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Meta Analysis
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Meta-Analysis Effects of Antenatal Care Visit and Knowledge on the Adherence of Iron Tablet and Folic Acid Consumption

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ABSTRACT

Background: Adherence to iron tablet and folic acid (IFA) supplementation is the main strategy for the prevention and control of iron deficiency and neural tube defects in pregnant women and the unborn child. This study aims to estimate the relationships of antenatal care (ANC) visits and maternal knowledge on IFA supplementation adherence in pregnant women.
Subjects and Method: This study is a systematic review and meta-analysis using the PRISMA flow chart and the PICO model. Population: pregnant women. Intervention: conduct antenatal care visits and have knowledge of IFA Supplementation. Comparison: did not make antenatal care visits and had no knowledge of IFA Supplementation. Outcome: IFA consumption compliance. The databases used are PubMed, Google Scholar, and SpringerLink with keywords ("Antenatal Care" OR "IFA Supplementation" OR "Compliance") AND "cross sectional". There were 11 cross-sectional studies published in 2011-2023 that met the inclusion criteria. Analysis was performed with RevMan 5.3.
Results: A meta-analysis of 11 cross-sectional studies from Ethiopia and Uganda was performed, with sample size= 4,367. This study showed that pregnant women who had regular ANC visits (aOR=2.22; 95% CI= 1.52 to 3.24; p < 0.001) and had good knowledge (aOR=2.48; 95% CI= 2.02 to 3.03; p<0.001) were more likely to adhere to IFA supplementation. The funnel plot indicates publication bias (overestimate).
Conclusion: Pregnant women with regular ANC visits and good knowledge have the possibility to adhere with IFA supplementation.

Keywords: antenatal care, knowledge, adherence.

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BACKGROUND

Accounting for more than 30% of the global population, the highest in developing countries including pregnant women, postpartum

women, and children aged 6-24 months are usually the group most affected by iron deficiency (Agegnehu et al., 2019). Iron deficiency anemia in pregnant women is known to reach 38.2% on a global scale (Aroke et al., 2020). The number of cases of anemia has been increasing lately from 37.10% (2013) to 48.90% (2018) in the population of pregnant women in Indonesia (Aji et al., 2020).

Several studies have reported that the use of antenatal iron and folic acid supplementation during pregnancy reduces the risk of neonatal and childhood mortality by preventing maternal anemia, low birth weight, and preterm birth (Assefa et al., 2019). The use of iron and iron intake will increase maternal hemoglobin and reduce the risk of iron deficiency in the first and second trimesters (Fite et al., 2021).

Regular antenatal care attendance is believed to guarantee healthier pregnancies and smooth deliveries, and women who miss visits are considered to be at risk for poor pregnancy outcomes (Al-Dankali et al., 2022). Antenatal care programs distribute iron supplements to pregnant women, the effectiveness of interventions that are useful for reducing maternal anemia is still inadequate (Fekadu et al., 2022). Pregnant women who do not do antenatal care and do not attend all counseling sessions are considered disobedient to the antenatal care guidelines carried out by health workers (Berhane and Belacew, 2022).

Pregnant women seek antenatal care relatively late during pregnancy, most of the first visits are in the fourth or fifth month of pregnancy, and less than 60% attend four or more antenatal care visits (Afolabi et al., 2022).

Based on the research results, it is known that women who have better knowledge about anemia tend to be more obedient when supplementing with iron tablets (Gomaa and Mohamed, 2020). Educated pregnant women are more likely to have good knowledge because they may have a wide source of information about the benefits and importance of taking oral iron and they can also be more concerned about the effects of unwanted pregnancy, resulting in more medication adherence than uneducated women (Kadir et al., 2021).

Mothers with low knowledge of IFA, iron, and anemia have a greater chance of developing anemia, this raises the possibility that women with adequate knowledge about the benefits and lack of signs/ symptoms of IFA and who know iron-rich food sources are more likely to use IFA or iron supplements, consume iron-rich foods, and detect and promptly treat anemia (Wemakor et al., 2022).

