Original Article

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Effect of vitamin C as an iron-supporting supplement in adolescents with suspected iron deficiency anemia: Is it effective for increasing hemoglobin levels?

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ABSTRACT

Background: Anemia is a global health problem that affects adolescents, adults, and children in both developed and developing countries. Anemia in adolescent girls (10–19 years of age) is defined as a hemoglobin level in the blood of <12 g/dL. In Indonesia, the prevalence of iron deficiency anemia in adolescent girls reaches 48.9%. Iron supplementation can be enhanced with vitamin C as a companion supplement. Vitamin C increases iron absorption in the body by reducing Fe^{3+} to Fe^{2+}, which requires an acidic environment for optimal dissolution and absorption. **Aim:** This study aims to assess the comparative effectiveness of iron supplementation with or without vitamin C in increasing hemoglobin levels. **Methodology:** An experimental design with consecutive sampling was conducted in September 2023 at Junior High School 1 Prambon, Nganjuk, East Java. The total sample consisted of 52 girls aged 12–13 years with anemia. The first group received iron and vitamin C, while the second group received iron only. Hemoglobin levels were by the fingerstick method. **Results:** There were 32 samples (53.33%) aged 13 years. The average change in hemoglobin levels before and after intervention in group 1 was 2.238 g/dL with < 0.05, while in group 2 it was 0.661 g/dL with <0.05. The average difference in changes in hemoglobin levels between groups 1 and 2 after intervention was 1.303 g/dL with <0.05. **Conclusion:** Iron supplementation with vitamin C results in more significant increases in hemoglobin levels.

Keywords: hemoglobin, anemia, iron supplementation, vitamin C

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INTRODUCTION

Anemia is a global health issue that affects teenagers, particularly adolescent girls, women of childbearing age, pregnant women, and children in both developed and developing countries. Indonesia is one of the developing countries still grappling with anemia.[1]

According to the World Health Organization (WHO), adolescents are described as individuals aged 10–19 years. During this period, teenagers have significant physical and psychological needs.[2,3]

The WHO and the Indonesian Ministry of Health define anemia as a condition where hemoglobin (Hb) levels in the blood are lower than normal values, which differ according to age group, gender, and physiological conditions. In adolescent females, normal hemoglobin levels range from 12 - 15 g/dl, and in adolescent males, they range from 13 - 17 g/dl. Anemia can result from various factors, including iron deficiency, vitamin B12 deficiency, folic acid deficiency, infectious diseases, congenital factors, and bleeding.[4] Degrees of anemia are classified as mild (11 - 11.9 mg/dL), moderate (8 - 10.9 mg/dL), and severe (< 8 mg/dL).[5]

It is estimated that 25% of the global population suffers from anemia, with iron deficiency accounting for 50% of all cases.[6] The prevalence of iron deficiency is higher in developing countries compared to developed nations such as the United States.[6,7] According to WHO data, the prevalence of iron deficiency anemia in adolescent girls in Southeast Asia is 41.9%.[8] In Indonesia, data from the 2018 Basic Health Research indicates an increase in anemia cases among young women, rising from 37.1% in 2013 to 48.9% in 2018. The proportion of anemia in the 15 - 24 year age group was 32%. Thus, anemia is still a significant public health issue in Indonesia that requires special attention from the government.[9]

In Indonesia, it is estimated that most cases of anemia are due to iron deficiency resulting from insufficient intake of iron-rich foods, particularly animal sources (heme iron). The primary sources of heme iron include liver, meat (beef and goat), poultry (chicken, duck, bird), and fish. Iron from animal sources can be absorbed by the body at rates between 20 - 30%. When dietary iron is insufficient, adolescents require iron supplementation. Iron supplementation for adolescents is one of the Indonesian government's initiatives to meet iron intake needs. Administering iron supplements at the appropriate dosage can prevent anemia and increase iron reserves in the body, especially in adolescent girls.[10]

To enhance iron absorption, iron supplementation can be taken with vitamin C. Vitamin C (ascorbic acid) increases the solubility of iron by converting ferric iron (Fe^{3+}) into ferrous iron (Fe^{2+}) and forming an ascorbate-iron complex, which dissolves and facilitates intestinal absorption.[11]

While several studies have examined the effectiveness of iron supplement tablets, there is limited research comparing the effectiveness of iron supplementation with or without vitamin C in increasing hemoglobin levels in adolescent girls aged 12 - 13 years with anemia. Therefore, this research serves as a preliminary study to compare the effectiveness of iron supplement tablets with or without vitamin C in increasing hemoglobin levels in this demographic and may inform clinical applications.

