

Meta Analysis

Effect of Early Initiation of Breastfeeding on Exclusive Breastfeeding and Stunting: A Meta-Analysis

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ABSTRACT

Background: Exclusive breastfeeding is the act of giving breast milk to babies from 0 to 6 months of age without giving any additional food or drinks, other than medicines. Stunting is a nutritional problem in which there is a linear growth disorder caused by chronic nutritional problems and recurrent infections characterized by a height-for-age index (HAZ) where the Z score is less than -2 SD. Early initiation of breastfeeding is one of the factors that influence exclusive breastfeeding and the incidence of stunting. This study aims to examine the effect of early initiation of breastfeeding on exclusive breastfeeding and the incidence of stunting.

Subjects and Method: Meta-analysis was carried out using the PRISMA flowchart and the PICO model (Population: mothers and children o to 59 months, Intervention: early initiation of breastfeeding, Comparison: no initiation of early breastfeeding, Outcome: exclusive breastfeeding and stunting). The databases used are PubMed, Science Direct, and Google Schoolar with keywords ((early breastfeeding initiation OR skin to skin contact OR breast crawl) AND (exclusive breastfeeding OR breast feeding) AND (stunting). There were 19 cross-sectional studies published in 2012-2022 that met the inclusion criteria. Analysis was performed with Revman 5.3.

Results: 19 articles with a cross-sectional study design originating from Bangladesh, China, Congo, Ecuador, Ethiopia, India, Indonesia, Malawi, Romania, Rwanda, Spain, and Tanzania involving 160,080 mothers and children o to 59 months. A meta-analysis of 11 cross-sectional studies showed that mothers and babies who initiated early breastfeeding were 2.16 times more likely to exclusively breastfeed than those who did not initiate early breastfeeding (aOR= 2.16, 95% CI= 1.76 to 2.65; p <0.001). A meta-analysis of 8 cross-sectional studies showed that mothers and babies who initiated early breastfeeding had a 0.89 times chance of not being stunted compared to those who did not initiate early breastfeeding (aOR= 0.89; 95% CI= 0.84 to 0.94; p < 0.001).

Conclusion: Early initiation of breastfeeding can increase exclusive breastfeeding. Early initiation of breastfeeding can reduce the incidence of stunting.

Keywords: exclusive breastfeeding, stunting incidence, early breastfeeding initiation, metaanalysis.

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BACKGROUND

Breastfeeding is the process of giving breast milk to babies which is a crucial process in

maternal and child health that starts when the baby is born until the child is two years old. WHO and UNICEF recommend exclu-

e-ISSN: 2549-0257 685 sive breastfeeding for children during the first 6 months after birth (WHO and UNI-CEF, 2016). Exclusive breastfeeding is the provision of breastmilk to babies from birth until they are 6 months old without additional food or other drinks, except medicines (Ministry of Health, 2021).

The prevalence of exclusive breast-feeding in the data (CDC, 2022) states that as many as 83.2% of babies born in 2019 received breastfeeding, but only 24.9% were given exclusive breastfeeding until the age of 6 months. The prevalence of exclusive breastfeeding in 57 low to middle income countries from 2010 to 2018 was only 45.7% (Zong et al., 2021). The prevalence of exclusive breastfeeding nationally states that the coverage of babies receiving exclusive breastfeeding in 2021 is 56.9% (Ministry of Health, 2021).

Adequate nutrition during the breast-feeding process plays a role in the growth and development of children. Babies who do not receive breast milk optimally have the potential to have less immunity to disease infections which can occur repeatedly so they are at risk of nutritional imbalance problems (Hadi et al., 2021). Stunting is a chronic nutritional problem that is a risk for every child to suffer in the form of growth retardation due to poor consumption patterns and repeated infections (Gebreayohanes and Dessie, 2022).

The prevalence of stunting in children under the age of 5 globally in 2020 is 22% or a total of 149.2 million children under five (World Health Organization, 2022). Stunting in Southeast Asia with a percentage of cases of 25% in 2021 (UNICEF East Asia and the Pacific Region, 2021). Meanwhile, the prevalence of stunting in toddlers nationally in 2021 will reach 24.4% (Ministry of Health RI, 2021).

