

Meta-Analysis the Effect of Exclusive Breastfeeding on Anemia in Children Under Five

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ABSTRACT

Background: The prevalence of iron deficiency anemia is still high, especially in children under five. One effort to prevent iron deficiency anemia is exclusive breastfeeding for newborns. This study aims to analyze exclusive breastfeeding on the incidence of anemia in children under five.

Subjects and Method: This study is a systematic review and meta-analysis, with PICO as follows: Population= toddlers aged <5 years; Intervention= exclusive breastfeeding; Comparison= non-exclusive breastfeeding; Outcome= iron deficiency anemia. The articles used in this study were obtained from several databases including PubMed, Springer Link, Science Direct, and Google Scholar, which were published from 2012 to 2022. The keywords to search for articles are as follows: "Children" AND ("exclusive Breastfeeding" OR "formula" OR "mixed feeding") AND (anemia OR "Iron deficiency"). The articles included in this study were full-text articles with a cross-sectional study design. Articles are collected using PRISMA flow diagrams. Articles were analyzed using the Review Manager 5.3 application.

Results: A meta-analysis of 9 cross-sectional studies from Ethiopia, Taiwan, Bangladesh and China concluded that exclusive breastfeeding is effective in reducing the risk of anemia in children under five. Toddlers who are exclusively breastfed have a risk of developing anemia 0.55 times compared to those who are not exclusively breastfed, and the reduced risk is statistically significant (aOR= 0.55; 95% CI= 0.32 to 0.92; p= 0.020).

Conclusion: Exclusive breastfeeding is effective in reducing the risk of anemia in children under five.

Keywords: exclusive breastfeeding, anemia, toddlers.

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BACKGROUND

Anemia is a condition in which the number of red blood cells (and resulting oxygen carrying capacity) is insufficient to meet the body's physiological needs (WHO, 2011).

According to WHO, in 2019, the global prevalence of anemia was 39.8% in children aged 6-59 months, or the equivalent of 269 million children who have anemia. The highest prevalence of anemia in toddlers is

in the African Region, which is 60.2%. Since 2000, the global prevalence of anemia in children under five has slowly decreased from year to year, from 48.0% to 39.8% and starting in 2010, the prevalence of anemia has stagnated. Anemia can affect cognitive and motor development in children, and reduce work capacity in adults, which can affect the country's economic development. Anemia is an indicator of malnutrition and poor health status (WHO, 2019).

Causes of anemia in children include iron deficiency, folate deficiency, vitamin B12 deficiency, hemoglobinopathy, infectious diseases such as malaria, tuberculosis, HIV, and parasitic infections (WHO, 2022). In several countries, especially malaria endemic areas, the prevalence of anemia in children caused by malaria infection is quite high. The most frequent cause of anemia in children globally is a problem of lack of nutritional intake, namely iron deficiency. It is estimated that around 50% of anemia in children is iron deficiency anemia (ADB) (Allali et al., 2017).

Children who get exclusive breast milk (ASI) for 6 months without being given other food and drink, the only source of iron they get is from breast milk. The iron content in breast milk ranges from 0.26–0.46 mg/L (Bzikowska-Jura et al., 2021). The need for iron in children aged 0–6 months with normal birth weight is 0.27 mg/day, which means that it is actually sufficient if only breast milk is given (Cai et al., 2017).

However, this is still controversial because it was found that the prevalence of anemia was still high in children aged 0–6 months who were exclusively breastfed (Krishnaswamy et al., 2017; Marol, 2021). There is research that the incidence of anemia is less experienced by children who receive formula milk or receive formula milk and breast milk compared to children who

receive exclusive breastfeeding (Ruangkit et al., 2021).

Various studies have been carried out with mixed results, but more in-depth analysis needs to be done to get conclusive results. Therefore, it is necessary to carry out a systematic analysis of relevant studies using meta-analysis to identify the effect of exclusive breastfeeding on the incidence of anemia in children under five.

