

Effect of Iron and Folic Acid Supplementation on the Infants Birth Weight: A Meta-Analysis

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ABSTRACT

Background: Low birth weight (LBW), defined as a birth weight of less than 2,500 grams, is associated with an increased risk of neonatal mortality and developmental disorders. Efforts to prevent and manage LBW can be made through the administration of iron and folic acid supplements during pregnancy. This study aims to estimate and analyze the effect of iron and folic acid supplementation on the birth of infants with low birth weight.

Subjects and Method: This study is a systematic review and meta-analysis of relevant previous studies conducted using the PRISMA guidelines. The population included pregnant women, interventions involving iron and folic acid supplementation compared to no supplementation, and outcomes related to low birth weight. Article searches were conducted in the PubMed, ScienceDirect, Scopus, and Google Scholar databases, published between 2013 and 2025. The search terms were ("Pregnant woman" OR "Expectant mother") AND ("Iron and folic acid supplements" OR "IFA supplements") AND ("Low Birth Weight" OR "Low-weight newborns"). Inclusion criteria included full-text articles with a cross-sectional study design and reporting adjusted odds ratio (aOR) values. Findings from the primary research articles were analyzed using Review Manager 5.3.

Results: The included primary studies comprised 21 articles from China, India, Nepal, Pakistan, Malawi, and Ethiopia. The results of this meta-analysis indicate that pregnant women who consumed iron and folic acid supplements had an average 0.87 unit lower risk of giving birth to LBW infants compared to pregnant women who did not consume iron and folic acid supplements (aOR= 0.87; 95% CI = 0.75 to 1.00; p= 0.040).

Conclusion: The administration of iron and folic acid supplements can reduce the incidence of low birth weight.

Keywords: low birth weight, iron and folic acid supplements, pregnant women.

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BACKGROUND

Low Birth Weight (LBW), defined as a birth weight of less than 2,500 grams, is an important indicator of maternal and infant

health and the quality of maternal health services. Globally, the prevalence of LBW in 2015 was 14.6%, highest in South Asia (16.0%) and Sub-Saharan Africa (9.5%), with

extreme variations in Ethiopia (17.3–36.0%) and India (14.5–41.3%) (Mare et al., 2025). Approximately 91% of cases occur in low- and middle-income countries, reflecting disparities in healthcare and nutrition services. The global decline from 17.5% (2000) to 14.6% (2015) has not yet achieved the WHO target. Risk factors include poor maternal nutrition, anemia, suboptimal gestational age, inadequate antenatal care, preterm birth, and hypertension (Sharma et al., 2025). Prevention requires a comprehensive approach: improving maternal nutrition, supplementation, and enhancing healthcare services.

Every year, 20–30 million babies are born LBW, >90% in developing countries, making it a serious public health issue (Eristu, Mamo, Zeleke, Tsegaw and Ayen, 2023) et al., 2023). India accounts for 27.6% and Indonesia 11.1% (third highest globally) (Herawati and Tridiyawati, 2023). LBW increases the risk of neonatal mortality, cognitive impairments, recurrent infections, and disabilities, especially when postnatal nutrition is also inadequate (Mohammed, 2014). Risk factors include prematurity, intrauterine growth restriction, pre-eclampsia, anemia, extreme maternal age, and insufficient antenatal visits (fewer than 4 visits increase the risk by 3 times) (Jumbale et al., 2018). Prevention requires optimal antenatal care, improved maternal nutrition, and early detection of complications (Eristu et al., 2023).

South Asia and Sub-Saharan Africa account for >70% of global cases (Okwaraji et al., 2024). South Asia has a prevalence of 20–28% (global contribution 44–48%), Sub-Saharan Africa 10–13% (global contribution 24–27%) (Bezie et al., 2024). progress is hindering the 2030 target (Blencowe et al., 2019). Determining factors include poor maternal nutrition, low antenatal care access, suboptimal maternal age, and weak

economies (Weyori et al., 2022). Prevention efforts should focus on sustainable nutrition interventions, maternal health access, and socioeconomic empowerment.

LBW increases the risk of neonatal mortality by 15–25 times compared to normal babies, especially in the first week, and the risk increases if the baby is not weighed at birth (Paixão et al., 2021). LBW is associated with motor and cognitive delays, autism, ADHD, increased susceptibility to infections, failure to thrive, and long-term disabilities (Kim et al., 2024). The Developmental Origins of Health and Disease (DOHaD) theory suggests that a history of LBW increases the risk of hypertension, heart disease, diabetes, and metabolic disorders in adulthood (Qi and He, 2021). Prevention and monitoring of LBW infant growth are crucial to reduce short- and long-term risks.

