## **Meta-Analysis**

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# Compliance with iron and folic acid supplementation and associated factors among pregnant women in Ethiopia: a systematic review and meta-analysis

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### **ABSTRACT**

**Background:** Anaemia is one of the world's leading cause of disability and the most serious global health issues. Globally about 38% (32 million) pregnant women are anaemic, from which 46.3% (9.2 million) are in Africa.

**Methods:** Works of articles from PubMed, Medline and Google Scholar journal data-base were considered. Entirely articles allied to compliance and determinants of AFA supplementation were captured. The authors used modified Newcastle-Ottawa quality appraisal rule for cross-sectional works to assess the excellence of the studies for consideration and, tracked preferred reporting items for systematic reviews and meta-analysis guideline. The pooled effect size was calculated with the review manager and compressive meta-analysis software.

**Results:** Eighteen studies with a total of 6649 pregnant women were included for analysis. Compliance of IFA supplementation in pregnancy in Ethiopia was 46.1%. Women who had experienced counselling on IFAS were 1.16 times, OR:1.16, (95% CI, 0.54, 2.50), knowledge on IFAS were 3.20 times, OR:3.20, (95% CI, 1.31, 7.85), knowledge of anaemia were five times OR:5.10, (95% CI, 1.87, 13.94), fourth visit for ANC were 1.58 times OR:1.58, (95% CI, 0.59, 3.42) and early registration for ANC were three times OR: 3.19, (95% CI, 0.77, 13.26) more likely to have compliance with IFAS compared to their counterpart.

**Conclusions**: There is low compliance of IFAS in different parts of Ethiopia. Lack of counselling on IFAS, knowledge of IFAS and anaemia, no fourth visit for ANC and timing in ANC registration were factors that hinder compliance of IFAS.

Keywords: Compliance, Anaemia, IFAS, Ethiopia

### INTRODUCTION

Anaemia is one of the world's leading cause of disability and the most serious global public health issues. Worldwide almost 38% (32 million) women in pregnancy are anaemic, from which 46.3% (9.2 million) are in Africa.<sup>1</sup> Though the causes are often vary; anaemia in pregnancy is extremely prevalent in global both industrialized and unindustrialized countries.<sup>2</sup> There is

considerable variation of prevalence anaemia in pregnancy within developed countries, in which the rate is 18% in USA, 20% in Australia, 67.8% in Singapore and 70% in China, whereas, the rates increase across trimesters.<sup>3-5</sup> However, the prevalence is increasing in developing countries, with rate of 50.1% in Ethiopia, 53% in Sudan, 71% in Guinea and 76.7% in Pakistan that is why anaemia has got consideration as public health concerns.<sup>6-8</sup>

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Anaemia in pregnancy has been connected to adverse pregnancy outcome and foetal development.9 These sound effects comprise; premature birth, LBW, abortion, delay psychomotor improvement and impairment of children's cognitive performance, and lesser totals on intelligence (IQ) test.10 Moreover, the effects of iron deficiency anaemia (IDA) in early stages of child and early childhood are not possibly to be adjusted by consequent iron treatment. 11 Iron consumption increase maternal mean haemoglobin concentration by 4.59 to 5.46 g/L. Hence, excessive consumption of iron at first or subsequent trimester pregnancy is meaningfully associated with decreased the threat of anaemia and, then lessens adverse birth outcome: premature birth and LBW. 6 Likewise, women in Sub-Saharan Africa consume low iron, calcium and folic having food assembly which is less than RDA (recommended dietary allowances) requirements in pregnancy for the reason that they were economically not established. 12

A plenty of works had examined multiple aspects upsetting anaemia in pregnancy. Therefore, maternal age, residence, literateness, antenatal care visit, interpregnancy interval, iron food consumption, dietary practice, micronutrient intake, dietary diversity, iron supplementation, parasite infection and gravidity were documented as factors related with anaemia in pregnancy. 13 Besides, women of third trimester pregnancy are more likely risky to develop anaemia as compared to first and second trimester.<sup>11</sup> To lessen burden of anaemia, WHO suggests day-to-day supplementation by 30-60 mg/d elemental iron+400 µg folic acid. Conversely, adherence to iron and folic-acid supplementation (IFAS) in Sub-Saharan Africa has to some extent better; quiet leftovers at substandard level in which adherence proportion ranges from 10.6% in Kenya to 79% in Mozambique.<sup>12</sup>