SUBJECTS AND METHOD

1. Design Study

This research is a systematic review and meta-analysis, using PRISMA diagrams using databases including PubMed, Springer Link, Science Direct, and Google Scholar. The keywords to search for articles are as follows: "Children" AND ("exclusive Breastfeeding" OR "formula" OR "mixed feeding") AND (anemia OR "Iron deficiency"). There were 9 studies with a cross-sectional study design that met the inclusion criteria. Analysis was performed using Review Manager (revMan) 5.3.

2. Steps of Meta-Analysis

The meta-analysis was carried out through 5 steps as follows:

- 1) Formulating research questions using the PICO model (PICO as follows Population = toddlers aged <5 years. Intervention = exclusive breastfeeding. Comparison = Non-exclusive breastfeeding. Outcome = Iron deficiency anemia).
- 2) Searching primary study research articles from electronic databases and libraries.
- 3) Conducting screening and quality assessment of primary research articles.
- 4) Extracting and analyzing data into the RevMan 5.3 application.
- 5) Interpreting the results and draw conclusions.

3. Inclusion Criteria

The inclusion criteria in this study included research subjects who were toddlers aged <5

years, full paper articles with cross-sectional observational studies, the size of the relationship used was adjusted odds ratio (aOR), and the research outcome was iron deficiency anemia.

4. Exclusion Criteria

Exclusion criteria in this study included articles with statistical results reported in bivariate form, articles published in languages other than English, and before 2012.

5. Operational Definition of Variables

Iron deficiency anemia is a child under 5 years of age who has a hemoglobin level <110 g/L. Anemia is categorized into anemia and not anemia, with a categorical measurement scale.

Exclusive breastfeeding is breast milk given to babies from birth for 6 (six) months, without adding and/or replacing it with other food or drinks. Exclusive breastfeeding is categorized into exclusive breastfeeding and not exclusive breastfeeding, with a categorical measurement scale.

6. Instrument

The quality assessment in this study uses the assessment criteria from the Cross-sectional Study Checklist published by the Center for Evidence Based Management (CEBMA) (2014).

7. Data Analysis

The articles in this study were collected using the PRISMA diagram and analyzed using the RevMan 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 initial search process in the database yielded 1,302 articles, after the process of deleting published articles, 871 were found, with 52 of them meeting the requirements for a full text review. A total of 9 articles with cross-sectional studies which can be seen in Figure 1. PRISMA Diagram.

The regional map in Figure 2 shows the distribution of primary study articles on the African continent consisting of 5 studies from Ethiopia and 1 study from Nigeria, as well as 3 studies from the Asian continent consisting of China, Bangladesh and Taiwan (Figure 2).

Assessing the quality of research using the Center for Evidence Based Management (CEBM) (2014) consists of 12 questions. A total of 9 primary studies were assessed for study quality (Table 1).

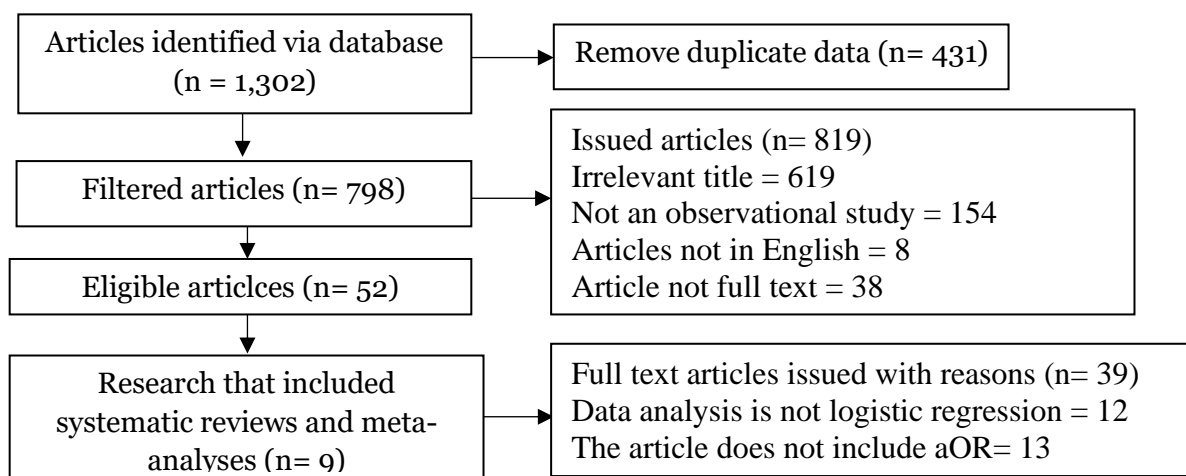


Figure 2. Map of the study area on the effect of bullying on the risk of suicide in adolescents