Failure to prevent LBW increases the risk of the double burden of malnutrition (DBM), both undernutrition and over-nutrition, and adds to the health care burden. Children with a history of LBW are at higher risk of stunting, wasting, and underweight, even with adequate socioeconomic factors (Jana, 2023). LBW accounts for 10–20% of child malnutrition variation in developing countries (Jana et al., 2021), increases first-year mortality, and worsens physical and cognitive development (Zoleko-Manego et al., 2021). DBM increases the risk of non-communicable diseases (NCDs) such as diabetes and heart disease (Nugent et al., 2020). Global economic losses are estimated at over 344 billion USD per year due to lost productivity and high healthcare costs (Jain et al., 2024). Prevention through improved maternal nutrition and enhanced quality of antenatal care is crucial.

Reducing LBW is a key indicator of the Sustainable Development Goals (SDGs) for maternal and child health. The global target is a 30% reduction between 2012 and 2030,

but the current rate is only 0.3% per year (Okwaraji et al., 2024). In 2020, 14.7% of babies were born LBW, with three-quarters in South Asia and Sub-Saharan Africa (Blencowe et al., 2019). Even in developed countries like Australia, LBW rates are rising among vulnerable groups (Huda et al., 2023). Risk factors include malnutrition, anemia, low antenatal care attendance, extreme maternal age, and low socioeconomic status. Effective interventions include iron/folate supplementation, nutrition education, improved antenatal care quality, smoking cessation programs, family planning counseling, and reproductive health education (Dewi, Hardjito and Kundarti, 2022). Given the contribution of LBW to neonatal mortality, stunting, and global economic losses, investment in mother-child interventions and accurate data systems is crucial (Krasevec et al., 2022).

Poor maternal nutritional status, characterized by low body weight, BMI, and upper arm circumference (MUAC) below standard levels, along with inadequate energy, protein, and micronutrient intake, consistently increases the risk of low birth weight (LBW) (Sana et al., 2025). Deficiencies in iron, folate, vitamin B12, calcium, and zinc in pregnant women also play a role (Fite et al., 2022). Low-quality antenatal care, limited ANC visits, inadequate anemia detection, limited nutrition education, and low supplementation coverage exacerbate the situation (Sharma et al., 2025). Targeted nutritional interventions through education, improved dietary patterns, and micronutrient supplementation are effective in reducing risks (Lopes et al., 2017). Prevention should focus on improving maternal nutrition before and during pregnancy, as well as the quality of maternal health services.

Iron and folic acid supplementation (IFA) during pregnancy has been proven to

reduce anemia, the risk of LBW, and neonatal mortality (Srivastava et al., 2024). Routine supplementation reduces anemia, increases average hemoglobin levels by 0.88 g/dL when combined with nutrition education (Anato and Reshid, 2025), and reduces the risk of LBW (RR 0.79) and neonatal mortality (RR 0.73) (Srivastava et al., 2024). However, IFA consumption adherence is low in many developing countries due to lack of education, limited ANC visits, low maternal knowledge, limited social support, and uneven access to supplements (Saragih et al., 2022). Strategies to improve the effectiveness of IFA include community-based nutrition education, strengthening ANC, equitable distribution, and counseling on side effects (Seidu et al., 2024).

Iron/folate supplements are effective in reducing maternal anemia and improving pregnancy outcomes. Daily iron supplementation can reduce anemia by up to 70% and iron deficiency anemia by up to 57%, as well as increase hemoglobin and ferritin levels in pregnant women (Finkelstein et al., 2024). Supplementation reduces the risk of low birth weight by 16–20% and increases birth weight by 30–58 grams, particularly among anemic mothers (Shi et al., 2021). Asian-African studies demonstrate stronger effectiveness in areas with high anemia prevalence, including reducing preterm birth (Chikakuda et al., 2018). Mild side effects such as digestive disturbances at doses ≥ 60 mg/day do not reduce benefits, and there is no evidence of increased malaria risk in endemic areas (Finkelstein et al., 2024). This intervention is recommended primarily in populations with high anemia prevalence.

Based on this background, comprehensive research with a meta-analysis is needed to determine the effect of iron and folate supplementation on the birth of low birth weight infants based on existing studies.

SUBJECTS AND METHOD

1. Study Design

This study is a systematic review and meta-analysis of relevant previous studies conducted using the PRISMA guidelines. The population includes pregnant women, interventions involving iron and folic acid supplementation with a control group without iron and folic acid supplementation, and outcomes related to the birth of infants with low birth weight. Article searches in this study were conducted in the PubMed, ScienceDirect, Scopus, and Google Scholar databases, published between 2013 and 2025. The keywords were ("Pregnant woman" OR "Expectant mother") AND ("Iron and folic acid supplements" OR "IFA supplements") AND ("Low Birth Weight" OR "Low-weight newborns").