Early breastfeeding initiation is a process of skin-to-skin contact between mother and baby and provides an opportunity for the baby with his instincts to be able to breastfeed immediately within the first hour of birth (JNPK-KR, 2017). Early breasftfeeding initiation increases the chances of exclusive breastfeeding, ensures that children get sufficient nutrition to prevent stunting (Susianto et al., 2022).

In this study, the authors were interested in conducting research through a meta-analysis regarding the effect of early initiation of breastfeeding on exclusive breastfeeding and the incidence of stunting using a meta-analysis.

SUBJECTS AND METHOD

1. Study Design

Meta-analysis was performed with the PRISMA flowchart using PubMed, Science Direct, and Google Schoolar databases. Keywords used (early breastfeeding initiation OR skin to skin contact OR breast crawl) AND (exclusive breastfeeding) AND (stunting). There were 19 studies with a cross-sectional study design published in 2012-2022 that met the inclusion criteria. Analysis was performed using RevMan 5.3.

2. Steps of Meta-Analysis

Meta-analysis is carried out through 5 steps as follows:

- Formulate research questions in PICO (Population, Intervention, Comparison, and Outcome).
- Searching for primary study articles from various databases including PubMed, Scopus, Science Direct, and Google Scholar.
- 3) Perform screening and conduct critical quality primary studies.
- 4) Perform data extraction and enter the estimated effect of each primary study into the RevMan 5.3 application.
- 5) Interpret the results and draw conclusions.

3. Inclusion Criteria

Full-text paper research articles using a cross-sectional study design. The relationship measure used is OR. Analysis using multivariate with adjusted Odds Ratio (aOR). The research subjects were mothers and children aged 0-59 months. Intervention in the form of early initiation of breast-feeding. One of the outcomes is exclusive breastfeeding and/ or stunting.

4. Exclusion Criteria

Articles published before 2012 and after 2022, and in languages other than English.

5. Operational Definition of Variables Exclusive breastfeeding is giving only breast milk to newborns until the age of the first 6 months of birth without additional food or other drinks except medicines.

Stunting is a linear growth disorder in children 0-59 months caused by chronic nutritional problems where the height-forage Z (HAZ) score is below minus two standard deviations (-2 SD) from the median population of the same age and sex.

Early Initiation of Breastfeeding is

process of skin contact between mother and baby so that the baby looks for the mother's nipple and starts breastfeeding for at least the first 1 hour after birth

3. Instrument

Quality assessment in this study used a critical appraisal checklist for cross-sectional studies published by the Joanna Briggs Institute.

4. Data Analysis

The articles in this study were collected using the PRISMA diagram and analyzed using the Review Manager 5.3 application by calculating effect sizes and heterogeneity to determine the combined research model and form the final results of the meta-analysis.

RESULTS

The search results for articles regarding the effect of early initiation of breastfeeding and the incidence of stunting yielded 19 articles using a cross-sectional study which can be seen in Figure 1. PRISMA Diagram.



Figure 2. Map of Research Area

The total articles in the initial search process were 2,054 articles with details of 248 Pub-Med database articles, 1,173 Science Direct database articles, and 633 Google Schoolar database articles. Furthermore, 1,687 articles were deleted with duplicate articles and 1,120 articles were filtered. From a total of 154 eligible full text articles, 19 were included in the synthesis meta-analysis. Full text articles included in the exclusion criteria are due to the following reasons:

- The intervention from the study was not initiation of early breastfeeding but skin contact intervention between mothers and other babies such as kangaroo mother care.
- 2. The outcome of the study was not exclu-

- sive breastfeeding but pre-lacteal feeding, and the outcome was not stunting but other nutritional problems such as wasting.
- 3. Does not include the Adjusted Odds Ratio (aOR) value as the result of multivariate logistic regression.