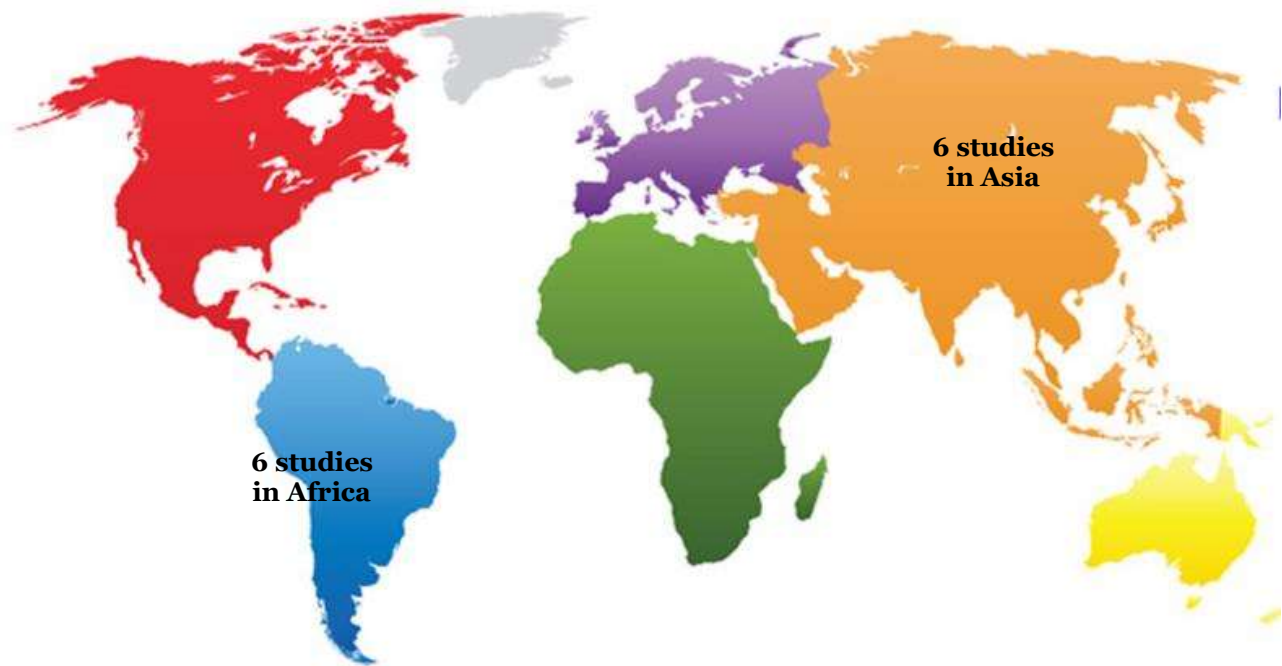


Figure 2. Map of research locations on the effect of bullying on the risk of suicide in adolescents

Table 1. Assessment of cross-sectional study quality in the meta-analysis

Primary Study	Questions Items												Total	
	1	2	3	4	5	6	7	8	9	10	11	12		
Asoba et al. (2019)	2	2	2	1	2	2	2	2	2	2	2	2	1	22
Aliyo et al. (2022)	2	2	2	1	2	2	2	2	2	2	2	2	2	23
Chen et al. (2019)	2	2	2	2	2	2	2	2	2	2	2	2	2	24
Gebreaweria et al. (2016)	2	2	2	2	2	2	2	2	2	2	2	2	2	24
Li et al. (2020)	2	2	2	2	2	2	2	2	2	2	2	2	2	24
Malako et al. (2018)	2	2	2	2	2	2	2	2	2	2	2	2	2	24
Mollah et al. (2021)	2	2	2	1	2	2	2	2	2	2	2	2	2	23
Osman et al. (2020)	2	2	2	2	2	2	2	2	2	2	2	2	1	23
Tekele et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	2	2	24

Question item description

- 1= Does the study formulate research questions (research problems) clearly?
- 2= Is the research method (study design) appropriate to answer the research question?
- 3= Are the methods for selecting research subjects clearly described?
- 4= Does the method of obtaining the sample lead to selection bias?
- 5= Is the sample representative of the target population of the study?

