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Meta-Analysis

The Effect of Maternal Anemia on Low Birth Weight: Meta Analysis

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ABSTRACT

Background: : Low birth weight is still a global public health problem that is associated with a number of risks. One of the factors that influence the occurrence of LBW is anemia. This study was aimed to estimate the risk of anemia in pregnant women to the incidence of LBW in several countries.
Subjects and Method: This study is a meta-analysis with PICO, Population: pregnant women. Intervention: maternal anemia. Comparison: no maternal anemia. Result: LBW. The articles used in this study were obtained from three databases namely Google Scholar, Pubmed, and Science Direct with a cohort study design from 2015 to 2022 that reported Adjusted Odds Odds Ratio in its multivariate analysis. The selection of articles was carried out using the PRISMA flow chart. Analysis of articles using the Review Manager 5.3 application.
Results: A total of 9 cohort studies involving 75,807 pregnant women from Taiwan, China, Japan, India, Bangladesh, Iran, and Colombia were selected for systematic review and meta-analysis. The data collected showed that pregnant women who were anemic during pregnancy had a 1.3 times higher risk of giving birth to babies with low birth weight than non-anemic mothers, but this result was not statistically significant (aOR= 1.30; 95% CI= 0.89 to 1.88; p= 0.170). With an intuitive index of 84%, so the effect between the studies is heterogeneous.
Conclusion: Mothers who experience anemia during pregnancy have a risk of giving birth to babies with low birth weight.

Keywords: anemia, pregnancy, low birth weight

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BACKGROUND

Low birth weight (LBW) is defined by the World Health Organization (WHO) as babies born weighing 2,500 grams. Low birth weight is still a global public health problem and is associated with a number of short-term and long-term consequences. It is estimated that 15% to 20% of all births worldwide are LBW, which represents more than 20 million births per year. There is considerable variation in the prevalence of low birth weight across regions and within countries. However, the majority of low birth weight births occur in low- and middle-income countries, especially in the most vulnerable populations (WHO, 2014).

The results of the regional survey stated that the prevalence of LBW in South Asia reached 28%, 13% in sub-Saharan Africa and 9% in Latin America (WHO,

2014). Meanwhile, according to UNICEF (2019) the prevalence of LBW in Southeast Asia reached 14.9%. In Indonesia, the prevalence of LBW in 2018 was 6.2%, this data tends to decrease when compared to previous years (Ministry of Health RI, 2018). However, this has not reached the global target of reducing prevalence of 2.7% per year until 2025 (WHO, 2014).

One of the parameters of newborn health is weight. Babies born with low birth weight have a higher risk of being born prematurely, born with jaundice disorder, and have lower heart rate, reflexes, muscle tone, and respiration (APGAR) scores when compared to babies born with normal birth weight. While the long-term impacts of LBW include not optimal child growth and development, the risk of heart disease to decreased intelligence and after adulthood will be at risk of experiencing hypertension, heart disease, and diabetes (Mitao et al., 2016). In addition, low birth weight accounts for 60-80% of all neonatal deaths and has a risk of death 20 times greater than normal weight infants (Putri, 2019).

One of the factors associated with the occurrence of low birth weight is anemia. Maternal anemia is a maternal condition with hemoglobin (Hb) less than 11 g/dl in the blood. WHO estimates that 40% of pregnant women worldwide are anemic. In Indonesia, maternal anemia reached 37.1% in 2013 and increased to 48.9% in 2019 (Basic Health Research, 2018).

If pregnant women experience anemia, it will cause metabolic disorders and asiutero-placental oxygen which results in stunted fetal growth so that it is very risky for low birth weight to occur. In addition, mothers who experience anemia are more prone to infection, the risk of bleeding before and during childbirth. This can certainly make a big contribution to the mortality rate, both the mortality rate and the infant mortality rate (Nur, 2018). The influence of anemia in pregnant women on the incidence of LBW encourages the need for information about how serious the problem is. Therefore, this analysis was carried out to determine the risk of anemia in pregnant women in LBW infants in several countries.

