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Review Article

Consumption of Iron Tablets and Hemoglobin Levels of Anemic Pregnant Women: A Meta-Analysis Study

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ABSTRACT

Iron Tablet Suplement (ITS) Consumption is expected to prevent anemia with increased hemoglobin levels. The 2023 Indonesian Health Survey report shows that 27.7% of pregnant women in Indonesia experience anemia which will have an impact on pregnancy and childbirth complications. The study aims to determine the effect of ITS consumption on increasing hemoglobin levels in anemia pregnant women, so that it can prevent complications of pregnancy, childbirth and the birth of stunted babies. This study uses meta-analysis using the random effect model method. Articles accessed from Google Scholar and PubMed databases. The selection of articles used the PICOTS framework, which included the population of pregnant women, ITS consumption interventions, comparison with the control group that did not consume ITS, the outcome of increasing hemoglobin levels, and the research design in the form of a quasi-experimental study. The inclusion criteria are research articles published in 2010–2022, using a quasi-experimental design, full text available, and mean difference data available. The search used the keywords "iron tablet" AND "hemoglobin" OR "anemic pregnant women" and "Fe tablets" OR "hemoglobin" OR "anemia in pregnant women". The selection process is presented in the PRISMA diagram, 10 eligible articles were obtained. Data analysis using Review Manager application 5.4. The forest plot showed that the pooled mean difference was significant (MD = 1.87: 1.29-2.44; p<0.00001; I^2 = 96%), then it can be concluded that the consumption of Blood Supplement Tablets significantly increases hemoglobin levels in anemia pregnant women by an average of 1.87 g/dl. The plot funnel shows the standard error of the left plot between 0.1-0.3 while the standard error of the right plot is 0.1-2.9 which shows an almost symmetrical distribution of research where the distribution of points is almost balanced between the left and right sides of the centerline, meaning that there is no publication bias. Consumption of Blood Supplement Tablets is effective in increasing hemoglobin levels in anemia pregnant women, it is recommended to ensure the appropriate dose (60 mg of iron per day), increase compliance through community-based education programs, regular mentoring, the use of reminders, and health policies that facilitate access to ITS for pregnant women, accompanied by regular examinations and distribution at health facilities.

INTRODUCTION

Pregnancy is a natural and physiological process that has a risk of experiencing nutritional and health problems, including iron anemia. Iron anemia in pregnant women is a condition in which hemoglobin levels are below 11 g/dl in the first and third trimester of pregnancy or below

10.5 g/dl in the second trimester of pregnancy.[1] Anemia is a serious health problem that requires special attention because it can increase the rate of maternal illness and death, and can affect *pregnancy outcomes*. Problems that can arise due to anemia are miscarriage *(abortion),* premature birth, long labor due to fatigue of the uterine muscles in contracting (*uterine inertia*), postpartum bleeding due to the absence of uterine muscle contractions (uterine atonia), shock, infections during childbirth, maternity infections, and severe anemia can cause decompensation of the cord.[2] Anemia during pregnancy can lead to pregnancy complications. A lack of hemoglobin reduces the blood's ability to transport oxygen, which can interfere with fetal development, increase the risk of premature birth, and low birth weight (LBW). In addition, anemia can worsen the risk of postpartum bleeding, increase her susceptibility to infections, and put more weight on the mother's heart which can trigger heart failure or preeclampsia. This condition is also associated with impaired fetal cognitive and physical development, as well as increasing the likelihood of complications such as gestational diabetes. In addition, anemia can cause impaired blood cell formation in the mother and fetus, worsen nutritional status, and increase the risk of anemia in the baby after birth. Therefore, managing anemia during pregnancy is essential to prevent complications that can harm the health of the mother and fetus.[3]

WHO data in 2015 shows that the incidence of anemia in pregnant women globally is 28-36 million people. Meanwhile, the highest number of anemias is in Asia (12-22 million people), and the lowest is in Oceania or the Pacific Ocean region (100-200 people). In Indonesia, the rate of anemia in pregnant women is still quite high, at 48.9%. The 2018 Riskesdas report shows that the prevalence of anemia in pregnant women has increased over the last 5 years, namely from 2013 (37.15%) to 2018 (48.9%), meaning that it has increased by 11.8%.[4] The younger the mother, the higher the prevalence of anemia in pregnant women, including 15-24 years old (84.6%), 25-34 years old (33.7%), 35-44 years old (33.6%), and 45-54 years old (24%).[5]

Anemia in pregnant women is caused by a variety of factors, the most common of which are a deficiency of iron, folic acid, and vitamin B12. An unbalanced diet, especially a deficiency of iron, folic acid, and vitamin B12, can lead to megaloblastic anemia, which interferes with the production of red blood cells and oxygenation of the mother's body and fetus.[6,7] Limited economic conditions can limit pregnant women's access to nutritious food and health services, increasing the risk of malnutrition leading to anemia.[8,9] In addition, the mother's health status, such as the presence of chronic diseases, indigestion, or infections such as malaria, can worsen the condition of anemia, either by affecting nutrient absorption or increasing blood loss.[10]

