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The effect of Dadih for the prevention of iron deficiency anemia in adolescent girls 12-15 years old

Pengaruh pemberian Dadih untuk pencegahan anemia defisiensi besi pada remaja putri 12-15 tahun

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Abstract

Adolescent girls are at risk of developing iron deficiency anemia. Dadih has high nutritional value and iron and probiotics. This study aimed to analyze the effect of administering Dadih to prevent iron deficiency anemia in adolescent girls aged 12-15. This study used a randomized controlled trial pre-posttest group design, which consisted of an intervention and control group totalling 40 participants taken randomly at the Sumatera Thawalib Parabek Bukittinggi Islamic Boarding School from February to June 2023. In both groups, serum ferritin and hemoglobin levels were measured before and after treatment for 14 days. The intervention group was administered 100 g of Dadih 1x a day, and the control group was administered a placebo. Data analysis was performed using the Wilcoxon statistical and Paired T-test at a 95%CI. Results: There was a significant difference in the hemoglobin levels before and after treatment (p=0,003). There was no significant difference in serum ferritin levels before and after treatment (p=0,191). In conclusion, the administration of 100 g of dadih did not increase serum ferritin and hemoglobin levels, and the independent administration of 100 g of Dadih to prevent iron deficiency anemia still needs to be considered.
Keywords: Anemia, fermented buffalo milk, ferritin, hemoglobin, iron intake

Abstrak

Remaja putri termasuk kelompok yang berisiko mengalami anemia defisiensi besi. Dadih mengandung nilai gizi tinggi, zat besi, serta probiotik. Penelitian bertujuan untuk menganalisis pengaruh pemberian dadih untuk mencegah anemia defisiensi besi pada remaja putri usia 12-15 tahun. Penelitian menggunakan *Randomized Controlled Trial (RCT) pre-posttest group design* yang terdiri dari kelompok intervensi dan kelompok kontrol dengan jumlah 40 peserta yang diambil secara acak di Pondok Pesantren Sumatera Thawalib Parabek Bukittinggi dari Februari sampai Juni 2023. Pada kedua kelompok ini dilakukan pengukuran serum feritin dan kadar hemoglobin sebelum dan sesudah diberikan perlakuan selama 14 hari. Kelompok intervensi diberikan dadih sebanyak 100 g 1x sehari sedangkan kelompok kontrol diberikan plasebo. Analisis data menggunakan uji Wilcoxon dan Paired T-tes 95%CI. Hasil, terdapat perbedaan yang signifikan kadar hemoglobin sebelum dan sesudah diberikan perlakuan (p=0,003). Tidak terdapat perbedaan kadar feritin serum sebelum dan sesudah perlakuan (p=0,191). Kesimpulan, pemberian dadih sebanyak 100 g belum dapat meningkatkan serum feritin dan kadar hemoglobin, pemberian dadih secara independen sebanyak 100 g untuk mencegah terjadinya anemia defisiensi besi masih perlu dipertimbangkan.
Kata Kunci: Anemia, asupan zat besi, susu kerbau fermentasi, feritin, hemoglobin

Introduction

Anemia is a public health problem experienced by all age groups, ranging from toddlers, adolescents, and adults to old age. In 2019, the World Health Organization (WHO) reported that approximately 30% of premenopausal women and 40% of under five year of age are anemic (Sekartini et al., 2010). Based on Indonesia National Basic Health Research (Riskesdas) data in 2018, as many as 32% of adolescents experienced anemia in Indonesia as much as 32% (Ainaya et al., 2022). Iron deficiency anemia (IDA) is a major cause of anemia (Kurniati, 2020).

In deficiency, anemia arises due to a decrease in the total amount of iron in the body so that iron reserves become empty and the iron supply for erythropoiesis decreases (Suega, 2015). The iron deficiency tests that are often used include hemoglobin and serum ferritin levels (Febriani & Sijid, 2021). Hemoglobin is a protein that contains iron in red blood cells and serves as an oxygen carrier from the lungs to the rest of the body (Amalia & Tjiptaningrum, 2016). Individuals who consume foods containing iron along with food components that increase iron absorption, including vitamin C, zinc, and vitamin A, will have increased hemoglobin levels in the blood (Hoppe et al. 2017; Al Rahmad, 2023). Ferritin level indicates the amount of iron stored in the body. Low serum ferritin levels indicate iron storage deficiency, whereas high ferritin levels indicate iron storage overload (Nasruddin et al., 2021).