Several published articles on compliance with iron and folic-acid supplementation (IFAS) in pregnancy in Ethiopia are documented. 14-31 Nevertheless there is no systematic review and meta-analysis conducted on prevalence and determinants of IFA supplementation. Empirically the current overall prevalence of IFAS in pregnancy is not identified in this setup. Therefore, the problem could be undetectable to policy makers. Thus, in order to sum up studies conducted in different corners of country and give overall prevalence and determinants of compliance with IFAS in Ethiopia.

### **METHODS**

Literature of articles from pubmed, medline and google scholar journal data base was retrieved. To raise the all-inclusiveness of the study findings, uniterms and bole operators in English were used in searching strategies. The search terms used were; compliance of iron and folic acid supplementation or compliance of iron and folic acid supplementation during pregnancy or determinants of

compliance of iron and folic acid supplementation and Ethiopia were used.

#### Literature search

All articles related to compliance of iron and folic acids supplementation were retrieved. Since year of publication were not limited, all artless published to February 25, 2020 were accessed for eligibility in the review. Studies of cross-sectional quantitative study design were included. Nevertheless, articles published in qualitative methods were excluded. All authors accessed the title and abstract independently. To avoid biases, all eligible articles were screened and selected after full abstract the paper were reviewed individually. Finally divergence was managed based on pre-set inclusion criteria.

### Data extraction and quality assessment

All authors involved were involved in data extraction. Data exaction template which include name of authors, publication years, study area, sample size, odds ratio, confidence intervals and p value, counselling on IFAS, knowledge of IFA supplementation, knowledge of anaemia, fourth visit for ANC and early registration for ANC were prepared before data extraction was performed. After all researchers extracted data independently. Results were cross checked and compared. All researchers discussed and came to consensus to if disparity was upraised.

In current study modified Newcastle-Ottawa scale (MNOS) quality appraisal rule was used for cross-sectional works to assess the excellence of the studies for consideration and, tracked preferred reporting items for systematic reviews and meta-analyses (PRISMA) guideline. The over-all mark for the MNOS for cross sectional works was nine stars as a highest for the total scale with the lowest of zero. Articles were considered as high excellence in condition if attained 7 out of 9, average if it attained 5 out of 9 and low if it attained below 5 out of 9.<sup>33</sup>

### **Outcome** interests

Prevalence of compliance with IFAS in pregnancy was the key outcome of this work. WHO defined antenatal care visit is care provided by skilled health personnel (doctor, nurse or midwife) during pregnancy. Trimester is the number of weeks during pregnancy (first, 1-12 weeks, second, 13-26 weeks, and third, 27-40 weeks). Good adherence was considered as a pregnant woman who took ≥65% of the total prescribed IFA supplementation per month; whereas the opposite is true for non-adherence.

### Statistically analysis

Extracted data prepared in Microsoft excel were exported to review manager software version 5.3 and compressive meta-analysis version 2 for analysis. Statistical

description related to compliance and determinants With IFAS was performed. We tested publication bias by funnel plot and additionally empirically by Egger's regression test and the degree of reliability was evaluated to assess the occurrence of statistical heterogeneity. Heterogeneity of studies was measured with the I-squared statistic, in which 25, 50, and 75% characterized low, moderate and high heterogeneity correspondingly. Subgroup analysis was done by the study sub-region and study type (community based or/and facility based). The influence of selected predictor's variables which include: intestinal parasite infection, IFA supplementation, third trimester pregnancy and dietary diversity score (DDS) was analyzed by isolated sets of meta-analysis. The results of the meta-analysis were displayed in forest pilot and odd ratio (OR) with 95% confidence interval (CI).

### **RESULTS**

### Literature search

In the beginning, we identified studies related to prevalence of compliance and determinants of IFA supplementation for inclusion in meta-analysis. Accordingly, we found complete of 135 published studies. From these, 110 were banned for the reason inclusion criterion was not contented. An overall 25 full text of studies were cleaned and carefully chosen for eligibility. Out of these 7 studies were removed due to poor statistical reports and deficient data occur. Lastly, 18 studies were added in analysis (Figure 1).