Iron needs in pregnant women vary depending on gestational age. In the first trimester, iron requirements increased from 0.8 mg/day to 6.3 mg/day in the third trimester. In the second and third trimester, iron needs cannot be met with food alone, even though the food consumed is of good quality and high iron bioavailability. Therefore, iron also needs to be obtained from other sources so that these needs are met. The total addition of iron during pregnancy is estimated to be about 1000 mg, which is very important for the fetus, placenta, and increased maternal blood volume.[11] Part of the increase in iron needs can be met from iron stores in the body and increased iron absorption more efficiently. However, if iron stores are low or non-existent, and iron absorption from food is very limited, then iron supplements are necessary. To overcome iron deficiency, it is recommended to consume 60-120 mg of Fe per day and increase iron intake from food sources such as meat, liver, fish, milk, yogurt, nuts, and green leafy vegetables.[12] The Indonesian government's policy regarding the consumption of Iron Tablet Suplement (ITS) for pregnant women stipulates a dose of one tablet per day for 90 days. Each tablet contains 60 mg of ferro sulfate, and 60 mg of ferro sulfate per day can increase hemoglobin levels by as much as 1 g% per month.[11]

In 2018, the coverage of giving ITS to pregnant women in Indonesia reached 81.42%, but the incidence of anemia in pregnant women is still high.[4,13] The results of various studies prove that there is a relationship between the consumption of tablets plus blood and hemoglobin levels, but some studies also show that there is no relationship between ITS consumption and hemoglobin levels in pregnant women. This is an important study whether the consumption of blood supplement tablets is related to increasing hemoglobin levels in pregnant women by examining various relevant research results. There have been quite a lot of studies related to the

effect of ITS consumption on pregnant women, but it is still limited that reviews its impact on pregnant women's hemoglobin levels using a meta-analysis approach. The purpose of this study is to present a comprehensive summary of the effect of ITS consumption on hemoglobin levels in pregnant women using the meta-analysis method. The hypothesis of this study is that the consumption of ITS significantly increases the hemoglobin levels of pregnant women who experience anemia.

METHODS

This study used a quantitative approach with a meta-analysis method to review the effect of ITS consumption on hemoglobin levels in anemic pregnant women. Independent variables were the consumption of blood-boosting tablets grouped into the intervention group (getting and administering ITS) and the control group (not consuming ITS). The dependent variable is the difference in hemoglobin levels in pregnant women with anemia before and after the consumption of blood plus tablets on a ratio scale. The stage of the data collection process (research article) uses a literature search engine from *the Google Scholar and Pubmed* databases. The selection of Google Scholar and PubMed compared to other databases is based on a wider coverage of articles and easier data accessibility. Google Scholar provides access to a wide variety of publications from a variety of disciplines, including articles, theses, books, and conference reports, allowing researchers to find more diverse and *up-to-date* sources of information. Meanwhile, PubMed, managed by *the National Library of Medicine*, specifically offers scientific articles in the fields of health and life sciences, with access to research that has gone through a rigorous peer-review process, providing high credibility. Both databases have user-friendly interfaces and allow for efficient literature search, making them the go-to choice for acquiring relevant and reliable data in a short period of time.

Research article searches are conducted using keywords and Boolean operators (OR, AND, NOT, or AND NOT) to broaden or narrow the search, making it easier to select relevant research articles. The keywords used include: "iron tablet" or "blood supplement tablet" or "anemia" and "anemia pregnant women". The inclusion criteria for research articles are quasi experimental research design, fulltext downloadable articles, using Indonesian or English, publications in 2010-2022, and the type of research variables according to the topic being studied. Meanwhile, the exclusion criteria include articles that are only available in abstract form and articles that cannot be downloaded. With this method, data from various studies can be categorized and analyzed to produce more general conclusions regarding the effects of ITS consumption on pregnant women with anemia.

The determination of research articles was carried out using the PICOTS strategy framework, which includes:

1. *Population/problem* refers to the group to be analyzed according to the theme of the meta-analysis, namely pregnant women
2. *Intervention* refers to management actions in the population/promblem, namely the consumption of blood-boosting tablets
3. *Comparison* refers to other management interventions used as a comparator, if there is none, a control group can be used, in this study it is a group that does not take blood-boosting tablets
4. *Outcome* is the outcome or output obtained from the intervention, namely an increase in hemoglobin levels.
5. *Study design* is a research design criterion used in the article to be reviewed, which is quasi-experimental.

