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COMPARISON OF IRON SUPPLEMENTATION DOSAGE WITH FERRITIN LEVELS IN PREGNANT WOMEN SYSTEMATIC LITERATURE REVIEW

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Abstract.

Anemia in pregnancy is a global health problem that affects nearly half of pregnant women. The World Health Organization (WHO) defines anemia in pregnancy as hemoglobin (Hb) <11 g/dL, or a hematocrit of 33% during pregnancy. The purpose of this study was to find out the effect of iron supplement dosage and ferritin levels in pregnant women based on a systematic literature review.The research design used is a qualitative systematic review. The population of this study were all published studies that discussed iron supplementation and ferritin levels in pregnant women. Of all the studies reviewed, it was concluded that giving 100 mg doses of iron supplementation per day to pregnant women is more effective in increasing ferritin levels.

Keywords: Iron Supplementation, Pregnant Women, Ferritin Levels, Systemic Review

1. INTRODUCTION

Anemia in pregnancy is a global health problem that affects nearly half of pregnant women. The World Health Organization (WHO) defines anemia in pregnancy as hemoglobin (Hb) <11 g/dL, or a hematocrit of 33% during pregnancy. The Centers for Disease Control and Prevention (CDC) defines anemia in pregnancy as having an Hb <11 g/dL, or a hematocrit of 33% during the first and third trimesters or a hematocrit of 32% in the second trimester.(Achebe and Gafter-gvili, 2017). Globally, anemia is found in more than 20% of pregnancies. The highest rates are found in developing countries with an estimated prevalence of 55.8% in Africa and 41.6% in Asia(da Costa et al., 2016). About 75 – 90% of cases of anemia in pregnant women are iron deficiency anemia(Abdu and Hussein, 2019). The main factors causing high anemia in pregnant women include poor diet, low adherence in taking iron tablets and irregularities in attending antenatal care services.(Nurmasari and Sumarmi, 2019).

The physiological need for iron in pregnant women and infants is very high with an estimated 1000-1200 mg of iron needed. About two thirds of iron is used to meet the needs of the mother, and one third for the needs of the placenta and fetus(Brannon and Taylor, 2017). WHO recommends daily supplementation of iron and folic acid in pregnant women at a dose of 30 mg to 60 mg of vitamin iron and 400 ng (0.4 mg) of folic acid as an effort to prevent anemia in the mother, puerperal sepsis, low birth weight, and low birth weight. premature(WHO, 2016). Regulation of the Minister of Health of the Republic of Indonesia No. 88 of 2014 also explains the standardization of iron supplement tablets for women of childbearing age and pregnant women. This effort includes administering iron tablets at least 90 tablets during pregnancy. According to the 2018 Riskesdas, only about 24% of pregnant women received ≥ 90 iron tablets, the rest only received < 90 items. The level of consumption of iron tablets is still quite low. Only 38.1% of pregnant women consumed ≥ 90 iron tablets, the remaining 61.9% only consumed <90 iron tablets(RI Ministry of Health, 2019).

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On researchVázquez et al., 2019stated that there was a relationship between ferritin levels and the dose of iron supplements in pregnant women. This early finding is supported by the research of Reddaiah et al., showing that iron supplementation is associated with increased serum ferritin levels. A greater magnitude of response to iron supplementation in women with suboptimal baseline haematological status has been suggested because of increased erythropoietin secretion. However, on researchAdaji et al., 2019Ferritin and hemoglobin levels decreased significantly after being given iron supplementation.

Therefore, researchers will analyze the relationship between ferritin levels and doses of iron supplements in pregnant women. This study aims to see the effectiveness of iron supplements in pregnant women in preventing and treating iron deficiency anemia by assessing ferritin levels.