MATERIALS AND METHODS

This research employed an experimental design with a consecutive sampling technique conducted in September 2023 at Junior High School 1 Prambon, Nganjuk, East Java. Inclusion criteria for this study included adolescent girls aged 12 - 13 year , suspected of having iron deficiency anemia (assessing only iron deficiency anemia, not all types of anemia), were included in this study. Were divided into two groups: the first group received iron and vitamin C supplementation, while the second group received iron supplementation alone.

Adolescent girls aged 12 - 13 years with hemoglobin levels < 12 g/dL who were willing to participate by signing informed consent. Exclusion criteria included allergies to vitamin C or iron, hemoglobin levels ≤ 7 g/dL, anemia with indications for transfusion, and a history of other diseases. Dropouts in this study were due to side effects (nausea, vomiting, diarrhea, decreased appetite, abdominal pain constipation) from vitamin C or iron, illness during the study, and consumption of medications or supplements other than the provided vitamin C and iron.

Hemoglobin levels were tested before the intervention in all adolescent girls aged 12–13 years, resulting in a total sample of 26 respondents in each group following the inclusion and exclusion criteria. The first group received iron supplement tablets contains ferrous fumarate (60 mg) and folic acid (0.4 mg) and vitamin C (250 mg). The second group received only iron supplement tablets. Iron supplement tablets with or without vitamin C were administered once a week for four weeks. Apart from providing supplementation, education regarding anemia and nutrition, including healthy meal proportions, was conducted over the four weeks. A second hemoglobin examination was performed after the intervention. Hemoglobin examinations before and after the intervention utilized the peripheral hemoglobin examination method (fingerstick) (Fig. 1).

Data analysis was performed using the T-test method with SPSS version 26. The dependent T-test assessed the significance of hemoglobin levels before and after the intervention for each group, while the independent T-test compared hemoglobin levels after the intervention between the two groups.