2. Steps of Meta-analysis

There are five steps in the meta-analysis, as described below:

- 1) Formulating the research problem using the PICO model (Population: pregnant women, Intervention: iron and folic acid supplementation, Comparison: iron and folic acid supplementation, Outcome: low birth weight).
- 2) Searching for primary research articles from electronic databases such as PubMed, ScienceDirect, Google Scholar, and Scopus.
- 3) Assess the quality of the primary research articles to be included using Critical Appraisal.
- 4) Combining results and analyzing data using Review Manager 5.3.
- 5) Placing findings in context by interpreting and drawing conclusions.

3. Inclusion Criteria

Inclusion criteria for articles to be included are full-text research articles, articles using an observational (cross-sectional) design and with an adjusted Odd Ratio (aOR), research articles published in English,

research articles published between 2013 and 2025, research articles with the subject of pregnant women, intervention involving iron and folic acid supplementation, and the research outcome is the birth of a baby with low birth weight.

4. Exclusion Criteria

Exclusion criteria for articles in this study include statistical results reported in the form of bivariate analysis, and research subjects who are pregnant women with comorbid conditions.

5. Operational Definition of Variables

Iron is an essential mineral that plays a role in the formation of hemoglobin to transport oxygen, while folic acid is a synthetic form of vitamin B9 that is important for DNA synthesis, cell division, and red blood cell formation. During pregnancy, both are needed to prevent anemia, support fetal growth, and reduce the risk of low birth weight and neural tube defects. The instruments used were an IFA (Iron and Folic Acid) supplement consumption questionnaire, medical records of pregnant women, or structured interviews regarding the frequency and adherence to supplement consumption during pregnancy. The measurement scale was categorical.

Low birth weight is defined as a baby born weighing less than 2500 grams, regardless of gestational age. Secondary data sources include the KIA book, medical records at healthcare facilities, or infant weighing results at birth. Continuous measurement scale.

6. Study Instruments

Research instruments are relevant articles published in databases on the effects of iron and folate supplementation on low birth weight. The study was conducted in accordance with the PRISMA flow diagram guidelines and article quality assessment using the Critical Appraisal Checklist for

Cross-Sectional Studies from the Center for Evidence-Based Management.

7. Data analysis

Data in this study were analyzed based on variations between studies using fixed-effect and random-effects models with Review Manager 5.3. Review Manager 5.3 was used to present overall mean differences and describe 95% confidence intervals (CI).

RESULTS

Study Selection

The search for articles to be included in the meta-analysis was conducted according to the PRISMA flow diagram in (Figure 1). Identification, screening, and eligibility

were considered in determining the selection of primary research articles. In the final review process, 21 articles were found to meet the qualitative and quantitative criteria for inclusion in the meta-analysis of the effect of iron and folic acid supplementation on the birth of LBW infants.

The primary studies on the effect of iron and folic acid supplementation on low-birth-weight infants consisted of 21 articles from two continents, Asia and Africa (Figure 2).

A summary of the 21 primary articles on the effect of iron and folic acid supplementation on the birth of infants with low birth weight included in this study is presented in Table 1.

