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Effective Methods to Prevent or Treat Anemia in Adolescent Women

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***Abstract*---**Anemia is a public health problem that can be experienced by all age groups from toddlers to the elderly. This condition is characterized by low levels of hemoglobin (Hb) in the blood, which is < 12 g/dl. The main cause of anemia is iron (Fe) deficiency, but deficiencies of other nutrients such as vitamins A, B12, and folic acid also play a role in the incidence of anemia. The deficiency occurs when the amount of Fe absorbed is not able to meet the body's needs. The program to prevent and control anemia in adolescent girls is carried out by providing iron-folate supplementation or known as Blood Add Tablets (TTD) since 1997 which is given on a daily basis when young girls are in their menstrual period. This study uses a systematic review approach, namely as many as 10 studies of Fe supplementation in adolescent girls 10-19 years which were obtained through electronic search of scientific publications using Google Scholar. The selected study criteria were regarding the intervention of Fe supplementation either alone or in combination with other methods to prevent and control Fe in adolescents during the period 2016-2021.

***Keywords*---**Anemia, Adolescent girls, Fe supplementation, education.

Introduction

Anemia is a public health problem that can be experienced by all age groups from toddlers to the elderly. This condition is characterized by low levels of hemoglobin (Hb) in the blood, which is < 12 g/dl. Riskesdas 2018 showed that the prevalence of anemia in women aged 15-24 years was 48.9% while the prevalence of anemia in pregnant women increased by 11.8% from 37.1% to 48.9%. It was further explained that the prevalence of anemia in adolescents was 32%, meaning that 3-4 out of 10 adolescents suffer from anemia. This is influenced by the habit of nutritional intake that is not optimal and lack of physical activity (Kemenkes RI, 2018a).

The main cause of anemia is iron (Fe) deficiency, but deficiencies of other nutrients such as vitamins A, B12, and folic acid also play a role in the incidence of anemia. The deficiency occurs when the amount of Fe absorbed is not able to meet the body's needs. This can occur due to low intake, decreased bioavailability in the body, increased body requirements due to a growth spurt or pregnancy (Swamilaksita 2016). Iron deficiency anemia is the main cause of Disability Adjusted Life Years (DALY's) in adolescent girls and reduces immunity, productivity, and learning achievement.

Teenage girls are very susceptible to anemia because they experience a lot of blood loss during menstruation. The World Health Organization (2016) estimates that as many as 27 percent of adolescent girls in developing countries suffer from anemia. The impact of anemia in adolescence can increase the risk of developing anemia during pregnancy. This will have a negative impact on the growth and development of the fetus in the womb and have the potential to cause complications in pregnancy and childbirth, and even cause the death of mother and child. The Maternal Mortality Rate (MMR) according to the 2015 Inter-Census Population Survey (SUPAS) was 305 per 100,000 live births and the main causes of maternal death were pre-eclampsia and eclampsia (32.4%) and postpartum hemorrhage (20.3%) (Kemenkes RI). RI, 2017).

The program to prevent and control anemia in adolescent girls is carried out by providing iron-folate supplementation or known as Blood Add Tablets (TTD) since 1997 which is given on a daily basis when young girls are in their menstrual period. The program was carried out independently in several areas to improve pre-pregnancy health and nutritional status in preparation for a mother, so that pregnant women are not anemic and give birth to healthy babies. In the framework of the National Movement for the Acceleration of Nutrition Improvement as stipulated in Presidential Regulation Number 42 of 2013, health and nutrition efforts are prioritized in the First 1000 Days of Life (HPK) to increase children's growth and development. Efforts to Accelerate Nutrition Improvement are carried out through specific and sensitive interventions which include integrated with anemia prevention programs to target groups of young women and WUS. In accordance with WHO recommendations in 2011, efforts to overcome anemia in adolescent girls and WUS are focused on promotion and prevention activities, namely increasing the consumption of iron-rich foods, supplementing iron-rich foods, and increasing fortification of foodstuffs with iron and folic acid (Ministry of Health RI, 2018b).

