

Meta-Analysis of Factors Affecting Compliance Behavior in Taking Iron Folate Supplements in Pregnant Women

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ABSTRACT

Background: Pregnant women can have a higher risk of iron and folic acid deficiency due to poor adherence to iron folate supplements. Factors that influence pregnant women during antenatal check-ups on adherence to taking iron folate supplements are getting counseling, having knowledge, attending antenatal care and diagnosing anemia. This study aims to analyze the factors that influence the behavior of adherence to taking iron folate supplements in pregnant women.

Subjects and Method: This was a meta-analysis study using PRISMA flowchart guidelines. The article search process was carried out between 2011 and 2021 using databases from PubMed, Google Scholar and ScienceDirect. Based on the database, there were 12 articles that met the inclusion criteria. The analysis was carried out using RevMan 5.3 software.

Results: A total of 12 articles reviewed in the meta-analysis showed that there were 7 articles discussing pregnant women who received nutritional counseling had higher adherence behavior to taking iron folate supplements and were statistically significant (aOR= 2.39; 95% CI= 1.92 to 2.96; $p < 0.001$), and there were 8 articles discussing pregnant women with anemia who had higher adherence to taking iron folate supplements and were statistically significant (aOR= 3.28; 95% CI= 1.56 to 6.87; $p = 0.002$).

Conclusion: Nutrition counseling and anemia status can improve the behavior of adherence to taking iron folate supplements in pregnant women.

Keywords: supplement, iron-folic acid, anemia, counseling

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BACKGROUND

Pregnancy can affect important stages of the life of pregnant women and their offspring (Siabani et al., 2018). Pregnant women may have a higher risk of iron and folic acid deficiency due to poor adherence to iron folate supplementation (Agegnehu et al., 2019). The incidence of iron folic acid deficiency is relatively high because there are physiological and hormonal changes

during pregnancy that will increase the need for iron folic acid (Mamo et al., 2021).

Factors that influence pregnant women during antenatal check-ups on adherence to taking iron folate supplements are getting counseling, having knowledge, number of antenatal visits, pregnancy history, having a diagnosis of anemia during pregnancy (Gebremariam et al., 2019; Molla et al., 2019), sociodemographic

factors such as age, education, marital status, religion (Nasir et al., 2020), clinical characteristics, obstetrics, gynecology, diet (Gebreweld and Tsegaye, 2018).

Anemia as a health problem that affects all age groups, especially pregnant women (Obai et al., 2016) Nationally, pregnant women experience anemia by 41.8% and pregnant women who comply with taking iron folate supplements are only 0.4% (Solomon et al., 2021). Lack of iron folate supplementation during pregnancy can lead to the risk of anemia (Ogundipe et al., 2012).

Another reason for the low non-adherence in pregnant women is fear of the side effects of taking iron folate supplements (Nimwesiga et al., 2021), inadequate counseling activities can affect the behavior of pregnant women towards non-adherence to taking iron folate supplements (Debi et al., 2020), the inability to motivate and provide appropriate counseling can reduce awareness of adherence to taking iron folate supplements in pregnant women (Felipe-Dimog et al., 2021).

Based on the factors that influence the adherence behavior of pregnant women to taking iron folate supplements that are poor and the need for prevention of anemia and nutritional counseling, researchers are interested in conducting a meta-analysis of factors that influence the behavior of adherence to taking iron folate supplements in pregnant women.

This study aimed to analyze the factors that influence the behavior of adherence to taking iron folate supplements in pregnant women when carrying out antenatal checks in health services, with a meta-analysis of previously conducted primary studies.

SUBJECTS AND METHOD

1. Study Design

This research was conducted using a meta-analysis research design with PRISMA flow chart guidelines. Article searches were performed using the following databases: PubMed, Google Scholar and ScienceDirect. Some of the keywords used are: "pregnant women AND anemia AND adherence to iron-folic acid supplementation", "pregnant women AND counseling AND adherence to iron-folic acid supplementation".

2. Inclusion Criteria

The inclusion criteria for this research article were full-paper cross-sectional study articles, articles in English, the size of the adjusted Odds Ratio (aOR), pregnant women who visited for antenatal check-ups, results of adherence to taking iron folate supplements.

3. Exclusion Criteria

The exclusion criteria for this research article were the statistical results of bivariate analysis and articles that did not use English.

