

The effect of iron tablets' side effects on the level of compliance to consuming iron tablets in pregnant woman: A systematic review

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Abstract

Iron tablet is one of the methods of preventing iron deficiency anemia during pregnancy. The consequences of ingestion include nausea, vomiting, constipation, diarrhea, epigastric pain, and dark stools. Pregnant women do not continue iron supplementation due to considering the negative effects. This behavior of not continuing to take the iron pills decreases the compliance of pregnant women to iron supplementation. This systematic literature review aims to assess the effect of iron tablets' side effects on the level of compliance to consuming iron tablets in pregnant woman. Four major electronic databases were used to explore a literature search: PubMed, Scopus, ScienceDirect, and Web of Science. There are fifteen eligible studies that fulfil the inclusion criteria. The PRISMA methodology was used to evaluate articles critically. EPHPP's technique for evaluating the quality of quantitative research was used to evaluate the quality of the kinds of literature (Effective Public Health Practice Project). Systematically, the findings are analyzed and summarized. Two main themes are used to classify the findings. Non-compliance and perceived risk to pregnancy can occur as a result of the first ANC visit at more than 16 weeks and less than 4 ANC visits during pregnancy. This is due to the lack of exposure to information and education from health professionals about iron tablets, the advantages of iron tablets, the side effects of iron tablets, and foods and beverages that could inhibit or accelerate the absorption of iron tablets.

Keyword: Compliance; Side Effects; Iron Tablet Supplements; Pregnancy

1. Introduction

The global prevalence of anemia in pregnancy exceeds 40% due to iron deficiency anemia in pregnant women. Iron supplements is one of treatment for iron deficiency anemia. The World Health Organization (WHO) recommends pregnant women take 90 iron tablets, each containing 0.4 g of folic acid and 30–60 mg of elemental iron [1]. Pregnant women who consume iron supplements may have nausea, vomiting, constipation, diarrhea, black stools, and abdominal pain. As a result, she often stops taking iron supplements [2].

Compliance with iron supplementation is defined as the behavior of pregnant women who comply with all the recommendations of health professionals. Insufficient compliance is caused not only by patient behavior but also by variables that are beyond the patient's control. It indicates that compliance to iron treatment is a subset of medical compliance. The main reasons that make people do not take their tablets are they do not like the side effects of iron pills and the frequency of pill consumption is too often. Other reasons include forgetting, the fear of having a big baby, and personal problems [3]. This literature study aims to discuss the correlation of side effects of iron tablets on the level of compliance, in which routine ANC visits as early as possible could increase the level of compliance and manage side effects after consuming.

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Purpose

This study aims to determine the impact of iron tablets effects on compliance level of iron tablets consumption in pregnant women. So, the research question is: Does the adverse effect of iron tablets' side effects on the level of adherence to consuming iron tablets in pregnant woman?

2. Material and methods

2.1. Design

This is a systematic review based on secondary research. Selected reporting elements are used in this review, which is methodical and adheres to PRISMA principles [4].

2.2. Searching the literature

This literature research used e-database: PubMed, Science Direct, Scopus, dan Web of Science using relevant keywords.

2.3. Inclusion criteria

2.3.1 Inclusion Criteria

- Research published in last five years (2018-2022)
- English Literature
- Full text, open-access literature, and original research
- The literature describes the impact of iron tablets effects on compliance level of iron tablets consumption in pregnant woman.

2.3.2 Exclusion Criteria

- Non-research studies (conference papers, book chapters, and reports) provide the literature.
- Studies are in the form of interventional, qualitative, systematic review, and case report studies.
- a pregnant mother with a chronic illness

2.4. Assessment of Quality

The Quality Assessment Tool for Quantitative Studies from the Effective Public Health Practice Project is used to evaluate the quality of the literature in this research (EPHPP). This instrument includes six broad evaluation components: selection bias (participants chosen), study design (research design), confounder (other factors relevant to outcomes that must be controlled), blinding (literature assessor), and data collecting method (proof of validity), withdrawals and dropouts (the number of people who entered or left the study). To make it easier for researchers to assess the quality of the literature covered, the results of this scoring system is divided into three rating of literature quality: (1=strong, 2=moderate, and 3=weak. These scales are based on component indicators and are used to evaluate the quality of the literature covered. After evaluating each component, it can be concluded that in general, a rating for literature is strong if there is no weak rating, moderate if there is one weak rating, and weak if there are more than two weak ratings. For each study, we extracted the following information: author, title, databased literature, journal, year, edition, volume, number, setting, research method, study design, participant, variables, instruments, statistical analysis, result of analysis, and summary of research result.