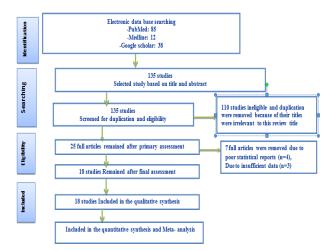


Figure 1: Flow diagram of the studies included in the meta-analysis.

### Characteristics of included studies

Twenty five cross-sectional articles were involved in the meta-analysis (Table 1).14-31

Score of modified

Table 1: Summary characteristics of included studies in meta-analysis.

Study authors	Year of publication	Regional location in Ethiopia	Sample size	Prevalence of anaemia in %	Newcastle–Ottawa scale
Sadore et al <sup>14</sup>	2015	SNNP	296	39.2	7
Taye et al <sup>15</sup>	2015	Amhra	628	20.4	8
Demis et al	2019	SNNP	422	43.1	7
Gashaaw et al	2018	Amhra	418	28.7	8
Gebreamlak et al	2017	Addis Aba	557	60	7
Gebremariam et al	2019	Amhra	241	40	6
Gebremedhin et al	2014	National	553	74.9	6
Gebremichael et al	2019	Tigray	200	10.5	7
Getachew et al	2018	Tigray	320	64.7	8
Dessie	2018	Amhra	348	19	6
Abdi et al	2018	Dire Dawa	217	76	5
Jikamo et al	2018	SNNP	365	69.59	8
Kassa et al	2019	SNNP	402	38.3	7
Molla et al	2019	Amhra	348	52.9	6
Boti et al	2018	SNNP	317	51.4	5
Niguse and Murugan	2018	Oromia	296	59.8	6
Shewasinad et al	2017	SNNP	326	70.6	7
Tarekegn et al	2019	Amhra	395	28.0	8

Out of these six studies (33.3%), were conducted in Amhara, six (33.3%) in Southern Nation Nationality and peoples of Ethiopia (SNNP), one (5.5%) in Oromia, two (11%) in Tigray, one (5.5%) in Dire Dawa city administration, one (5.5%) in Addis Ababa city

administration and one (5.5%) national study. The highest sample size was from Amhara with sample size of 628 and the minimum was from Tigray with sample size of 200 and the mean age of the respondent was 27 years. 17,21 Out of eighteen included studies; fourteen of the studies were facility based and the rest four were community based. 16-18,21-25,27-31,33

# Prevalence of compliance toward iron and folic-acid supplementation

The minimum prevalence of compliance 10.5% was observed from study conducted in Tigray.<sup>21</sup> The highest (74.9%) was observed in study conducted at National

level.<sup>20</sup> The pooled prevalence of compliance with Iron and folic-acid supplementation (IFAS) among pregnant women in Ethiopia was 46.1% (95% CI, 0.388-0.558). The heterogeneity test revealed  $I^2$ =98.14% and statistical evidence of heterogeneity, p≤0.00001). Therefore, random-effect analysis was used. The Bag's and Egger's test for publication bias also showed, no statistical evidence of publication bias, p=0.704 and p=0.459 respectively (Figure 2).

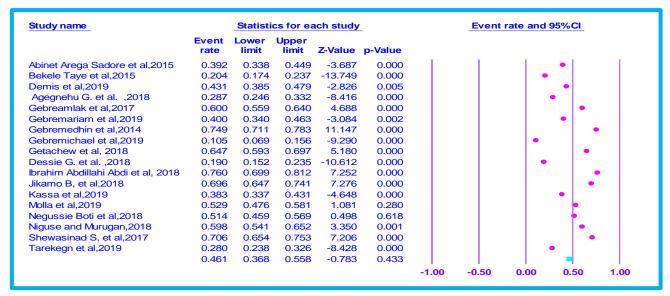


Figure 2: Forest plot displaying the pooled prevalence of compliance with IFAS in pregnancy in Ethiopia.

Table 2: Subgroup analysis of prevalence of compliance with iron and folic acid among pregnant women in Ethiopia.