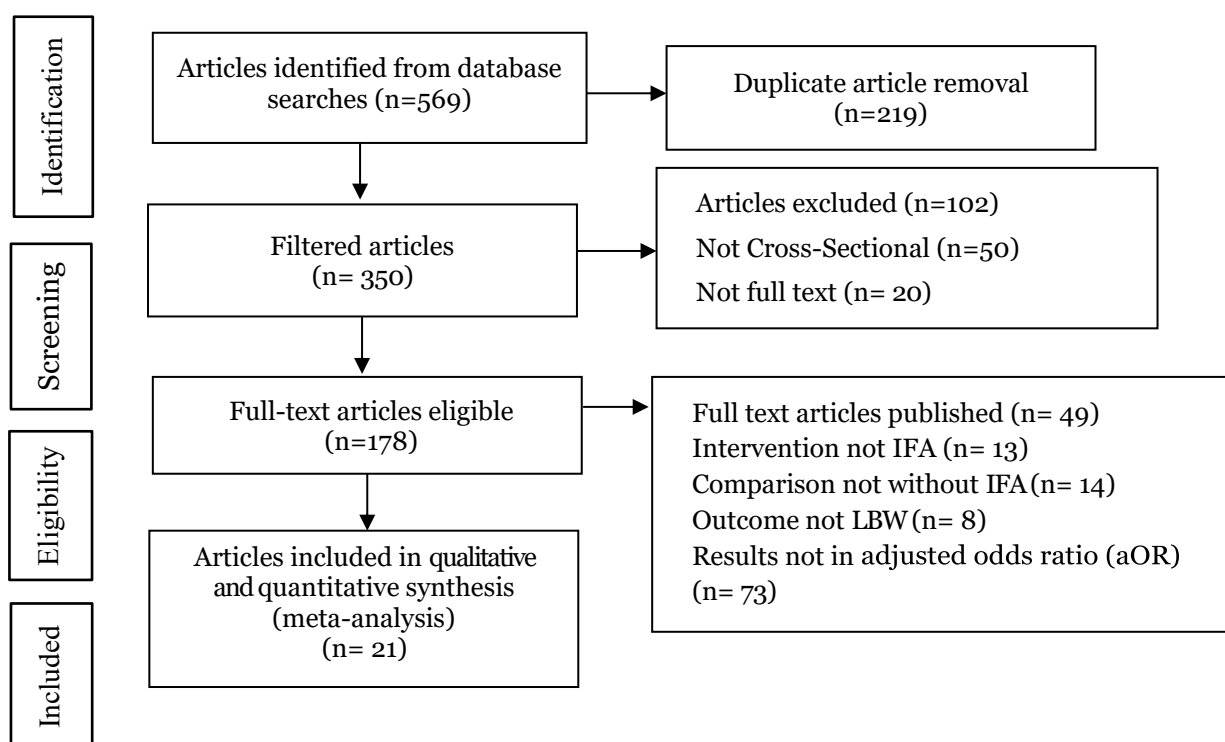


Figure 1. PRISMA flow diagram of the effect of iron and folate supplementation on the birth of LBW infants

Included Studies

Table 1 describes the primary studies included in the meta-analysis. A total of nine article of included this study. Four studies were conducted in Asia, all of which from

Indonesia. Five studies were conducted in Africa, all of which from the Ethiopia (Figure 2). A detailed description of the study characteristics, including the PICO, is summarized in Table 1. Critical appraisal

uses the Joanna Briggs Institute (JBI)
Critical Appraisal Tools for Use in JBI

Systematic Reviews, Checklist for Analytical
Cross-sectional Study (Table 2).



Figure 2. Map of the study areas on the effect of iron and folate supplementation on the birth of LBW infants

Table 1. Description of the primary research included in the meta-analysis

| Author (Year) | Country | Sample | P | I | C | O |
|--------------------------|---------|---------|-------------------------------------|--|--|-----|
| Zhou et al. (2019) | China | 287 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Balarajan et al. (2013) | India | 22.648 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Chatterjee et al. (2021) | India | 7.897 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Malhotra et al. (2014) | India | 124.385 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Pal et al. (2020) | India | 2611 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Rai et al. (2021) | India | 120.374 | Pregnant women or expectant mothers | Consumption of more than 100 IFA | Consumption of less than 100 IFA | LBW |
| Khanal et al. (2014) | Nepal | 2845 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Khanal et al. (2024) | Nepal | 4935 | Pregnant women who have given birth | Consumption of IFA for more than 90 days | Consumption of IFA for less than 90 days | LBW |

| Author (Year) | Country | Sample | P | I | C | O |
|-------------------------------|----------|--------|---|--|--|-----|
| Tapa et al. (2022) | Nepal | 308 | Pregnant women who have given birth | IFA consumption or adherence | No IFA intake or non-adherence | LBW |
| Nisar et al. (2014) | Pakistan | 5692 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Chicakuda et al. (2018) | Malawi | 220 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Casto et al. (2018) | Ethiopia | 432 | Postpartum women with newborn infants | Consumption of IFA for more than 90 days | Consumption of iron-folate supplements for less than 90 days | LBW |
| Chanie et al. (2018) | Ethiopia | 243 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Ekubagew argies et al. (2019) | Ethiopia | 240 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Gudeta et al. (2019) | Ethiopia | 1980 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Jember et al. (2020) | Ethiopia | 358 | Postpartum pregnant women with newborn babies | IFA consumption | No IFA consumption | LBW |
| Lake et al. (2019) | Ethiopia | 304 | Pregnant women who have given birth to newborn babies | IFA intake | No IFA consumption | LBW |
| Liyew et al. (2021) | Ethiopia | 2110 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Mulatu et al. (2017) | Ethiopia | 457 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Tadesse et al. (2022) | Ethiopia | 337 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |
| Toru et al. (2020) | Ethiopia | 196 | Pregnant women who have given birth | IFA consumption | No IFA consumption | LBW |

The adjusted Odds Ratio (aOR) and 95% CI for the effect of iron and folic acid supplementation on low birth weight infants are presented in Table 2.

Quality assessment of cross-sectional studies on the effect of iron and folic acid

supplementation on low birth weight infants. The results of the Critical Appraisal Checklist for Cross-Sectional Studies in Table 3.