- 6= Was the sample size estimated taking into account the results of preliminary studies of statistical power?
- 7= Is the minimum response rate achieved?
- 8= Is the measurement (questionnaire) valid and reliable?
- 9= Was a statistical significance test carried out?
- 10= Did the researcher report the confidence interval?

- 11= Are there any confounding factors that have not been taken into account?
 12= Can the results be applied in practice/community?
- Note:**
 0 = No
 1 = Hesitant
 2 = Yes

Table 2. Description of the primary studies included in the meta-analysis

Author (Year)	Country	Study Design	Total Popul asi	P	I	C	O
Asoba et al. (2019)	Nigeria	Cross-sectional	1,227	Toddlers <5 years old	exclusive breastfeeding	Not exclusive breastfeeding	Anemia
Aliyo et al. (2022)	Ethiopia	Cross-sectional	350	Child <5 years old	exclusive breastfeeding	Not exclusive breastfeeding	Anemia
Chen et al. (2019)	Taiwan	Cross-sectional	2,804	1 year old toddler	exclusive breastfeeding	Not exclusive breastfeeding	Anemia
Gebreha weria et al. (2016)	Ethiopia	Cross-sectional	2,554	Toddlers aged 6-23 months	exclusive breastfeeding	Not exclusive breastfeeding	Anemia
Li et al. (2020)	China	Cross-sectional	5,529	Toddlers aged 6 to 71 months	exclusive breastfeeding	Not exclusive breastfeeding	Anemia
Malako et al. (2018)	Ethiopia	Cross-sectional	485	Toddlers aged 6 to 23 months	exclusive breastfeeding	Not exclusive breastfeeding	Anemia
Mollah et al. (2021)	Bangladesh	Cross-sectional	258	Toddlers aged <5 years in rural areas	exclusive breastfeeding	Not exclusive breastfeeding	Anemia
Osman et al. (2020)	Ethiopia	Cross-sectional	500	Toddlers aged <5 years	exclusive breastfeeding	Not exclusive breastfeeding	Anemia
Tekele et al. (2021)	Ethiopia	Cross-sectional	1,301	Toddlers aged 6-59 months	exclusive breastfeeding	Not exclusive breastfeeding	Anemia

A total of 9 cross-sectional observational study articles as a source of meta-analysis of the effect of exclusive breastfeeding on the

incidence of anemia in children under five (Table 2).

The size of the aOR relationship of 9

cross-sectional observational study articles as a source of meta-analysis of the effect of exclusive breastfeeding on the incidence of anemia in children under five (Table 3).

The forest plot in Figure 3 shows that exclusive breastfeeding is effective in reducing the risk of anemia in children under five. Toddlers who are exclusively breastfed have a risk of developing anemia 0.55 times compared to those who are not exclusively breastfed, and the reduced risk is statistically significant (aOR= 0.55; 95% CI= 0.32

to 0.92; p= 0.020). The forest plot also shows high heterogeneity of effect estimates between primary studies I²= 87%; p<0.001. Thus, the calculation of the average effect estimate is carried out using the random effect model approach.

The funnel plot in Figure 4 shows a fairly balanced distribution of effect estimates to the right and left of the average vertical line of estimates. Thus, the funnel plot does not indicate publication bias.