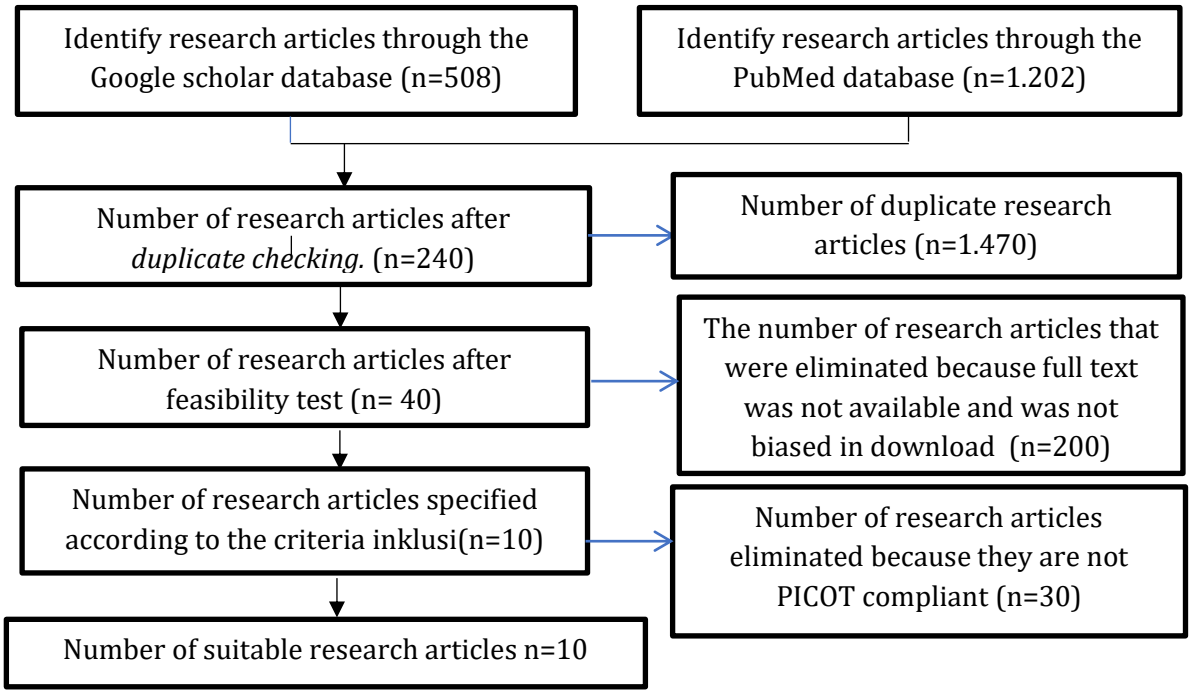


Figure 1. PRISMA Diagram of Research Article Selection

The data collection process is presented in the form of *Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA)* diagrams. The PRISMA chart shows that 508 articles were selected from *the Google Scholar* database, while 1,202 articles were selected from the international journal PubMed. The next stage is filtering based on abstracts, which aims to ensure that each article corresponds to the established independent and dependent variables. During the screening process, the completeness of the article is also evaluated and articles that are not available in full text form will be removed from the selection. In addition, articles that are not accessible are also excluded through the exclusion process. The final results of the article search and those that meet the criteria for analysis are 10 research articles. Data is extracted through a systematic selection process from relevant articles. The parameters used in the data extraction use the PICOTS framework. Parameters used in data extraction such as sample characteristics and changes in mean and deviation patterns of hemoglobin levels.The extraction results are presented in the form of a table.

Data processing and analysis using *Review Manager 5.4* software with *the weighted mean differences* (WMD) method. The data analysis aims to test the variance of the data through the variance homogeneity test, which can be seen from the results of *the Funnel Plot* and *Forest Plot*. *Forest Plot* is used to describe how much variation there is between studies, while *Funnel Plot* is used to show the results of the analysis of the relationship between the size of the study effect and the sample size of the various articles analyzed. The results of the variance homogeneity test can be seen through *the Forest Plot;* if the study shows heterogeneous (significant) variations, then the analysis uses *the Random Effects model.* On the other hand, if the variance of data between studies is not homogeneous (varies), then the model used is the *Fixed Effects model*. The selection of *the random effect* model in this study was based on the level of heterogeneity between studies detected using the value of I^2. A high I^2 value ($I^2 \geq 50\%$, p value ≤ 0.05) then using *a random effect (heterogeneous data variance)* indicates significant variation between the results of different studies, reflecting differences in the study design, population, or methodology used. In this case, *the random effect* model is more appropriate because it can account for these variabilities by providing more flexible weights for each study, resulting in more realistic estimates and better generalizations. Conversely, if the I^2 value is low ($I^2 < 50\%$, p value > 0.05), then the data analysis uses *a fixed effect model (homogeneous data variance)* that indicates that the studies have greater similarity in the results, the *fixed effect* model is more suitable because it assumes that the

measured effects are consistent across studies. Therefore, *the random effect* model was chosen in this study to account for the considerable heterogeneity between the studies analyzed. If there are biased factors or uncontrolled characteristics in the studies being analyzed, the results of the *random effect model* may be less accurate. *Cochrane Q test* results to assess the heterogeneity of statistical data. Sensitivity analysis to test statistical heterogeneity. *The effect size* used is a combination of each study with a specific statistical technique, which generally does not have basic data in the study. In this study, *the Effect Size* was calculated using *mean differences*. Publication bias analysis is seen from the results of *the Funnel plot* by looking at the standard error values and the distribution of research articles from the centre *line*. The results of the analysis were validated through sensitivity analysis to ensure consistency of the study results even though some studies were removed from the analysis. The first step in validation is to make a comparison between *fixed effect* and *random effect models* to assess the stability of the estimates obtained. If the results of the two models are similar, this suggests that heterogeneity between studies is low, and the conclusions drawn are likely to be stable. Next, sensitivity analysis was performed by removing one or more studies from the meta-analysis to see if the results remained consistent. If the deletion of a particular study causes a significant change in the results, this suggests that the findings from those studies may have a major influence on the conclusions. Conversely, if the results remain stable, this provides confidence that the research findings are robust enough and do not depend on one particular study. Thus, sensitivity analysis helps confirm the validity and resilience of the meta-analysis results to variations in the data.