Adolescent girls are among the groups prone to iron-deficiency anemia. Anemic adolescent girls will later become prospective mothers if pregnant and unfulfilled iron are at risk of giving birth to babies with low birth weight and premature birth. This situation poses the risk of stunting (Meikawati et al., 2021; Yani et al., 2023). One strategy to prevent the impact of iron-deficiency anemia is to consume foods containing iron, such as meat, chicken, liver, and fish (Piskin et al., 2022), including dadih. Many studies have been conducted to prevent and treat anemia, including studies on children with iron deficiency anemia who received iron preparations with Lactobacillus reuteri 3 × 108 CFU for 14 days, showing a higher ret-he level in the intervention group (Manoppo et al., 2019). A study on adolescent girls with anemia who were given green bean juice with 6,7 mg iron for 14 days found that there was a difference in hemoglobin levels before and after the intervention ($p<0,05$). (Carolin et al., 2021)Study on adolescent girls who were given probiotic supplementation in the form of Yakult with a content of $6,5x10^9$ CFU has reduced the level of anemia in the intervention group. (Rekha, 2015). In addition, studies on children aged 5-18 years who received low-dose iron tablets supplemented with L. plantarum 299v for 6-8 weeks showed a high increase in ferritin levels in the intervention group (Rosen et al., 2019).

Dadih is a functional food derived from fermented buffalo milk, which is native to West Sumatra. Dadih contains energy of 237,68 cal per 100 g, protein 43,56 g per 100 g, fat 162 g per 100 g, and carbohydrates 32,12 g per 100 g (Helmizar et al., 2018). Protein content in the dadih plays a role in the transport and absorption of iron in the small intestine (Mani et al., 2020). Dadih contains essential minerals and vitamins that increase iron absorption (Purnasari et al. 2021). Iron in 100 g of dadih as much as 6,53 mg (Taufiqa et al., 2021). Iron plays a role in the formation of hemoglobin and transport of oxygen throughout the body (Wong, 2017). Vitamin C content can increase iron absorption (Rieny et al., 2021) and vitamin A affects iron metabolism, which can increase hemoglobin concentration (Jus'at et al., 2014)Additionally, dadih is a probiotic food source. In 100 g of dadih there are lactic acid bacteria $6,4x10^9$ CFU/ml (Taufiqa et al., 2021). Previous studies demonstrated the ability of probiotics to increase iron absorption. Lactobacilli, through their mechanism of lowering intestinal pH (Hoppe et al., 2017), create an acidic environment in the intestinal tract that makes iron more easily absorbed. Dadih, a high-nutrient food, is expected to improve health and prevent iron-deficiency anemia in adolescent girls by enhancing bioavailability and stimulating iron absorption.

Adolescent girls require more iron because they experience blood loss every month and during their growth period. Iron intake and foods that increase good iron absorption can be an intervention to prevent deficiency anemia in adolescent girls. The incidence of anemia in teenagers in Bukittinggi in 2017 was 41,75%. (Yunita et al., 2021). Research on dadih in

adolescent girls, especially dadih as a source of probiotics to prevent iron-deficiency anemia, has never been conducted.

Therefore, this study aimed to analyze the effect of dadih administration on serum ferritin and hemoglobin levels to prevent iron deficiency anemia in healthy adolescent girls 12-15 years old at Sumatera Thawalib Parabek Bukittinggi Islamic Boarding School.

Methods

This study used a Randomized Controlled Trial (RCT) with a prepost-test group design. This study provided treatment to two groups: 20 participants in the intervention group and 20 participants in the control group, which were formed in a random manner so that both could be considered equal. This study was conducted at the Sumatra Thawalib Parabek Bukittinggi Islamic Boarding School from February to June 2023, involving healthy adolescent girls 12-15 years old who attended the Islamic Boarding School.