The Indonesian government has adjusted to the TTD program launched by the WHO in 2011, which is given once a week on a school basis. The provision of school-based TTD is based on the proportion of young women who attend school, which is around 70 percent. Several studies have shown the effectiveness of the iron supplementation program and its effect on the incidence of anemia and other health effects in adolescent girls. For example, one study gave young women 200 mg of fumarate (group A) weekly for 3 months, group B received iron supplementation and nutrition education, and group C was not given any intervention. The results of the study showed that Hb levels increased significantly after supplementation in both groups A and B (Jalambo et al. 2018).

Another study on the effects of supplementation combined with an increase in dietary Fe intake for 12 weeks in adolescents showed that supplementation showed a better effect on hemoglobin in anemic adolescent girls, while no difference was observed between supplementation and dietary intervention in adolescents (Neto et al. al. 2018). Based on this description, it is necessary to review the effect of Fe supplementation either independently or in combination with other methods such as nutrition education or dietary intervention to assess or draw conclusions about effective methods to prevent or treat anemia in adolescent girls.

Materials and Methods

This study uses a systematic review approach, namely as many as 10 studies of Fe supplementation in adolescent girls 10-19 years which were obtained through electronic search of scientific publications using Google Scholar. Then, meta-synthesis is carried out to get new theories and concepts to get a deeper and broader level of understanding. The selected study criteria were regarding the intervention of Fe supplementation either alone or in combination with other methods to prevent and control Fe in adolescents during the period 2016-2021. The list of studies used is in Table 1.

Table 1
List of Studies Used in Research

Author	Intervention	Research Period	Study Results
Neto *et al.*	1. Fesupplementation 2. Dietary intervention	12 weeks	1. There was no significant difference between Hb in the group of adolescents with dietary intervention and adolescents with Fe supplementation (-1.43 g/L [95% CI: -6.02, 3.16]; P = 0.54, I^2 , 89%, P < 0.01). 2. There was no difference between serum ferritin in the dietary intervention and Fe supplementation group (44.81 pmol/mL [95% CI: -7.58, 97.19], P = 0.09; I^2,

			96%, P < 0.01). 3. The incidence of anemia in adolescent girls who were given Fe supplements was lower (4.3%) than the group of adolescent girls with dietary intervention (9.7%)
Jalambo *et al.*	1. Fumarate (A) 2. Fumarate + NE (B) 3. Control (C)	3 months	1. Hb levels increased in groups A and B. 2. 2. At the follow-up stage (3 months after discontinuation of the intervention), iron and hemoglobin levels in group B continued to increase and malonyl dialdehyde decreased
Fernadez-Gaxiola and De-Regil	1. Intermitten IFA vs control (no intervention) 2. Intermittent IFA vs daily IFA	3-6 months	1. The group receiving intermittent iron supplements had 5.19 grams more Hb per liter (95% CI 3.07-7.32) than those who did not receive the intervention or placebo. 2. The incidence of anemia was reduced in adolescents receiving daily supplementation compared with intermittent (RR 1.09, 95% CI 0.93 to 1.29; 1749
Min *et al.*	1. Folate 2. IFA 3. IFA + Vit A	12 weeks	1. Changes in serum ferritin and body iron were significantly higher in IFA and IFA + VitA. 2. IFA + Vita A increase the efficacy of supplementation and reduce inflammation.
Arini *et al.*	1. IFA	3 months	1. Giving iron supplements to adolescent girls who experience anemia has a significant impact on reducing the incidence of anemia in adolescent girls. 2. The average decrease in the incidence of anemia in adolescent girls is 24.9%.
Permatasari *et al.*	1. IFA	4 months	1. The prevalence of anemia (Hb <12g/dl) before the

			program was 20.7% and decreased to 15.2% after 4 months of intervention. 2. The results of logistic regression analysis show that the factors that influence the increase in Hb levels, namely the initial Hb status (p<0.05;OR=3.52;CI95%=1. 40-8.85).
Kaur and Sangha	1. IFA + NE 2. IFA + IAP + NE	3 months	1. Hemoglobin levels were higher in the IAP group (from 10.1 ± 0.13 to 11.70 ± 0.09g/dl) than in the IFA group (from 9.9 ± 0.12 to 10.32 ± 0.09 g/dl) 2. Consumption of foods rich in iron and vitamin C increases after nutrition education
Pinho-Pompeu *et al.*	1. 40 mg elemental Fe	2x a day during pregnancy	1. Iron supplementation reduces the occurrence of negative birth outcomes among pregnant adolescents such as prematurity and infant mortality
Bansal *et al.*	1. IFA 2. IFA +B12	1. 26 weeks 2. B12 500 mcg (6 weeks) and 15 mcg (20 weeks)	1. The mean Hb increased in groups A and B after the intervention (P<0,001). 2. The decrease in the prevalence of anemia in both groups was greater in group B (39.7%) than in group A (35.9%). 3. Serum ferritin deficiency also decreased more in group B (6.4%) than in group A (15,2%).
Shah *et al.*	1. IFA	52 weeks	1. The average increase in hemoglobin seen among adolescent boys is 1.5 gm/dl and for adolescent girls is 1,3 gm/dl.