RESULT

Iron Tablet Suplement Consumption in Pregnant Women with Anemia

Table 1 shows that at the Talang Health Center in Tegal Regency, 16 people were given Blood Supplement Tablets and 16 people were given date Blood Supplement Tablets, with a total of 32 respondents, so that the compliance percentage reached 50%.[2] Meanwhile, the results of the research at the Purwoyoso Semarang Health Center involved a sample of 21 people, of which 11 people obediently took Blood Supplement Tablets and 10 people did not comply. This non-compliance is caused by work outside the home, such as being a private worker or civil servant. Limited food availability in the environment of working mothers and irregular dietary conditions affect the level of compliance, so that the percentage of compliance is recorded at 52.4%.[4]

The results of the study on 50 pregnant women in the first trimester with a quasi-experimental design with a prospective cohort design, iron supplementation intervention in the form of 90 tablets was carried out, obtained results of 100% of pregnant women consuming Blood Supplement Tablets.[14] The results of another study at the Garuda Health Center from 60 pregnant women, only 20 pregnant women with anemia (30%) consumed ITS.[15]

Table 1. Excise Data from Research Articles on the Effect of Iron Tablet Suplement Consumption on Hemoglobin Levels in Anemic Pregnant Women

Author	Researcher title	Research Results
Dian Litasari (2014)[4]	Compliance with Taking Blood Supplement Tablets with Increased HB Levels of Pregnant Women at Purwoyoso Health Center Semarang	Before taking iron tablets, the hemoglobin level of pregnant women was recorded at 11 g/dl, which is relatively low, and increased to 11.62 g/dl after consuming 90 iron tablets. Most pregnant women (85.7%) admitted to consuming the iron tablets. Compliance rates vary, with a low of 81% and a high of 100%. The average blood hemoglobin level of pregnant women before consuming iron tablets was 10.9 gr%±1.0486 gr% SD. After consuming iron tablets, the average hemoglobin level increased to 11.6 gr%± 0.35857gr% SD. There was an increase in average hemoglobin levels by 0.7 gr% (p value = 0.002 < 0.05).
Durrotun Munafiah (2019)[2]	Giving ITS Mama (Date Honey, Increasing	Hemoglobin levels before ITS administration and Date Honey (Mama) companion therapy had a

Author	Researcher title	Research Results
	Pregnancy Hemoglobin Yield Levels in Preparation for Childbirth at the Talang Health Center, Tegal Regency	median of 10,000 g/dl, while after ITS and companion therapy the median hemoglobin level increased to 11,350 g/dl. The results of *the Wilcoxon signed ranks test* showed a significant difference between the administration of ITS and Mama's companion therapy (Date Honey) to hemoglobin levels in preterm pregnancies (p-value = 0.000).
Hilma Triana (2020)[16]	Effect of Beet Powder (Beta Vulgaris) with Fe Supplementation Increased Hemoglobin, Hemoatocrit, and Erythrocyte Levels in Pregnant Women with Anemia at Welahan 1 Health Center, Jepara Regency	Hemoglobin levels before consuming ITS 8.00 g/dl increased after consuming ITS to 10.90g/dl. Pregnant women with anemia who received significant Fe supplementation were able to significantly increase hemoglobin levels (p-value = 0.000), hematocrit levels (p-value = 0.000), and erythrocyte count (p-value = 0.001), resulting in significant differences in blood hemoglobin levels, hematocrit, and erythrocyte count in the intervention and control groups before and after treatment.
Lailahtul Mustaghfiroh (2017)[14]	Increase in Hemoglobin Levels in Pregnant Women with Iron Supplementation at BPM Ummi Haniek Jepara	The results showed that the average hemoglobin level before consuming ITS was 12.216 grams, while after consuming ITS increased to 13.128 grams. The results of the t-test indicated a significant effect of iron supplements on the increase in hemoglobin levels in pregnant women ($p < 0.05$), with an average increase of 0.912 gr%.
Liva Marita (2016)[15]	The Effect of Giving Green Spinach with Fe Preparation for Changes in Hemoglobin Levels in Pregnant Women at the Garuda Health Center	Differences in hemoglobin levels before and after taking ITS showed a p-value of 0.811 > 0.05, which means that there was no significant difference between hemoglobin levels before and after taking Fe tablets.
Rini Hariani Ratih (2017)[17]	The Effect of Iron (Fe) Administration on the Increase in Hemoglobin in Pregnant Women with Anemia at the Laboratory of RSIA Zainab Pekan Baru	The average hemoglobin level of pregnant women who experienced anemia before being given ITS was 8.81 gr/dl, while after ITS it increased to 12.59 gr/dl. Based on the dependent t-test, it was shown that there was an effect of ITS administration on increasing hemoglobin levels in pregnant women who were anemic (p-value 0.001< 0.05).
Rini Rahmayati (2017)[18]	Differences in the Effectiveness of ITS Administration on Hemoglobin Levels of Anemic Pregnant Women at the Air Padang Children's Health Center	The intervention group that received ITS plus red guava juice had an average hemoglobin level of 9.55 before administration, and increased to 11.17gr/dl after administration. Meanwhile, the average hemoglobin level in the control group that was only given ITS was 8.84 gr/dl, and increased to 11.48 gr/dl after 7 days of ITS administration. There was no difference in effectiveness between the administration of ITS plus guava juice compared to the administration of ITS alone on the hemoglobin levels of pregnant women who were anemic.
Umi Romayati Keswara (2017)[19]	The Effectiveness of ITS Administration on Increasing HB Levels in Pregnant Women at the Kamlin Inpatient Health Center in Bandar Lampung	The average hemoglobin level of pregnant women before being given ITS was 10.530 with a standard deviation of 1.1298, the highest hemoglobin level was 12.2 and the lowest was 8.0. After ITS administration for 1 month, the average hemoglobin level of pregnant women increased to 12.145 with a standard deviation of 0.6591, the highest hemoglobin level was 13.6 and the lowest was 10.8. There was a significant difference in the hemoglobin