The adolescent girls who participated in this study met the inclusion and exclusion criteria. The inclusion criteria for being a study subject were in good health and no history of disease, having an Hb value of ≥ 11 g/dl, not taking iron supplements or multivitamins in the 5-7 days before the study, not consuming products containing probiotics during the study and not consuming tea 2 hours before and after the intervention. The exclusion criteria were as follows: absence of menarche, menstruation, history of milk allergy, major surgery within the last six months, and unwillingness to have their blood drawn in this study.

The number of research subjects in each group was 20, according to the calculation of the number of samples. The intervention group was administered dadih, while the control group was administered a placebo, which is gelatin whose texture and color resemble dadih. The treatment was administered once per day at as much as 100 g for 14 days.

The dadih comes from buffalo milk in the Kamang area, Agam Regency, and West Sumatra. Buffalo milk was first pasteurized at 65^0C for 30 min (Helmizar et al., 2018), and then placed into bamboo tubes at 37^0C-40^0C as much as 130 cc to obtain 100 g of dadih. The bamboo tube was covered with plastic and fermented for 48 hours. During treatment, researchers and appointed personnel supervised the monitoring of the level of compliance of the research participants with treatment.

Before treatment, the research participants were educated about food intake according to the recommended nutritional adequacy rate (RDA) for adolescent girls 12-15 years old. During the study, researchers and trained personnel in the field continued to provide motivation so that research subjects could consume food as recommended by the RDA and then assess daily food intake obtained through interviews using food recall. To examine serum ferritin and hemoglobin levels, blood samples were drawn to assess serum ferritin and hemoglobin levels before treatment. On day 15, blood samples were collected again to assess the serum ferritin and hemoglobin levels after treatment.

This study involved laboratory analysis of blood samples from the research subjects. Blood was collected by collecting as much as 5 mL of blood; 2 cc was inserted into the EDTA tube for hemoglobin level examination, and 3 cc into the separator tube for serum ferritin examination. Hemoglobin levels were checked using the SYSMEX SN 550 tool, while the separator tube was taken to the Biomedical Laboratory of the Faculty of Medicine, Andalas University for centrifugation at 3000 rpm for 15 min and then stored at -20^0 °C to be checked together after the sample met. Ferritin was examined using Biochem Canada Inc. The CAN-F-4280 diagnostic tool version 10.0.

This study was approved by the Health Research Ethics Commission of the Faculty of Medicine, Diponegoro University (code number 185/EC/KEPK/FK-UNDIP/V/2023). Analysis of research data begins with proving that the data are normally distributed, namely, using the Shapiro-Wilk test. Wilcoxon test and paired t-test were used to determine differences before and after treatment in the same group. The Mann–Whitney test was used to determine the differences in variables between the intervention and control groups.

Result and Discussion

An overview of the adolescent girls who participated in this study is presented in Table 1. The age of the study participants in the

intervention and control groups was 14 years old. BMI in the intervention group was 20,9 kg/m^2 and in the control group it was 20,6 kg/m^2. Based on the statistical output using the independent t-test obtained for the BMI parameter value of p>0,05, it was concluded that there was no difference in BMI between the control and intervention groups. The results show that the study subjects in both groups could be considered equal.

Table 1. Distribution of age, weight, height, and body mass index (BMI) of research subjects

Parameters	Group Control	Group intervention	Mean Difference (95% CI)	p-value
	Mean±SD	Mean±SD		
Age (years)	14,2±0,83	13,8±0,5	0,5 (0,004-0,904)	0,056*
Weight (kg)	47,9±5,7	48,7±6,5	0,7 (3,195-4645)	0,710**
Height(m)	1,5±0,05	1,5±0,06	0,004 (3,195-4,645)	0,848**
BMI (kg/m^2)	20,6±1,8	20,9±2,7	0,702 (1,192-1,755)	0,892**

*Mann-Whitney, **Independent T-test

Food intake assessments were conducted on the research subjects. A description of the subjects' food intake during treatment is shown in Figures 1.