Figure 2. Shows the distribution area of primary study articles in 4 continents, namely 9 articles on the African Continent (Congo, Tanzania, Ethiopia, Malawi, and Rwanda), 7 articles on the Asian Continent (Bangladesh, China, India, and Indonesia), 2 articles on the Continent Europe (Romania and Spain), and 1 article Americas (Ecuador).

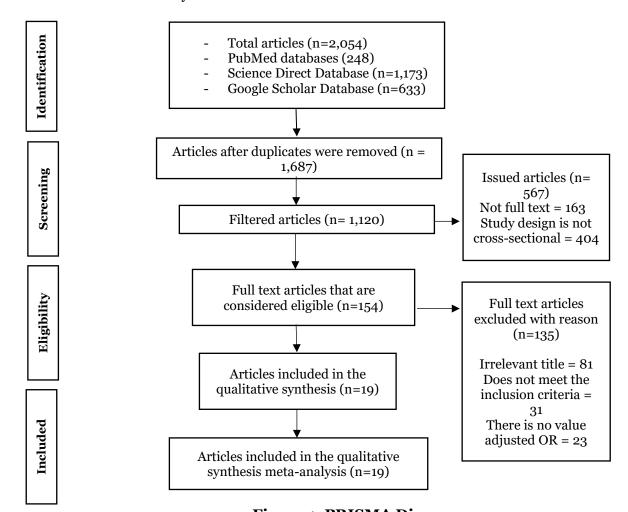


Figure 1. PRISMA Diagram

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Table 1. Assessment of article quality with a cross-sectional study design

	14010 1111	Cozma-					Jebena			Liben	Shi	Alrnom	Vienul	Muhim	Nsereko	Rah	Tariku	Tello	Martínez	Walter
No		Petrut et al. (2017)	et al.	et al.	et al.	et al.	et al. (2022)	et al.	et al.,	et al.	et al.	et al.	et al.	bula et al. (2019)	et al. (2022)	et al.	et al. (2017)	et al. (2022)	-vázquez et al.	
1	Were the criteria for inclusion in the sample clearly defined? Were the	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
2	research subjects and settings described in detail?	2	2	2	2	2	2	2	2	1	2	2	2	2	2	2	2	2	1	2
	Is exposure measured in a valid and reliable way? What are the	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
4	standard criteria used for objective condition measurement?	2	2	1	2	1	2	2	1	2	1	2	2	1	2	1	2	2	2	1
5	Were confounding factors identified? Was a strategy	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
6	for dealing with confounding factors stated? Are the results	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	measured in a valid and reliable way?	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
8	Has proper statistical analysis been used?	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
	Total of Score	16	16	15	16	15	16	16	15	15	15	16	16	15	16	15	16	16	15	15

Note: 2= Yes, 1= Can't tell, 0: No

Table 2. Study description of the effect of early breastfeeding initiation on exclusive breastfeeding