Author	Researcher title	Research Results
		levels of pregnant women after taking ITS for 1 month at a dose of 60 mg/day (p-value < 0.001).
Utary Dwi Listiarini (2021)[20]	The Impact of ITS Consumption on Increased Hemoglobin in Pregnant Women in the 11th Trimester at the Kuaalanamu Deli Serdang Emplasmen Health Center	The average hemoglobin level before consuming ITS was 9.64 g/dl, after consuming ITS the average (mean) hemoglobin level increased to 11.62 g/dl. This shows that there is a significant relationship between ITS consumption and hemoglobin levels that there is an increase in maternal hemoglobin levels after consuming ITS (p-value 0.000 <0.05)
Wini Hadiyani (2019)[21]	The Effect of ITS Consumption Compliance on Hemoglobin Levels of Pregnant Women at the Cibuntu Health Center	The mother's Hemoglobin level increased from 10.3 g/dl to 11.1 g/dl after obediently consuming ITS. The results showed that ITS consumption adherence had a significant effect on increasing hemoglobin levels (p-value 0.003 <0.05)

The results of the study at the RSIA Zainab Pekanbaru Laboratory involved a sample of 30 people, with distribution based on the age of pregnant women who were anemic. At the age of <20 years, there were 3 people who took Fe tablets; at 21-35 years old, there are 20 people; and at the age of 36-50 years, there were 7 people who took Blood Supplement Tablets. Of the 30 samples, 20 of them consumed ITS, resulting in a compliance percentage of 67%.[6] The results of the research in the Air Padang Children's Health Center area showed that the sample used by 30 people was 100% obtained.[18] The results of the study in the Kamling Bandar Lampung Inpatient Health Center area found that the study on 31 respondents for all pregnant women so that the presentation obtained was 100%.[19] The results of the research at the Kualanamu Deli Serdang Emplasmen Poskesdes revealed that there were 15 respondents involved in the study and complied in consuming ITS regularly.[20] The results of research in the Welahan Health Center area of Jepara Regency show that presentations that consume ITS are only 50%.[16]

The results of the study in the Cibuntu Health Center area showed that more than half of pregnant women were not compliant in consuming ITS (64.5%). Pregnant women's non-compliance in taking ITS is influenced by several factors, such as nausea or even vomiting after consuming Fe Tablets, as well as lazy and forgetful factors. In addition, consumption behavior is also a factor that affects the consumption of blood-boosting tablets.[21] The results of research in the Purwoyoso Health Center area of Semarang show that non-compliance in consuming ITS is caused by work factors outside the home, such as becoming a Civil Servant or private worker and others. The limited availability of food in the environment of working mothers can affect irregular diets, thus contributing to a compliance rate that reaches only 52.4%.[4]

Hemoglobin Levels in Pregnant Women with Anemia

The results of several studies showed that there was an increase in hemoglobin levels before and after ITS consumption. The results of the study in the Welana 1 Health Center area of Jepara Regency, from the 7 articles analyzed, found the lowest value of hemoglobin levels which was 8.00 g/dl due to pregnant women experiencing anemia, which then increased to 10.90 g/dl after consuming ITS.[16] The results of the study in the Purwoyoso Semarang Health Center area showed that there were still respondents with a compliance rate of taking Blood Supplement Tablets of less than 100%, namely 3 respondents (14.4%). Non-compliance is caused by forgetfulness or nausea after taking Blood Supplement Tablets.[4]

The results of the study in the Talang Health Center area of Tegal Regency found that the median hemoblobin level in preterm pregnancy before ITS was given was 10 g/dl after ITS was given increased to 11.00g/dl, meaning that there was a significant increase before and after ITS consumption.[2] The results of the study at BPM Ummi Haniek Jepara found that the average hemoglobin level before the intervention was 12.216 gr% then increased to 13.128 gr% after ITS consumption, there was an increase in Hemoglobin level by 0.912 gr% (p-value < 0.05).[14]