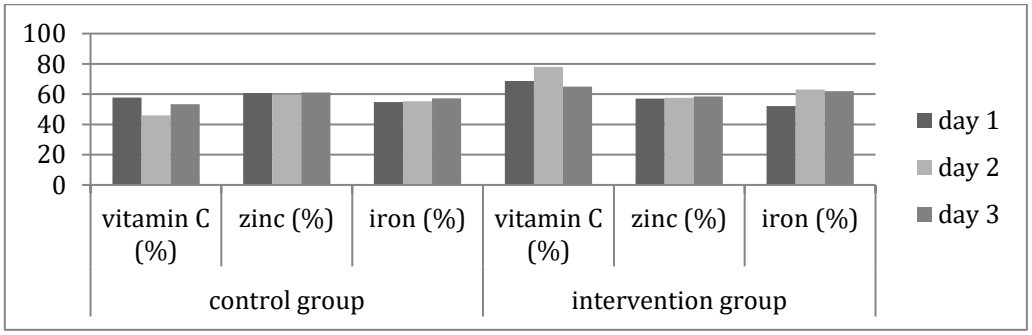

Figure 1. Percentage of vitamin c, zinc, and iron intake in control and intervention group

After evaluating the food intake of the research participants in both groups, the percentages of vitamin C, zinc, and iron intake were obtained. The micronutrient intake percentage increased and some decreased during the study. Based on the nutritional adequacy rate (RDA) in 2019, the nutritional adequacy of adolescent 13-15 years old is iron of 15 mg, zinc 9 mg of zinc, and 65 mg of vitamin C (Kementerian Kesehatan Republik Indonesia, 2019). After comparison with the RDA, the percentage of vitamin and mineral intake of the study participants was still lacking. The drug was administered daily to the intervention group during the study period. The dadih given contains 162,48 kcal, carbohydrates 5,65%, protein 10,31%, and fat 10,96%. The lactic acid bacterial content in the dadih ranged from 10^8 CFU. Dadih also contains as much iron as 3,4 mg. The acceptability of the dadih by participants was 100%. This study analyzed serum ferritin and hemoglobin levels before and after treatment (Tables 2 and 3).

Table 2. Changes in serum ferritin levels before and after treatment

Serum ferritin content (ng/ml)	Control group Mean±SD	Intervention group Mean±SD	Mean Difference (95% CI)	p-value
Before	46,3±29,6	44,92±28,0	1,3 (17,150-19,765)	0,850*
After	40,6±25,4	41,0±28,2	0,4 (17,605-16,757)	0,787*
Mean Difference (95% CI)	3,6 (1,929-13,354)	2,9 (1,033-10,726)		
p-value	0,135**	0,191**		

*Mann-Whitney, **Wilcoxon test

(Table 2) The study found no significant difference in serum ferritin levels before and after treatment between the control and intervention groups. The Mann–Whitney test also showed no significant difference in serum ferritin levels after treatment in both groups. Therefore, the study concluded that treatment did not affect the serum ferritin levels.

Table 3. Changes in serum hemoglobin levels before and after treatment

Hemoglobin Level (g/dl)	Control group Mean±SD	Intervention group Mean±SD	Mean Difference (95% CI)	p-value
Before	13,3±1,3	13,9±1,6	0,7 (0,267-1,587)	0,401*
After	12,4±1,2	13,3±1,1	0,1 (0,145-1,594)	0,080*
Mean Difference (95% CI)	13,6 (13,174-14,071)	12,8 (12,451-13,219)		
p-value	0,000**	0,003***		

*Mann-Whitney, **Paired Sample T-test, ***Wilcoxon test

Table 3 shows the changes in hemoglobin levels before and after treatment. The paired sample t-test 95%CI showed a significant difference in hemoglobin levels, while the Wilcoxon test showed a significant difference. The results suggest that there was a significant difference in hemoglobin levels before and after treatment in both groups, with a decrease in levels remaining within normal levels after administration.

Research on the effect of dadih as a source of probiotics to prevent iron deficiency anemia is a new study and an input to previous studies that discuss the ability of probiotics to increase iron absorption and improve iron status in humans. This study analyzed the effect of dadih consumption on iron status based on serum ferritin parameters and hemoglobin levels in healthy adolescent girls 12-15 years old. After the researchers conducted the interviews using questionnaires, the average food intake and sleep duration during the study were obtained. The average intake of iron and vitamin C in the study participants was less than 77% RDA. The adequacy of iron and vitamin C is considered a deficit if < 77% RDA and normal if ≥77% RDA (Herawati et al., 2019). This finding suggests that the study participants experienced iron and vitamin C deficiencies, which are useful for iron metabolism. The results of this study are in line with research conducted at the Darul Ulum Peterongan Islamic Boarding School Jombang, which found the level of consumption of energy, protein, vitamin C and iron of female students in the category of less (Sya' Bani & Sumarmi, 2016).