II. METHODS

The research design used is a qualitative systematic review. The population of this study were all published studies that discussed iron supplementation and ferritin levels in pregnant women. The sample in this study was taken by total sampling, namely the technique of taking all samples that met the inclusion and exclusion criteria. The sampling technique in this study was to collect studies available on e-databases: Google Scholar, PubMed, ScienceDirect and Scopus. This research was conducted at the researcher's residence from June 2022 - December 2022. The instrument used in this study was hardware in the form of a laptop to process data. The application of the PRISMA method to avoid duplication and process the research studies obtained so that they fit the inclusion criteria.Ah*Mixed Appraisal Tool*(MMAT).Data processing was carried out using the PRISMA method to analyze all research studies obtained. The purpose of the PRISMA method is to avoid duplication and filter research studies. Screened studies will be assessed with the Mixed Appraisal Tool (MMAT).Research studies that have been carried out critical appraisal by assessing the completeness of the contents of the research study, the methods used and the results of the research conducted.

III. RESULTS AND DISCUSSION

Assessment of the quality of the literature that has been selected uses the Mixed Appraisal Tool (MMAT), which is a critical assessment tool for the assessment stage of systematic mixed studies reviews, namely reviews that include literature with qualitative, quantitative and mixed methods methods. Assessment of the methodological quality of five categories for studies: qualitative research, randomized controlled trials, non-randomized controlled trials, descriptive quantitative, and mixed methods (Hong et al., 2018).

This tool is divided into three categories with different methodological quality criteria depending on the study design and methods, namely, qualitative, quantitative (categorized as: randomized controlled, nonrandomized, and descriptive), and mixed methods. Before being assessed, all literature was given a screening question to show that the literature includes empirical studies and can be assessed using the MMAT.

Each literature will be given a 'Yes', 'No', or 'Can't Tell' answer to the question according to the type of research method. The overall score on methodological quality varies from 0% (low quality), 25% (low quality), 50% (moderate quality), 75% (moderate quality), and 100% (high quality) (El-Awaisi et al., 2018). Then each literature will answer 5 questions according to the research methods of each literature. The results of the assessment of the quality of the literature can be seen in the table.

Research F. Ahamed et al. (2018), G. Karakoc et al. (2022), S. Shinar et al. (2017), Goonewardene et al. (2018), J. Adaji et al. (2019), and L. Iglesias et al. (2019) used a randomized controlled quantitative research method. The questions asked were regarding the target population, the type of measurement used for the research results, the complete data, the confounders in the design and analysis, and the interventions given. All of the literature has an MMAT value of 75%.

The study of M. Naess-Andresen et al. (2019) and P. Crispin et al. (2019) uses a non-randomized quantitative research method. The questions asked were regarding the target population, the type of measurement used for the research results, the complete data, the confounders in the design and analysis, and the interventions given. In the study of M. Naess-

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Andresen et al. (2019) obtained an MMAT value of 75%, whereas in the study of P. Crispin et al. (2019) got an MMAT score of 100%.

Table 1. Assessment of Literature Quality

No	Author, year	MMAT Score (%)	Score quality
1	(Ahamed et al., 2018)	75	Reasonable
2	(Karakoc et al., 2022)	75	Reasonable
3	(Næss-Andresen et al., 2019)	75	Reasonable
4	(Crispin et al., 2019)	100	Tall
5	(Shinar, Skornick-Rapaport and Maslovitz, 2017)	75	Reasonable
6	(Goonewardene and Senadheera, 2018)	75	Reasonable
7	(Adaji et al., 2019)	75	Reasonable
8	(Iglesias Vazquez et al., 2019)	75	Reasonable