2.5. Data Extraction

The data preparation procedure includes converting significant data from the chosen literature into certain formats or tables to make it simpler for researchers to discover literature.

3. Results

3.1. Search results

To identify the relevant research, a literature review was conducted for this study using the electronic databases PubMed, Web of Science, SCOPUS, and Science Direct. Using the Boolean operator containing OR/AND search phrases like "compliance" OR "compliance" AND "side effect" AND "iron supplementation" OR "iron folic acid" AND "pregnancy," a literature review was conducted.

The initial search of the electronic database found 2,693 items. Then screening was analyzed based on the inclusion and exclusion criteria, resulting in a total of fifteen articles for completing literature research in this subject presents a flowchart of the PRISMA search and selection method. **Figure 1** Below is the research and article selection processes.

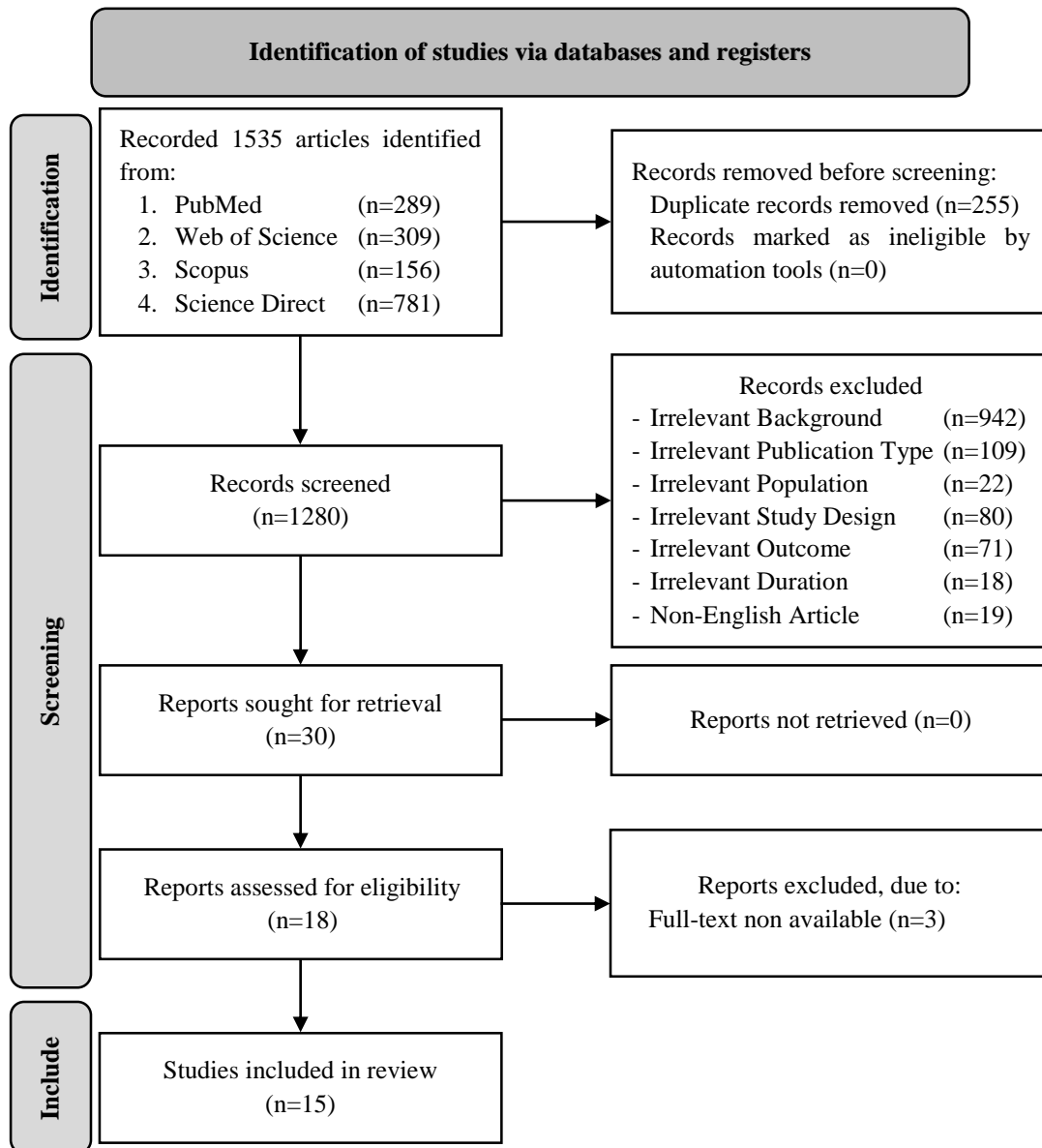


Figure 1 PRISMA flow diagram of study selection process

3.2. Characteristic of the study

Data is extracted from each literature review to determine the characteristics of the literature. The 15 studies included 5194 participants, with 12 cross-sectional studies and 3 randomized controlled trials, which included the study designs. Ethiopia, Kenya, and Nigeria are the sources of 12 literatures from the African continent, and three literatures are from the Asian continent (India and Saudi Arabia). The characteristics of the literature are summarized in Table 1 below.

Table 1 Data on the characteristics of the literature reviewed

No.	Author	Details
1.	[5] Adaji et al	Article title: Daily versus twice daily dose of ferrous sulphate supplementation in pregnant women
		Place: Abuja, Nigeria
		Study design: Randomized Clinical Trial
		Time: March to December 2015
		Number of participants: 182 participants