Sub group	No. included in studies	Prevalence (95% CI)	Heterogeneity statistics	Tau squared	p value	$\mathbf{I}^2$
By region				-		
Addis Ababa	1	60 (0.559,0.64)	-	-	-	-
Amhara	6	30.5 (0.213,0.415)	139.04	0.349	< 0.000	96.403
Dire Dawa	1	76 (0.699,0.812)	-	-	-	-
National	1	74.9 (0.711,0.783)	-	_	-	-
Oromia	1	59.8 (0.541,0.652)	-	-	-	-
SNNP	6	52.3 (0.404,0.639)	147.25	0.348	< 0.000	96.624
Tigiray	2	31.8 (0.031,0.874)	112.958	3.3444	< 0.000	99.115
By study type						
Facility based	14	47.2 (0.372,0.574)	577.334	0.597		97.797
Community based	4	42.7 (0.206,0.681)	320.783	1.148		99.065

### Subgroup analysis

We performed a subgroup analysis by classifying studies into corresponding regional location in Sub-Saharan Africa in order to calculate and relate the prevalence of compliance of IFA supplementation athwart various participants' characteristics. Grounded on this analysis,

the lowest magnitude of compliance of IFA supplementation in pregnancy was documented In Tigiray region 31.8 (CI: 0.031, 0.874) and the highest was in Dire Dawa city administration 76 (CI: 0.699, 0.812). A higher magnitude (44.3 %) of compliance with IFAS in pregnancy was documented studies investigated at facility level than community based studies 47.2 (CI: 0.372, 0.574) (Table 2).

### Counselling on iron and folic acid supplementation

Out of eighteen studies included in meta-analysis; seven of them documented as counselling on IFA supplementation was associated with compliance of IFAS supplementation in pregnancy. 14,16,18,19,22,25,31 Likewise, the result of meta-analysis showed, women who had experiences of counselling on IFA supplementation infections in their course of pregnancy were 31.16 times

more likely to adhere compared to those with no experience of counselling during pregnancy, OR:1.16 (95% CI 0.54, 2.50). We performed heterogeneity test and the  $I^2$ =94% and statistical indication of heterogeneity, p $\leq$ 0.00001). Therefore, random-effect analysis was second hand. The Bag's and Egger's test for publication bias also exhibited, no statistical indication of publication bias, p>0.05 and p=0.953 correspondingly (Figure 3).

### Knowledge of iron folic acid supplementation

Association of lack of knowledge of iron folic-acid supplementation and risk of developing noncompliance to IFAS during pregnancy was reported in seven studies. 14,15,19,23,26-28 The result of meta-analysis showed that, pregnant women who had knowledge on supplementation of IFAS were 3.20 times more likely to have compliance of IFAS during pregnancy compared to those with women who had no knowledge of IFAS, OR: 3.20, (95% CI, 1.31, 7.85). The heterogeneity test showed I²=96% and statistical evidence of heterogeneity, p≤0.0000). Therefore, random-effect analysis was used. The Bag's and Egger's test for publication bias also showed, no statistical evidence of publication bias, p=0.710 and p=0.918 respectively (Figure 4).

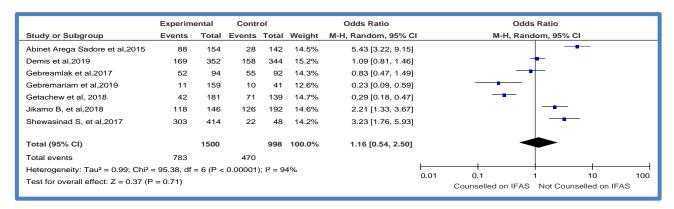


Figure 3: Forest plot displaying association of counseling on Iron and folic acid supplementation with compliance with IFAS among pregnant women in Ethiopia.

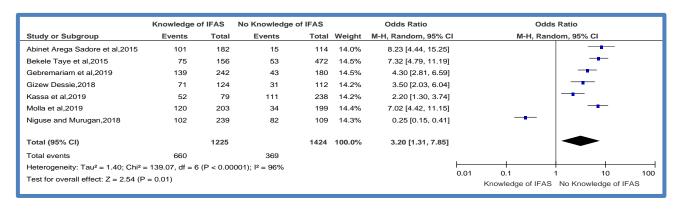


Figure 4: Forest plot displaying association of Knowledge of iron folic acid supplementation with compliance with IFAS among pregnant women in Ethiopia.