SUBJECTS AND METHOD

1. Study Design

This study is a meta-analysis study. The articles used in this study were obtained from several databases, namely Google Scholar, PubMed, and Science Direct between 2020 and 2021. The selection of articles was carried out using Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA). Keywords to search for articles are as follows: “Anemia” OR “Low Hb” AND Maternal OR Pregnancy AND Neonatal Outcome OR Low Birth Weight.

2. Inclusion Criteria

The inclusion criteria in this study article are: full-text article using an English-language cohort study design, study subjects are pregnant women who experience anemia, the results are low birth weight babies, multivariate analysis with Adjusted Odds Ratio (aOR) to measure the effect estimated.

3. Exclusion Criteria

The exclusion criteria in this study article are: articles published in languages other than English and articles published in the last 10 years.

4. Operational Definition of Variable

The search for articles used in this study was adjusted to the eligibility criteria using PICO. The population in this study were pregnant women with the intervention experiencing anemia during pregnancy, the ratio of not experiencing anemia during

pregnancy, and the results given were low birth weight.

Maternal anemia are pregnant women with hemoglobin (Hb) conditions in the blood less than 11 g/dl. The instruments used are medical records and data collection records for officers related to the diagnosis of maternal anemia. The measurement scale is categorical.

Low birth weight are infants born weighing 2,500 grams in the medical records and officer data collection records related to the diagnosis of low birth weight babies. The measurement scale is categorical.

5. Instrument Study

The study was guided by the PRISMA flow chart and quality assessment using the Critical Assessment Skills Program (CASP, 2018).

6. Data Analysis

The data in this research article will be analyzed using the RevMan 6.4 application. The results of data processing are then presented in the form of forest plots and funnel plots to determine the effect size and heterogeneity. Fixed Effect Model is used for homogeneous data, while Random Effect Model is used for heterogeneous data across studies.

RESULTS

The search for articles in this study was conducted through several journal databases, including Google Scholar, Pubmed, and Science Direct. The review process for related articles can be seen in the PRISMA flow chart in Figure 1. The initial search for supporting articles in this study found 275,555 articles. Then the articles are sorted according to topic, substance of analysis and full text, and 22 articles were obtained. Of the 22 articles, the most relevant were selected, which were 9 articles.

Articles that fulfilled the quality assessment were then included in a quantitative synthesis using meta-analysis. It can be seen in Figure 2 that the research articles came from four continents, namely East Asia (Taiwan, China, Japan), South Asia (India, Bangladesh), West Asia (Iran) and South America (Colombia). Table 1 showed the quality of the study and Table 2 showed that 12 articles from the cohort study provide evidence of the relationship of maternal anemia to the incidence of low birth weight.

Based on the results of the Forest Plot, this study showed that pregnant women who were anemic during pregnancy had a 1.3 times greater risk of having a low birth weight baby than mothers who did not have anemia, but this result was not statistically significant (aOR= 1.30; 95%). CI= 0.89 to 1.88; p= 0.170). The heterogeneity of the research data showed I^2= 84% so that the distribution of the data was declared heterogeneous and used the Random Effect Model.

The results of the Funnel Plot showed that there was a potential for publication bias which was indicated by an overestimate effect which is characterized by an asymmetric distribution between the right and left plots. There were four plots on the right, three plots on the left, and two plots touching the vertical line. The plot on the right side of the chart has a standard error (SE) between 0 and 0.8. The plot on the left side of the graph has a standard error (SE) between 0 and 0.4.