A study involving pregnant women from Indonesia found that better adherence was found in pregnant women who had good knowledge about taking oral iron (Kadir et al., 2021). Adherence to IFA is the main strategy for preventing and controlling iron deficiency and neural tube defects for pregnant women and the unborn child, this is still rarely implemented in developing countries (Kassa et al., 2019). Adherence to routine iron supplementation among pregnant women has the potential to predict maternal and fetal health during pregnancy, labor and after delivery (Moshi et al., 2021).

Based on several research findings on the determinants of adherence of pregnant women, it was found that there was a gap between the results of one study and another, namely that there was a difference in the value of adjusted odds ratio (aOR) and the p-value between the effect of antenatal care visits and knowledge of compliance in pregnant women with iron and folid consumption. acid supplementation. Some of these studies were also conducted in several countries at different times. Based on the Gap of

Knowledge, the researcher will conduct research using a systematic review and meta-analysis of various results of previous primary studies.

The data obtained by the researchers will be analyzed using a meta-analytic study design, which is an epidemiological study that provides the strongest evidence in terms of causality by combining and statistically unifying the results of a number of independent primary studies that can be combined (Murti, 2018).

This study aims to analyze and estimate the size of the Gap of Knowledge or the influence of antenatal care visits and knowledge on the adherence of pregnant women to iron and folid acid supplementation. based on the results of similar previous studies.

SUBJECTS AND METHOD

1. Study Design

This research was conducted by systematic review and meta-analysis using primary data, namely data from similar previous research results. Article search using several databases, namely: Google Scholar, PubMed, and Springer Link. The keywords used are ("Antenatal Care" OR "Iron and Folid Acid supplementation" OR "Compliance") AND "aOR". There were 11 primary studies that met the inclusion criteria of this study.

2. Steps of Meta-Analysis

1) Formulate research questions through the PICO format (Population= Pregnant women; Intervention= Conduct antenatal care visits and have knowledge of IFA supplementation; Comparison= Did not make antenatal care visits and had no knowledge of IFA supplementation; and Outcome= IFA consumption compliance.
2) Searching for primary study research articles from several databases, namely Springer Link Google Scholar, and PubMed.
3) Conducting article selection by determining inclusion and exclusion criteria and conducting critical assessments.
4) Extracting selected primary study data and synthesizing effect estimates using the RevMan 5.3 application.
5) Interpret results and draw conclusions.

3. Inclusion Criteria

This full-text article uses a cross-sectional study design, the subject of the study is pregnant women, the outcome of the study is adherence of pregnant women, and the results of the analysis used are multivariate analysis with adjusted odds ratio (aOR) to measure the estimated effect.

4. Exclusion Criteria

Articles published in languages other than English, articles prior to 2011, and outcome measures in studies are incomplete or do not clearly describe results.

5. Operational Definition of Variable

Antenatal Care is a health service provided to pregnant women in health institutions by trained health workers at least 4 times, provided during pregnancy to ensure better mother and baby outcomes through risk identification, prevention and management of pregnancy-related or concomitant diseases.

Knowledge is Knowledge is a process experienced by someone to know something through sensing a certain object, whether obtained formally or informally. Informal knowledge can be obtained from the mass media, other people's experiences, family or information provided by health workers.

Compliance is the obedience or regularity of pregnant women in consuming iron and folic acid for a minimum of 90 days during pregnancy up to 42 days after the postpartum period. Those who are able to take at least seventy-two IFAS pills or more or 80% of the total intake time are considered to be compliant in taking IFAS, while those who are unable to take less than seventy-two IFAS tablets or less than 80% of the total intake period are considered non-adherent to intake IFAS.

6. Instrument

The quality assessment of the main article in this study used the Primary Study Quality Assessment for Cross-Sectional Observational Study Design in Meta-Analytic Research sourced from the Public Health Sciences Masters Study Program, Postgraduate School, Sebelas Maret University.

7. Data Analysis

The articles in this study were collected using the PRISMA diagram and analyzed using the Review Manager 5.3 application (RevMan 5.3) by calculating the effect size and heterogeneity (I^2) to determine the combined research model and form the final results of the meta-analysis. The results of data analysis are presented in the form of forest plots and funnel plots.