Previous studies have reported differences in the nutrient content and lactic acid bacteria in different regions that produce dadih. The dadih from Tanah Datar contained 14,92% carbohydrates, 12,41% protein, and 5,7% fat. The calories of the Tanah Datar dadih are 160,62 kcal per 100 g. Dadih from Palupuah and Gaduik contain 8,3% carbohydrates, 10.89% protein and 18,00% fat. Calories from Palupuah and Gaduik dadih were 237,68 kcal per 100 g. Tanah Datar, Palupuah, and Gaduik dadih contain 10^6-10^8 CFU of lactic acid bacteria (LAB) (Helmizar et al., 2018). The dadih given to the research subjects came from Kamang Agam Regency. The nutritional value of dadih is almost equivalent to the results of previous studies that showed that dadih contains macro-and micronutrients and probiotics. Dadih contains calories 162,48 kcal, carbohydrates 5,65%, protein 10,31%, fat 10,96%, and iron 3,4 mg. In addition, this dadih contained probiotics ranging from 10^8 CFU. The International Scientific Association for Probiotics and Prebiotics defines probiotics as live microorganisms that provide health benefits when administered in adequate amounts (Hoppe et al., 2017; Fikri et al., 2022). The standard conditions for probiotics to provide benefits are at least 10^6 CFU per gram (Korčok et al., 2018). Probiotics produce LAB through several mechanisms that can affect the gut microbiota and increase iron absorption by reducing ferric ions ($Fe3^+$) to ferrous ions ($Fe2^+$), thus making iron more easily absorbed (Barkhidarian et al., 2021; Wulandari, 2021).

After data analysis, there was no significant difference in the serum ferritin levels between the groups. Thus, it can be concluded that dadih or placebo administration had no effect on the serum ferritin levels. Table 3 shows the serum ferritin levels of study participants. As shown in Table 3, the lowest average serum ferritin levels in the control and intervention

groups were < 30 ng/ml. Ferritin levels < 30 ng/ml indicate iron deficiency (Al-Naseem et al., 2021; Soppi, 2018). These results show that the research subjects were already at the stage of iron deficiency, namely, iron depletion or iron-deficient erythropoietin. At this stage, no clinical signs were found, but iron deposits were reduced, as can be seen from the low serum ferritin levels. However, hemoglobin levels remain normal (Kurniati, 2020; Fitriany & Saputri, 2018; Ritonga et al., 2023). Iron and vitamin C deficiencies in the study subjects in both groups caused iron stores to be used and transported with ferritin to carry out erythropoiesis. In iron-deficient conditions without anemia, the recommended oral dose of iron to improve serum ferritin levels is approximately 28-50 mg of iron daily for 25 days (Al-Naseem et al., 2021; Rahmad, 2017). This study provided dadih containing as much iron as 3,4 mg and probiotics (108 CFU). The average iron intake of research subjects was less than 15 mg based on the RDA (2019), so this content did not sufficiently increase serum ferritin levels, which may result in no effect of treatment on serum ferritin levels in either group. The results of this study are in line with the research conducted by Rosen et al. (2019), who administered low doses of iron sulfate (1-3 mg/kg/day) with or without 10^{10} CFU probiotics from the probiotic Lactobacillus plantarum 299v for 6-8 weeks to treat iron deficiency in pediatric patients. The results showed no significant difference in the increase in serum ferritin levels between the probiotic and control groups. The probiotic Lactobacillus plantarum 299v did not improve this treatment (Rosen et al., 2019).