4. Operational Definition of Variables

The articles included in this study were PICO-adjusted. The search for articles was carried out by considering the eligibility criteria determined using the following PICO model: Population= pregnant women who had antenatal checkups, Intervention= nutrition and anemia counseling. Comparison= no nutrition counseling and no anemia, Outcome= adherence to taking iron folate supplements.

Nutrition counseling is to provide guidance and health education to optimize adherence to taking iron folate supplements in pregnant women. Nutrition counseling is categorized as nutrition counseling and not nutrition counseling. The measurement scale is categorical.

Anemia is a condition where the body lacks red blood cells and does not function

properly. The incidence of anemia during pregnancy has an increased need for hemoglobin, so it is necessary to comply with taking iron folate supplements. Anemia is categorized as anemia and not anemia. The measurement scale is categorical.

Iron folate supplements can provide benefits to pregnant women to prevent anemia and reduce nutritional deficiencies. The measurement scale is categorical.

5. Data Analysis

Articles were analyzed using the Review Manager (RevMan) 5.3 application to cal-

culate effect size and heterogeneity, and form the final results of the meta-analysis. The results of data processing are presented in the form of forest plots and funnel plots.

RESULTS

Process of searching article was carried out by searching several journal databases including Google Scholar, Pubmed, and Science Direct. it can be seen using the PRISMA FLOW flowchart shown in Figure 1.