RESULTS

The process of searching for primary articles related to the effect of antenatal care visits and knowledge on the adherence of pregnant women to consumption of iron and folic acid supplementation. In this meta-analysis study, it was conducted on several databases and the results obtained were 11 articles which can be seen in Figure 1 PRISMA Flow Diagram. The total number of articles in the initial search process was 2,076 articles. After the process of deleting published articles, 150 articles were found, with 87 of them meeting the requirements for a full text review. Furthermore, as many as 11 articles that met the quality assessment were included in the quantitative synthesis using meta-analysis.

Figure 2 shows the distribution area of the 11 primary articles used in this study, namely from the African continent was conducted in Ethiopia and Uganda.

1. The effect of ANC visits on the adherence to IFA supplementation consumption

Table 2 presents a description of 10 observational cross-sectional study as a source of meta-analysis of the effect of antenatal care visits on adherence of pregnant women to iron and folic acid supplementation.

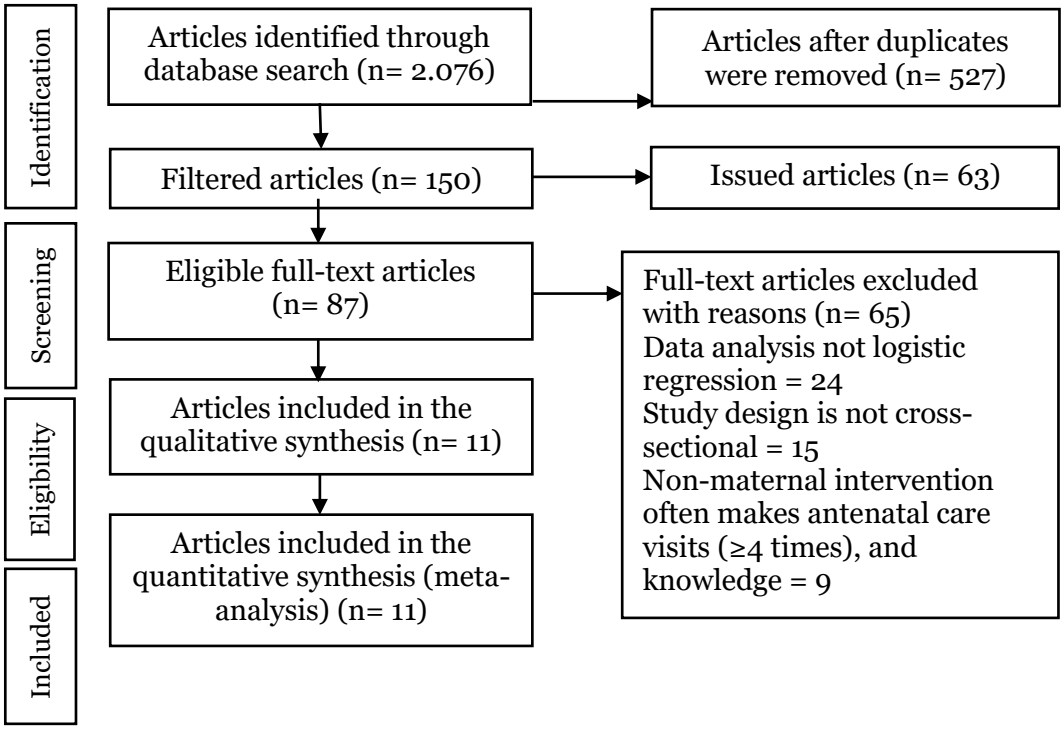

Figure 1. PRISMA flow diagram

Figure 2. Map of the studies distribution

Table 1. Results of the quality assessment of the cross-sectional study on the effect of antenatal care visits and knowledge on adherence of pregnant women to consumption of iron and folic acid supplementation

Author (Year)	Criteria of Question							Total
	1	2	3	4	5	6	7	
Demisse et al. (2021)	2	2	2	2	2	2	2	14
Molla et al. (2019)	2	2	2	2	2	2	2	14
Demis et al. (2019)	2	2	2	2	2	2	2	14
Solomon et al. (2021)	2	2	2	2	2	2	2	14
Kiwanuka et al. (2017)	2	2	2	2	2	2	2	14
Gebremariam et al. (2019)	2	2	2	2	2	2	2	14
Gebremichael and Welesamuel (2020)	2	2	2	2	2	2	2	14
Tarekegn et al. (2019)	2	2	2	2	2	2	2	14
Nigussie et al. (2022)	2	2	2	2	2	2	2	14
Tefera et al. (2021)	2	2	2	2	2	2	2	14
Ridwan and Shafi (2021)	2	2	2	2	2	2	2	14