Author (year)	Country	Study Design	Sample	Population	Intervention	Comparison	Outcome
Cozma-Petruţ et	Romania	Cross-	1,399	Mother and baby	Early Breastfeeding	No Early Breastfeeding	Exclusive
al. (2021)		sectional		aged 0-23 months	Initiation	Initiation	breastfeeding
Duan et al.	China	Cross-	5,287	Mothers and babies	Early Breastfeeding	No Early Breastfeeding	Exclusive
(2022)		sectional		aged < 6 months	Initiation	Initiation	breastfeeding
Ervina et al,	Indonesia	Cross-	158	Mother and baby	Early Breastfeeding	No Early Breastfeeding	Exclusive
(2020)		sectional		aged 0-12 months	Initiation	Initiation	breastfeeding
Giang et al.	Vietnam	Cross-	1,812	Mother and baby	Early Breastfeeding	No Early Breastfeeding	Exclusive
(2022)		sectional		aged 0-24 months	Initiation	Initiation	breastfeeding
Gizaw et al.	Ethiopia	Cross-	258	Mother and baby	Early Breastfeeding	No Early Breastfeeding	Exclusive
(2017)		sectional		aged 0-24 months	Initiation	Initiation	breastfeeding
Jebena dan	Ethiopia	Cross-	649	Mother and baby	Early Breastfeeding	No Early Breastfeeding	Exclusive
Tenagashaw, (2022)		sectional		aged o-6 months	Initiation	Initiation	breastfeeding
Lenja et al. (2016)	Ethiopia	Cross-	396	Mothers and babies	Early Breastfeeding	No Early Breastfeeding	Exclusive
		sectional		aged < 6 months	Initiation	Initiation	breastfeeding
Li et al. (2021)	Cina	Cross-	494	Mother and baby	Early Breastfeeding	No Early Breastfeeding	Exclusive
		sectional		aged o-5 months	Initiation	Initiation	breastfeeding
Liben et al.	Ethiopia	Cross-	346	Mothers and babies	Early Breastfeeding	No Early Breastfeeding	Exclusive
(2016)	_	sectional		aged < 6 months	Initiation	Initiation	breastfeeding
Martínez-vázquez	Spanyol	Cross-	1,200	Breastfeeding	Early Breastfeeding	No Early Breastfeeding	Exclusive
et al. (2022)		sectional		mothers and babies during hospital care	Initiation	Initiation	breastfeeding
Shi et al. (2021)	China	Cross-	5,327	Mothers and babies	Early Breastfeeding	No Early Breastfeeding	Exclusive
		sectional		aged < 6 months	Initiation	Initiation	breastfeeding
Akram et al.	Bangladesh	Cross-	17,863	Mother and child	Early Breastfeeding	No Early Breastfeeding	Stunting
(2018)		sectional		aged 0-59 months	Initiation	Initiation	
Kismul et al.	Congo	Cross-	9,030	Mother and child	Early Breastfeeding	No Early Breastfeeding	Stunting
(2017)	· ·	sectional		aged 6-59 months	Initiation	Initiation	
Muhimbula et al.	Tanzania	Cross-	110	Mother and child	Early Breastfeeding	No Early Breastfeeding	Stunting
(2019)		sectional		aged 0-24 months	Initiation	Initiation	

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Penulis (Tahun)	Negara	Desain Studi	Sampel	Populasi	Intervensi	Comparison	Outcome
Nsereko et al. (2018)	Rwanda	Cross- sectional	1,634	Mother and child aged 0-24 months	Early Breastfeeding Initiation	No Early Breastfeeding Initiation	Stunting
Rah et al. (2015)	India	Cross- sectional	109,903	Mother and child aged 0-59 months	Early Breastfeeding Initiation	No Early Breastfeeding Initiation	Stunting
Tariku et al. (2017)	Ethiopia	Cross- sectional	1,295	Mother and child aged 6-59 months		No Early Breastfeeding Initiation	Stunting
Tello et al. (2022)	Ecuador	Cross- sectional	625	Mother and child aged 0-23 months	Early Breastfeeding Initiation	No Early Breastfeeding Initiation	Stunting
Walters et al. (2019)	Malawi	Cross- sectional	2,294	Mother and child aged 0-23 months	Early Breastfeeding Initiation	No Early Breastfeeding Initiation	Stunting

Assessment of study quality was carried out quantitatively and qualitatively, this study used a critical appraisal checklist cross-sectional study (Joanna Briggs Institute, 2017). Critical appraisal which consists of 8 questions. Each "yes" answer is given a score of 2, "unclear" answer is given a score of 1 and "no" answer is given a score of 0.

Table 1 shows the assessment of study quality by checklist of cross-sectional studies. Based on the answers from the quality assessment, the total score of the answers ranged from 15 to 16 scores, this indicates

that the quality of the article is feasible for meta-analysis.

The study description in Table 2 shows the effect of early initiation of breastfeeding on exclusive breastfeeding. There are 11 articles with a total sample of 17,326 breastfeeding mothers and babies aged 0 to 6 months.