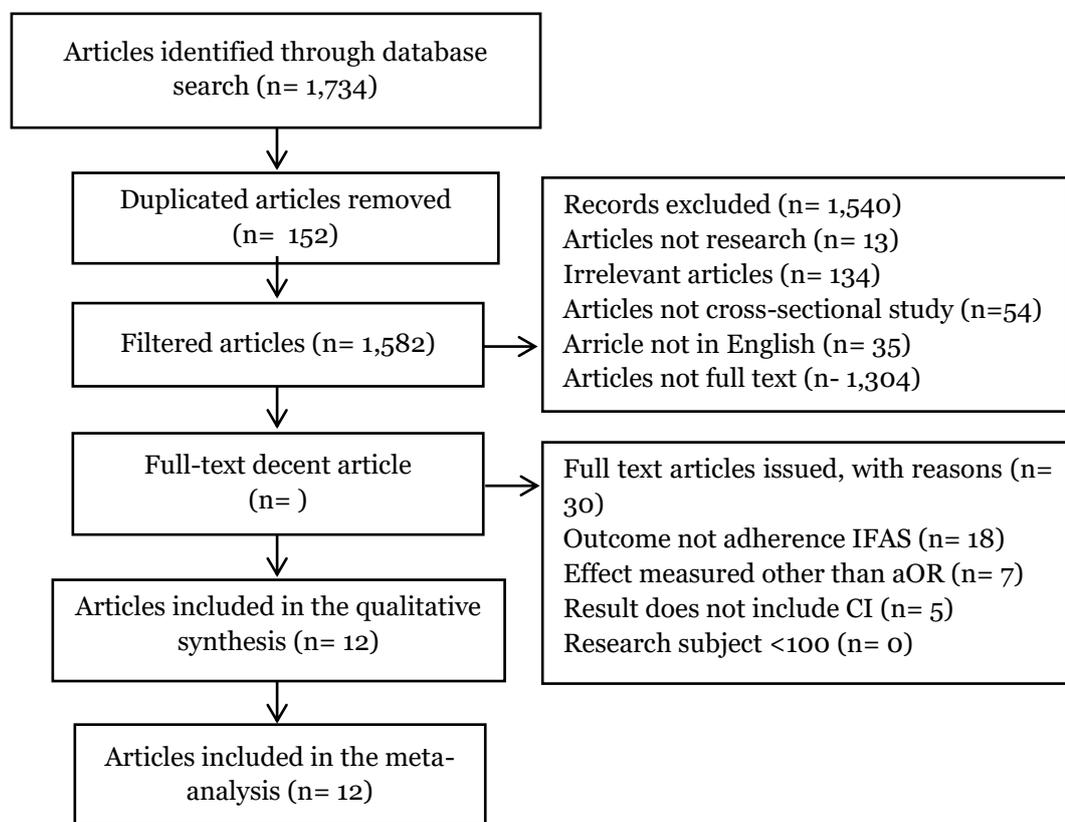


Figure 1. Results of Prisma Flow Diagrams

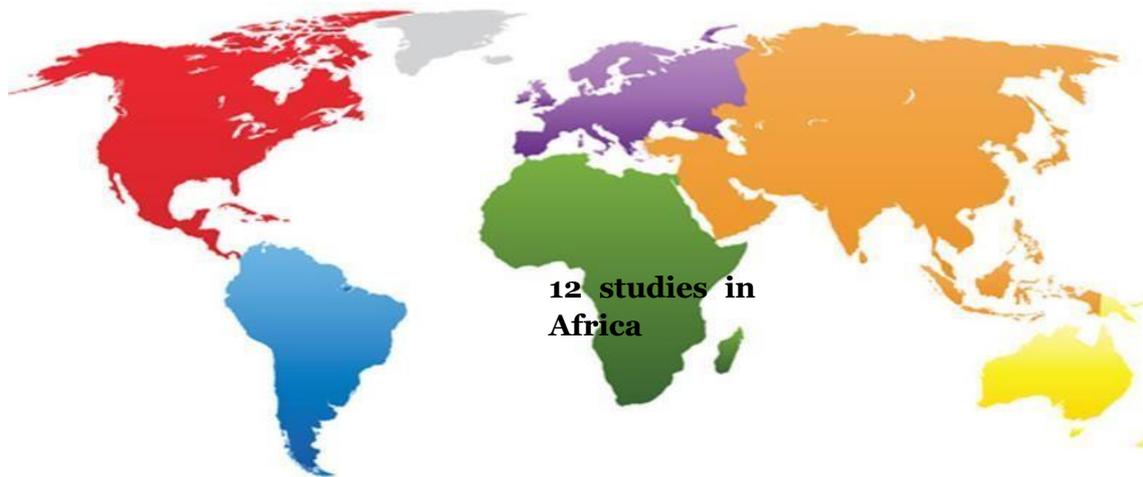


Figure 2. Research Distribution Map

Table 1. showed that the research consists of 12 articles from the initial search process yielding 1,734 articles. A total of 12 articles that met the quality assessment were included in the quantitative synthesis using meta-analysis. The research comes from 1 continent, namely African continent, namely Ethiopia 9 articles, Uganda 2 articles and Tanzania 1 article.

Assessment of the quality of research articles using the Critical Appraisal Checklist for cross-sectional study which can be seen in table 1. The criteria for evaluating articles with cross-sectional study design are as follows:

1. Does the study formulate the research question (research problem) clearly?
2. Is the cross-sectional research method appropriate to answer the research question?
3. Is the method for selecting research subjects clearly described?

4. Does the sampling technique not introduce bias (selection)?
5. Is the sample representative of the research target population?
6. Is the sample size based on consideration of the results of previous studies regarding statistical power?
7. Is the minimum response rate achieved?
8. Is the instrument in determining screen time and fast food valid and reliable?
9. Has statistical significance been tested?
10. Did the researcher report confidence intervals?
11. What confounding factors have been taken into account?
12. Are the results applicable in practice or in the community?

Table 2. shows a description of the main studies included in the primary study meta-analysis.

Table 1. Results of Quality Assessment of a Cross-sectional Study of Factors Affecting Compliance Behavior in Taking Iron Folate Supplements in Pregnant Women.

Primary Study	Criteria												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Ogundipe <i>et al.</i> (2012)	2	2	2	2	2	2	2	2	2	2	2	2	24
Gembremariam <i>et al.</i> (2017)	2	2	2	2	2	2	2	2	2	2	2	2	24
Kiwanuka <i>et al.</i> (2017)	2	2	2	2	2	2	2	2	2	2	2	2	24
Birhanu <i>et al.</i> (2018)	2	2	2	2	2	2	2	2	2	2	2	2	24
Boti <i>et al.</i> (2018)	2	2	2	2	2	2	2	2	2	2	2	2	24
Molla <i>et al.</i> (2019)	2	2	2	2	2	2	2	2	2	2	2	2	24
Gebremichael <i>et al.</i> (2019)	2	2	2	2	2	2	2	2	2	2	2	2	24
Gebremichael <i>et al.</i> (2020)	2	2	2	2	2	2	2	2	2	2	2	2	24
Demisse <i>et al.</i> (2021)	2	2	2	2	2	2	2	2	2	2	2	2	24
Nimwesiga <i>et al.</i> (2021)	2	2	2	2	2	2	2	2	2	2	2	2	24
Mamo <i>et al.</i> (2021)	2	2	2	2	2	2	2	2	2	2	2	2	24
Mekonnen <i>et al.</i> (2021)	2	2	2	2	2	2	2	2	2	2	2	2	24