		The results of the study: The level of compliance with taking iron tablets (ferrous sulphate) was divided into two intervention groups, namely the 75% once-daily dose (65 mg) and 55% twice-daily dose (130 mg) groups. Side effects were the most prevalent reason for noncompliance (nausea, vomiting, epigastric pain) [OR = 0.41, CI = 0.210–0.790, P = 0.009]. The 25% who received the once-daily dose were much more compliant than the 45% who received the twice-daily dose, as an indication that failure to comply with intake caused side effects. The perception of compliance significantly impacts how the side effects of iron pills are experienced.
2.	[6] Ahamed et al	Article title: Effect of directly observed oral iron supplementation during pregnancy on iron status in a rural population
		Place: Haryana, India
		Study design: Randomized Clinical Trial
		Time: January to December 2014
		Number of participants: 368 participants
		The results of the study: Compliance in the intervention group was 69.1% vs. 60.4% in the control group (P = 0.001). In the control (44%) and intervention (30%) groups, side effects were a common reason for low compliance. Constipation/diarrhea, upper abdominal pain, and nausea/vomiting were side effects that were experienced more frequently in the intervention group. Significantly higher compliance to IFA therapy is related to an increase in side effects associated with intermittent IFA therapy (one weekly dose).
3.	[7] Birhanu et al	Article title: Compliance to iron and folic acid supplementation in pregnancy
		Place: Gondar, Northwest Ethiopia
		Study design: Cross-sectional
		Time: 8 th March to 10 th April, 2017
		Number of participants: 418 participants
		The results of the study: Compliance for supplementing iron and folic acid was 55.3% (95% CI: 50.74%, 60.26%). The primary reason for not taking supplements as advised was the fear of negative effects. 143 pregnant women (34.2%) reported having anemia. The length of ANC visits, the quantity of pills given, how often iron is given at each ANC visit, and anemia status all have an impact on the adverse effects of iron tablets, which consequently influence the effectiveness of iron-folate supplements.
4.	[8] Boti et al	Article title: Compliance to Iron-Folate Supplementation and Associated Factors among Pastoralist's Pregnant Women
		Place: Burji Districts, Southern Ethiopia
		Study design: Cross-sectional
		Time: March to April
		Number of participants: 317 participants

