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Research

Relationship between Formula Milk and the Incidence Obesity in Children Under Five: Meta-Analysis

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ABSTRACT

Background: Obesity is a nutritional disorder that most often occurs in children. Obesity is associated with worse health outcomes in children, including asthma and sleep apnea. This study aimed to examine the relationship between formula feeding and obesity in children under five.

Subjects and Method: This was a meta-analysis study conducted by systematically reviewing articles from PubMed, Science Direct, Springer Link, and Google Scholar. The articles used in this research are articles that have been published from 2008-2016. The search for articles was carried out by considering the eligibility criteria using the PICO model, P: toddlers, I: formula feeding, C: breastfeeding, O: obesity. The key words for finding articles were as follows: "OR" Formula milk "OR" Infant Formula") AND" Breast Feeding "AND (Obesity OR" Body Mass Index"). The inclusion criteria used were full paper, used English, cohort and cross-sectional observational study design and the results reported were adjusted odds ratio. Articles were collected using PRISMA diagrams, and analyzed using the Review Manager 5.3 application.

Results: A total of 9 articles were conducted meta-analysis in this study with a sample size of 26,119. The results of the meta-analysis of the cohort study showed that formula feeding increased the incidence of obesity in children under five (aOR= 1.10; 95% CI= 0.78 to 1.56; p= 0.570). The results of the meta-analysis of cross-sectional studies showed that formula feeding increased the incidence of obesity in children under five (aOR= 1.25; 95% CI= 0.59 to 2.63; p= 0.560).

Conclusion: Formula feeding increases the incidence of obesity in children under five.

Keywords: Obesity, formula, toddlers, meta-analysis

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BACKGROUND

Childhood obesity is a major public health problem (Mallan et al., 2018). Obesity is the most common nutritional disorder in children. Preventing obesity in children should be a useful strategy in preventing future heart disease because weight loss interventions in obese children are difficult and rarely successful (Campoy et al. al., 2018).

In 2016, an estimated 38.3 million children were overweight or obese. The problem of obesity has grown to epidemic proportions, with more than 4 million people dying each year as a result of being overweight or obese in 2017 according to the global disease burden (WHO, 2020).

Obesity is associated with worse health outcomes in children, including asthma and sleep apnea and adults who are obese have an increased risk of cardiovascular disease (CVD), type 2 diabetes and some cancers. Therefore, reducing the risk of obesity is a priority for public health (Lanigan, 2020).

The World Health Organization (WHO) and the United Nations International Children's Fund (UNICEF) recommend early initiation of breastfeeding within 1 hour of birth, exclusive breastfeeding during the first 6 months of life, and introduction of nutritionally adequate and safe complementary foods at 6 months of age together with continued breastfeeding until 2 years of age or more. However, many babies and children do not receive optimal nourishment.

WHO is actively promoting breastfeeding as the best source of food for infants and young children, and is working to increase the rate of exclusive breastfeeding during the first 6 months to at least 50% by 2025 (WHO, 2020).

Formula milk is prepared as a nutritional substitute for breast milk, but due to differences in biology and constituents, it can cause obesity and growth disorders in infants (Synaii, 2019). The difference between formula milk and breast milk is that formula milk is just-food. In contrast, breast milk is a complex, living nutrient liquid containing antibodies, enzymes and hormones, all of which have health benefits (Savino et al., 2009). Children who are fed formula milk earlier after delivery are more likely to show rapid growth than children who are breastfed. Children who are fed formula milk are more often obese and come from families with lower social status than children who are breastfed alone (Toftlund et al., 2018).

SUBJECTS AND METHOD

1. Study Design

This was a meta-analysis research. Data search was carried out systematically and comprehensively through PubMed, Science Direct, Springer Link, and Google Scholar databases. Search keywords used were: "Children Under Five" AND ("non Breast Feeding" OR "Formula milk" OR "Infant Formula") AND "Breast Feeding" AND (Obesity OR "Body Mass Index").