Note: Answer 2= Yes; 1= Hesitant; 0= No

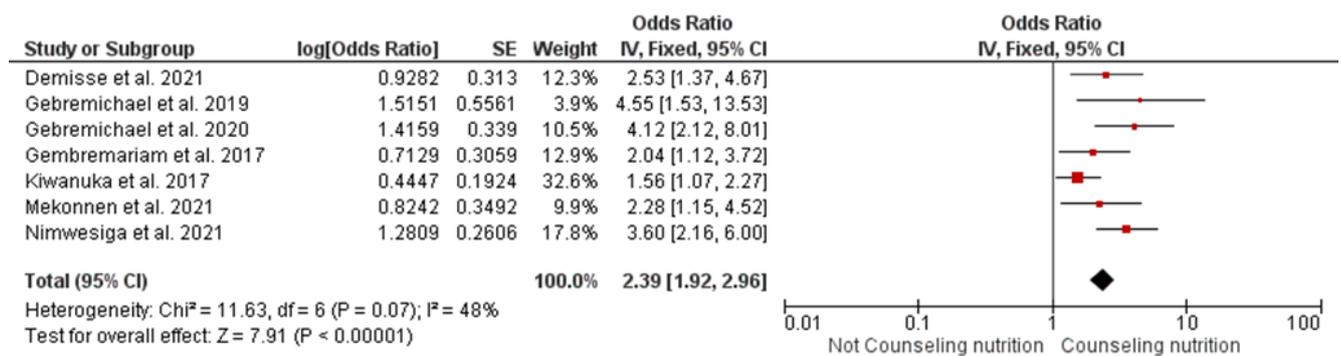


Figure 3. Forest plot Effect of Nutritional Anemia Status on Compliance Behavior of Taking Iron Folate Supplements in Pregnant Women

Based on the results of the forest plot, in Figure 3 shows that pregnant women who received nutrition counseling had a 2.39 times higher adherence behavior to taking iron folate supplements compared to pregnant women who did not receive nutri-

tion counseling, and the results were statistically significant (aOR= 2.39; 95% CI= 1.92 to 2.96; p< 0.001). Meta-analysis of 7 articles showed heterogeneity value I²= 48%, the analysis model used was fixed effect.

Table 2. Description of Primary Research included in the Meta-Analysis

No	Author (Year)	Country	Study Design	Sample		Population (P)	Intervention (I)	Comparison (C)	Outcome (O)	aOR (CI 95%)
				Total	NC					
1	Gembremariam <i>et al.</i> (2017)	Ethiopia	Cross-sectional	241	94	Pregnant women who have performed ANC at least 2 times at Debre Tabor General Hospital and received iron folate supplementation for at least 1 month.	Pregnant women ANC visit <16 weeks, received counseling about iron folate supplementation had anemia, had knowledge about iron folate supplementation.	Pregnant women did not receive counseling about iron folate supplementation, did not have anemia, did not have knowledge about iron folate supplementation	Compliance with taking iron folate supplement	2.04 (1.12 to 3.75)
2	Kiwanuka <i>et al.</i> (2017)	Uganda	Cross-sectional	370	132	Pregnant women in the 2nd or 3rd trimester who perform ANC at Mulago National Referral Hospital and receive iron folate supplements	High number of ANC visits, receiving counseling about iron folate supplementation, number of supplements received >14 tablets, HIV positive status, not taking other medications, not formal workers or not working	Low number of ANC visits, did not receive counseling about iron folate supplementation, number of supplements received 14 tablets, negative HIV status, taking other drugs, formal workers	Compliance with taking iron folate supplement	1.56 (1.07 to 2.29)
3	Gabremichel <i>et al.</i> (2019)	Ethiopia	Cross-sectional	200	159	pregnant women who attended ANC follow-up at Ayder	Living in rural areas, receiving health education and nutrition	Living in urban areas, not receiving health education and nutri-	Compliance with taking iron folate supplement.	4.55 (1.53 to 13.51)