Description of the question criteria:

1. Formulation of research questions in the acronym PICO

a. Was the population in the primary study the same as the population in the PICO meta-analysis?

b. Is the operational definition of exposure/ intervention in the primary study the same as the definition intended in the meta-analysis?

c. Was the comparison used in the primary study the same as that planned for the meta-analysis?

d. Were the outcome variables studied in the primary study the same as those planned in the meta-analysis?

2. Methods for selecting research subjects

a. Descriptive cross-sectional study: Was the sample randomly selected?

b. Analytic cross-sectional study: Was the sample chosen randomly or purposively?

3. Methods for measuring comparisons (intervention) and outcome

a. Were exposure/ intervention and outcome variables measured by the same instrument (measuring instrument) in all primary studies?

b. If variables are measured on a categorical scale, are the cutoffs or categories used the same between the primary studies?

4. Design-related bias

a. What is the Response Rate?

b. Is non-response related to outcome?

5. Methods to control confounding

a. Was there any confusion in the results/ conclusions of the primary study?

b. Did the primary study investigator use appropriate methods to control for the effects of ambiguity?

6. Methods of statistical analysis

a. In a cross-sectional study, was multivariate analysis performed? Multivariate analysis included multiple linear regression analysis, multiple logistic regression analysis, and Cox regression analysis.

b. Does the primary study report effect sizes or relationships on multivariate analysis? (eg, adjusted OR, adjusted regression coefficient).

7. Conflict of Interest

Is there a conflict of interest with the research sponsor?

Rating guide:

1. If on one question all items answer "Yes", then give a score of "2" to that question.
2. If in one question there is one item whose answer is "No", then give a score of "1" to that question.
3. If on one question all the items the answer is "No", then give a score of "0" to that question.

Table 2. Study descriptions of primary antenatal care visits included in the meta-analysis

Author (Year)	Country	Sample	Population	Inter-vention	Comparison	Outcome
Demisse et al. (2021)	Ethiopia	400	Pregnant women	Regular ANC visit	Irregular ANC visit	IFA Consumption Compliance
Molla et al. (2019)	Ethiopia	348	Pregnant women	Regular ANC visit	Irregular ANC visit	IFA Consumption Compliance
Demis et al. (2019)	Ethiopia	422	Pregnant women	Regular ANC visit	Irregular ANC visit	IFA Consumption Compliance
Solomon et al. (2021)	Ethiopia	416	Pregnant women	Regular ANC visit	Irregular ANC visit	IFA Consumption Compliance
Kiwanuka et al. (2017)	Uganda	370	Pregnant women	Regular ANC visit	Irregular ANC visit	IFA Consumption Compliance
Gebremichael and Welesa-muel 2020)	Ethiopia	629	Pregnant women	Regular ANC visit	Irregular ANC visit	IFA Consumption Compliance
Tarekegn et al. (2019)	Ethiopia	395	Pregnant women	Regular ANC visit	Irregular ANC visit	IFA Consumption Compliance
Nigussie et al. (2022)	Ethiopia	527	Pregnant women	Regular ANC visit	Irregular ANC visit	IFA Consumption Compliance
Tefera et al. (2021)	Ethiopia	308	Pregnant women	Regular ANC visit	Irregular ANC visit	IFA Consumption Compliance
Ridwan and Shafi (2021)	Ethiopia	290	Pregnant women	Regular ANC visit	Irregular ANC visit	IFA Consumption Compliance

Based on table 2, the description of primary research on the effect of antenatal care visits on adherence of pregnant women to iron and folic acid supplementation was conducted through a meta-analysis of 10 articles. The research locations varied, namely Ethiopia and Uganda. In this study, similarities were found, namely the research design used cross-sectional, the research subjects were pregnant women, the interventions

provided were antenatal care and not antenatal care. In this study, there were differences in the number of samples used, namely the smallest was 290 and the largest sample was 629. The total number of samples included in the meta-analysis of the effect of exclusive breastfeeding on the incidence of stunting in toddlers was 4,024 toddlers.