### Knowledge of anaemia during pregnancy

Association of lack of knowledge iron folic-acid supplementation and risk of developing noncompliance to IAFAS during pregnancy was reported in eight studies.<sup>14-16,22,25,27,31</sup> The result of meta-analysis showed that, pregnant women who had knowledge of anaemia during pregnancy were 5.42 times more likely to have

compliance of IFAS during pregnancy compared to those women who had no knowledge of anaemia, OR: 5.42, (95% CI, 1.51, 13.43). The heterogeneity test showed  $I^2$ =97% and statistical evidence of heterogeneity, p≤0.0000). Therefore, random-effect analysis was used. The Bag's and Egger's test for publication bias also showed, no statistical evidence of publication bias, p=0.907 and p=0.371 respectively (Figure 5).

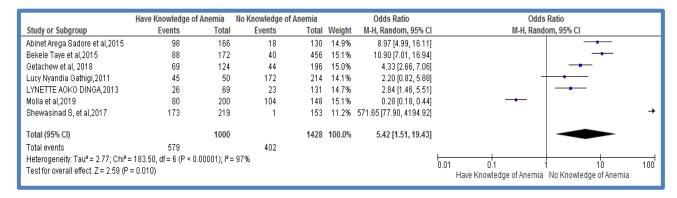


Figure 5: Forest plot displaying association of knowledge of anaemia during with compliance with IFAS among pregnant women in Ethiopia.

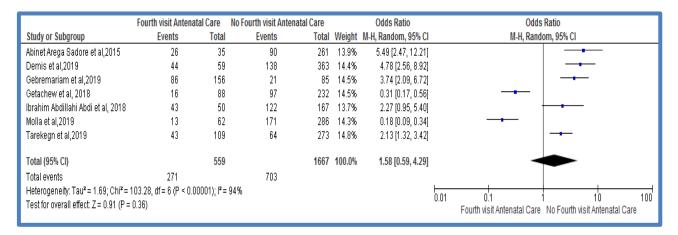


Figure 6: Forest plot displaying association of fourth visit for antenatal care with compliance with IFAS among pregnant women in Ethiopia.

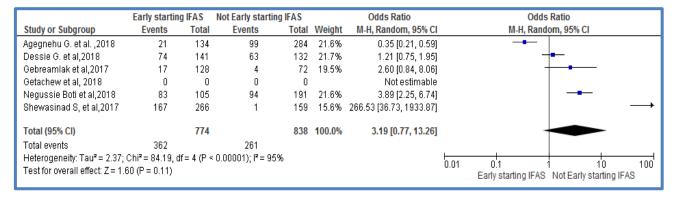


Figure 7: Forest plot displaying association of early timing antenatal care registration with compliance with IFAS among pregnant women in Ethiopia.

### Fourth visit for antenatal care (ANC)

Association of lack of fourth visit for antenatal care and risk of developing noncompliance to IFAS during pregnancy was reported in seven studies. 16,19,22,24,27,30 The result of meta-analysis showed that, pregnant women who had fourth visit for ANC during pregnancy were 1.58 times more likely to that, compliance with IFAS during pregnancy compared to those women who had no

fourth visit for ANC, OR: 1.58, (95% CI, 0.59,3.42). The heterogeneity test showed  $I^2$ =94% and statistical evidence of heterogeneity, p≤0.00001). Therefore, random-effect analysis was used .The Bag's and Egger's test for publication bias also showed, no statistical evidence of publication bias, p=0.930 and p>0.0.05 respectively (Figure 6).

### Early timing antenatal care registration

Association of non-early timing of registration of antenatal care and risk of developing noncompliance to IFAS during pregnancy was reported in seven studies.  $^{14,18,22,23,28,31}$  The result of meta-analysis showed that, pregnant women who had early registered for antenatal care during pregnancy were 3.19 times more likely to have compliance with IFAS in relation to those women who had late registration for antenatal care, OR 3.19, (95% CI, 0.77, 13.26). The heterogeneity test showed  $I^2$ = 95% and statistical evidence of heterogeneity, p≤0.00001). Therefore, random-effect analysis was used. The Bag's and Egger's test for publication bias also showed, no statistical evidence of publication bias, p=0.2427and p=0.256 respectively (Figure 7).