No	Author (Year)	Country	Study Design	Sample		Population (P)	Intervention (I)	Comparison (C)	Outcome (O)	aOR (CI 95%)
				Total	NC					
4	Gabremichael et al. (2020)	Ethiopia	Cross-sectional	623	512	Comprehensive Specialized Hospital who received iron folate supplements during the study period Pregnant women who perform the second ANC or more at the Adwa city government health institution and have received iron folate supplements for at least 1 month	counseling, family size 4, frequency of pregnancy 2, number of ANC visits 2. Pregnant women are 25-29 years old, have knowledge about iron folate supplements, get nutritional counseling, get partner support	tion counseling, family size <4, pregnancy frequency <2, number of ANC visits <2. Age of pregnant women 35 years, did not have knowledge about iron folate supplementation, did not receive nutritional counseling, did not receive partner support	Compliance with taking iron folate supplements	4.12 (2.12 to 8.03)
5	Nimwesiga et al. (2021)	Uganda	Cross-sectional	438	62	Pregnant women who perform ANC at least 2 times at Bwindi Community Hospital and receive iron folate supplements a month before	Primigravida, parity <3, received supplements, education about the benefits and harms of supplements, received adequate nutritional counseling	Number of pregnancies ≥4, parity 3, did not have a did not receive health education about the benefits and harms of supplements, did not receive nutritional	Compliance with taking iron folate supplements	3.6 (2.16 to 4.30)

No	Author (Year)	Country	Study Design	Sample		Population (P)	Intervention (I)	Comparison (C)	Outcome (O)	aOR (CI 95%)
				Total	NC					
						data collection		counseling sufficient		
6	Demisse et al. (2021)	Ethiopia	Cross-sectional	400	336	Pregnant women who make ANC visits at least 2 times and take iron folate supplements at least 1 month before the study is conducted	Having anemia, getting counseling about iron folate supplements, having knowledge about iron folate supplements	Do not have anemia, do not get counseling about iron folate supplements, do not have knowledge about iron folate supplements	Compliance with taking iron folate supplements	2.53 (1.37 to 4.66)
7	Mekonnen et al. (2021)	Ethiopia	Cross-sectional	414	325	Pregnant women take iron folate supplements for at least 1 month	Have a history of premature delivery, anemia, have a high perception of benefits, high self-efficacy	Does not have a history of premature delivery, anemia, does not have a high perception of benefit, does not have high self-efficacy	Compliance with taking iron folate supplements	2.28 (1.15 to 4.53)

Table 3. Description of the primary study in the meta-analysis of the effect of anemia status on adherence to taking iron folate supplements in pregnant women

No	Author (Year)	Country	Study Design	Sample		Population (P)	Intervention (I)	Comparison (C)	Outcome (O)	aOR (CI 95%)
				Total	NC					
1	Ogundipe et al. (2012)	Tanzania	Cross-sectional	21,889	471	Pregnant women performing ANC at Kilimanjaro Christian Medical College	Age of pregnant women >35 years, work as a housewife, has a history of malaria, suffers from HIV, has a history of preeclampsia or eclampsia, has anemia, has malaria, has other infectious diseases	Pregnant women age 26-35 years, work as a professional, do not have a history of malaria, do not suffer from HIV, do not have a history of preeclampsia or eclampsia, do not have anemia, do not have malaria, do not have other infectious diseases	Compliance with taking iron folate supplements	10.81 (8.72 to 13.39)
2	Gembre-mariam et al. (2017)	Ethiopia	Cross-sectional	241	47	Pregnant women who have performed ANC at least 2 times at Debre Tabor General Hospital and received iron folate supplementation for at least 1 month.	Multigravida, Primipara or multipara, primipara or multipara, had children, ANC visit <16 weeks, received counseling about iron folate supplementation, had anemia, had knowledge about iron folate supplementation	Primigravida, Nullipara, had no children, ANC visit >16 weeks, did not receive counseling about iron folate supplementation, did not have anemia, did not have knowledge about iron folate supplementation	Compliance with taking iron folate supplements	2.22 (1.15 to 4.29)

No	Author (Year)	Country	Study Design	Sample		Population (P)	Intervention (I)	Comparison (C)	Outcome (O)	aOR (CI 95%)
				Total	NC					
3	Birhanu et al. (2018)	Ethiopia	Cross-sectional	418	143	Pregnant women who perform ANC at the University of Gondar Hospital and receive iron folate supplements	Living in urban areas, married status, family size 4, first visit of ANC in the 1st trimester, experiencing anemia, number of supplements given each time ANC visit is 30 tablets	Lives in rural areas, single status, family size <4, the first ANC visit in the 3rd trimester, does not experience anemia, the number of supplements given every ANC visit is >30 tablets	Compliance with taking iron folate supplements	1.9 (1.17 to 3.12)
4	Boti et al. (2018)	Ethiopia	Cross-sectional	373	141	Pregnant women aged 15-49 years who follow ANC and receive iron folate supplementation for at least 1 month	Age <35 years, education status of mother and husband at least basic education, family size 4, multigravida, trimester 2 or 3, pregnancy registration ≤16 weeks, has a history of anemia, has knowledge about anemia, has knowledge about iron folate supplements	Age 35 years, mother and husband did not receive formal education, family size <4, primigravida, trimester 1, pregnancy registration >16 weeks, did not have a history of anemia, did not have knowledge about anemia, did not have knowledge about iron folate supplements	Compliance with taking iron folate supplements	2.02 (1.09 to 3.72)