Table 2. Adjusted Odds Ratio (aOR) and 95% CI data on the effect of iron and folic acid supplementation on low birth weight infants

| Author (Year) | aOR | Lower Bound | Upper Bound | p |
|------------------------------|-------|-------------|-------------|---------|
| Zhou et al. (2019) | 1.09 | 1.61 | 0.751 | - |
| Balarajan et al. (2013) | 0.82 | 0.72 | 0.94 | - |
| Chatterjee et al. (2021) | 0.686 | 0.049 | 0.050 | - |
| Malhotra et al. (2014) | 1.06 | 0.96 | 1.18 | - |
| Pal et al. (2020) | 3.86 | 2.54 | 5.87 | 0.000 |
| Rai et al. (2021) | 0.84 | 0.80 | 0.89 | <0.001 |
| Khanal et al. (2014) | 0.67 | 0.98 | 0.45 | - |
| Khanal et al. (2024) | 0.69 | 0.90 | 0.54 | - |
| Tapa et al. (2022) | 0.47 | 1.00 | 0.22 | 0.002 |
| Nisar et al. (2014) | 0.82 | 0.71 | 0.96 | <0.0001 |
| Chicakuda et al. (2018) | 0.41 | 0.11 | 1.63 | 0.208 |
| Casto et al. (2018) | 1.78 | 0.07 | 0.40 | - |
| Chanie et al. (2018) | 0.40 | 0.03 | 5.50 | 0.50 |
| Ekubagewargies et al. (2019) | 0.62 | 2.32 | 0.17 | - |
| Gudeta et al. (2019) | 0.34 | 0.72 | 0.16 | - |
| Jember et al. (2020) | 1.51 | 5.26 | 0.43 | 0.53 |
| Lake et al. (2019) | 0.96 | 2.52 | 0.37 | 0.948 |
| Liyew et al. (2021) | 0.86 | 1.19 | 0.63 | - |
| Mulatu et al. (2017) | 0.30 | 0.09 | 0.99 | - |
| Tadesse et al. (2022) | 0.27 | 0.10 | 0.72 | - |
| Toru et al. (2020) | 0.176 | 0.031 | 1.001 | - |

Table 3. Results of the Critical Appraisal Checklist for Cross-Sectional Studies

| Primary Study | Criteria Question | | | | | | | | | | | | | Total |
|------------------------------|-------------------|---|---|---|---|---|---|---|---|----|----|----|----|-------|
| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | |
| Zhou et al. (2019) | 2 | 2 | 2 | 2 | 2 | 0 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 23 |
| Balarajan et al. (2013) | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 23 |
| Chatterjee et al. (2021) | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 24 |
| Malhotra et al. (2014) | 1 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 24 |
| Pal et al. (2020) | 2 | 2 | 2 | 0 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 23 |
| Rai et al. (2021) | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 24 |
| Khanal et al. (2014) | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 1 | 1 | 2 | 2 | 2 | 23 |
| Khanal et al. (2024) | 2 | 2 | 2 | 2 | 0 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 23 |
| Tapa et al. (2022) | 1 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 23 |
| Nisar et al. (2014) | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 0 | 2 | 2 | 2 | 23 |
| Chicakuda et al. (2018) | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 24 |
| Casto et al. (2018) | 2 | 2 | 2 | 0 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 23 |
| Chanie et al. (2018) | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 24 |
| Ekubagewargies et al. (2019) | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 24 |
| Gudeta et al. (2019) | 1 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 24 |
| Jember et al. (2020) | 2 | 2 | 2 | 2 | 2 | 0 | 1 | 2 | 2 | 2 | 2 | 2 | 2 | 23 |
| Lake et al. (2019) | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 23 |
| Liyew et al. (2021) | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 23 |
| Mulatu et al. (2017) | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 23 |
| Tadesse et al. (2022) | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 23 |
| Toru et al. (2020) | 2 | 0 | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 2 | 2 | 23 |

Criteria: Yes = 2, Undecided = 1, No = 0

Question Criteria:

Formulation of research questions in the acronym PICO

1. Is the population in the primary study the same as the population in the PICO meta-analysis?
2. Is the operational definition of intervention, i.e., exposed status in the primary study the same as the intended definition in the meta-analysis?
3. Is the comparison, i.e. the unexposed status used in the primary study the same as the intended definition in the meta-analysis?
4. Is the outcome variable examined in the primary study the same as the intended definition in the meta-analysis?

Methods for selecting research subjects

5. In analytic cross-sectional studies, do researchers select samples from the population randomly (random sampling)?
6. Alternatively, if in an analytic cross-sectional study the sample is not randomly selected, do researchers select the sample based on outcome status or based on intervention status?

Methods for measuring exposure (intervention) and outcome variables

7. Are exposure and outcome variables measured with the same instrument(s) across all primary studies?
8. If the variable is measured on a categorical scale, are the cutoffs or categories used the same across primary studies?

Design-related bias If the sample is not randomly selected

9. Whether the researcher has made efforts to prevent bias in selecting research subjects. For example, selecting subjects based on the outcome status is not affected by the exposure status (intervention), or selecting subjects based on the exposure status (intervention) is not affected by the outcome status.

Methods to control for confounding

10. Whether the primary study researchers made efforts to control for confounding (e.g., conducted multivariate analyses to control for confounding).