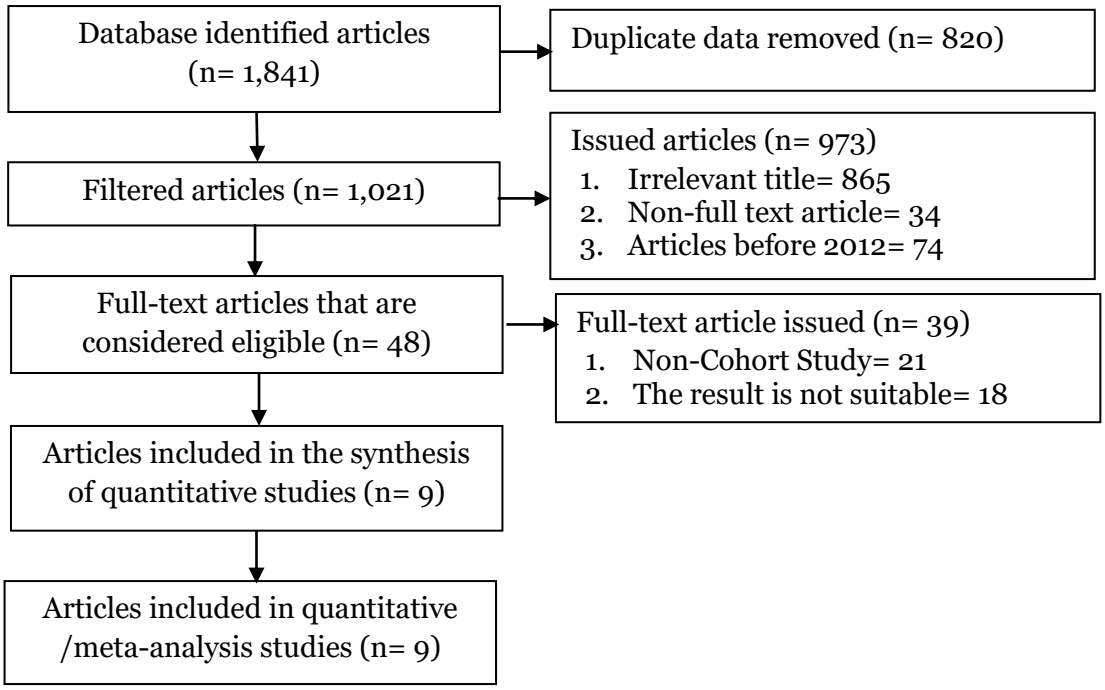

Figure 1. PRISMA flow Chart

Figure 2. Study area map of maternal anemia on LBW

Table 1. Assessment of study quality published by the Critical Appraisal Skills Program (CASP)

No.	Indicator	Publication (Author and Year)								
		Biswas et al. (2019)	Carpenter et al. (2021)	Chu et al. (2020)	Heydar-pour et al. (2019)	Jwa et al. (2015)	Masu-kume et al. (2015)	Nair et al. (2016)	Puerto et al. (2021)	Sun et al. (2021)
1.	Does this research have a clear research focus?	1	1	1	1	1	1	1	1	1
2.	Is the cohort study process clearly defined?	1	1	1	1	1	1	1	1	1
3.	Is exposure measured accurately so as to minimize bias?	1	1	1	1	1	0	1	1	1
4.	Are the results measured accurately to minimize bias?	1	1	1	1	1	1	1	1	1
5.	Do the authors identify important confounding factors? Were confounding factors considered in the design or analysis?	1	1	1	1	1	1	1	1	1
6.	Is the follow-up on the subject complete? Is the follow-up period sufficient?	1	1	1	0	1	1	1	1	1
7.	Are the results of the study using AOR?	1	1	1	1	1	1	1	1	1
8.	Are the research results accurate?	1	1	1	1	1	1	1	1	1
9.	Do you believe the results of this study?	1	1	1	1	1	1	1	1	1
10.	Can this research be applied to the local population?	1	1	1	1	1	1	1	1	1
11.	Are the results of this study in accordance with the existing evidence?	1	1	1	1	1	1	1	1	1
12.	Do the results of this study have any implications?	1	1	1	1	1	1	1	1	1
Total		**12**	**12**	**12**	**11**	**12**	**11**	**12**	**12**	**12**