The study description in Table 3 shows the effect of early breastfeeding initiation on the incidence of stunting. There are 8 articles with a total sample of 142,754 breastfeeding mothers and children aged o to 59 months.

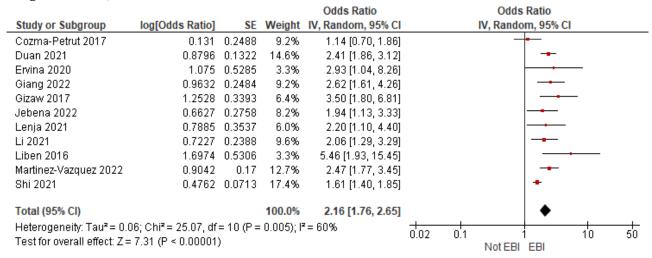


Figure 3. Forest Plot of the effect of early breastfeeding initiation on exclusive breastfeeding

The forest plot in Figure 3 shows that early initiation of breastfeeding is effective in increasing the likelihood of exclusive breastfeeding and the effect is statistically significant. Mothers and babies who initiate early breastfeeding have the possibility of exclusive breastfeeding 2.16 times compared to those who do not initiate early breastfeeding (aOR= 2.16; 95% CI= 1.76 to 2.65; p<0.001). The forest plot also shows heterogeneity in the estimation of the effect of early breastfeeding initiation between primary studies which were meta-analyzed with I²= 60% (p= 0.005) so that the analysis used the

Random Effect Model (REM).

The funnel plot in Figure 4 shows that the distribution of effect estimates between studies is not symmetrical, that is, there is more distribution to the right of the vertical line of average effect estimates than to the left. Thus, this funnel plot shows that there is publication bias, because the distribution of effect estimates is more to the right of the vertical line, the average effect estimate in the funnel plot is the same as the average effect estimate which is located to the right of the forest plot, the publication bias tends to overstate overestimate the true effect.

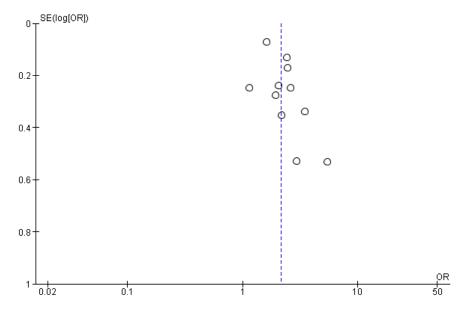


Figure 4. Funnel plot of the effect of early initiation of breastfeeding on exclusive breastfeeding

The forest plot in Figure 5 shows that early initiation of breastfeeding is effective in reducing the likelihood of stunting and this effect is statistically significant. Mothers and babies who initiate early breastfeeding have a 0.89 times chance of not having stunting compared to those who do

not initiate early breastfeeding (aOR= 0.89, 95% CI= 0.84 to 0.94; p<0.001). The forest plot also shows the heterogeneity of the estimated effect of early breastfeeding initiation between primary studies which was meta-analyzed with I^2 = 11% (p=0.34) so that the analysis used Fixed Effect Model.

				Odds Ratio	Odds Ratio
Study or Subgroup	log[Odds Ratio]	SE	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Akram 2018	-0.1393	0.069	18.4%	0.87 [0.76, 1.00]	-
Kismul 2017	-0.1985	0.0807	13.5%	0.82 [0.70, 0.96]	
Muhimbula 2019	-0.9163	0.5356	0.3%	0.40 [0.14, 1.14]	
Nsereko 2018	0.1484	0.1295	5.2%	1.16 [0.90, 1.50]	+-
Rah 2015	-0.1054	0.0413	51.4%	0.90 [0.83, 0.98]	=
Tariku 2017	-0.1054	0.121	6.0%	0.90 [0.71, 1.14]	 -
Tello 2022	-0.0408	0.2842	1.1%	0.96 [0.55, 1.68]	
Walters 2019	-0.1744	0.1468	4.1%	0.84 [0.63, 1.12]	
Total (95% CI)			100.0%	0.89 [0.84, 0.94]	•
Heterogeneity: Chi ^z =	7.86, df = 7 (P = 0 .	34); l² = 1	1%		
Test for overall effect:					0.2 0.5 1 2 5 Not EBI EBI