The results showed that there was a significant difference in hemoglobin levels before and after treatment in the control and intervention groups, but there was a decrease in hemoglobin levels after the administration of dadih or placebo. This decrease is due to the intake of iron and vitamin C, and encouraging food iron absorption does not match the daily value (RDA). Iron and vitamin C deficiency causes the body to be unable to produce hemoglobin, disrupting the erythropoiesis process. Fewer iron intakes than RDA, increased iron needs, and consumption of foods that increase iron absorption are still lacking, thus affecting bioavailability and resulting in a decrease in hemoglobin levels. mg iron of 3,4 mg and probiotics containing 10^8 CFU in a state of iron deficiency did not sufficiently increase the hemoglobin level of the study subjects. In addition, based on the schedule of activities at Islamic boarding schools, research subjects were taking exams when research was carried out, so the quality of sleep of research subjects was disturbed (Utomo et al., 2023). The disruption of sleep quality triggers oxidative stress. Oxidative stress can lead to the production of reactive oxygen species (ROS), which can result in lipid peroxidases. This condition is characterized by increased malondialdehyde (MDA) levels. This state is reactive and can damage the cell membranes of erythrocytes. Peroxidase on erythrocyte membranes results in hemolysis, which can further reduce hemoglobin levels (Sasputra, 2019). The conduct of the exam also affected participants' anxiety levels. Each individual has a different way of responding to this situation: there can be an increase in food intake or a decrease in food intake, which causes a lack of nutritional intake, including iron (Wardana & Dinata, 2016). This condition results in the disruption of hemoglobin production, which can be seen from the decrease in hemoglobin levels in the research subjects. The results of this study are inversely proportional to the research conducted by Manoppo et al. (2019), who delivered tablets of ferrous sulfate 300 mg or at a dose of 2 × 60 mg iron plus probiotics Lactobacillus reuteri DSM 17938 as many as 3×10^8 for 14 days in children with iron-deficiency anemia. The results obtained influence reticulocyte hemoglobin equivalent (Ret-He) levels; there was an increase in Ret-He levels after treatment (Manoppo et al., 2019). The difference with this study is that this study only provided dadih without additional iron preparations, whereas previous studies provided probiotics and iron preparations. The effects of dadihing were evaluated at the end of the study. The study subjects did not complain of vomiting, nausea, or the negative effects of dadih administration. The study participants reported increased appetite, a more comfortable stomach, and regular bowel movements. This illustrates that the provision of dadih provides good benefits for the digestive tract of the research subjects.

The limitation of the study was that it was conducted on healthy adolescent girls with criteria only looking at hemoglobin levels,

although with this parameter, it could not be seen that the study subjects had experienced iron depletion or iron deficiency. In addition, researchers have conducted education about the dietary intake of research subjects according to the RDA and assessed other factors that affect iron status parameters, such as sleep time and stress conditions; however, researchers have not controlled these factors in good condition, as expected.

Conclusion

Giving 100 g of dadih did not increase the iron parameters in the serum and hemoglobin levels. Independent administration of as much as 100 g/day of dadih to prevent iron-deficiency anemia still needs to be considered. The intervention should pay attention to the stage of iron deficiency anemia, which can be affected by serum ferritin levels.

Future studies should include serum ferritin levels as an inclusion criterion with normal category measurement results, so that the effect of dadih administration on iron status in healthy adolescents can be used to prevent iron deficiency anemia. In addition, daily consumption of dadih is recommended to increase iron intake to prevent iron-deficiency anemia.

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References

Ainaya, N. A., Apriningsih, Wahyuningtyas, W., & Makkiyah, F. A. (2022). Faktor-faktor yang memengaruhi niat remaja putri dalam mengonsumsi Tablet Tambah Darah (TTD) di Desa Sirnagalih, Kabupaten Bogor. *Jurnal Penelitian Kesehatan Suara Forikes*, *13*(2), 365–371. https://doi.org/p-ISSN 2086-3098 e-ISSN 2502-7778

Al-Naseem, A., Sallam, A., Choudhury, S., & Thachil, J. (2021). Iron deficiency without anemia: a diagnosis that matters. *Clinical Medicine, Journal of the Royal College of Physicians of London*, *21*(2), 107–113. https://doi.org/10.7861/CLINMED.2020-0582

Al Rahmad, A. H. (2023). Scoping Review: The role of micronutrients (Fe, Zn, Iodine, Retinol, Folate) during pregnancy. *Jurnal Kesehatan Manarang*, *9*(1), 1–13. https://doi.org/https://doi.org/10.33490/jkm.v9i1.812