Statistical analysis methods

11. Did the researchers analyze the data in this primary study using a multivariate analysis model (e.g., multiple linear regression analysis, multiple logistic regression analysis)?
12. Whether the primary study reported the effect size or relationship of the multivariate analysis (e.g., adjusted OR, adjusted regression coefficient).

Conflict of interest

13. Are there no possible conflicts of interest with the sponsor of the research, which could bias the conclusions?

Based on the results of the study quality assessment with Critical Appraisal Analytical Cross-Sectional Studies, a total of 21 articles were found eligible with each article getting a total point of 23 and 24 so that the article was considered eligible for meta-analysis research. The total score of a primary study ≥ 22 , then the study can be included in the meta-analysis.

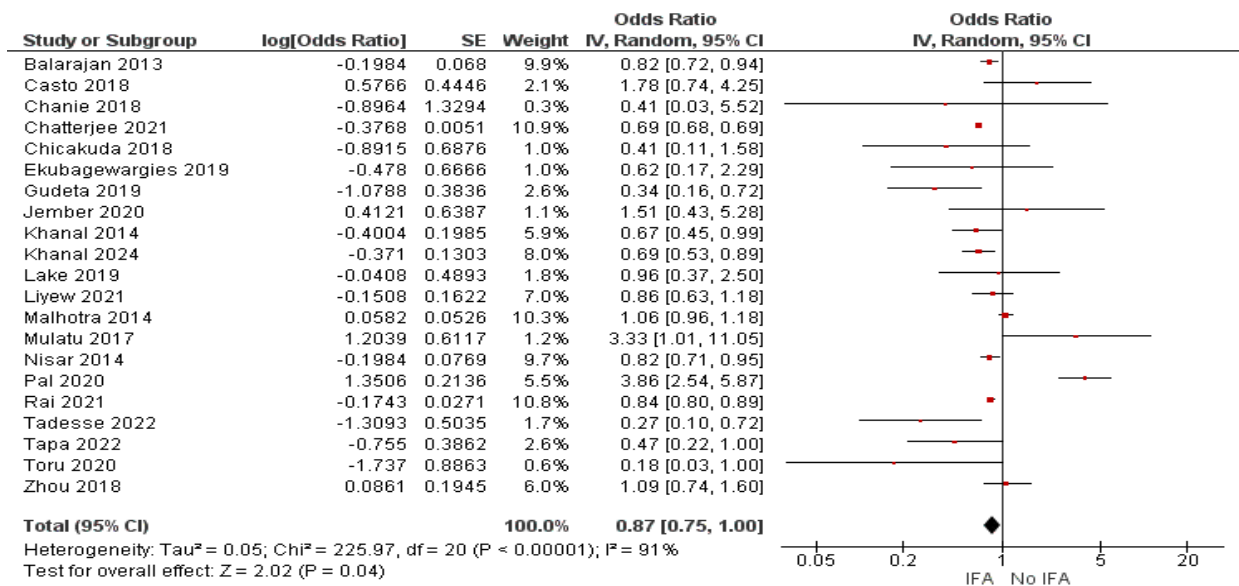


Figure 3. Forest plot meta-analysis of the effect of iron and folic acid supplementation on the birth of low birth weight babies.

Based on Figure 3 show that the forest plot in Figure 6 shows that there is a statistically significant effect of iron and folic acid supplementation on the birth of low birth weight babies in pregnant women. Pregnant women who consumed iron and folic acid supplements had an average 0.87 units lower rate of low birth weight babies

compared to pregnant women who did not consume iron and folic acid supplements (aOR = 0.87; 95% CI = 0.75 to 1.00; $p = 0.040$). The forest plot also indicates high heterogeneity of effect estimates across studies ($I^2 = 91\%$; $p < 0.001$), therefore the average effect estimate was calculated using the random effects model approach.