Note: IFA: Iron Folic Acid; IAP: Amla Powder; NE: Nutrition Education

Results and Discussions

Before adolescence, the nutritional needs of boys and girls are not differentiated, but entering adolescence there are specific biological and physiological changes in the body according to gender (gender specific) so that nutritional needs are different. For example, teenage girls need more iron because they have menstruation every month. In addition to these changes, adolescents experience psychological and social changes. There are variations in the time and duration of the transition from children to adults which are influenced by socio-cultural and economic factors. In addition, adolescents are homogeneous groups even though they are in the same socio-cultural environment regarding development, maturity or maturity, and lifestyle.

The wrong understanding of nutrition, where a slim body is often a dream for every teenager, especially women, causes frequent nutritional problems. This happens because to maintain their slimness they apply food that does not meet the rules of good nutrition so that their nutritional needs are not met in quantity and quality (not in accordance with the recommended Nutritional Adequacy Rate/RDA). The RDA for women is presented in Table 2 (Permenkes RI No. 28 of 2019).

Table 2
Nutritional Adequacy Rates for Young Women

Nutrients	**Age Range (years)**			
	10-12	**13-15**	**16-18**	**19-29**
Energy (kcal)	1900	2050	2100	2250
Protein (g)	55	65	65	60
Carbohydrate (g)	65	70	70	65
Total fat (g)	280	300	300	360
Fiber (g)	27	29	29	32
Water (ml)	1850	2100	2150	2350
Vit A (RE)	600	600	600	600
Vit D (mcg)	15	15	15	15
Vit E (mcg)	15	15	15	15
Vit K (mcg)	35	55	55	55
Vit B1 (mg)	1,0	1,1	1,1	1,1
Vit B2 (mg)	1,0	1,0	1,0	1,1
Vit B3 (mg)	12	14	14	14
Vit B5 (mg)	5,0	5,0	5,0	5,0
Vit B6 (mg)	1,2	1,2	1,2	1,3
Folate (mcg)	400	400	400	400
Vit B12 (mcg)	3,5	4,0	4,0	4,0
Biotin (mcg)	20	25	30	30
Choline (mg)	375	400	425	425
Vit C (mg)	50	65	75	75
Calsium (mg)	1200	1200	1200	1000
Phosphorus (mg)	1250	1250	1250	700
Magnesium (mg)	170	220	230	330
Iron (mg)	8	15	15	18

Nutrients	Age Range (years)			
	10-12	**13-15**	**16-18**	**19-29**
Iodine (mcg)	120	150	150	150
Zink (mg)	8	9	9	8
Selenium (mcg)	19	24	26	24
Manganese (mg)	1,6	1,6	1,8	1,8
Fluorine (mg)	1,9	2,4	3,0	3,0
Chromium (mcg)	26	27	29	30
Potassium (mg)	4400	4800	5000	4700
Sodium (mg)	1400	1500	1600	1500
Chlorine (mg)	2100	2300	2400	2250
Copper (mcg)	700	795	890	900

Note: According to WHO, adolescents are residents in the age range of 10-19 years

At the age of adolescence, the need for energy and nutrients is indicated for the deposition of body tissues, where the total need for energy and nutrients is higher than the age range before and after. Moreover, at that time is an important transition period of growth from children to adults. Balanced nutrition at this time will greatly determine the next stage of life. In addition, at this time there are rapid changes so that nutrient intake must be considered in order to grow optimally. Physical activity in adolescents is generally more for activities at school, extracurricular, sports, hobbies, and courses, all of which will certainly drain energy which leads to having to adjust to a balanced nutritional intake.