The results of the research in the Garuda Health Center area found that the average hemoglobin level before ITS consumption was 8.81 g/dl, then increased after consuming ITS to 11.48 g/dl.[18] Research at the RSIA Zainab Pekanbaru Laboratory found that the average level

before consuming ITS of 8.81 g/dl increased to 12.58 g/dl.[17] The results of the study in the Kamling Inpatient Health Center area of Bandar Lampung showed that the average hemoglobin level before consuming ITS of 10,694 gdl increased to 12,206 g/dl after consuming ITS.[19]

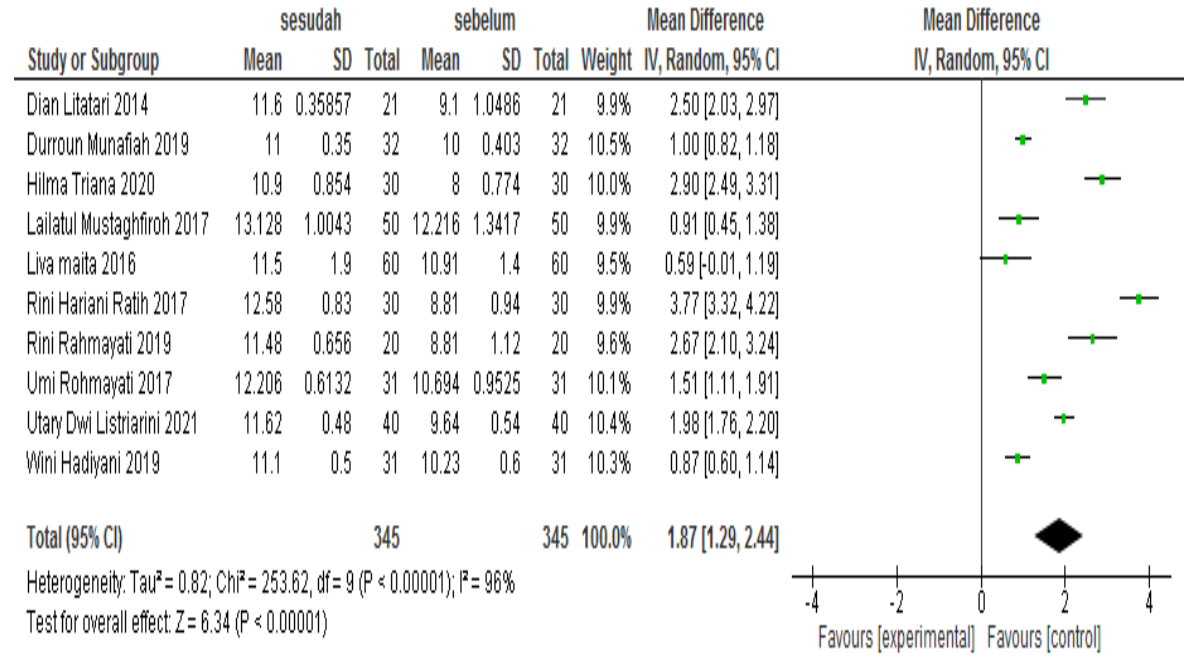
Compliant with ITS consumption can increase hemoglobin levels from 9.64 g/dl to 11.62 g/dl. Hemoglobin is made up of Fe (iron), protoporphyrin, and globin (1/3 of the weight of HB is made up of Fe). Free iron comes in two forms, namely ferrous (Fe2+) and ferrous (Fe3+).[20] The results of the study in the Cibuntu Health Center area showed an increase in hemoglobin levels before consuming (10.23 g/dl) increased after consuming Blood Supplement Tablets (11.1 g/dl).[21]

Iron Tablet Suplement Consumption and Hemoglobin Levels

The effect of Blood Supplement Tablet consumption on hemoglobin levels can be seen through the results of the Forest Plot in Figure 2 and the Funnel Plot in Figure 3.

Figure 2 shows that there is variation between heterogeneous studies, which is evidenced by the p-value in the heterogeneity test that is smaller than 0.05, namely p-value = 0.00001, and the I2 value of 96%. Therefore, this analysis uses a random effect model. The Forest Plot in Figure 2 shows that the pooled mean difference obtained is 1.87 (range 1.29-2.44), and the results are statistically significant with a p-value < 0.00001, which is smaller than 0.05. Thus, it can be concluded that ITS consumption has a significant influence on increasing hemoglobin levels in pregnant women who experience anemia.

Figure 3 shows a funnel plot that illustrates the effect of Blood Supplement Tablet consumption on hemoglobin levels in anemia pregnant women. The plot on the left side has an error standard between 0.1 and 0.3, while the plot on the right side has an error standard between 0.1 and 2.9. This plot funnel shows an almost symmetrical distribution of the research, with an almost balanced distribution of points between the left and right sides of the centerline. This shows that there is no publication bias in the studies analyzed.