Figure 5. Forest Plot of the effect of early breastfeeding initiation on the incidence of stunting

The funnel plot in Figure 6 shows that the distribution of effect estimates between studies is asymmetric, that is, there is more distribution to the left of the vertical line of the average effect estimates than to the right. Thus this funnel plot shows that there is publication bias, because the distribution of effect estimates is more to the left of the vertical line, the average effect estimate in the funnel plot is the same as the average

effect estimate which is located to the left of the forest plot, the publication bias tends to overstate overestimate the real effect (over estimate).

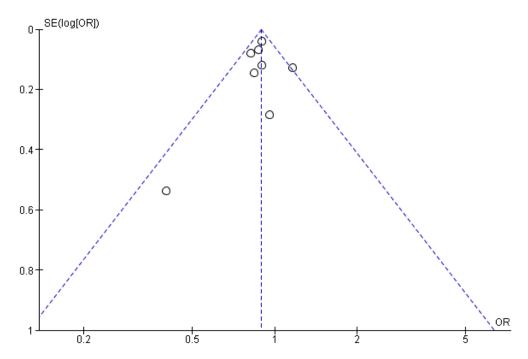


Figure 6. Funnel plot of the effect of early breastfeeding initiation on the incidence of stunting

DISCUSSION

Effect of early initiation of breastfeeding on exclusive breastfeeding

Exclusive breastfeeding is giving only breast milk to babies from 0 to 6 months of age without giving any additional food or drinks, other than medicines. Babies who do not receive exclusive breastfeeding have the potential to have reduced immunity against disease infections which can occur repeatedly, putting them at risk for chronic nutritional imbalance problems (Hadi et al., 2021).

Early initiation of breastfeeding can increase exclusive breastfeeding, this result is in accordance with the hypothesis. A meta-analysis of 11 cross-sectional articles with a total sample of 17,326 mothers and infants aged 0 to 6 months showed that mothers and babies who initiated early breastfeeding had 2.16 times the likelihood of exclusive breastfeeding compared to those who did not initiate early breastfeeding (aOR= 2.16,

95% CI= 1.76 to 2.65; p<0.001). The heterogeneity of effect estimates between primary studies shows I²= 60% (p=0.005) so the analysis uses the Random Effect Model (REM).

Early initiation of breastfeeding affects the secretion of the hormone's prolactin and oxytocin in the mechanism of the prolactin reflex and let down reflex which correlate with milk production during breastfeeding. Nipple stimulation during early initiation of breastfeeding stimulates the release of oxytocin which is associated with increased prolactin levels, reduced ACTH and cortisol levels (stress hormones and gastrointestinal hormones), increased bounding and reduced anxiety (Uvnas-Moberg et al., 2020).

Early initiation of breastfeeding reduces the risk of delaying lactogenesis II (Fok et al., 2019). After the baby is born and the placenta is released, there is a decrease in the levels of the hormones progesterone,

estrogen, HPL, and PIF and an increase in the hormone prolactin. Early initiation of breastfeeding stimulates an increase in the hormone prolactin which stimulates alveoli cells to secrete colostrum (G/slassie et al., 2021).

Huang et al., (2022) stated that the baby's ability to breastfeed is better obtained by early initiation of breastfeeding. Babies who carry out early initiation of breastfeeding have experience in finding the mother's nipple until they are able to suckle. The ability to breastfeed is related to the intrinsic reflexes of newborns in the form of rooting reflex, sucking reflex and swallowing reflex.

The results of this study are in line with those conducted by (Vila-Candel et al., 2018) which stated that mothers and babies who do IMD have a 0.1 times chance of exclusive breastfeeding (aOR= 0.1; 95% CI= 0.0 to 0.1). Research (Cato et al., 2019) also stated that early initiation of breastfeeding had an effect of 2.61 times on exclusive breastfeeding (OR= 2.61; 95% CI= 1.80 to 3.78). Similar research was also conducted in Ecuadorian by (Espin et al., 2021).