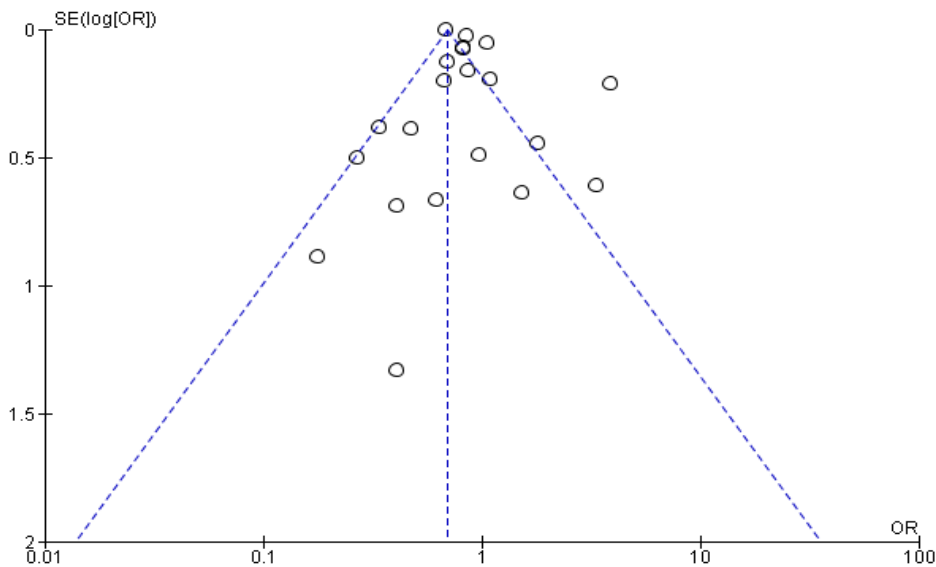


Figure 4. Funnel plot meta-analysis of the effect of iron and folic acid supplementation on low birth weight.

Based on Figure 3 show that the funnel plot above shows the distribution of studies in the meta-analysis based on standard error and odds ratio. Overall, the plot appears symmetrical around the combined effect line, but there is slight asymmetry at the bottom, with more studies on the right side. This suggests the possibility of mild publication bias, as the distribution of effect estimates is opposite to the location of the diamond (♦) in the forest plot in Figure 6, which is to the left of the vertical null hypothesis line. This publication bias tends to underestimate the true effect estimate.

DISCUSSION

Low birth weight (LBW) is an important indicator of maternal and neonatal health that can affect infant survival and development. Various maternal factors contribute to LBW, including the mother's nutritional status during pregnancy. Iron and folic acid (IFA) supplementation during pregnancy has been widely recommended as an intervention to reduce maternal anemia and improve birth outcomes.

The prevalence and patterns of IFA supplement consumption, based on various studies, show significant variation in the level of IFA supplement consumption among pregnant women. According to a study by Ekubagewargies, the majority (86.7%) of pregnant women received iron/folic acid supplementation during antenatal care. However, the optimal duration of consumption remains a challenge (Ekubagewargies et al., 2019). According to Kastro's study, out of 355 women (92%) who consumed iron and folic acid supplements at least once, only 264 women (61.1%) received fewer than 90 tablets during their last pregnancy (Kastro, Demissie and Yohannes, 2018). A similar pattern was reported by Chanie & Dilie, where out of 213 mothers who consumed iron tablets, only 27 mothers

(11.1%) consumed them for more than 90 days (Chanie and Dilie 2018).

The association between IFA supplementation and low birth weight is that several studies have shown a consistent protective effect of IFA supplementation against the occurrence of LBW. According to Zhou's research, not consuming antenatal supplements containing folic acid was positively associated with LBW (AOR = 1.32, 95% CI = 1.00 to 1.74) (Zhou et al., 2019). This finding is supported by several other studies showing an increased risk of LBW among mothers who did not consume IFA supplements. Liyew reported that mothers who did not consume iron with folic acid during pregnancy had a 3.51 times higher risk of giving birth to LBW infants compared to mothers who consumed the supplements (AOR = 3.51; 95% CI= 1.3 to 9.49) (Liyew, Sisay and Muche, 2021).

Similar results were found by Mulatu, who discovered that mothers who did not consume iron and folic acid supplements during pregnancy were nearly three times more likely to give birth to babies with low birth weight (AOR = 2.814; 95% CI= 1.73 to 4.57), (Mulatu, 2017). Tadesse's research also confirmed these findings, reporting a 3.1-fold increase in risk (AOR = 3.1; 95% CI= 1.6 to 6.0) (Tadesse et al., 2023).

The duration of IFA supplement consumption showed a significant association with the prevention of LBW. A study conducted by Chatterjee and Dubey found that mothers who consumed iron and folic acid supplements for more than three months during pregnancy were less likely to have children with LBW (OR= 0.74 with a p-value= 0.049), (Chatterjee and Dubey, 2022). These findings align with Khanal's research, which showed that mothers who consumed iron and folic acid supplements for at least 90 days had a lower risk of giving birth to LBW infants (AOR= 0.67; 95% CI:

0.47 to 0.96) (Khanal et al., 2014). Tapa's study reinforces this evidence by reporting that IFA consumption for ≥ 90 days during pregnancy was significantly associated with a reduced risk of LBW (AOR: 0.57; 95% CI: 0.39 to 0.85), indicating a protective effect of IFA supplementation (Thapa et al., 2022). The Rai study even demonstrated a stronger protective effect in mothers who consumed ≥ 100 IFA tablets, with a reduced risk of Extremely Low Birth Weight (ELBW) (OR= 0.54; 95% CI= 0.31 to 0.95), Very Low Birth Weight (VLBW) (OR= 0.71; 95% CI= 0.59 to 0.84), and LBW (OR= 0.84; 95% CI= 0.80 to 0.89) (Rai et al., 2021).