Teenagers need more energy and protein than adults, as well as vitamins and minerals. A young woman needs an average of 2,000 calories per day to maintain body condition. Vitamins B1, B2 and B3 are important for carbohydrate metabolism into energy, folic acid and vitamin B12 for the formation of red blood cells, and vitamin A for tissue growth. In addition, bone growth requires adequate calcium and vitamin D. In addition, vitamins A, C and E are important to meet to maintain new tissues to function optimally.

The need for minerals increases during growth spurts, such as calcium, iron, and zinc. Iron is very important for young women for metabolism and the formation of red blood cells. The average iron requirement for prepubertal children is 10 mg/day, while the adolescent diet contains only 6 mg/1000 kcal, so girls who generally require lower calories will have difficulty meeting their iron needs. Iron deficiency will cause iron deficiency, whereas excess intake in patients with certain genetic predispositions causes iron overload. Teenage girls who are menstruating need higher iron. Good sources of iron in the diet, liver, beef, dried beans, spinach, and fortified grains and cereals.

Adolescence is an important age to be introduced to a variety of foods, both variety, type and taste of food. Teenagers generally like high-calorie foods that lack vitamins and minerals, thus making the body fatter. At this age it is difficult to change his eating habits, unless he sees the impact and benefits. They must see the relationship between the desired condition and the food that must be eaten, before making a decision. In this context, it is not a diet that must be taken, but an attitude to like nutritious food.

Iron Supplementation for Teenagers

The need for micronutrients, especially from food is not able to meet the need for iron, so it needs to be added from supplementation. Giving iron supplementation regularly for a certain period of time aims to increase hemoglobin levels quickly, and needs to be continued to increase iron stores in the body. Types and doses of Fe supplementation in adolescent girls in various studies are shown in Table 3.

The data in Table 3 shows that of the 10 studies reviewed, the supplementation given was in the form of iron alone or in combination with folic acid and other vitamins. The most widely used combination is iron with folic acid (IFA). There are 3 studies that use single iron, both Fe elemental and Fumarate. The usual single dose of iron given ranged from 40-60 mg of elemental Fe, while the dose for Fumarate in a study conducted on adolescent girls in Palestine was 200 mg. IFA also has various doses ranging from 60 mg to 120 mg of iron, combined with folic acid at a dose of 400 mcg to 2.5 mg. Some studies have combined it with Vitamin A, Vitamin B12, and IAP (Amla Powder) which contains Vitamin C.

Table 3
Types and Dosage of Fe Supplementation in Adolescent Girls

Author	Location	Types	Dose
Neto *et al.*	Meta analysis (PRISMA)	Single Fe tablets	Not mentioned
Jalambo *et al.*	Palestina	Fumarate	200 mg
Fernadez-Gaxiola and De-Regil	Country of origin (meta-analysis)	IFA	60-120 mg Fe elemental
Min *et al.*	Myanmar	1. Folat 2. IFA + Vit A 3. IFA + Vit A	2, 5 mg folate 15000 IU Vit A 60 mg Fe Elemental
Arini *et al.*	Bali	IFA	60 mg Fe + 400 mcg FA
Permatasari *et al.*	Bogor	IFA	60 mg Fe + 0,25 FA
Kaur and Sangha	India	1. IFA+NE 2. IFA+IAP+NE	150 mg Ferrous sulphate + 500 mcg FA Vit C 678mg/100g)
Pinho-Pompeu *et al.*	Brazil	Single Fe tablets	40 mg Fe elemental
Bansal *et al.*	India	1. IFA 2. IFA + B12	Fe 100 mg + Folate 500 mcg Fe 100 mg + folate 500 mcg + B12 500 mcg
Shah *et al.*	India	IFA	100 mg Fe + 500 mcg FA

Note: IFA: Iron Folic Acid; IAP: Amla Powder; NE: Nutrition Education

It has been previously explained that Fe supplementation, either alone or in combination with other nutrients, was given based on different doses between studies. Of course, differences in supplementation methods and their dosages will produce different outcomes. The data in Table 4 shows that Fe supplementation with a combination of other nutrients has a fairly good impact on increasing Hb and serum ferritin. In fact, the combination of IFA with Vitamin A can reduce the

incidence of inflammation in adolescents. There is 1 study which states that single iron supplementation does not significantly affect Hb or serum ferritin. However, the incidence of anemic adolescents is much lower who is given supplementation than those who are not given supplementation (Neto et al. 2018). However, studies conducted on pregnant adolescents showed that there was an improvement in pregnancy outcomes in adolescents who were given single iron supplementation. The intended pregnancy outcomes are reducing the incidence of prematurity, low birth weight, infant mortality, and maternal death during childbirth. (Pinho-Pompeu et al. 2016).