2. Inclusion Criteria

The author developed the inclusion criteria, namely full text English articles with a cohort and cross-sectional study design. The research subjects were children aged 1 month - 5 years. The therapy given is formula milk. The analysis used was multivariate with adjusted odds ratio and the outcome was obesity.

3. Exclusion Criteria

The exclusion criterion in this study was a non cross-sectional study, articles that were not full text and published before 2005. Articles published in languages other than English and not a multivariate analysis study.

4. Operational Definition of Variables

The article search was carried out by considering the eligibility criteria defined using the PICO model. The population in the study were toddlers with intervention in the form of formula milk, comparison of breastfeeding and obesity outcomes.

Obesity is a body condition that is assessed based on indicators of body weight according to body length, which is more than 3 standard deviations above the median of the Child Growth Standard. The instrument used was a height measuring instrument, a weight measuring instrument with a continuous measuring scale.

Formula feeding is defined as a condition in which a child is given formula milk, either partially or totally at the age of less

than 6 months. The instrument was a questionnaire with a dichotomy measuring scale.

5. Data Analysis

Articles were collected using PRISMA diagrams, and analyzed using the Review Manager 5.3 application by calculating the effect size and heterogeneity to determine which research models were combined to form the final meta-analysis result.

RESULTS

The article review process can be seen in the PRISMA flow diagram Figure 1. This meta-analysis analyzes 9 primary studies conducted in the Netherlands, Sweden, China, Brazil, Australia and Indonesia.