The results of this study are not in line with those conducted by (Nisrina et al., 2019) which stated that early initiation of breastfeeding was not related to exclusive breastfeeding (p= 0.574. Similar results were stated by (Syamsuriyati et al., 2019) early initiation of breastfeeding was not associated with the practice of exclusive breastfeeding.

The effect of early breastfeeding initiation on the incidence of stunting

Stunting is a nutritional problem where there is a linear growth disorder caused by chronic nutritional problems and recurrent infections characterized by a height-for-age index (HAZ) where the Z score is less than -2 SD (Chandra, 2020). Stunting has an impact on increasing morbidity and mortality, poor academic development and ability,

increased risk of infection and non-communicable diseases, insulin resistance, risk of diabetes, hypertension, dyslipinemia, and reproductive disorders (Soliman et al., 2021).

Early initiation of breastfeeding can reduce the risk of stunting, this result is in accordance with the hypothesis. The results of a meta-analysis of 8 articles with a total sample of 142,754 mothers and children o to 59 months related to the effect of early breastfeeding initiation on the incidence of stunting showed that mothers and babies who initiate early breastfeeding have a 0.89 times chance of not being stunted compared to those who do not initiate early breastfeeding (aOR= 0.89; 95% CI= 0.84 to 0.94; p<0.001). The heterogeneity of effect estimation between primary studies shows I2= 11% (p=0.34) so the analysis uses the Fixed Effect Model (FEM).

Early breastfeeding initiation is an early breastfeeding intervention. The nutritional content of breast milk changes according to each stage of lactation and the needs of the baby (Harmancioğlu and Kabaran, 2019). Smooth milk production can support exclusive breastfeeding and ensure that babies receive optimal nutrition and prevent disease infections and nutritional imbalance problems, including stunting (Susianto et al., 2022).

Total protein and immunoglobin levels decrease dramatically in infants within a few days after birth. Colostrum that babies receive from the time of initiation of early breastfeeding contains nutritional and immunological components that can increase intestinal maturation, infection resistance, and epithelial recovery after infection (Simanjuntak et al., 2018). Colostrum produces natural immunity in infants, reducing the risk of hypoglycemia and hypothermia (Gebreayohanes and Dessie, 2022).

Similar research results were found (Dahliansyah, 2020) which stated that infants who received early initiation of breastfeeding had a 0.3 times chance of not experiencing stunting (OR= 0.32; 95% CI= 0.12 to 0.84). Research (Roche et al., 2017) where early initiation of breastfeeding is a protective factor from stunting (OR= 0.58; 95% CI= 0.33 to 0.99; p<0.05). As well as research (Cato et al., 2019) which explained that delayed early initiation of breastfeeding had an effect on the incidence of stunting (OR= 2.61, 95% CI= 1.80 to 3.78).

Research results that were inconsistent were found in a study (Smith et al., 2021) in Tanzania which stated that early breastfeeding initiation was not related to stunting, but was associated with an increased risk of infant death in the first 6 months after birth. Research (Satapathy et al., 2021) in Odhisa also states that early initiation of breastfeeding is not a factor in the incidence of stunting, but the main determinant is exclusive breastfeeding. As well as stydy by Aakre et al. (2017) in Saharawi that early initiation of breastfeeding is not related to stunting.

The limitation of this study is that there is research bias because it only uses 3 databases, namely Google Scholar, PubMed, and Science Direct, thus ignoring research from other databases. As well as language bias where the selected articles are only published in English, thus ignoring articles published in other languages.

AUTHOR CONTRIBUTION

Tsamarah Iffah Zahrotin Nisa as the main researcher who chose the topic, conducted a search for data collection in this study. Rita Benya Adriani and Bhisma Murti conducted data analysis and reviewed research documents.

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CONFLICT OF INTERESTS

There is no conflict of interest in this study.

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