No	Author (Year)	Country	Study Design	Sample		Population (P)	Intervention (I)	Comparison (C)	Outcome (O)	aOR (CI 95%)
				Total	NC					
5	Molla et al. (2019)	Ethiopia	Cross-sectional	348	31	Pregnant women making ANC visits at the health center, West Dembia district	Have knowledge about anemia, have knowledge about iron folate supplements, number of ANC visits 4, have a history of anemia, have a history of malaria	No knowledge of anemia, no knowledge of iron folate supplementation, number of ANC visits 2, no history of anemia, no history of malaria	Compliance with taking iron folate supplements	13.87 (3.75 to 51.35)
6	Mekonnen et al. (2021)	Ethiopia	Cross-sectional	414	90	Pregnant women who visit ANC at Simada district health centers and take iron folate supplements for at least 1 month	Have a history of premature delivery, have a history of anemia, get counseling about iron folate supplements, have a high perception of benefits, have high self-efficacy	Does not have a history of premature delivery, anemia, does not receive counseling about iron folate supplements, does not have a high perception of benefit self-efficacy	Compliance with taking iron folate supplements	1.67 (0.74 to 3.76)
7	Mamo et al. (2021)	Ethiopia	Cross-sectional	396	61	Pregnant women who visit ANC and receive iron folate supplements for at least 1 month	ANC frequency 4, have a history of anemia, have good knowledge about anemia and iron	ANC frequency <4, no history of anemia, no good knowledge about anemia and iron	Compliance with taking iron folate supplements	1.87 (1.01 to 3.47)

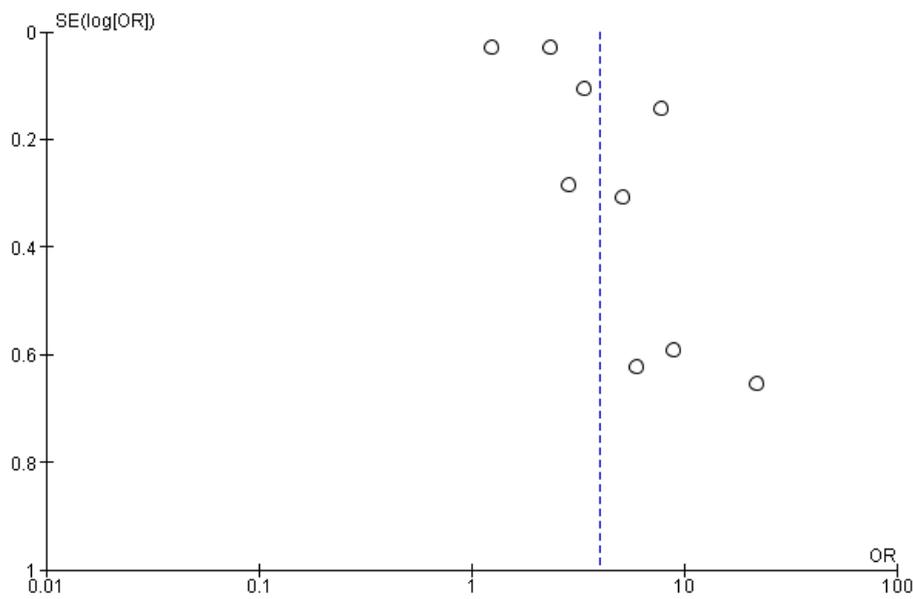


Figure 4. Funnel Plot Effect of Nutritional Anemia Status on Compliance Behavior of Taking Iron Folate Supplements in Pregnant Women

Based on figure 4. the funnel plot showed that there is a potential for publication bias with an overestimated effect characterized by an asymmetric distribution between plots (2 plots on the left, 3 plots on the right and 2 plots stuck in the middle). The plot on the left of the graph appears to have a

standard error (SE) between 0.2 and 0.4, while the plot on the right of the graph has a standard error (SE) between 0.1 and 0.6. The occurrence of bias can also be seen from the imbalance in the plot distance between studies, both on the right and left of the Funnel plot.