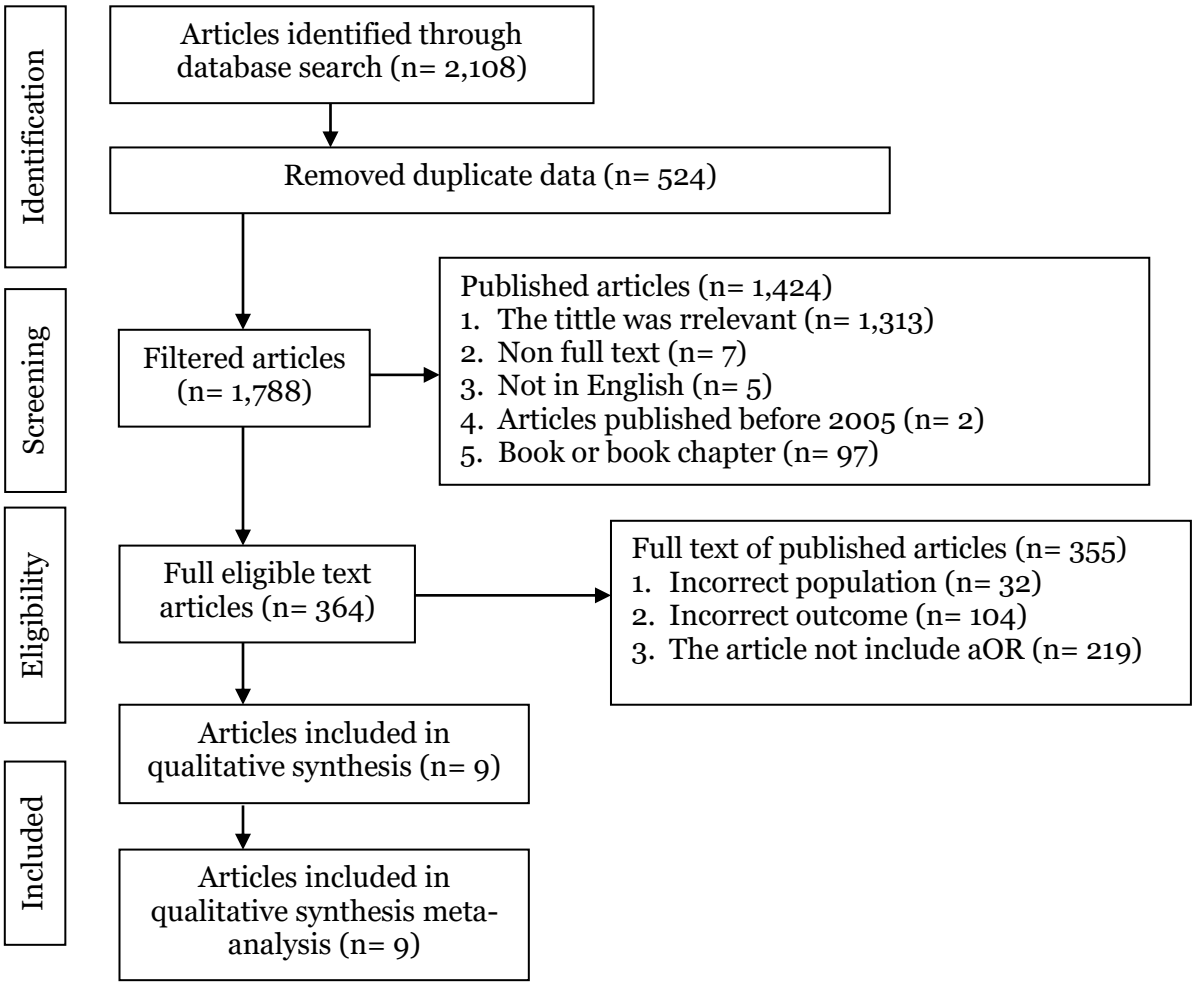

Figure 1. PRISMA flow diagram

The study quality assessment was carried out quantitatively. This study uses the Critical Appraisal Skills Program (CASP) for Cohort Study (Center for Evidence Based Management, 2014; NHS, 2004; 2006). Assessment of the quality of the study research was also carried out using critical appraisal tools from the center for evidence-based management in a cross-sectional design.

Table 1. Assessment of the quality of the cohort study

Primary Study	Criteria												
	1	2	3	4	5	6	7	8	9	10	11	12	Total
Contarato et al. (2016)	1	1	1	1	1	1	1	0	1	1	1	1	11
Huang et al. (2014).	1	1	1	1	1	1	1	1	1	1	1	1	12
Huss et al. (2008).	1	1	0	0	1	1	1	1	1	1	1	1	10
Kuperset al. (2015).	1	1	1	1	1	1	1	1	1	1	1	1	12
Pluymenet al. (2018)	1	1	1	1	1	0	0	1	1	1	1	1	10
Zhang et al. (2013).	1	1	1	1	1	1	0	0	1	1	1	1	10

Table 2. Assessment of the quality of the cross-sectional design study

Primary Study	Criteria												
	1	2	3	4	5	6	7	8	9	10	11	12	Total
Gopinath et al. (2012)	1	1	1	0	1	1	1	1	1	1	1	1	11
Mangrio et al. (2012)	1	1	1	0	0	0	1	1	1	1	1	1	9
Rachmi et al. (2016)	1	1	1	0	1	1	1	1	1	1	0	1	10

a. Formula feeding against obesity

Research related to the relationship of formula feeding with the incidence of obesity in children under five consisted of 9 articles from 4 continents, namely the Asian Continent (3 articles), the Americas (1 article), the European Continent (4 articles) and the Australian Continent (1 article). Nine articles prove the link of formula feeding to obesity.