Note:
1: Yes; 0: No

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

Author (Year)	Country	Study Design	Sample		P Population	I Intervention	C Comparison	O Outcome	aOR (95%CI)
			Mother Who Gives Birth	Maternal Anemia					
Biswas et al. (2019)	India	Prospective cohort	1,976	988	Registered postnatal mothers from April 2015 – March 2017	Experiencing anemia during pregnancy	Not experiencing anemia during pregnancy	LBW, Primi Parity, Premature	2.11 (1.51 to 2.95)
Carpenter et al. (2021)	Bangladesh	Prospective cohort	1,665	114	List of postnatal mothers between July 2019 and April 2020	Experiencing anemia during pregnancy	Not experiencing anemia during pregnancy	LBW	0.96 (0.63 to 1.45)
Chu et al. (2020)	Taiwan	Retrospective cohort	13,026	1,795	List of postnatal mothers from 2001 to 2016	Limits of anemia Hb levels in women	Not experiencing anemia	LBW, Feto-placental Vasculogenesis and Angiogenesis	0.88 (0.69 to 1.12)
Heydarpour et al. (2019)	Iran	Retrospective cohort	2,742	756	List of maternal pregnancies in 2017	Experiencing anemia during pregnancy	Not experiencing anemia during pregnancy	LBW, Neonatal mortality, Premature, Cesarean delivery	0.66 (0.46 to 0.93)
Jwa et al. (2015)	Japan	Retrospective cohort	1,986	907	List of pregnancies between 34 and 41 weeks in 2010 and 2011	Experiencing anemia during pregnancy	Not experiencing anemia during pregnancy	LBW, Placenta Weight	2.00 (1.30 to 3.10)

Table 3. Description of Main Studies Included in the Meta-Analysis Primary Study

Author (Year)	Country	Study Design	Sample		P Population	I Intervention	C Comparison	O Outcome	aOR (95%CI)
			Mother Who Gives Birth	Maternal Anemia					
Masukume et al. (2015)	China	Prospective cohort	5,609	125	List of pregnancies in New Zealand, Australia, England and Ireland	Experiencing anemia (hemoglobin <11g/dL)	Not experiencing anemia during pregnancy	LBW, Placental Weight	1.31 (0.62 to 2.76)
Nair et al. (2016)	India	Retrospective cohort	1,007	651	List of pregnant women from January-	Experiencing anemia during pregnancy	Not experiencing anemia during pregnancy	PPH, LBW, Prenatal Death	6.19 (1.44 to 26.71)
Puerto et al. (2021)	Colombia	Prospective cohort	1,218	930	Pregnant women who give birth in 2021 are 18-42 years old	Experiencing anemia during pregnancy and low Ferritin	Not experiencing anemia during pregnancy	LBW	0.48 (0.28 to 0.82)
Sun et al. (2021)	China	Retrospective longitudinal cohort	46,578	7,555	List of postnatal mothers since	Experiencing anemia during pregnancy and low Ferritin	Not experiencing anemia during pregnancy	LBW, Premature	0.74 (0.63 to 0.88)