		The results of the study: The number of IFAS pills consumed (four tablets per week) was used to assess iron and folate supplement compliance (51.4%). Nearly 2.5 times [AOR = 2.47, 95% CI = 1.13–4.97] more obedient were pregnant women with a formal education compared to those with a primary education. There is a significant relationship between levels of compliance and IFAS side effects. reducing IFAS side effects to increase pregnant women's psychological tolerance to the IFAS
5.	[9] Choudhuri et al	Article title: Compliance to iron and folic acid tablets among pregnant women attending antenatal clinic
		Place: Agartala, Tripura, India
		Study design: Cross- sectional
		Time: 15 th June to 14 th September 2019
		Number of participants: 240 participants
		The results of the study: The compliance of participants to IFA supplements was 52.5%. Constipation, gastritis, and vomiting were the most common tablet side effects (35.09%). At an adequate compliance level, there is no association between side effects and taking IFA tablets ($P > 0.05$). To increase pregnant women's compliance, health professionals need to provide counselling, education, and education.
6.	[10] Elsharkawy et al	Article title: Effectiveness of Health Information Package Program on Knowledge and Compliance among Pregnant Women with Anemia
		Place: Sakaka, Al-Jouf, Saudi Arabia
		Study design: Randomized Clinical Trial
		Time: January to May 2021
		Number of participants: 196 participants
		The results of the study: The maximum iron tablet consumption for three months is 90 tablets. Low compliance was less than 45 tablets (50%), medium compliance was 45–67 tablets (50%–75%), and high compliance was between 68–90 tablets (75%). IFAS side effects include gastrointestinal issues (vomiting, constipation, flatulence, headache, and taste disturbance). In comparison to the control group, the intervention group (90.8%) showed higher compliance. The side effects of iron supplements are significantly associated with compliance with taking IFAS.
7.	[11] Gebremichael et al	Article title: Compliance to iron-folic acid supplement and associated factors among antenatal care attending pregnant mothers
		Place: Adwa, Tigray, Ethiopia
		Study design: Cross- sectional
		Time: 1 st May to 6 th July, 2018
		Number of participants: 623 participants
		The results of the study: Compliance with iron-folic acid supplements was 40% [95% CI: 37.0%–44.7%]. There were 240 (78.2%) pregnant women who reported epigastric pain, constipation, and vomiting as IFAS supplement side effects. Effects were significantly associated with consumption and compliance level.
8.	[12] Kamau et al	Article title: Effect of a community-based approach of iron and folic acid supplementation on compliance by pregnant women
		Place: Kiambu, Kenya
		Study design: Cross- sectional
		Time: June 2016 to March 2017
		Number of participants: 340 participants

		The results of the study: Pregnant women are considered compliant if they consume a minimum of five iron tablets (70%) per week. Compliance rates in the first (63.8%–71.4%) and final (68.5%–74.3%) groups [DID 0.02 and CI -0.20, 0.24]. The number of people in the intervention group who discontinued taking IFAS (22.6%–9.8%) because of negative effects decreased because of improved knowledge about IFAS, indicating a strong association between non-compliance and consuming IFAS.
9.	[13] Kamau et al	Article title: Compliance with Iron and folic acid supplementation (IFAS) and associated factors among pregnant women
		Place: Kiambu, Kenya
		Study design: Cross- sectional
		Time: June to October 2016
		Number of participants: 364 participants
		The results of the study: The iron-folic acid supplementation level of compliance was 32.7%. 56.3% had a side effect [aPR = 1.15; 95% CI = 0.84-1.58, p <0.001]. High compliance was significantly associated with IFAS side effects. Pregnant women who do not receive counselling have a lower proclivity to be obedient, which contributes to insufficient iron supplement consumption.
10.	[14] Kassa et al	Article title: Compliance with iron folic acid and associated factors among pregnant women through pill count
		Place: Hawassa, South Ethiopia
		Study design: Cross- sectional
		Time: 1 st November to 30 th December
		Number of participants: 422 participants
		The results of the study: There was 38.3% compliance with the iron-folic acid supplementation. Consuming a minimum of four tablets per week (four times per week) or for more than 90 days during the third trimester of pregnancy is considered adhering to iron-folate supplementation. In pregnant women, side effects had an 8.5 times greater likelihood of reducing compliance [AOR = 0.34, 95% CI: 0.16-0.76]. As a result, the intensity of the side effects of iron-folate acid tablets has a major influence on how well pregnant women comply with the treatment.
11.	[15] Kedir et al	Article title: Iron and Folic Acid Supplementation Compliance and Associated Factors among Pregnant Women Attending Antenatal Clinic
		Place: Shalla, Southwest Ethiopia
		Study design: Cross- sectional
		Time: February to April 2019
		Number of participants: 402 participants
		The results of the study: According to the pill count and respondents' self-reports, 154 (38%; 95% CI, 33.5%–43.1%) and 171 (42.5%) of the study's total participants were compliant with iron and folate supplements, respectively. Pregnant women who were using tablets reported gastrointestinal discomfort, vomiting, constipation, and diarrhea (59.2%). The frequency of using iron-folate supplements is significantly associated with compliance with counselling services, knowledge of the benefits of IFA, and side effects.
12.	[16] Nasir et al	Article title: Compliance to iron and folic acid supplementation and prevalence of anemia among pregnant women attending antenatal care clinic
		Place: Tikur, Anbessa, Addis ababa, Ethiopia
		Study design: Cross- sectional