Amalia, A., & Tjiptaningrum, A. (2016). Diagnosis dan tatalaksana anemia defisiensi besi diagnosis and management of iron deficiency anemia. *Majority*, *5*, 166–169. https://juke.kedokteran.unila.ac.id/index.php/majority/article/viewFile/944/777

Barkhidarian, B., Roldos, L., Iskandar, M. M., Saedisomeolia, A., & Kubow, S. (2021). Systematic review probiotic supplementation and micronutrient status in healthy subjects: A systematic review of clinical trials. *Nutrients*, *13*(9), 1–20. https://doi.org/10.3390/nu13093001

Carolin, B. T., Suprihatin, Indirasari, & Novelia, S. (2021). Pemberian sari kacang hijau untuk meningkatkan kadar hemoglobin pada siswi anemia. *Journal for Quality in Women's Health*, *4*(1), 109–114. https://doi.org/10.30994/jqwh.v4i1.111

Febriani, A. Y. U., & Sijid, S. T. A. (2021). Review : anemia defisiensi besi. *Jurnal Alauddin*, *November*, 137–142. https://doi.org/10.24252/psb.v7i1.23466

Fikri, B., Ridha, N. R., Putri, S. H., Salekede, S. B., Juliaty, A., Tanjung, C., & Massi, N. (2022). Effects of probiotics on immunity and iron homeostasis: A mini-review. *Clinical Nutrition ESPEN*, *49*, 24–27. https://doi.org/10.1016/j.clnesp.2022.03.031

Fitriany, J., & Saputri, A. I. (2018). Anemia defisiensi besi. *Kesehatan Masyarakat*, *4*(1202005126), 1–30.

Helmizar, H., Yuswita, E., & Putra, A. E. (2018). Analysis of the nutrients and microbiological characteristics of the indonesian dadih as a food supplementation. *Global Journal of Health Science*, *11*(1), 155. https://doi.org/10.5539/gjhs.v11n1p155

Herawati, A. N., Palupi, N. S., Andarwulan, N., &

Efriwati, E. (2019). Kontribusi asupan zat besi dan vitamin C terhadap status anemia gizi besi pada balita Indonesia. *Penelitian Gizi Dan Makanan (The Journal of Nutrition and Food Research)*, *41*(2), 65–76. https://doi.org/10.22435/pgm.v41i2.1886

Hoppe, M., Önning, G., & Hulthén, L. (2017). Freeze-dried Lactobacillus plantarum 299v increases iron absorption in young females—Double isotope sequential single-blind studies in menstruating women. *PLoS ONE*, *12*(12), 1–15. https://doi.org/10.1371/journal.pone.0189141

Jus'at, I., . S., . S., & Fitrah, F. (2014). Hubungan kekurangan vitamin A dengan anemia pada anak usia sekolah. *Gizi Indonesia*, *36*(1), 65–74. https://doi.org/10.36457/gizindo.v36i1.117

Kementerian Kesehatan Republik Indonesia. (2019). *Angka Kecukupan Gizi*. http://hukor.kemkes.go.id/uploads/produk_hukum/PMK_No__28_Th_2019_ttg_Angka_Kecukupan_Gizi_Yang_Dianjurkan_Untuk_Masyarakat_Indonesia.pdf

Kurniati, I. (2020). Anemia defisiensi zat besi (Fe). *Jurnal Kedokteran Universitas Lampung*, *4*(1), 18–33. https://doi.org/10.23960/jkunila4118-33

Korčok, D. J., Tršić-Milanović, N. A., Ivanović, N. D., & Đorđević, B. I. (2018). Development of probiotic formulation for the treatment of iron deficiency anemia. *Chemical and Pharmaceutical Bulletin*, *66*(4), 347-352. https://doi.org/10.1248/cpb.c17-00634

Mani, L., Fatimah-muis, S., & Kartini, A. (2020). Korelasi kadar hepcidin dan asupan makanan dengan serum transferrin reseptor dan hemoglobin pada remaja stunted overweight. *Jurnal Gizi Indonesia, 8*(1), 51–59. https://doi.org/10.14710/jgi.8.1.51-59

Manoppo, J., Tasiringan, H., Wahani, A., Umboh, A., & Mantik, M. (2019). The role of Lactobacillus reuteri DSM 17938 for the absorption of iron preparations in children with iron deficiency anemia. *Korean Journal of Pediatrics, 62*(5), 173–178. https://doi.org/10.3345/kjp.2018.07024