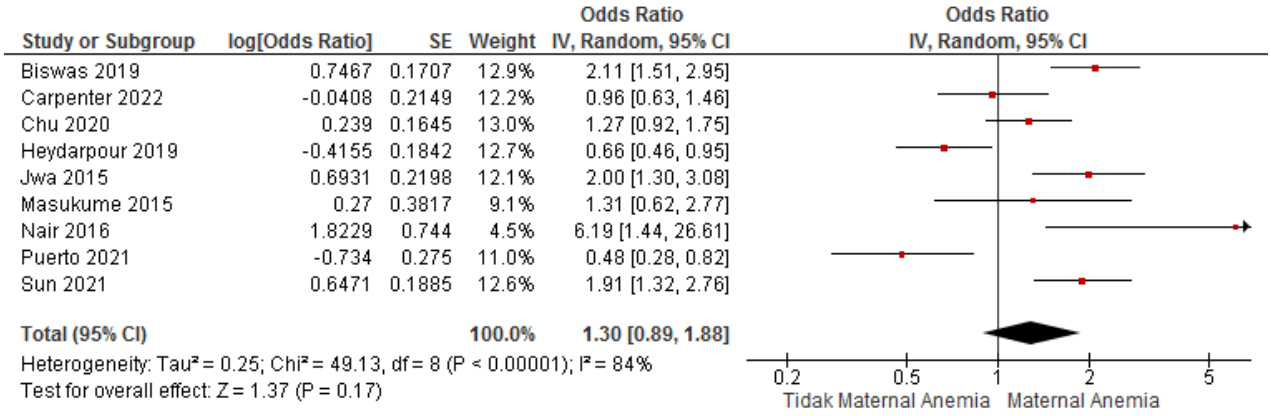

Figure 3. Forest Plot of the Effect of Maternal Anemia on LBW

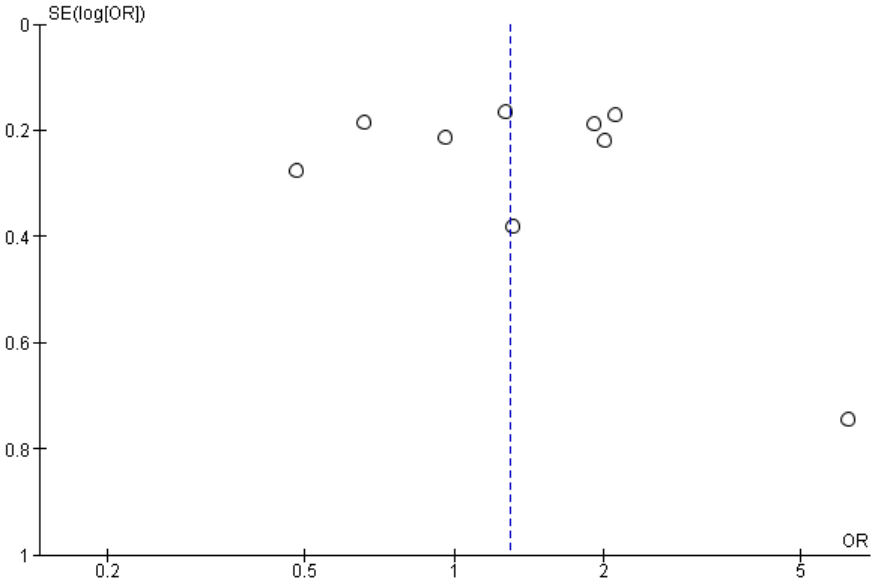

Figure 4. Funnel Plot of the Effect of Maternal Anemia on LBW

DISCUSSION

Based on the results of this systematic study and meta-analysis, anemia in pregnant women increased the incidence of LBW by 1.30 times compared to non-maternal anemia (aOR= 1.30; 95%CI= 0.89 to 1.88). According to WHO, anemia in pregnancy is defined as a hemoglobin level of less than 11 g/dl. In developing countries anemia is a major problem and is associated with increased maternal and child mortality, preterm delivery, low birth weight babies, and others. This is in line with a study conducted by Anwar in 2019 at the Department of Gynecology and Obstetrics of Civil Servant Shifa Karachi Pakistan which stated that anemia in pregnant women increased the risk of LBW by 2.48 times. In addition to increasing the risk of LBW, the study stated that low maternal hemoglobin levels were associated with an increased risk of preterm delivery, APGAR score <5 in the first 1 minute and IUGR (Anwar et al., 2019).

The biggest cause of anemia is due to iron deficiency or often referred to as iron deficiency anemia. Iron deficiency anemia is a type of anemia that is often found in developing countries due to poor eating habits, impaired iron absorption due to helminth infections, malaria, and so on. There are two factors that cause iron

deficiency, namely direct causative factors and indirect causative factors. The first direct factor is that the iron content in food is not enough, this is due to the low iron content in food, improper food processing, and low socioeconomic status. The second direct cause is low Fe absorption, this situation is caused by indirect causes, namely the composition of food is less diverse and there are substances that can inhibit the absorption. The third direct cause is the increased need for Fe, this is caused by indirect causes due to physical growth and conditions of pregnancy and lactation. The last direct cause is blood loss, which is caused by indirect causes due to chronic bleeding, parasites, infections and poor health services (Kadir, 2018).