Table 3 lists the results of a statistical summary of the estimated effect with the highest aOR value of 6.97 and the lowest aOR value of 0.46. CI 95% with the largest range of 3.25 to 14.96, while the smallest range is 0.15 to 1.41.

Table 3. Adjusted Odds Ratio (aOR) value of the effect of antenatal care visits on adherence of pregnant women to IFAS consumption

Author	aOR	95% CI	
		Lower Limit	Upper Limit
Tarekegn et al. (2019)	4.14	2.14	8.01
Gebremichael et al. (2020)	1.40	0.88	2.22
Demisse et al. (2021)	1.69	0.76	3.22
Kiwanuka et al. (2017)	1.49	1.12	1.97
Solomon et al. (2021)	3.15	1.16	9.05
Molla et al. (2019)	6.97	3.25	14.96
Demis et al. (2019)	2.94	1.39	6.21
Tefera et al. (2021)	3.05	1.23	7.58
Nigussie et al. (2021)	0.46	0.15	1.41
Ridwan and Shafi (2021)	1.99	1.09	3.61

The forest plot in Figure 3 shows that there is an effect of antenatal care visits on the adherence of pregnant women in consuming iron and folic acid supplementation. Pregnant women who make regular antenatal care visits are more likely to adhere to iron and folic acid supplementation by 2.22 times compared to those who do not make regular antenatal care visits (aOR=2.22; 95% CI= 1.52 to 3.24; p<0.001).

Estimation of effects between studies showed high heterogeneity (I^2=71%; p= 0.004), with the calculation of the average effect estimation using the Random Effect Model (REM) approach.

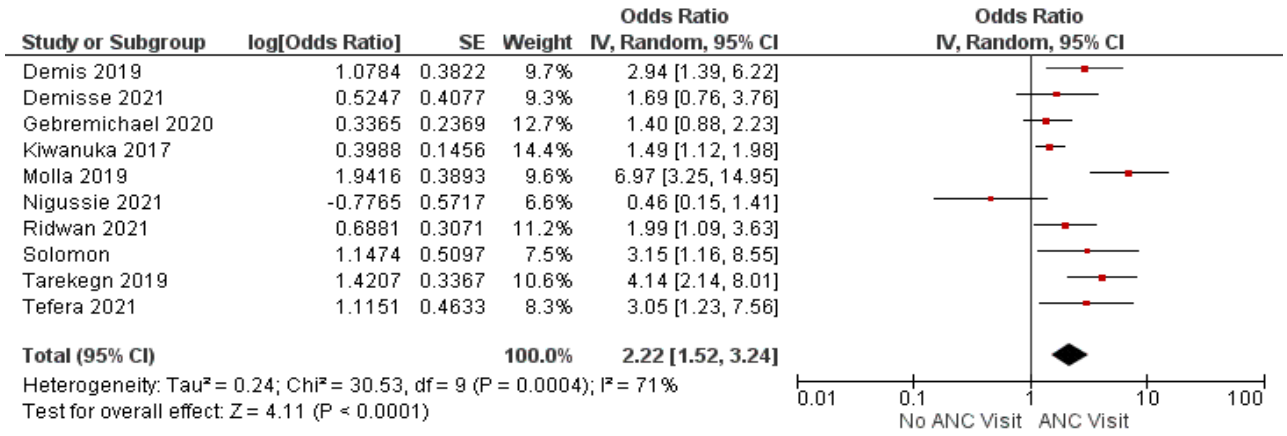

Figure 3. Forest plot of the effect of antenatal care visits on compliance of pregnant women consuming iron and folic acid supplementation

The funnel plot in Figure 4 shows that the distribution of effect estimates is more to the right than to the left of the average vertical line for small sample primary studies, thus indicating publication bias because the distribution is more to the right of the average vertical line.