Biological mechanisms of the study Gudeta explains the biological mechanisms underlying the relationship between iron deficiency and LBW (Gudeta et al., 2019). Mothers who do not consume iron are more likely to have babies with low birth weight because low hemoglobin levels and reduced erythrocyte formation result in low oxygen supply to the fetus. Low oxygen concentrations can affect fetal metabolism and result in low birth weight. Research conducted by Balarajan confirms that maternal iron deficiency anemia is associated with an increased risk of low birth weight, preterm birth, and perinatal mortality. Iron and folic acid supplementation during pregnancy is a widely recommended intervention to reduce maternal anemia and improve birth outcomes (Balarajan et al., 2013).

Quantitative impact of IFA supplementation, Malhotra provides a quantitative perspective on the benefits of IFA supplementation. Their study showed that IFA consumption during pregnancy for 1 month increased birth weight by 6.46 grams. Thus, there could be an increase of 19.38 grams in birth weight if mothers consume IFA supplements for three months, which is the minimum duration of IFA consumption according to current guidelines (Malhotra et

al., 2014). Nisar's research supports these findings by reporting that daily antenatal iron-folate supplementation is associated with a reduced risk of low birth weight, where babies born to mothers who received IFA had significantly higher average birth weights compared to babies whose mothers did not receive supplements (Nisar and Dibley, 2016).

According to research by Chanie and Dilie (2020), mothers who experienced anemia during pregnancy were significantly associated with low birth weight (AOR = 0.13; 95% CI = 0.01 to 1.01). Low iron tablet intake is also significantly associated with neonatal birth weight (AOR = 4.33, 95% CI = 1.54 to 12.22). Kastro's research adds a broader nutritional perspective by reporting that mothers who did not consume fruit daily during pregnancy had a significantly higher odds of giving birth to babies with low birth weight. This may be due to the complementary nutritional benefits of fruits as a primary source of micronutrients, which, when consumed especially during the first trimester, can enhance fetal organ development (Kastro et al., 2018).

According to the study, the importance of antenatal care is emphasized, reporting that the odds of LBW are 3.79 times higher in mothers who did not undergo antenatal care compared to those who did. During ANC visits, routine nutritional and medical advice is provided, along with supplementation (Jember et al., 2020).

Consistency of Findings Across Geographic Settings Findings on the protective effects of IFA supplementation against LBW show consistency across various geographic settings. According to a study by Lake & Fite, institutional research in northwestern Ethiopia revealed that prematurity, lack of antenatal care, malaria during pregnancy, anemia during pregnancy, and lack of iron supplementation were independent risk

factors influencing low birth weight (Lake and Fite, 2019). According to Mulatu's study, their findings are consistent with previous research conducted in Gondar and Tigray, Ethiopia (Mulatu, 2017). According to Pal's research, similar results were reported from a national sample in India, where multivariate analysis revealed that the odds of low birth weight among mothers who did not consume IFA tablets during pregnancy were significantly higher (OR= 1.46; 95% CI= 1.23 to 1.72) compared to those who did (Pal et al., 2020).

Based on a review of various studies, there is strong and consistent evidence that iron and folic acid supplementation during pregnancy provides a protective effect against low birth weight. This protective effect appears to be optimal when supplementation is provided for an adequate duration (≥ 90 days or ≥ 3 months) and within the context of comprehensive antenatal care. The biological mechanisms underlying this protective effect are related to the prevention of maternal iron deficiency anemia, which can impair oxygen supply to the fetus and affect fetal metabolism and growth. Additionally, IFA supplementation should be supported by a balanced diet, including consumption of fruits rich in micronutrients. Policy implications of these findings emphasize the importance of ensuring universal access to high-quality IFA supplementation during pregnancy, improving adherence to consumption over an adequate duration, and integrating IFA supplementation into comprehensive antenatal care packages. Maternal health programs should emphasize not only the provision of supplements but also education on the importance of adherence and optimal duration to achieve maximum benefits in preventing LBW.

A meta-analysis was conducted on 21 primary research articles with a cross-

sectional design. The articles included were from China, India, Nepal, Pakistan, Malawi, and Ethiopia. The total sample size was 273,388 pregnant women. This meta-analysis concluded that pregnant women who consumed iron and folic acid supplements had an average 0.87 unit lower rate of low-birth-weight babies compared to pregnant women who did not consume iron and folic acid supplements (aOR= 0.87; 95% CI= 0.75 to 1.00; $p= 0.040$). The distribution of effects across studies indicated publication bias that underestimated the true effect.

AUTHORS CONTRIBUTION

Atiqoh Khoirunnisa' Maftuch as the main researcher who conducted the topic selection, data search and collection as well as the analysis process in this study. in this study. Bhisma Murti and Setyo Sri Rahardjo as observers in analyzing the research data and preparing the publication.

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CONFLICT OF INTEREST

There was no conflict of interest in this study.

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