b. Forest plot

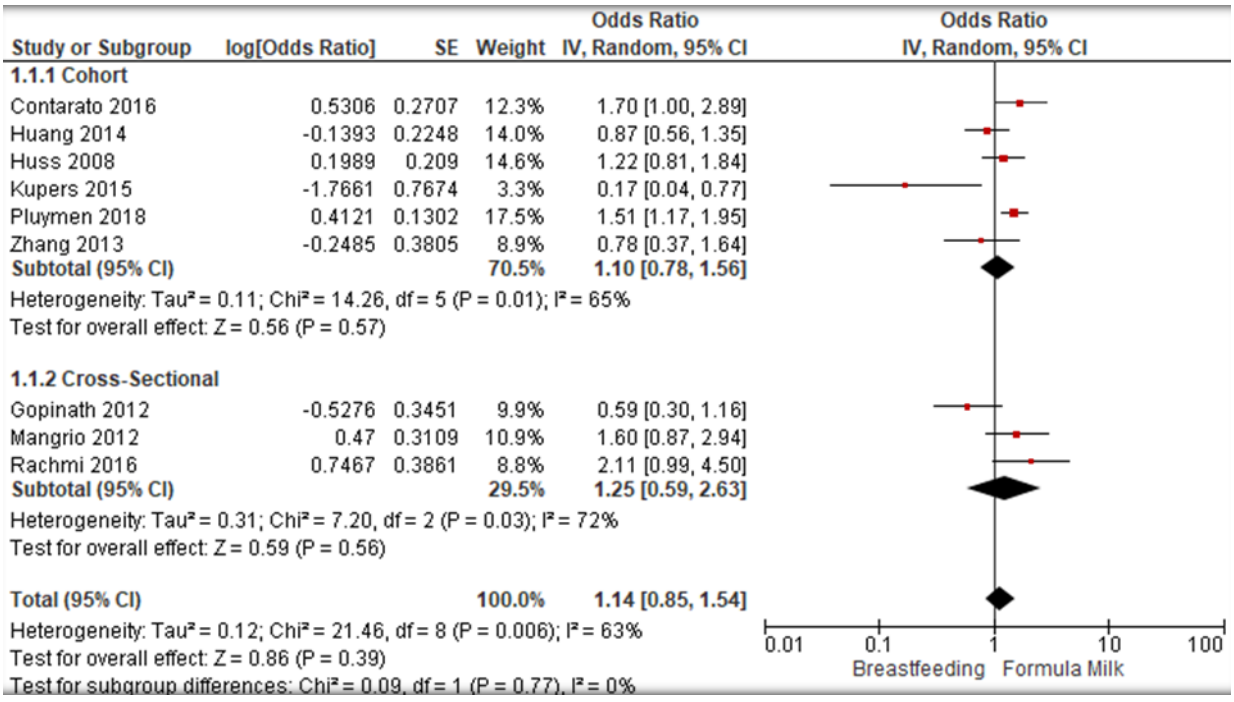

Figure 2. Forest plot of feeding relationship formula with the incidence of obesity in toddlers

Table 3. Descriptions of primary studies included in the meta-analysis

Author (Year)	Country	Study Design	Sample	P (Population)	I (Intervention)	C (Comparison)	O (Outcome)
Contarato *et al.* (2016).	Brazil	Cohort	435	Children 12-24 months of age.	Formula feeding.	Exclusive breastfeeding, juice, fruit or tea.	Overweight, obese.
Gopinath *et al.* (2012).	Australia	*Cross-sectional*	731	Children aged 3-4 years.	Children who are not exclusively breastfed, including formula feeding.	Exclusive breastfeeding and duration.	Difference in BMI and obesity.
Huang *et al.* (2014)	Cina	Cohort	1,093	Infants 3-12 months of age.	Formula feeding	Breastfeeding	Growth and obesity.
Huss *et al.* (2008)	Swedia	Cohort	7,356	Children aged 5 years.	Children who are not exclusively breastfed, including formula feeding.	Exclusive breastfeeding.	Obesity.
Kupers *et al.* (2015).	Belanda.	Cohort	2,475	Children aged 1-24 months.	Formula feeding.	Breastfeeding.	Growth patterns, obesity.
Mangrio *et al.* (2012).	Swedia	*Cross-sectional*	9,009	4 year old child.	Children who are not exclusively breastfed, including formula feeding.	Exclusive breastfeeding.	Obesity.
Pluymen *et al.* (2018)	Belanda	Cohort	2,611	Infants 3-12 months of age.	Providing formula milk and complementary foods from an early age.	Breastfeeding.	Obesity
Rachmi *et al.* (2016)	Indonesia	*Cross-sectional*	1,311	Children aged 2.0-4.9 years.	Complementary feeding before 6 months of age, including formula feeding.	Exclusive breastfeeding.	Being overweight and obese.
Zhang *et al.* 2013).	Cina	Cohort	1,098	2 years old children	Mixed breastfeeding includes formula feeding.	Exclusive breastfeeding.	Obesity