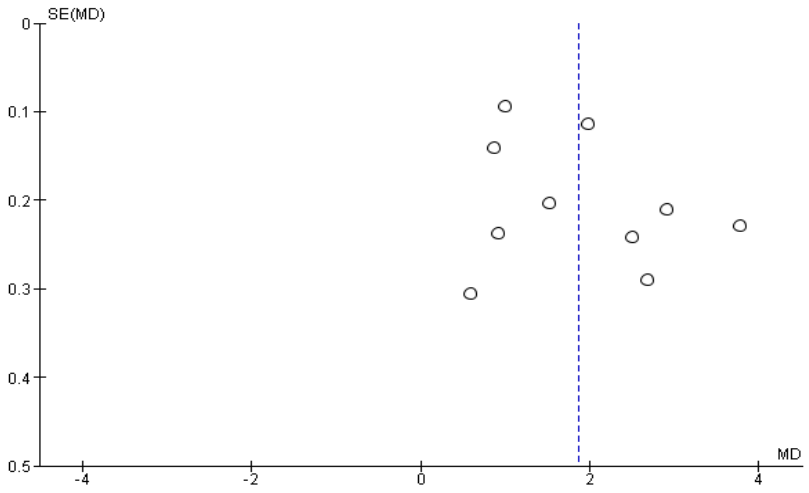


: The Green Squares show the weight of each study.

: Black Diamond Depicts *Pooled Mean Difference*

: Horizontal Line Illustrates Confidens Interval 95%

Figure 2. *Forest Plot* The Effect of Iron Tablet Suplement Consumption on Hemoglobin Levels in Pregnant Women with Anemia



Information:

SE : Standard Error

○ : MD Value per Article

------- : *Center Line* to see the symmetry of the plot

Figure 3. *Funnel Plot* The Effect of Iron Tablet Suplement Consumption on Hemoglobin Levels in Pregnant Women with Anemia

Sensitivity Test

Sensitivity test to identify heterogeneity. The results of the sensitivity test were carried out by comparing the differences between *the fixed effect model* and *the random effect model.* The results of the sensitivity test in Table 2 show that *the mean difference* value in *the fixed effect model* is lower than the *mean difference* in the random effect model, although the difference is not very significant. Based on the results of the homogeneity test, a p-value (0.00001) was obtained < 0.05, which indicates variation between studies. The results of this meta-analysis are considered robust (relatively stable to change).

Table 2. Comparison of *Pooled Mean Difference* between *Fixed Effect Models dan Random Effect Model*

Research variables	n	*Homogeneity (p-value)*	*Fixed Effect Model*	*Random Effect Model*
			Mean difference 95% CI	*Mean difference 95% CI*
Effect of Blood Supplement Tablet Consumption on Hemoglobin Levels in Anemic Pregnant Women	10	< 0.00001	1.60 (1.49 – 1.70)	1.87 (1.29 –2.44)

DISCUSSION

There were 10 research articles combined in a meta-analysis on the effect of Blood Supplement Tablet consumption on hemoglobin levels in pregnant women with anemia. All of these articles used a quasi-experimental study design. The results showed a mean difference of 1.87 (1.29-2.44), which is statistically significant with a p-value < 0.0001, which is smaller than 0.05. Thus, it can be concluded that the consumption of blood-boosting tablets has a significant effect on increasing hemoglobin levels in pregnant women who are anemic. Other studies also

support these findings, which suggest that the consumption of Blood Supplement Tablets may increase hemoglobin levels in pregnant women. Pregnant women who consume less blood-boosting tablets are at higher risk of anemia.[22,23,24,25]

Iron nutrients are very important for the body, and can be obtained from animal, plant, or blood-boosting tablets. Iron plays a role in the formation of hemoglobin which can bind to CO2 after releasing O2. About 15% of the CO2 in the blood is transported by hemoglobin molecules. CO2 reacts with the terminal α-amino group on hemoglobin, forming carbamates and releasing protons. Hemoglobin binds to two protons for every four O2 molecules released, which also affects the blood's carrying capacity. This process is reversed in the lungs, where O2 binds to hemoglobin which is in a deoxygenated state (without O2), protons are released and combine with bicarbonate to form carbonic acid. Carbonic acid then breaks down into CO2 gas (with the help of the enzyme carbonic anhydrase), which is eventually exhaled out of the body.[26] The results of Ratih (2017) research show that low hemoglobin levels in pregnant women are influenced by lack of consumption of iron-containing foods and unhealthy lifestyles.[17] The physical condition of pregnant women who are easily weak, lethargic and bleeding events cause low hemoglobin levels.[2]

As the gestational age increases, the need for iron in pregnant women is also increasing. Therefore, every pregnant woman needs to take Iron Tablet Suplement Consumption. In the first trimester, no iron is needed because the growth of the fetus is still relatively slow. However, in the second and third trimester, iron requirements need to be increased by 9 mg.[27] In the second and third trimester of pregnancy, the mother will experience an increase in blood volume by 35%, which is equivalent to 450 mg of iron, to produce new red blood cells. The addition of red blood cells is needed to meet the needs of oxygen and nutrients for the fetus until birth. The lower the addition of red blood cells, the less nutrients the fetus receives, which can affect its growth and development, as well as increase the risk of health problems in the fetus.[28]