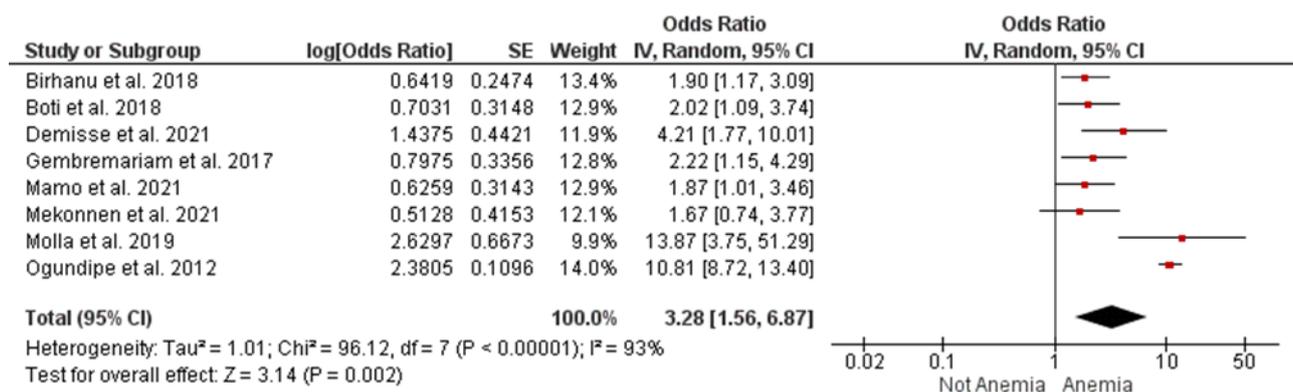


Figure 5. Forest plot Effect of Nutritional Anemia Status on Compliance Behavior of Taking Iron Folate Supplements in Pregnant Women

Based on the results of the forest plot, in Figure 5 showed heterogeneity value of I²= 93%, the analysis model used was random effect. The forest plot in Figure 4 shows that pregnant women with anemia

had 3.28 times higher adherence to taking iron folate supplements compared to pregnant women who were not anemic, and the results were statistically significant (aOR= 3.28; 95% CI = 1.56 to 6.87; p = 0.002).

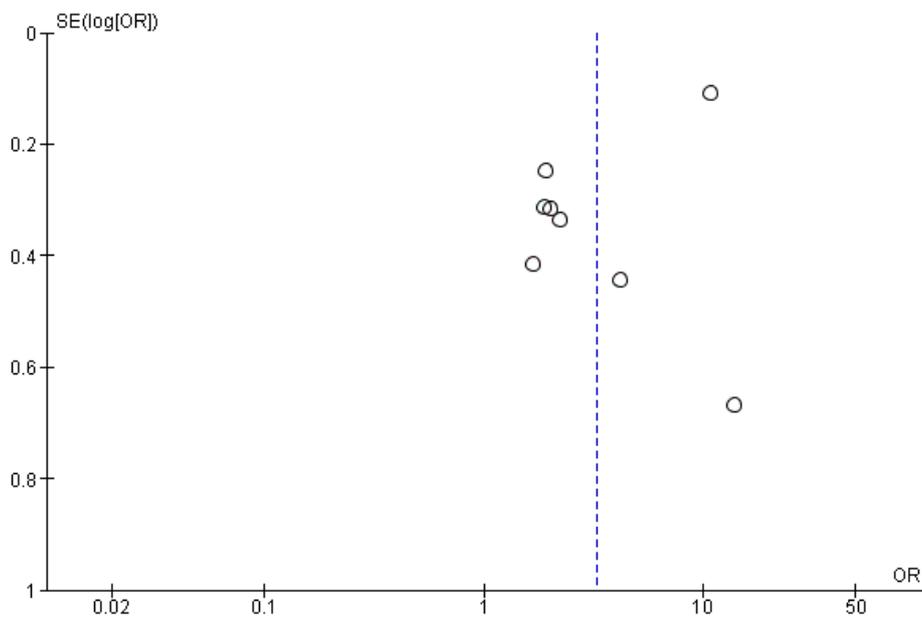


Figure 5. Funnel plot Effect of Nutritional Anemia Status on Compliance Behavior of Taking Iron Folate Supplements in Pregnant Women

The funnel plot in Figure 5 shows that there is a potential for publication bias with an underestimate effect characterized by an asymmetric distribution between plots (5 plots on the left and 3 plots on the right). The plot on the left of the graph appears to have a standard error (SE) between 0.2 to 0.4, while the plot on the right of the graph has a standard error (SE) between 0.1 and 0.7. The occurrence of bias can also be seen from the imbalance in the plot distance between studies, both on the right and left of the Funnel plot.