c. Funnel plot

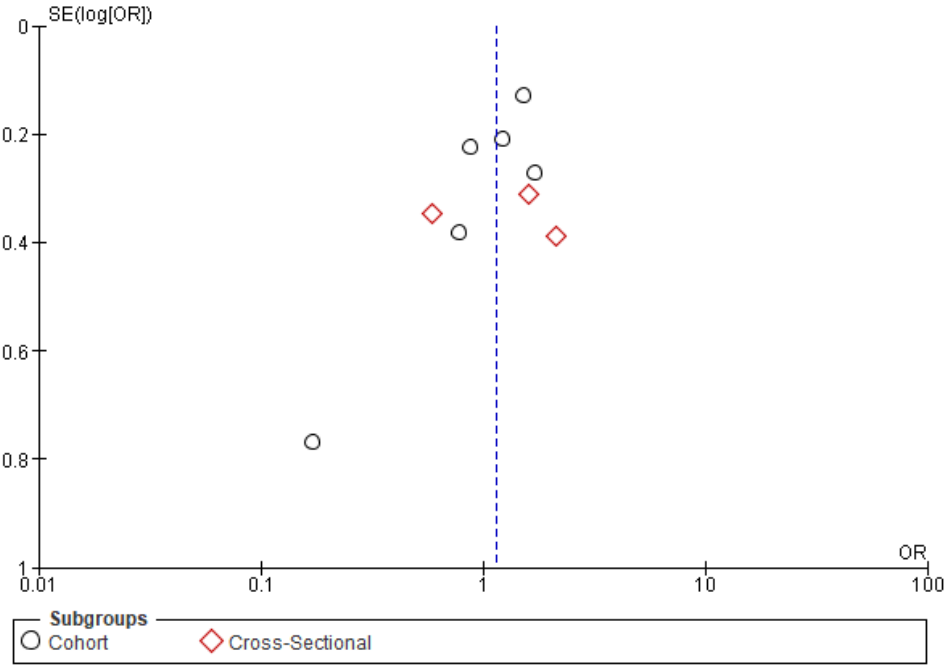

Figure 3. Funnel plot of formula feeding with the incidence of obesity in toddlers

The results from the forest plot (Figure 2) show that formula feeding increases the incidence of obesity in children under five. The meta-analysis results of the cohort study showed that formula feeding increased the incidence of obesity in children under five by 1.10 times compared to breastfeeding (p= 0.570). The heterogeneity of the research data shows I^2= 65% so that the distribution of the data is declared heterogeneous (random effect model).

The results of the meta-analysis of cross-sectional studies showed that formula feeding increased the incidence of obesity in children under five by 1.25 times compared to breastfeeding (p= 0.560). The heterogeneity of the research data shows I^2= 72% so that the distribution of the data is stated to be heterogeneous (random effect model).

The funnel plot (figure 3) shows that the plots on the right and left are not symmetrical with each other and do not form an inverted funnel, with 5 plots on the right and 4 plots on the left. The plot on the left of the graph appears to have a standard error between 0.2 and 0.8 and the plot on the right has a standard error between 0 and 0.6. This indicates that there is a publication bias in the study.