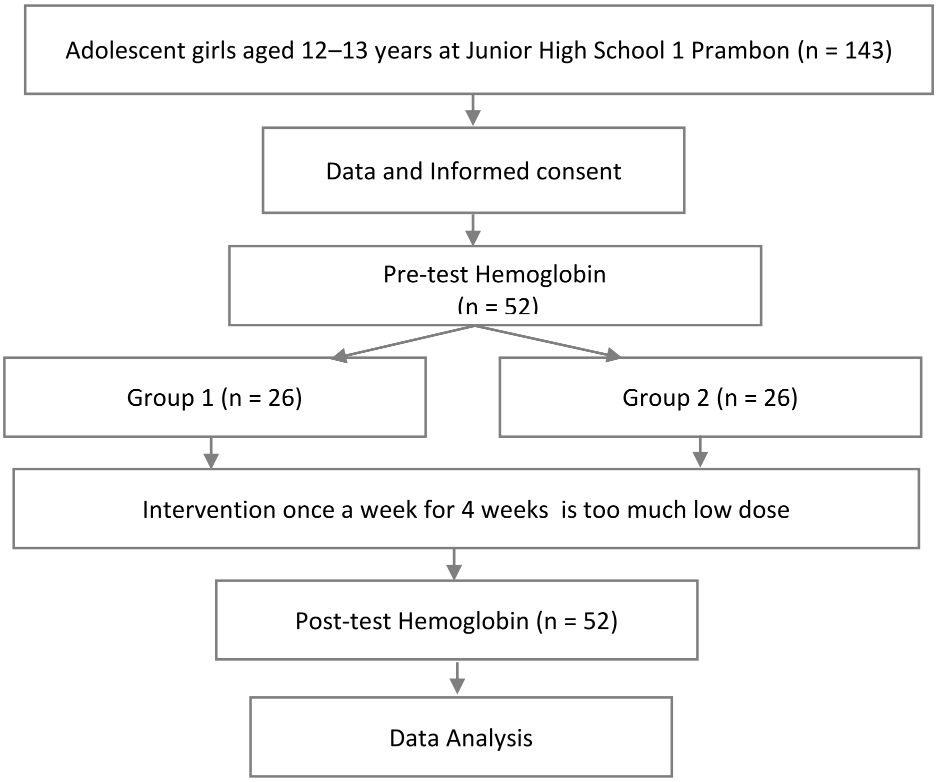

Figure 1: Research Workflow

RESULTS

The total sample in this study consisted of 52 respondents divided into two groups with 26 respondents (50%) in each group. There were 32 respondents (61.53%) aged 13 years and 20 respondents (38.47%) aged 12 years (Table 1).

The average hemoglobin level before intervention in the first group was 10.57 g/dL, and the average hemoglobin level after intervention was 12.82 g/dL. The difference in average hemoglobin levels before and after intervention in the first group was 2.25 g/dL. The maximum and minimum changes in hemoglobin levels before and after intervention were 4.9 g/dL and 0.8 g/dL, respectively (Table 2).

In the second group, the average hemoglobin level before the intervention was 10.85 g/dL, and the average hemoglobin level after the intervention was 11.54 g/dL. The difference in average hemoglobin levels before and after intervention in the second group was 0.69 g/dL. The maximum and minimum values of changes in hemoglobin levels before and after intervention were 2.5 g/dL and 0.1 g/dL, respectively (Table 3).

Data analysis of changes in hemoglobin levels utilized the T-test. The dependent T-test indicated that the first group experienced a difference in average hemoglobin levels before and after intervention of 2.25 g/dL with a p value = 0.000. A value < 0.05 indicates a significant increase in hemoglobin levels before and after the intervention. In the second group, the difference in average hemoglobin levels before and after intervention was 0.69 g/dL with a value = 0.000, also indicating a significant increase (Table 4).

Comparative analysis of the average increase of 0.42 g/dL in hemoglobin levels after intervention in groups. and 2 was conducted using an independent T-test. The analysis revealed a difference in average hemoglobin levels after intervention of 1.28 g/dL with = 0.000. A value < 0.05 indicates a significant difference in average hemoglobin levels between the two groups after the intervention. (Table 5)

Table 1: Demographic characteristics.

Age (year)	No.	Percentage (%)
12	20	38.47%
13	32	61.53%

Table 2: Average, maximum, and minimum values of hemoglobin levels before and after group 2 intervention.

	Before	After	Difference
Average (g/dL)	10.57	12.82	2.25
Maximum(g/dL)			4.9
Minimum (g/dL)			0.8

Table 3: Average, maximum, and minimum values of hemoglobin levels before and after group 1 intervention.

	Before	After	Difference
Average (g/dL)	10.85	11.54	0.69
Maximum(g/dL)			2.5
Minimum(g/dL)			0.1

Table 4: Difference in Hemoglobin Levels Before and After Intervention in Groups 1 and Group 2

	T-test Dependent		Evidence
	Group 1	Group 2	*p* < 0.05, significant increase in hemoglobin levels.
Average (g/dL)	2,25	0,69	
P value	0.0000.0000.000	0,000	

Table 5: Difference in hemoglobin levels after intervention in groups 1 and group 2

	T-test Independent	*p* value
Average difference (g/dL)	1.28	0,000

DISCUSSION

Fifty two (36.6%) adolescent girls aged 12 – 13 years experienced anemia,the total population of adolescent girls aged 12–13 years at Junior High School 1 Prambon, Nganjuk, East Java. These results are consistent with research conducted by Abilash et al. in India in 2019, which reported that 124 (48.63%) of 255 adolescent girls had anemia, with a prevalence of 47.34% in the 10 - 14 year age group and 52.64% in the 15-19 years is 52.64%.12 The high prevalence of anemia in adolescent girls is attributed to their increased need for macro and micronutrients, including iron, for physical growth, maturation of reproductive organs, and cognitive development.13,14 Additionally, the onset of menstruation increases the risk of anemia in adolescent girls. 15,16