Table 3. Adjusted Odds Ratio (aOR) cross-sectional study of the effect of exclusive breastfeeding on the incidence of anemia in toddlers

Primary Study	aOR	95%CI	
		Lower Limit	Upper Limit
Asoba et al. (2019)	0.57	0.39	0.84
Aliyo et al. (2022)	0.39	0.11	2.09
Chen et al. (2019)	0.23	0.11	0.47
Gebrehaweria et al. (2016)	0.73	0.54	0.98
Li et al. (2020)	1.58	1.04	2.42
Malako et al. (2018)	0.38	0.21	0.71
Mollah et al. (2021)	0.88	0.32	2.2
Osman et al. (2020)	0.11	0.11	0.23
Tekele et al. (2021)	0.57	0.39	0.83
Asoba et al. (2019)	0.57	0.39	0.84

a. Forest Plot

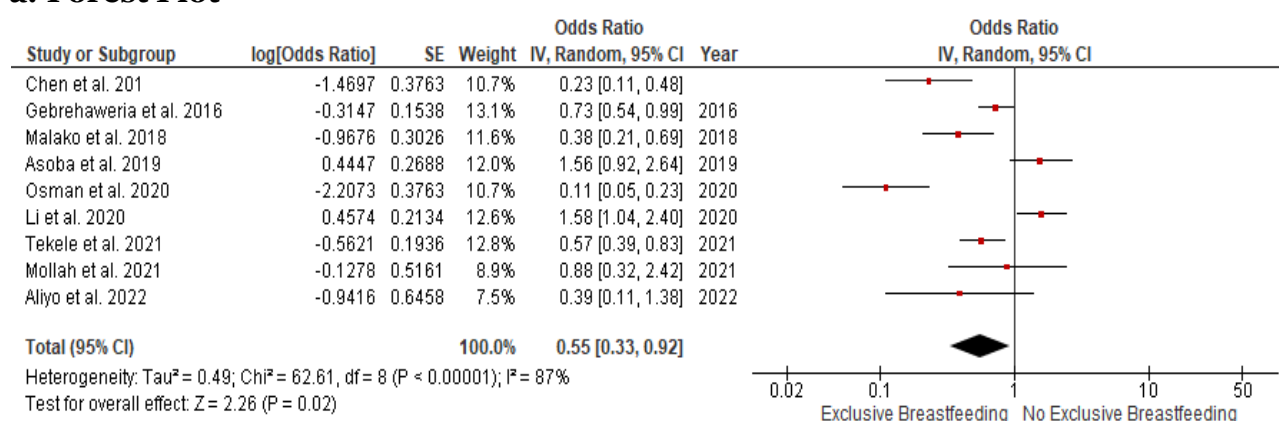


Figure 3. Forest plot of the effect of exclusive breastfeeding

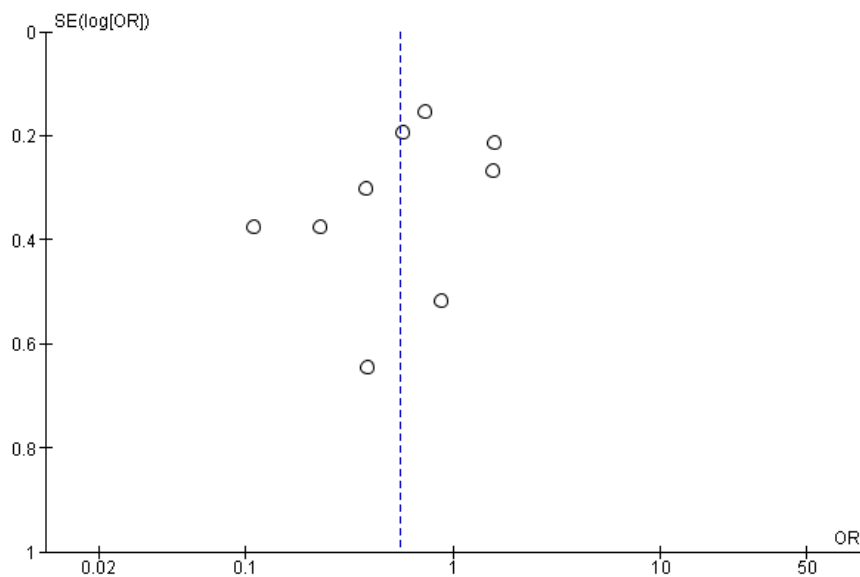


Figure 4. Funnel plot of the effect of exclusive breastfeeding on the incidence of anemia in toddlers