DISCUSSION

This systematic study and meta-analysis research raises the theme of formula feeding on the incidence of obesity in children under five. The independent variable analyzed was formula feeding.

This meta-analysis study was conducted using a study that controls the confounding factor which can be seen from the study inclusion requirements, namely multivariate analysis and the statistical result reported is the adjusted odds ratio (aOR). Estimates of the combined relationship between formula feeding and the inci-

dence of obesity in children under five were processed using the RevMan 5.3 application. The results of the systematic study and meta-analysis are presented in the form of a forest plot and a funnel plot.

Formula feeding against obesity

The results of the forest plot indicate that formula feeding increases the incidence of obesity in children under five. The results of the meta-analysis of the cohort study showed that formula feeding increased the incidence of obesity in infants by 1.10 times compared to breastfeeding and the meta-analysis of cross-sectional studies showed that formula feeding increased the incidence of obesity in children under five by 1.25 times compared to breastfeeding.

A study by Hopkins et al. (2015) which aims to determine the effect of feeding the type of milk during infants on child recovery shows that formula feeding is associated with faster weight gain and height than breastfeeding (p = 0.001). This study is in line with the research of Synaii et al. (2019) which aims to compare the growth patterns of formula-fed and breast-fed babies in Iran. The results showed that BMI was significantly higher in the infant formula group (p = 0.020).

The meta-analysis research conducted by Owen et al. (2005) stated that formula feeding was associated with a slightly higher BMI than those who received breast milk (p= 0.002). Other research conducted by Beckett and Meldrum (2018) shows that there is evidence that unhealthy feeding practices, namely the introduction of solid food too early and formula feeding are predictive factors for obesity in early childhood.

Formula-fed babies grow differently from breastfed in that they are heavier after four to six months of age. This difference should be anticipated to limit formula feeding or dietary intake (Dietitians of Canada and Canadian Pediatric Society, 2010). Formula milk has a higher protein content than breast milk. The results showed a positive relationship between initial protein intake and obesity, there was a higher BMI in the high protein intake compared to the low protein group (Davanzo et al., 2016).

Exclusive breastfeeding is recommended until the baby is around six months old. Therefore, giving formula milk before 6 months of age is not recommended (Wilson, 2008). In the recommended pre-age formula feeding, several things should be considered, namely when there is a medical contraindication to breastfeeding, the milk production is really low and has fully informed the mother that bottle feeding is a better alternative in certain circumstances.

Effective intervention programs can facilitate improvements in feeding practices to further support healthy care among infants and toddlers (Taha et al., 2020). Factors that help mothers not to provide other than breast milk until the age of six months is a trusting relationship with health workers, consistent advice and recommendations so that the mother accepts it easily and enthusiastically (Walsh et al., 2015).

Policies to overcome the burden of malnutrition and the threat of obesity and obesity rests on three main pillars. The first is scaling up specific nutrition or direct interventions, which include infant and young child feeding, changes in communication behavior to improve nutritional status, micronutrient supplementation, and treatment of severe acute malnutrition. The second objective is to cultivate or be sensitive to indirect nutritional interventions. These include food insecurity alleviation, promotion of agricultural nutrition-friendly, aquaculture, introducing nutrients into

social safety net programs, sanitizing water, and promoting preventive measures against overweight and obesity. The third objective is to promote multi-sectoral efforts and coordination of all actions at the national level (Ahmed, 2017).

The limitation in this study is that there is a publication bias that is shown in the funnel plot, language bias occurs because in this study the selected articles are only those published in English so that they ignore articles that use other languages, as well as search bias because in this study the researchers only used 4 databases (PubMed, Science Direct, Springer Link, and Google Scholar) thus ignoring other search sources.

AUTHOR CONTRIBUTION

Elma is the principal researcher who selects topics, searches and collects research data. Yulia Lanti and Bhisma Murti played a role in analyzing data and reviewing research documents.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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