The results of hemoglobin examinations in group 1 showed significant changes before and after the intervention 60 mg ferrous fumarate 0.4 mg folic acid and vitamin C with an average increase in hemoglobin levels of 2.25 g/dL and < 0.05. This finding is supported by previous research conducted by Niayi et al. in China in 2020, which reported an average increase in hemoglobin levels of 3.2 g/dL after four weeks with p < 0.05.17

The results of group 2 showed significant changes, with an average increase in hemoglobin levels of 0.69 g/dL and p < 0.05. This finding aligns with research conducted by Sukhdeep et al. in India in 2016, which reported an average increase in hemoglobin levels in the group receiving iron supplementation alone 0.42 g/dL with < 0.05.18

The difference in the average increase in hemoglobin levels between the two groups after the intervention was 1.28 g/dL with < 0.05. These results indicate that vitamin C supplementation has a more pronounced effect in increasing hemoglobin levels. This conclusion is consistent with research conducted by Jessica et al. in Jakarta in 2021, which found a significant difference in the average increase in hemoglobin levels between the group receiving vitamin C as an additional iron supplement and the group receiving iron supplementation alone, with an average difference of 0.85 and < 0.05.19

Iron is a crucial micronutrient involved in various metabolic processes. It plays an important role in oxygen and electron transport, cell division, and gene expression regulation. Approximately 70% of the body's iron is utilized in hemoglobin synthesis,which is essential for oxygen transport to tissues. The amount of circulating iron in the body is relatively small compared to daily iron requirements, necessitating the breakdown of old red blood cells to maintain erythropoiesis balance. Additionally, increased iron intake is essential to meet daily needs. Dietary iron is categorized into , namely non-heme (Fe^{3+}) and heme (Fe^{2+}). The primary source of heme iron meat, while non-heme iron is predominantly found in vegetables. About 1 - 2 mg of iron is absorbed from food.20,21 Fe^{3+} (ferric) is more stable but less soluble in water. Ferric iron binds to proteins such as transferrin, which facilitates absorption. In contrast, Fe^{2+} is less stable but more soluble in water and possesses reactive properties. Fe^{2+} is typically oxidized to Fe^{3+}. Before absorption, Fe^{3+} from food must be reduced to Fe^{2+} to enhance intestinal absorption. This reduction is facilitated by the enzyme ferric reductase duodenal cytochrome B (DCYTB) on the apical membrane of enterocytes. Fe^{2+} is absorbed through the apical membrane of enterocytes via divalent metal transporter 1 (DMT1), which is the primary regulatory unit for iron absorption in the duodenum and ileum. Uptake of Fe^{2+} at the apical membrane can be utilized for cellular metabolism, stored in ferritin, or transported in circulation. Fe^{2+} is transported via ferroportin (FPN1) and must be oxidized by hephaestin (Hp) or ceruloplasmin to become Fe^{3+} before binding to transferrin (Tf) in circulation.21,22

The reduction of Fe^{3+} to Fe^{2+} requires an acidic environment, which can be created by vitamin C. Forms a complex with Fe^{3+} to facilitate the reduction process. The bond between vitamin C and iron is based on the properties of vitamin C and its derivatives, which bind metals, including iron.23

This research has several limitations. First, the sample was specifically for adolescent girls aged 12–13 years at Junior High School 1 Prambon, Nganjuk, which may not represent the entire population of adolescent girls. Second, the anemia variable in this study is not specific to the type of anemia experienced. Third, this study did not assess the nutritional intake of participants during the intervention.

CONCLUSION

Based on the research, it is evident that vitamin C forms a complex with Fe^{3+} to facilitate the reduction process, enhancing the bioavailability of iron and improving its absorption and utilization in the body. Supplementation with both iron and vitamin C results in a more significant increase in hemoglobin levels compared to iron supplementation alone.

This research has several limitations. First, the sample is specifically limited to adolescent girls aged 12–13 years at Junior High School 1 Prambon, Nganjuk, which may not represent the entire population of adolescent girls. Second, the anemia variable in this study is not specific to the type of anemia experienced. Third, this study did not assess the nutritional intake of participants during the intervention.

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