DISCUSSION

This systematic study and meta-analysis raised the theme of the effect of nutritional counseling and anemia status on the behavior of adherence to taking iron folate supplements in pregnant women. The independent variables analyzed were nutritional counseling and anemia status. The dependent variable analyzed was the behavior of adherence to taking iron folate supplements.

This research on the behavior of adherence to taking iron folate supplements in

pregnant women is important because pregnant women are very at risk of experiencing iron and folate deficiency and have low adherence to taking iron folate supplements. Agegnehu et al. (2019) states that pregnant women are more susceptible to the incidence of anemia and iron deficiency in the body so that it can reduce nutrients that affect life. The main strategy by implementing iron and folic acid supplementation to reduce anemia is to provide counseling about the benefits of taking iron folate supplements to pregnant women.

The primary studies that met the criteria were 12 articles from the African continent, 9 from Ethiopia, 2 from Uganda and 1 from Tanzania. This study shows that nutritional counseling and anemia status statistically significantly influence the behavior of adherence to taking iron folate supplements in pregnant women.

Nutrition counseling can improve adherence to taking iron folate supplements in pregnant women, these results are in accordance with the hypothesis. The results of the forest plot of 7 primary studies con-

ducted showed the magnitude of the effect of nutritional counseling on the behavior of adherence to taking iron folate supplements in pregnant women, namely 1.18 increasing adherence to taking iron folate supplements (aOR= 2.39; 95% CI= 1.92 to 2.96; $p < 0.001$). The heterogeneity of the research data shows $I^2 = 48\%$ so that the distribution of the data is declared homogeneous (fixed effect model).

Research by Nimwesiga et al. (2021) showed that adherence to taking iron folate supplements in pregnant women in Uganda was due to advice and counseling from health workers about the good effects of iron folate supplements and knowledge about health benefits. Research by Demisse et al. (2021) recommend strengthening nutritional counseling in health institutions because knowledge about iron and folic acid affects adherence to taking iron folate supplements in pregnant women. This is supported by the research of Mekonnen et al. (2021) which showed that pregnant women in Ethiopia who received appropriate health counseling and education about iron folate supplementation could improve adherence to taking iron folate supplements in pregnant women.

The results of the study were in line with that carried out by Gembremariam et al. (2017) which states that nutritional counseling can improve adherence to taking iron folate supplements in pregnant women in Ethiopia (aOR= 2.04, 95% CI= 1.12 to 3.75). Other similar studies were found in Uganda (Kiwauka et al., 2017), and Ethiopia (Gebremichael et al., 2019; Gebremichael et al., 2020).

In addition to nutritional counseling, anemia status in pregnant women, both anemia that occurred during pregnancy and a history of previous anemia, can increase adherence to taking iron folate supplements in pregnant women, these results are in

accordance with the hypothesis. The results of the forest plots from 8 primary studies that were conducted showed the magnitude of the effect of anemia status on the behavior of adherence to taking iron folate supplements in pregnant women, which was 3.28 increasing adherence to taking iron folate supplements (aOR= 3.28; 95% CI= 1.56 to 6.87; $p = 0.002$). The heterogeneity of the research data shows $I^2 = 93\%$ so that the distribution of the data is said to be heterogeneous (random effect model).

The research of Mamo et al. (2021) in Ethiopia showed that pregnant women who had a previous history of anemia had higher adherence to taking iron folate supplements. This is also in line with Molla et al. (2019) which showed that women who had a history of anemia during pregnancy were more likely to adhere to it compared to women who had no history of anemia. This is presumably because women who have a history of anemia drink more iron folate supplements for fear of side effects, and health workers will usually place more emphasis on anemic clients than non-anemic patients.

Similar studies were also found in Tanzania (Ogundipe et al., 2012) and Ethiopia (Gembremariam et al. 2017; Birhanu et al., 2018; Boti et al., 2018; Demisse et al. 2021; Mekonnen et al., 2021).

This study conclude that that pregnant women who received nutritional counseling and had anemia status had higher adherence behavior to taking iron folate supplements compared to pregnant women who did not receive nutritional counseling .

AUTHOR CONTRIBUTION

Farida Nur Aisyiyah contributed in choosing topics, searching for and collecting research data. Eltigeka Devi Apriliani contributes in data processing, analyzing data and reviewing research documents.

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This study is self-funded.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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