DISCUSSION

Systematic review and meta-analysis in this study were carried out with the aim of increasing the generalization of findings and obtaining convincing conclusions from the results of various similar studies regarding exclusive breastfeeding for the incidence of anemia in toddlers. Primary studies that met the criteria totaled 9 articles originating from the African continent, namely 6 studies from Ethiopia, and 3 articles originating from the Asian continent, consisting of 1 study from China, 1 study from Taiwan, and 1 study from Bangladesh.

A total of 9 cross-sectional observational research articles as a source of meta-analysis of exclusive breastfeeding on the incidence of anemia in toddlers. This study shows that exclusive breastfeeding is effective in reducing the risk of anemia in children under five. Toddlers who are exclusively breastfed have a risk of developing anemia 0.55 times compared to those who are not exclusively breastfed, and the reduced risk is statistically significant (aOR= 0.55; 95% CI= 0.32 to 0.92; p= 0.020). The forest plot also shows high heterogeneity of effect

estimates between primary studies $I^2= 87\%$; $p<0.001$. Thus, the calculation of the average effect estimate is carried out using the random effect model approach. This study shows that the distribution of effect estimates is fairly balanced to the right and left of the average vertical line of estimation. It indicates that there is no publication bias.

Supriyati's research (2018) showed that babies aged 6 months who were not exclusively breastfed had a risk of developing anemia by 2.16 compared to babies who were exclusively breastfed, and these results were statistically significant (OR= 2.16; 95% CI= 1.16 to 4.19; p = 0.022). This is in accordance with previous research, the factors that cause anemia in infants are exclusive breastfeeding, the sex of the baby, and the socioeconomic level of the family (Helmyati et al., 2007; Spinelli et al., 2005; Malkanthi et al., 2010; Laite et al., 2010; Laite et al., 2005; al., 2013).

Therefore, exclusive breastfeeding is recommended to be given to babies up to 6 months of age and by providing complementary foods at the beginning of 6 months of

age, after which it is continued by continuing to provide breastfeeding until 2 years of age (Sawitri, 2017). Infants who are not exclusively breastfed for 4–6 months have a risk of 18.4 times experiencing iron deficiency anemia compared to infants who are exclusively breastfed. Meanwhile, a history of exclusive breastfeeding and toddlers with poor nutritional status have a risk of 61 times and 10.4 times experiencing iron deficiency anemia (Sawitri, 2017). Exclusive breastfeeding by parents for 6 months to 24 months of age for toddlers aims to provide nutritional intake (Faiqah et al., 2018). Exclusive breastfeeding for newborns is an effort to prevent infectious diseases, malnutrition, and death in infants and toddlers (Ibrahim and Rahayu, 2021).

Prevention of iron deficiency anemia or iron deficiency in infancy plays an important role in the occurrence of long-term effects. Prevention that can be done includes primary and secondary prevention. Primary prevention includes counseling at health centers regarding adequate iron intake and providing iron supplementation and iron fortification in the diet. Secondary prevention includes screening and early diagnosis and appropriate management of iron deficiency. Sekartini et al. (2005) reported that giving iron supplementation to children who had received fortified formula from the age of 6 months did not differ significantly in increasing hemoglobin levels compared to the placebo group, so that in this group it was recommended to have a screening test at the age of 15-18 months.

This study concluded that exclusive breastfeeding is effective in reducing the risk of anemia in toddlers. This study recommends that researchers conduct further research regarding the effect of exclusive breastfeeding on the incidence of anemia in toddlers, so that it can reduce the severity and even death in toddlers with anemia.

AUTHOR CONTRIBUTION

Fikri Dian Dinu Azizah as the main researcher who chose the topic, conducted a search for data collection in this study. Eti Poncorini Pamungkasari and Bhisma Murti conducted data analysis and reviewed articles selected.

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This study is self-funded.

CONFLICT OF INTERESTS

There is no conflict of interest.

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