Preventing pregnant women from anemia needs to be a priority program in the health sector. Pregnant women with anemia have Intrauterine Growth Restriction (IUGR), Low Birth Weight (LBW) premature birth, fetal death, and postnatal infant mortality.[29,30,31] Pregnant women with anemia are 2.8 times more likely to give birth to babies with IUGR than pregnant women who are not anemic. Babies born with IUGR are at risk of developing brain neurodevelopmental disorders.[32] A cohort study conducted in Pakistan showed that pregnant women with anemia were 2.4 times more likely to give birth to LBW than mothers who were not anemic..[32] The lower the hemoglobin level of a pregnant woman, the higher the risk of the baby being born with LBW condition.[27,33] Pregnant women with anemia are 4.5 times more likely to give birth to a premature baby than mothers who are not anemic..[32] The lower the mother's hemoglobin level, the higher the risk of premature birth. Mothers with severe anemia have a higher risk of giving birth prematurely than mothers who have moderate anemia.[33] Mothers who experience anemia in the second and third trimesters are at a higher risk of premature birth than mothers who are not anemic..[30,34] Mothers with anemia have a higher risk of stillbirth than mothers who are not anemic. The risk of stillbirth also increases if the mother has a poor nutritional status (BMI less than 18 kg/m2). The lower the hemoglobin level of pregnant women, the higher the risk of stillbirth. Pregnant women who have severe anemia are at higher risk of stillbirth than pregnant women who are not anemic.[33] Pregnant women with anemia in the second and third trimester of pregnancy are more likely to have stillbirths.[30,34] The higher the severity of anemia in pregnant women, the greater the risk of newborn death.[35] If pregnant women are affected by anemia in the first trimester, they have a higher risk of newborn death than mothers who are anemic in the third trimester.[32]

The funnel plot shows an almost symmetrical distribution of the research, which indicates the absence of publication bias, there is still the possibility of other biases that can affect the results of the research, such as *selection bias*. *Selection bias* can occur when studies included in the meta-analysis are not representative of the broader population, for example because only studies with positive or significant results are more likely to be published or more accessible, leading to inaccurate estimates of effects. In the context of this study, *selection bias* may arise if only studies with certain inclusion criteria, such as studies involving pregnant women with mild levels of

anemia or those with easier access to Blood Supplement Tablets, are included in the analysis. This can lead to results that do not describe the effects of the intervention on a broader and more diverse population. In addition, *selection bias* can also arise from differences in study design, the way hemoglobin levels are measured, or differences in sample characteristics (e.g., age of the pregnant woman, severity of anemia, or socio-economic factors), which may affect the results. Therefore, even if no publication bias was found based on the plot funnel, it is still important to consider the potential *selection bias* and its impact on the validity and generalization of these meta-analysis findings.[36]

The limitations of this study were not to conduct an analysis based on categories such as the trimester of pregnancy and the level of compliance with ITS consumption, because not all of the articles analyzed provided information related to the trimester of pregnancy. This limits the ability to explore potential differences in the effectiveness of ITS consumption based on stage of pregnancy or level of adherence. In addition, although the plot funnel is used to detect publication bias, this analysis is not entirely adequate to identify bias more comprehensively. Therefore, it is recommended for future researchers to use Egger's test to confirm the results of the funnel plot. These limitations are a consideration for future improvements and recommendations for future researchers to improve the accuracy of the analysis and reduce potential bias.

CONCLUSIONS

The results of the meta-analysis study proved that there was a significant effect of blood tablet consumption on hemoglobin in anemia pregnant women. Recommendations for health workers and policymakers to focus on improving education for pregnant women about the importance of regular consumption of ITS. This education should include information about the long-term benefits for the health of the mother and baby, as well as the potential risks if you do not follow the recommendations for ITS consumption. In addition, monitoring of pregnant women's compliance with ITS consumption needs to be improved through regular visit at health facilities or posyandu, by involving families in supporting pregnant women to take supplements as recommended. Policymakers should consider policies that make it easier for pregnant women to access ITS, either by providing free or affordable supplements, as well as developing better monitoring systems to ensure optimal compliance. This will help maximize the positive impact of ITS consumption in preventing anemia in pregnant women and improving maternal and infant health.

The research suggests that further research needs to be conducted that considers factors that can affect the effectiveness of ITS consumption, such as the trimester of pregnancy and the level of compliance with consumption. Researchers can categorize the data by trimester of pregnancy to explore whether the effects of ITS differ in the early, middle, or late stages of pregnancy. Additionally, it is important to measure and report pregnant women's compliance levels with ITS consumption, as low adherence can affect the results of studies and reduce the effectiveness of interventions. Researchers are also advised to use additional tests such as Egger's test to confirm the results of the plot funnel in detecting publication bias, which can provide a more accurate picture of potential bias in the studies being analyzed. By paying attention to these factors, further research can provide more comprehensive and useful findings for more effective health policies in preventing anemia in pregnant women.

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