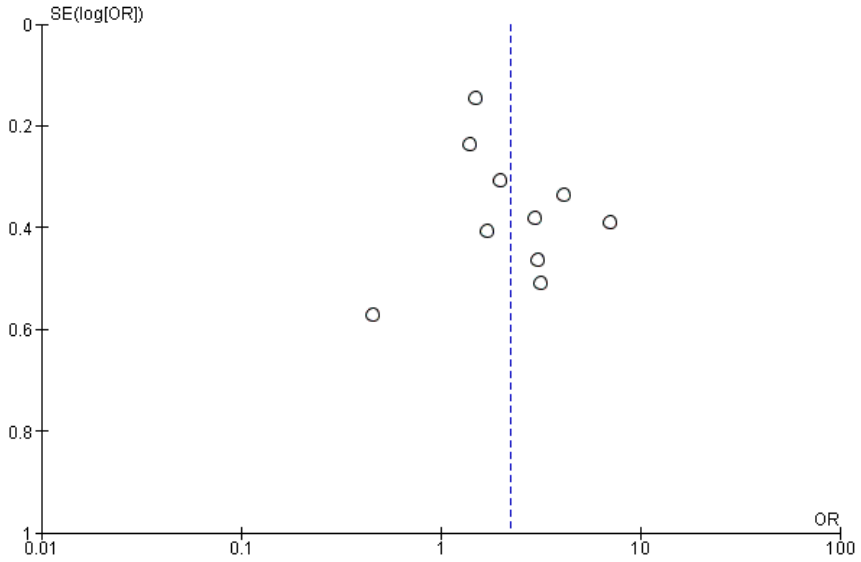

Figure 4. Funnel plot of the effect of antenatal care visits on compliance of pregnant women consuming iron and folic acid supplementation

2. Effect of maternal knowledge on adherence to IFA supplementation consumption

Table 4 presents a description of 8 observational cross-sectional study articles as a source of meta-analysis of the effect of knowledge on adherence of pregnant women to iron and folic acid supplementation.

Based on Table 4, it presents primary research on knowledge of adherence of pregnant women to consumption of iron and folic acid supplementation, which was conducted in a number of 8 articles with Ethiopian research locations, with a total sample of 3,294. There are similarities, namely the cross-sectional study design, the research subjects are pregnant women, the interventions given have knowledge of IFA supplementation. In this study there were also differences in the number of samples, the smallest being 262 pregnant women and the largest being 629 pregnant women. Table 5 lists the results of a statistical summary of the estimated effect with the highest aOR value of 3.56 and the lowest aOR value of 2.09.

Table 4. Description of the primary study knowledge included in the meta-analysis

Author (Year)	Country	Sample	Population	Intervention	Comparison	Outcome
Demisse et al. (2021)	Ethiopia	400	Pregnant women	Good knowledge of IFA	Poor knowledge of IFA	IFA Consumption Compliance
Molla et al. (2019)	Ethiopia	348	Pregnant women	Good knowledge of IFA	Poor knowledge of IFA	IFA Consumption Compliance
Demis et al. (2019)	Ethiopia	422	Pregnant women	Good knowledge of IFA	Poor knowledge of IFA	IFA Consumption Compliance
Solomon et al. (2021)	Ethiopia	416	Pregnant women	Good knowledge of IFA	Poor knowledge of IFA	IFA Consumption Compliance

Author (Year)	Country	Sample	Population	Inter-vention	Comparison	Outcome
Gebremichael and Welesamuel (2020)	Ethiopia	629	Pregnant women	Good knowledge of IFA	Poor knowledge of IFA	IFA Consumption Compliance
Gebremariam et al. (2019)	Ethiopia	262	Pregnant women	Good knowledge of IFA	Poor knowledge of IFA	IFA Consumption Compliance
Nigussie et al. (2022)	Ethiopia	527	Pregnant women	Good knowledge of IFA	Poor knowledge of IFA	IFA Consumption Compliance
Ridwan and Shafi (2021)	Ethiopia	290	Pregnant women	Good knowledge of IFA	Poor knowledge of IFA	IFA Consumption Compliance

Table 5. Adjusted Odds Ratio (aOR) value of the effect of knowledge on adherence of pregnant women to IFAS consumption

Author	aOR	95% CI	
		Lower Limit	Upper Limit
Gebremariam and Welesamuel (2019)	3.27	1.80	5.95
Gebremichael et al. (2020)	2.16	1.37	3.40
Demisse et al. (2021)	2.1	1.29	3.44
Solomon et al. (2021)	3.56	1.42	8.54
Molla et al. (2019)	2.82	1.52	5.23
Demis et al. (2019)	2.47	1.47	4.16
Nigussie et al. (2021)	2.79	1.42	5.51
Ridwan and Shafi (2021)	2.09	1.13	3.85