### **DISCUSSION**

The current review was conducted to determine the prevalence and determinants of compliance with iron and folic-acid supplementation among pregnant women in Ethiopia. Eighteen studies and total of 6649 pregnant women were included for the review. The heterogeneity test shows statistical evidence of heterogeneity which was explained by variation of geographical location by region and types of study (community and facility based). The pooled meta-analysis of this review found that, the prevalence of compliance with IFAS was 46.1% in Ethiopia. Study conducted in Iran reported that, prevalence compliance of IFAS among pregnant women was 71.6%. <sup>32</sup> Also in Egypt more than one-third of the pregnant women were not taking iron-folate tablets during pregnancy. <sup>33</sup> Finding in India again revealed that,

compliance of IFAS among pregnant women was 64%.<sup>34</sup> In Mozambique the level of adherence with IFAS during pregnancy were 79%.<sup>35</sup> The pooled prevalence of compliance with IFAS among pregnant women in this study was lower than of studies conducted in Iran, India and Mozambique and comparable with study done in Egypt and Kenya.

The current pooled meta-analysis showed that, pregnant women who had knowledge of IFAS was almost three times more likely to have compliance with IFAS during pregnancy compared to those women who had no knowledge of IFAS and pregnant women who had knowledge of anaemia during pregnancy were more than five times more likely to have compliance of IFAS compared to those women who had no knowledge of Anaemia. Studies done in Egypt and Kenya revealed that, there was a high statistically significant positive correlation between women's core of knowledge about folic acid, iron and anaemia and their score of compliance to iron /folate supplementation during pregnancy. 33,34

The pooled effect of current meta-analysis showed that pregnant women who had fourth visit for ANC during pregnancy were almost two times more likely to have compliance with IFAS during pregnancy compared to those women who had no fourth visit for ANC. Similarly an investigation conducted in five Asian countries (India, Indonesia, Nepal, Pakistan, and the Philippines) revealed that, pregnant women who had received at least three antenatal care visits were much more likely to adhere to at least 90 days of iron tablet or syrup or iron and folic acid tablets supplementation and also suggested antenatal care-seeking visits seem to be a particularly effective ways of reaching women and in increasing the likelihood of uptake of iron only or iron and folic acid supplements.<sup>36</sup> An investigation in South Africa also suggested that, compliance was thought to be influenced by the regular good attendance of antenatal care clinic service.<sup>37</sup>

The result of meta-analysis showed pregnant women who had early registered for antenatal care during pregnancy was three times more likely to have compliance with IFAS in relation to those women who had late registered for antenatal care. Similarity study done in Malawi reported, attending antenatal care during the first trimester were significantly associated with increased odds of taking iron supplementation for 90 days or more during pregnancy.<sup>38</sup>

### Strength and limitation

This review used extensive exploration method and more than one reviewer had taken part in all course of review process. PRISMA guideline was carefully tracked throughout review path. Nevertheless, this review has certain defects. Firstly, study lacks representativeness as, no data was found from some of regions in the countries such as Gambela and Benushangul Gumuz regions. Secondly, studies have been omitted due to poor statistics report, small sample size, inadequate data and qualitative studies. Finally, since only cross sectional studies were involved outcome variable may possibly be affected by confounding variable. Thus, this limitation might influence the overall prevalence of compliance among pregnant women in Ethiopia.

### **CONCLUSION**

Current paper finding suggests that lack of compliance of IFAS in pregnancy is rampant (all most half) in Ethiopia. Factors comprise; lack of counselling on IFAS, lack of knowledge on IFAS and anaemia during pregnancy, lack of fourth visit antenatal care and non-early timing of antenatal care registration were statistically related with compliance of IFA supplementation. These call the careful appraisal of Government and non-Governmental organization focus on interventions to promote the strengthening of antenatal care, supplementation of IFAS and establishment counselling of pregnant women to adhere to IFA supplementation during their pregnancy and measures are required to escalate compliance with IFA Supplementation in pregnancy in Ethiopia. Probable suggestion for supplementation needs to make sure that

women be given IFAS in pregnancy as WHO reference (minimum 90 tablets).

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