surviving to day 2 and who were breastfed successfully Exclusion criteria: Multiple births, non-initiators and those interviewed outside the neonatal period Loss to follow up: <5 %
Intervention	Initiation of breastfeeding: [1] Early versus [2] late Type of breastfeeding: [1] Exclusive, [2] partial and [3] predominant
Outcome	All infectious disease related neonatal mortality

Risk of bias

Item	Author's judgment	Description
Reverse causality	Mild	Risk was reduced as all deaths in 1st 2 days were excluded
Misclassification	Moderate	24 h recall for feeding status at 1 month, but 4 weeks for timing of initiation
Confounding	Gender, birth size, gestational age, congenital anomaly, health on day of birth, health at time of interview, mother's health at delivery, mother's age, parity, education, cash income, household water supply, place of defecation, antenatal visits, place of birth and presence of birth attendant	Controlled

Kasla 1995

Methods	Cohort study
Participants	537 newborns in a hospital in Bombay, India
	Inclusion criteria: Newborns
	Exclusion criteria: Birth weight <2,000 g, seriously ill in early neonatal period
	Loss to follow up: 12 %
Intervention	Type of breastfeeding: [1] Exclusive, [2] artificial and [3] mixed
Outcomes	Total morbidity and morbidity due to gastrointestinal and respiratory infections

Risk of bias

Item	Author's judgment	Description
Misclassification	Mild	Disease classification based on mother's recall and classification
Confounding	Possible confounding not described	Not adjusted in the analysis

Lopez-Alarcon 1997

Methods	Cohort study
Participants	216 newborns in a community and a hospital in Mexico City, Mexico
	Inclusion criteria: Singleton, full-term, healthy and weighing >2,500 g at birth
	Exclusion criteria: Congenital malformations and those who moved out
	Loss to follow up: 22 %
Intervention	Type of breastfeeding: [1] Exclusively breastfed, [2] partially breastfed and [3] formula fed
Outcomes	Diarrhea and acute respiratory infection related morbidity

Risk of bias

Item	Author's judgment	Description
Misclassification	Mild	Babies shifted during the 6 month period in the three feeding groups
		Misclassification of outcome unlikely as the diagnosis was clear and the physicians were blinded to the feeding history
Confounding	Possible—differences by feeding groups not described	Not controlled

Mullany 2008

Methods	Cohort study
Participants	23,662 newborns between 2002 and 2006 as part of a randomized control trial in a rural community in Southern Nepal
	Inclusion criteria: Newborns
	Exclusion criteria: If two or more of the following conditions were present
	1. Difficulty breathing
	2. Stiffness of the back or convulsions
	3. Dysentery
	4. Presence of watery stools five or more times within 24 h
	5. Severe chest in drawing
	6. Axillary temperature >37.8 °C
	7. Respiratory rate <70 breath/min
	Loss to follow up: 1.4 %
Interventions	Initiation on breastfeeding: [1] Early versus [2] late
Outcomes	Neonatal mortality and morbidity

Risk of bias

Item	Author's judgment	Description
Reverse causation bias	Low	Early deaths excluded
Recall bias	Low	Feeding classification based on 24 h recall
Confounding	Birth weight, gestation, sex, maternal literacy, chlorhexidine use, maternal hand washing, death of siblings, parity, maternal fever, ethnicity	Controlled

Sinha 2003

Methods	Case control study
Participants	933 infants born between 1990 and 1998 in a hospital in Boston, Massachusetts, United States
	Inclusion criteria: Infants delivered ≥37 weeks gestation with respiratory tract infection (LRTI but not pneumonia) diagnosed after discharge
	Exclusion criteria: Pneumonia and delivery <37 weeks
	Loss to follow up: 1 %
Intervention	Type of breastfeeding: [1] Exclusive breastfed, [2] mixed breastfed and [3] not breastfed
Outcomes	Neonatal morbidity

Risk of bias

Item	Author's judgment	Description
Selection bias or measurement bias	Mild	Electronic search of feeding records
Confounding and adjustment	Year of birth, season of birth, presence of siblings, and socioeconomic status	Controlled

Victora 1987

Methods	Case control study
Participants	510 Neonates in urban area in Southern Brazil
	Inclusion criteria: Infant deaths 7–364 days of life
	Exclusion criteria: Very low birth weight (<1,500 g), multiple births, more than 15 days in hospital immediately before death and congenital malformation or cerebral palsy
	Loss to follow up: <2 %

continued

Methods	Case control study
Intervention	Cases were deaths due to diarrhea, respiratory and other infections (meningitis, skin infections, measles, whooping cough, neonatal sepsis and tuberculosis
	Controls were neighbors aged 7–364 days
	Type of feeding: [1] Breastfeeding, [2] mixed and [3] artificial
Outcomes	Neonatal deaths

Risk of bias

Item	Author's judgment	Description
Interviewer bias	Mild	Reduced as information on outcome (diarrhea) was collected at the end of interview
Reverse causality	Mild	Feeding classified as status before illness
Confounding	Age, social status, birth weight, type of housing, piped water, birth interval, maternal education, family income	Controlled

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