Anemia is a decrease in the capacity of the blood to carry oxygen caused by a decrease in the number of red blood cells or a decrease in the concentration of hemoglobin in the blood circulation. During pregnancy, there is an increase in plasma which results in an increase in blood volume in pregnant women. The increase in plasma is not in balance with the number of red blood cells, resulting in a decrease in hemoglobin levels. Therefore, pregnant women must have adequate iron intake by consuming iron tablets of at least 90 tablets during pregnancy in addition to iron intake from food. In a study conducted by Bhaskar in 2015 stated that supplementation of blood- supplemented tablets in pregnant women is associated with the incidence of LBW. Pregnant women who consume less than 90 blood- supplemented tablets for 90 days have a nearly 3 times higher chance of giving birth to LBW babies compared to mothers who take blood-supplemented tablets for more than 90 days (Bhaskar et al., 2015).

The results showed that the nutritional status of malnutrition is a risk factor for anemia in pregnant women. Nutritional status is a person's health condition as a result of food consumption, absorption and use of nutrients (Angraini et al., 2020). A study in Ethiopia stated that pregnant women who consume a varied diet (milk, foods of animal origin, fruits and vegetables rich in vitamin A) have a lower risk of anemia, low birth weight and premature birth (Zerfu et al., 2016). Improving the nutritional status and health of pregnant women is the best way to overcome anemia in pregnant women. Fetal nutrition depends entirely on maternal nutrition, therefore, pregnant women must receive adequate nutriation. Insufficient energy and protein intake in pregnant women can cause Chronic Energy Deficiency (CED) (Angraini et al., 2020). According to a study conducted by Feresu, Harlow and Woelk (2015), it is stated that if the mother's upper arm circumference is less than 28.5, the risk of experiencing low birth weight is 1.35 times.

Beside the CED in pregnant women, there are other factors that influence the incidence of LBW in this meta-analysis study. A research by Biswas (2018) concluded that in addition to low birth weight, other factors that could influence the incidence of anemia in pregnancy were significantly related to female newborns, primiparity, incomplete ANC visits. Antenatal check-ups are important for high-risk mothers, monitoring weight gain during pregnancy, early detection of anemia, providing nutritional supplements, as well as early detection of complications and death in mother and baby. In this study, pregnant women with ANC less than four times had a 2.7 times chance of giving birth to LBW babies. Strengthening adolescent and maternal health with interventions that focus on anemia screening and prevention among women in the reproductive age

group can reduce the incidence of LBW infants (Biswas et al., 2019).

In a study related to Hb and LBW levels, Bakacak (2015) reported that low Hb levels were associated with the incidence of LBW only in the first trimester. The results of the analysis in this research article are in line with the research conducted by Masukume (2015) which states that anemia is not significantly associated with preterm birth, SGA and LBW. Although the association was not significant, problems related to pregnancy outcomes tended to occur more frequently in anemic mothers than in non-anemic mothers. On the other hand, a study conducted in Iran explained that if Hb concentrations in the first, second and third trimesters were associated with infant birth weight and the incidence of low birth weight (LBW), because low Hb (anemia) could cause fetal growth restriction (Moghaddam et al., 2015).

In this meta-analysis, the incidence of LBW is also related to the condition of pregnant women with preeclampsia, eclampsia and chronic hypertension. Other factors that influence the occurrence of LBW in this meta-analysis are smoking habits, nutritional status (less and obese) in pregnant women, maternal HIV status, maternal height, maternal education, place of residence, malaria infection, and others. (Mitao et al., 2016; Feresu et al., 2015).

The weakness of this meta-analysis is that the reference year is limited to the last seven years. This is because the context of anemia in pregnant women and the incidence of LBW requires data from the latest study results to be relevant to the current situation. In addition, this study has a language bias because many articles are in English.

AUTHOR CONTRIBUTION

Elsa Tursina and Fahmi Adhimukti were the main researchers who chose the topic, searched for and collected study data and were the authors of this research article.

FUNDING AND SPONSORSHIP

This study is self-funded.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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