Table 2. Literature Characteristics

No	Author, year	Article Title	Research methods	Country	Research subject	Conclusion
1	(Ahamed et al., 2018)	*Effect of directly observed oral iron supplementation during pregnancy on iron status in a rural population in Haryana: A randomized controlled trial.*	*Randomized controlled clinical trial*	India	400 pregnant women in North India, with gestational age of 12 – 16 weeks.	- In the control group with a supplementation dose of 100 mg of iron, it showed an increase in ferritin levels of 12.1 ng/L - In the intervention group with a supplementation dose of 100 mg of iron, showed an increase in ferritin levels of 12.8 ng/L
2	(Karakoc et al., 2022)	*Is every other day iron supplementation effective for the treatment of the iron deficiency anemia in pregnancy?*	*Randomized controlled clinical trial*	turkey	264 pregnant women aged 14 – 28 weeks of gestation	- The daily intake group was given elemental iron 100 mg per tablet every day, showing an increase in

						ferritin levels of 4.9 ng/L - The every other day intake group was given elemental iron 100 mg per tablet every day, showing an increase in ferritin levels of 3.9 ng/L
3	(Næss-Andresen et al., 2019)	*Serum ferritin, soluble transferrin receptor, and total body iron for the detection of iron deficiency in early pregnancy: a multiethnic population-based study with low use of iron supplements.*	*Cross-sectional*	Oslo, Norway	792 pregnant women of 6 ethnicities (Western Europe, South Asia, Middle East, Sub-Saharan Africa, East Asia and Eastern Europe) with gestational age ≤ 20 weeks	The best indicator of iron deficiency anemia is ferritin
4	(Crispin et al., 2019)	*First trimester ferritin screening for pre-delivery anemia as a patient blood management strategy.*	*Case control/retrospective*	Canberra, Australia	4102 pregnant women	Serum ferritin level in the first trimester is the best marker to predict anemia in the third trimester
5	(Shinar, Skornick-Rapaport and Maslovitz, 2017)	*Iron supplementation in singleton pregnancy: Is there a benefit to doubling the dose of elemental iron in iron-deficient pregnant women? a*	*Randomized controlled clinical trial*	Bnei Brak, Israel	324 pregnant women in the second trimester	- In group 1 with a dose of 34 mg of iron per day, it showed an increase in ferritin levels of 4.5 ng/L - In group 2, the dose of 68 mg of iron per day showed an increase in

		randomized controlled trial.				ferritin levels of 4.8 ng/L.
6	(Goonewardene and Senadheera, 2018)	*Randomized control trial comparing the effectiveness of weekly versus daily antenatal oral iron supplementation in preventing anemia during pregnancy.*	*Randomized controlled clinical trial*	Sri Lanka	292 pregnant women with gestational age of 14 – 22 weeks	- In group 1, the administration of 120 mg of iron per day showed that it did not improve ferritin levels - In group 2, the administration of 60 mg of iron per day showed that it did not improve ferritin levels
7	(Adaji et al., 2019)	*Daily versus twice daily dose of ferrous sulphate supplementation in pregnant women: A randomized clinical trial*	*Randomized controlled clinical trial*	Abuja, Nigeria	182 pregnant women with gestational age of 14 – 24 weeks	- In group 1, the administration of 65 mg of iron per day showed that it did not improve ferriti levels - In group 1, the administration of 130 mg of iron as much as 2 capsules per day showed that it did not improve ferritin levels.
8	(Iglesias Vazquez et al., 2019)	*The Effectiveness of Different Doses of Iron Supplementation and the Prenatal Determinants of Maternal Iron Status in Pregnant Spanish*Wom	*Randomized controlled clinical trial*	Catalonia, Spain	791 pregnant women with gestational age ≤ 12 weeks	- Strata 1 with a dose of iron supplementation of 40 – 80 mg/day succeeded in protecting iron deficiency at the 36th week of pregnancy

		en: ECLIPSES Study.				- Strata 2 with a dose of iron supplementation of 20 – 40 mg/day increases ferritin levels at 36 weeks of pregnancy

From searching and filtering articles, it produces 8 journals. The 8 journals come from India, Turkey, Norway, Australia, Israel, Sri Lanka, Nigeria and Spain. The methods used varied, consisting of 6 journals using randomized controlled clinical trial, cross sectional, and case control methods. The articles I took were articles from 2017 to 2022.