Table 4
Effects of Fe Supplementation on Young Women

Author	Treatment	Hasil					
		Hb	Serum Feritin	MDA	Inflammation	Consumption of Fe and Vitamin C	Pregnancy results
Neto *et* al.	Single Fe tablets	-	-	-	-	-	-
Jalambo *et al.*	Fumarat +NE	√	√	√	-	√	-
Fernadez-Gaxiola dan De-Regil	IFA	√	-	-	-	-	-
Min *et al.*	Vit A + IFA	√	√	-	√	-	-
Arini *et al.*	IFA	√	-	-	-	-	-
Permatasari *et al.*	IFA	√	-	-	-	-	-
Kaur dan Sangha	IFA + IAP + NE	√	-	-	-	√	-
Pinho-Pompeu *et al.*	Single Fe tablets	√	-	-	-	-	√
Bansal *et al.*	1. IFA 2. IFA + B12	√	√	-	-	-	-
Shah *et al.*	IFA	√	-	-	-	-	-

Note: IFA: Iron Folic Acid; IAP: Amla Powder; MDA: Malonil Dialdehid

Combination of Fe Supplementation and Nutrition Education for Teenagers

Referring to Table 4 that Fe supplementation is not only combined with other vitamins or minerals, but some studies also combine it with nutritional education. Better outcomes are expected to occur, especially in changing adolescent behavior to increase consumption of healthy foods. It turns out that 2 studies conducted in Palestine and India, where researchers combined Fe supplementation with nutritional education showed that the consumption of Fe and Vitamin C in adolescents increased better than the group of adolescents who were not given nutrition education.

Interestingly, among the studies that did not get significant results from the administration of iron alone, but when the administration was accompanied by the provision of nutrition education, the results were much better. The results in question are increased levels of Hb, serum ferritin, and consumption of healthy foods, especially sources of Fe and Vitamin C, as well as decreased levels of malonyl diladehid (MDA). MDA is a reactive compound that occurs naturally and is usually used as a marker of oxidative stress.

Discussion

The need for micronutrients must be met given that it plays an important role in the body's metabolism. One way to improve the inadequate intake of micronutrients is to supplement these nutrients singly or in combination. The impact of combination supplementation of two or more nutrients is the possibility of interaction of the two nutrients, either synergistically or antagonistically. The mechanisms that can occur in the interaction of micronutrients, namely: (1) one type of micronutrient can directly affect the absorption of other micronutrients, and (2) if the body experiences a deficiency or excess of one type of micronutrient, it affects the metabolism of micronutrients. other. Furthermore, it can be explained that the interaction of nutrients can occur in food, in the absorption phase, or in the body. Food contains a mixture of various nutrients and other ingredients that allow for the interaction of nutrients. In the absorption phase, food is digested and nutrients are released to be absorbed. During the digestive process, micronutrients affect the availability or absorption of other micronutrients, for example by increasing solubility or by regulating intestinal function (Ridwan 2012).

Some interactions of iron with other micronutrients, such as between iron and folic acid, vitamin A, and vitamin C are often found in several studies. For example, the interaction of iron with folic acid will cause a synergistic effect if given together with food and drinks. While the combination of iron and vitamin C supplementation will have a real effect, namely an increase in Hb or anemia status, if given to subjects with anemia.

Folate or called folic acid is needed for the formation of red blood cells and growth. Folic acid can be obtained by consuming green leafy vegetables and liver. Folate is not stored in the body in large amounts so it is necessary to obtain it through daily food intake to maintain normal levels. In folate deficiency anemia, the red blood cells are abnormally large. Large cells are called megalocytes or megaloblasts in the bone marrow (Saptyasih, Widajanti, and Nugraheni 2016). Therefore, Fe supplementation is usually combined with folic acid in order to produce a better outcome for the incidence of anemia.