The forest plot in Figure 5 shows that there is an effect of knowledge on the compliance of pregnant women in consuming iron and folic acid supplementation. Pregnant women who have good knowledge are 2.48 times more likely to comply with iron and folate supplementation than mothers who do not have knowledge (aOR= 2.48; 95% CI= 2.02 to 3.03; p<0.001). Inter-study effect estimates show low heterogeneity (I^2= 0%; p= 0.90), with the calculation of the average effect estimation using the Fixed Effect Model approach.

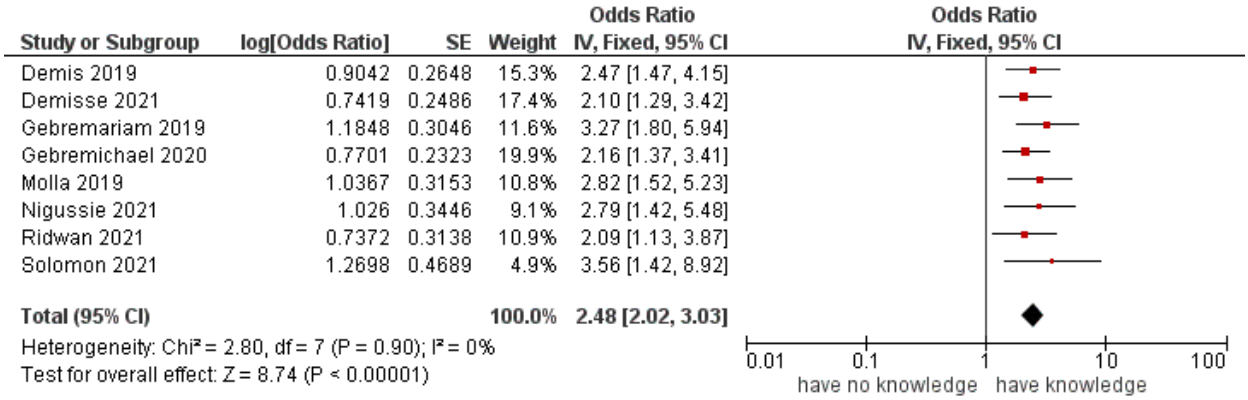

Figure 5. Forest plot of the effect of knowledge about iron and folic acid on the compliance of iron and folic acid supplementation

The funnel plot in Figure 6 shows that the distribution of effect estimates is located to the right rather than to the left of the average vertical line. Figure 6 shows that there is a

publication bias (overestimate).

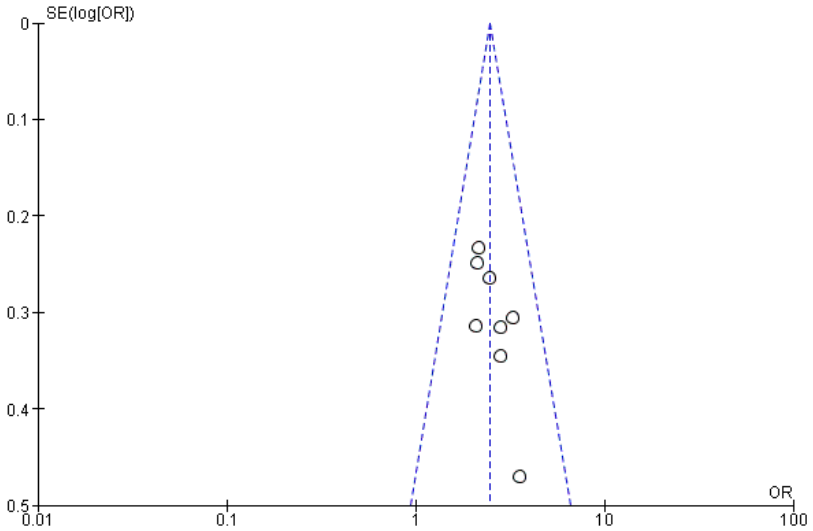

Figure 6. Funnel plot of the influence of knowledge on adherence of pregnant women to iron and folic acid supplementation