		Time: 5 th April to 5 th June, 2019
		Number of participants: 257 participants
		The results of the study: The percentage of IFAS compliance is 63.6%. WHO advises a daily supplemental dosage of 30 to 60 mg iron and 400 mg of folic acid, beginning as soon as possible. The primary cause of noncompliance with IFAS is adverse effects. It is optimal to take IFAS with meals and before bed to reduce adverse effects and improve compliance. There was a statistically significant correlation between using IFA supplements consistently and the side effects.
13.	[17] Ridwan et al	Article title: Compliance to iron folate supplementation and associated factors among pregnant women attending antenatal care at public hospitals
		Place: Jigjiga, Somali, Ethiopia
		Study design: Cross- sectional
		Time: 1 st - 30 th 2020
		Number of participants: 290 participants
		The results of the study: Compliance with iron and folate supplementation was quite poor. The IFAS compliance percentage is 54.9%. Women who are pregnant take four or more iron and folate supplements per week. Constipation/diarrhea, epigastric pain, and nausea/vomiting were reported as side effects (27.7%). More than four ANC visits during pregnancy were associated with almost twice as many compliant pregnant women [AOR: 1.991; 95% CI: 1.098–3.610; P = 0.023]. Compliance was statistically significantly affected by IFA supplement side effects.
14.	[18] Tarekegn et al	Article title: Antenatal care and mothers' education improved iron-folic acid compliance
		Place: Denbiya, Northwest Ethiopia
		Study design: Cross- sectional
		Time: 2 nd April to 27 th May, 2016
		Number of participants: 395 participants
		The results of the study: The results show that pregnant women who used IFA supplements had a favorable compliance rate of 28.01 percent (95% CI, 24.01, 35.9). stomach pain caused by IFA supplement side effects. Negative antenatal effects of IFA supplementation are significantly associated with low compliance with IFA supplementation in pregnant women.
15.	[19] Tegodan et al	Article title: Compliance to Iron and Folic Acid Supplements and Associated Factors Among Pregnant Mothers Attending ANC
		Place: Gulele, Addis ababa, Ethiopia
		Study design: Cross- sectional
		Time: May to June, 2019
		Number of participants: 398 participants
		The results of the study: Pregnant women obediently use supplements at least four times per week [95% CI = 57.5–67.0]. Pregnant women most often report side effects as the reason for non-compliance. Epigastric pain, black stools, nausea, and vomiting is all regarded as side effects. Health information on the side effects of iron and folic acid supplements became a statistically significant component associated with IFA supplement consumption at a p<0.05.

4. Discussion

The majority of the fifteen articles that were analyzed come from either Africa (Ethiopia, Kenya, and Nigeria) or Asia (Saudi Arabia and India). These regions are categorized as developing and impoverished countries, respectively, based

on the HDI (Human Development Index). Three parameters are used to classify: knowledge, an acceptable quality of living, and a long and healthy life. This literature cannot describe compliance globally because there is no literature from developed countries, such as those on the European continent. According to the participant literature in the fifteen publications reviewed, many of the participants are illiterate, and the majority barely completed elementary school. This may have an impact on a woman's level of knowledge since a mother with a higher level of education will have greater access to information sources and be more aware of the importance of iron supplements during pregnancy [16].

Pregnant women with low knowledge often have a negative perspective on adverse reactions to iron supplements, like nausea, vomiting, diarrhea, constipation, epigastric discomfort, and black faces [5,6,12]. This causes pregnant women to consistently forget or stop consuming according to WHO's advised standards [5]. The total pill of iron tablets consumed and poor management or missed iron supplement consumption indicate the quality of adherence in pregnant women [10]. Side effects after consuming iron supplements can reduce compliance to taking the prescribed number of pills as recommended by health workers [7,11,13,14]. Compliance and perceived risk significantly impacted the pregnancy of pregnant women who had ANC visits before 16 weeks of pregnancy and/or less than four times over the duration of their pregnancy [15,16,18]. This is due to exposure to healthcare workers' information and advice on iron supplementation, its benefits and drawbacks, as well as drinks and foods that may potentially obstruct or boost iron absorption [8,9,19].

5. Conclusion

Pregnant women with low knowledge often have a negative perspective on adverse reactions to iron supplements. This causes pregnant women to consistently forget or stop consuming according to the WHO's advised standards. Side effects after consuming iron supplements can reduce compliance with taking the prescribed number of pills. Compliance and perceived risk significantly impacted the pregnancy of pregnant women who had ANC visits before 16 weeks of pregnancy and/or less than four times over the duration of their pregnancy.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest

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