Iron deficiency anemia can be exacerbated if there is a deficiency of Vitamin A. Therefore, the administration of Fe supplementation in combination with Vitamin A has a beneficial effect on iron deficiency anemia. The combination of vitamin A and iron supplements for reducing anemia appears to be more effective than iron or vitamin A supplements alone. The role of Vitamin A in the body, among others, for the growth and differentiation of erythrocyte progenitor cells, the body's immunity to infection, and mobilization of iron reserves from all tissues. The

interaction of vitamin A with iron is synergistic, this can be seen when the administration of vitamin A can reduce the prevalence of anemia and improve iron utilization compared to only vitamin A supplementation or iron alone. In addition, it was also found that if the body is in a state of vitamin A deficiency, the transport of iron from the liver and/or the incorporation of iron into erythrocytes will be disrupted. In the study, it was shown that the interaction of Vitamin A with Fe, which was characterized by a decreased prevalence of anemia, decreased serum transferrin receptors, which meant improved erythropoiesis.
The interaction of Vitamin C with Fe has long been known, namely Vitamin C as a strong promoter of the absorption of Fe from food and can counteract the inhibitory effects of phytate and tannins. Several studies have shown a positive effect of Vitamin C on Hb levels, but not a few are less successful. The inconsistency of research results depends on the characteristics of the food consumed. Sources of non-heme Fe which are often found in plant foods are the largest source of Fe for people in developing countries. Vitamin C can increase the absorption of Fe if taken at the same time, because Vitamin C will convert Fe from ferric to ferrous which is more easily absorbed. In addition, Vitamin C forms an iron-ascorbate group which remains soluble at higher pH in the duodenum (Ridwan 2012).

The interaction of Fe shown from the research results is not only with folic acid, Vitamin A, and Vitamin C, but also with Vitamin B12. The lack of adolescents in consuming good sources of Vitamin B12 (liver, meat, shrimp, and shellfish) and the food consumed has a low absorption of Fe, so the intake becomes inadequate to meet the needs. The cause of anemia is not only caused by a lack of nutrient input. If the input of nutrients is sufficient but the red blood cell production process is disrupted due to improper digestion or stomach abnormalities so that important nutrients cannot be absorbed and are wasted with feces, then over time the body will experience anemia. Vitamin B12 and folic acid are needed as keys in cell metabolism and are needed for the development of red blood cells in the bone marrow. Vitamin B12 along with folic acid is needed in the final maturation of red blood cells so that a lack of this vitamin causes developing cells to be unable to reproduce DNA before division, so that the resulting RBC (Red Blood Cell) is large (megaloblastic). Therefore, IFA with the concurrent administration of Vitamin B12 is synergistic and can reduce the incidence of anemia.

The results of the study explained that a very good effect of supplementation was given in conjunction with nutrition education, where changes were not only related to physical or clinical aspects but also in the long term how attitudes and behavior of adolescents to be aware of the importance of healthy food were also instilled. Nutrition education is carried out through counseling as an effort to instill an understanding of nutrition, introduction to eating problems, meal planning and agreed diet planning. Nutrition education can be carried out in two ways, namely directly through face to face, or indirectly. Direct nutrition education can be carried out through counseling both individually and in groups, while indirect nutrition education can be through mass media, reading books, electronics, leaflets and so on.

The success of nutrition education directly depends on the delivery method, the messenger, the recipient of the message and the place where the counseling takes

place. Mahdanijah (2004) further explained that nutrition education or counseling is an educative approach to produce individual or community behavior that is needed to improve food improvement and nutritional status. The hope from this effort is that people can understand the importance of food and nutrition, so they are willing to act and act according to nutritional norms. Basically the nutrition education program aims to change unhealthy behavior into healthier behavior, especially eating behavior

4 Conclusion

Meeting the iron needs of adolescents can provide supplementation either alone or in combination with other nutrients. The nutrient that is usually combined is folic acid because its effect is more than iron alone. However, the administration of iron and folic acid will have a better impact on increasing Hb and serum ferritin when combined with other nutrients such as Vitamin A, Vitamin C, or Vitamin B12, and there are even other positive effects that can be obtained such as lowering MDA and lowering inflammation. However, the most effective result was when providing supplements only accompanied by nutrition education because it was not associated with an increase in Hb and serum ferritin only, but also an increase in adolescent food consumption, especially an increase in consumption of sources of Fe and Vitamin C.

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