DISCUSSION

1. The effect of ANC visits on the adherence to iron and folic acid supplementation

Optimal adherence to folic acid supplementation during pregnancy reduces the risk of anemia-related morbidity in the mother, and congenital anomalies such as neural tube defects in the fetus as well as IFA intake below the recommended period during pregnancy have adverse neonatal outcomes such as; miscarriage, stillbirth, prematurity, low birth weight, congenital anomaly, perinatal morbidity and death. Compliance with IFA supplementation plays a major role in the prevention and treatment of iron deficiency anemia, especially in pregnant women whose iron requirements increase due to the needs of the fetus and mother (Desta et al., 2019).

A total of 10 cross-sectional research articles as a source of meta-analysis of the effect of antenatal care visits on adherence of pregnant women to iron and folic acid supplementation. This study shows that there is an effect of antenatal care visits on pregnant women's adherence in consuming iron and folic acid supplementation. Pregnant women who make regular antenatal care visits are more likely to adhere to iron and folic acid supplementation by 2.22 times compared to those who do not make regular antenatal care visits (aOR= 2.22; 95% CI= 1.52 to 3.24; p<0.001) and the results were statistically significant. The heterogeneity of the research data shows I2 = 71% so that the spread of the data is declared heterogeneous (random effect model).

The results of this study are in line with Ridwan and Shafi (2021), women with four or more ANC service visits are more compliant than women who have less than four ANC service visits. Possible reasons for this may be due to the fact that women who visit more often have more information exposure who are more likely to know about supplements and also healthcare providers can assist women during their ANC visits by discussing the benefits of IFS, then concluding with IFS adherence.

The results of this study are in line with the research by Sendeku et al. (2020), pregnant women who start early antenatal care have a higher likelihood of adherence to

iron-folic acid supplementation. This may be because pregnant women who order ANC services early and receive repeated counseling can gain better knowledge about the benefits of IFAS on their pregnancy outcomes.

2. Effect of knowledge on the adherence to iron and folic acid supplementation

Knowledge of pregnant women about IFA supplements is another factor found to be associated with supplement adherence. Compared with women who did not have satisfactory knowledge of IFA supplements, those who had satisfactory knowledge of IFA supplements were twice as likely to comply with the supplements. This can happen because pregnant women with satisfactory knowledge are aware of the consequences of iron and folic acid deficiency in both mother and child, enabling them to stick to the recommendations of health workers (Gebremichael and Welesamuel, 2020)

A total of 8 cross-sectional research articles as a source of meta-analysis of the effect of knowledge on adherence of pregnant women consuming iron and folic acid supplementation. shows that there is an effect of knowledge on compliance of pregnant women in consuming iron and folic acid supplementation. Pregnant women who have good knowledge have a 2.48 times more likely to comply with iron and folic acid supplementation than mothers who do not have knowledge (aOR= 2.48; 95% CI= 2.02 to 3.03; $p<0.001$), and the results are statistically significant . The heterogeneity of the research data shows $I^2 = 0\%$ so that the distribution of the data is declared homogeneous (fixed effect model).

The results of this study are in line with Sendeku et al. (2020), pregnant women who receive health education about IFAS are more likely to comply with IFAS than those who do not receive health education. The possibility of this can happen if pregnant women get health education so that they can increase the level of knowledge, attitudes and practices regarding IFAS compliance in pregnant women.

The results of this study are in line with Desta et al. (2019), women who have good knowledge about IFA supplementation have a greater chance of complying with the recommended IFA supplementation than mothers who have poor knowledge. Possible explanations for this could be due to the fact that mothers who have good knowledge about supplementation attain higher levels of education, are more likely to obtain information regarding iron-folate requirements and understand educational messages conveyed through various media.

In this study, knowledge of iron folate supplementation is positively related to compliance. Pregnant women who are aware of the importance of iron folate supplementation during pregnancy are more likely to consume tablets than mothers who do not have knowledge (Molla et al., 2019).

AUTHORS CONTRIBUTION

Siti Fatimah ANPA as a researcher who selects topics, searches for and collects research data. Uki Retno Budhiastuti and Rita Benya Adriani analyzed the data and reviewed research documents.

FUNDING AND SPONSORSHIP

This study is self-funded.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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