The journal consists of various doses of iron supplementation given to pregnant women, such as 1 x 1 per day with a dose of 100 mg iron, 1 x 1 per day with a dose of 34 mg iron, 2 x 1 per day with a dose of 68 mg iron, weekly 10 mg of iron, daily dose of 60 mg of iron, 1 x 1 per day with a dose of 65 mg of iron, 2 x 1 dose of 130 mg of iron, there is a dose according to the Hb value, that is, if the Hb is 110 – 130 g/L given a dose 40 – 80mg of iron, if Hb > 130g/L given a dose of 20 – 40mg of iron. The gestational age selected was 12 to 26 weeks.

Because there are variations in the amount and dosage of iron supplementation in pregnant women, the type of disease varies, it also affects the levels of ferritin. There are several journals which state that the ferritin value increases after iron supplementation, and several journals also say that the ferritin value does not improve after iron supplementation.

Effect of Dosage of Iron Supplementation in Pregnant Women with Ferritin Levels

There are six studies that discuss how the effect of iron supplementation doses on ferritin levels, in which two of them have decreased ferritin levels and four other studies have increased ferritin levels. Six studies are randomized controlled clinical trials. Some of these studies show that the results of iron supplementation doses do not improve ferritin levels. One study said that taking 1 capsule containing 100 mg of elemental iron in one day increased ferritin levels by 12.8 ng/L 100 days after iron supplementation.

Characteristics of Research Subjects of Iron Deficiency Anemia in Pregnant Women

Based on the characteristics of the study subjects, the most iron deficiency anemia in pregnant women was at 12-26 weeks of gestation, namely the second trimester, except in the study by L. Iglesias et al. (2019) at gestational age ≤ 12 weeks. Almost all research subjects were pregnant women with indications of iron deficiency anemia in the early trimester of pregnancy, except in the study by J. Adaji et al. (2019) who chose non-anemic pregnant women as research subjects. Research subjects received doses of iron supplementation in study subjects varying from 1 capsule in one day, 2 capsules in one day, up to weekly doses.

Relationship between Iron Supplementation Doses and Ferritin Levels in Pregnant Women

In the study of F. Ahamed et al. (2018) obtained results with a supplementation dose of 100 mg of iron per day, showing an increase in ferritin levels of 12.8 ng/L. In the study of G. Karakoc et al. (2022) given 100 mg of elemental iron per tablet every day, showed an increase in ferritin levels of 4.9 ng/L. In the study of S. Shinar et al. (2017) showed that giving a dose of 34 mg of iron per day showed an increase in ferritin levels of 4.5 ng/L. In the study of Goonewardene et al. (2018) showed that giving 60 mg and 120 mg of iron per day showed that it did not improve ferritin levels. In the study of J. Adaji et al. (2019) gave the result that giving 65 mg 1 capsule per day and 130 mg of iron as many as 2 capsules per day, showed that it did not improve ferritin levels.

The results of a systematic literature review study of the relationship between doses of iron supplementation and ferritin levels in pregnant women obtained 3 literatures stating that there was an increase in ferritin levels after iron supplementation, 2 literatures stating that after iron supplementation the results did not improve ferritin levels, 1 literature which states that ferritin is the best indicator of iron deficiency anemia in pregnant women, and 1 literature states that ferritin levels in the first trimester is the best marker for predicting anemia in the third trimester.

Some studies do not include complete data on ferritin levels after iron supplementation. There are variations in supplementation doses and target age ranges so that there are differences regarding ferritin levels. Some researchers do not pay attention to the dosage limits of supplementation, causing significant side effects. The presence of confounding variables in each study was different, such as gestational age, time of day, and the rules for administering iron supplementation, causing the possibility of bias in this review.

IV. CONCLUSION

Of all the studies reviewed, it was concluded that giving 100 mg doses of iron supplementation per day to pregnant women is more effective in increasing ferritin levels. Future research is expected to consider gestational age, administration rules and doses of iron supplementation. It is hoped that in the future further research will be carried out regarding concrete assessment references of ferritin levels either increasing or decreasing after iron supplementation.

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