Meikawati, W., Rahayu, D. P. K., & Purwanti, I. A. (2021). Berat badan lahir rendah dan anemia ibu sebagai prediktor stunting pada anak usia 12–24 bulan di Wilayah Puskesmas Genuk Kota Semarang. *Media Gizi Mikro Indonesia*, *13*(1), 37–50. https://doi.org/10.22435/mgmi.v13i1.5207

Nasruddin, H., Faisal Syamsu, R., & Permatasari, D. (2021). Angka kejadian anemia pada remaja di Indonesia. *Cerdika: Jurnal Ilmiah Indonesia*, *1*(4), 357–364. https://doi.org/10.59141/cerdika.v1i4.66

Piskin, E., Cianciosi, D., Gulec, S., Tomas, M., & Capanoglu, E. (2022). Iron absorption: Factors, limitations, and improvement methods. *ACS Omega*, *7*(24), 20441–20456. https://doi.org/10.1021/acsomega.2c01833

Rahmad, A. H. (2017). Pengaruh asupan protein dan zat Besi (Fe) terhadap kadar hemoglobin pada wanita bekerja. *Jurnal Kesehatan*, *8*(3), 321–325. https://doi.org/10.26630/jk.v8i3.509

Rekha, T. R. (2015). *A study to assess the effectiveness of probiotic supplementation on level of anaemia among adolescent girls studying at selected school master of science in nursing a study to assess the effectiveness of probiotic supplementation on level of anaemia among*. http://repository-tnmgrmu.ac.in/1419/1/3001297rajthangarekhar.pdf

Rieny, E. G., Nugraheni, S. A., & Kartini, A. (2021). Peran kalsium dan vitamin C dalam absorpsi zat besi dan kaitannya dengan kadar hemoglobin ibu hamil: Sebuah tinjauan sistematis. *Media Kesehatan Masyarakat Indonesia*, *20*(6), 423–432. https://doi.org/10.14710/mkmi.20.6.423-432

Ritonga, E., & Maigoda, T. (2023). Effects of a mixture hylocereus polyrhizus (Red Dragon Fruit) juice and moringa leaf powder towards hemoglobin level in adolescent girls. *AcTion: Aceh Nutrition Journal, 8*(3), 478-484. http://dx.doi.org/10.30867/action.v8i3.1088

Rosen, G. M., Morrissette, S., Larson, A., Stading, P., Griffin, K. H., & Barnes, T. L. (2019). Use of a probiotic to enhance iron absorption

in a randomized trial of pediatric patients presenting with iron deficiency. *Journal of Pediatrics*, *207*, 192-197.e1. https://doi.org/10.1016/j.jpeds.2018.12.026

Sasputra, I. N. (2019). Hubungan kualitas tidur dengan kadar hemoglobin mahasiswa Fakultas Kedokteran Undana. *Cendana Medical Journal, 17*(2), 158–163. https://doi.org/10.35508/cmj.v7i2.1780

Sekartini, R., Widjaja, N. A., Manikam, N. R. M., Jo, J., Basrowi, R. W., & Dilantika, C. (2010). Review Article: Iron-Deficiensy Anemia: Indonesia striving. *Journalism*, *11*(3), 369–373. https://doi.org/10.1177/1461444810365020

Soppi, E. T. (2018). Iron deficiency without anemia – a clinical challenge. *Clinical Case Reports*, *6*(6), 1082–1086. https://doi.org/10.1002/ccr3.1529

Suega, K. (2015). *Aspek biologik dan klinik dari besi: Dari anemia defisiensi besi sampai anemia dengan kelebihan besi*. https://erepo.unud.ac.id/id/eprint/19824

Sya`Bani, I. R. N., & Sumarmi, S. (2016). Hubungan status gizi dengan kejadian anemia pada santriwati di Pondok Pesantren Darul Ulum Peterongan Jombang. *Jurnal Keperawatan Muhammadiyah*, *1*(1), 8–15.

Taufiqa, Z., Chandra, D. N., Helmizar, H., Lipoeto, N. I., & Hegar, B. (2021). Micronutrient content and total lactic acid bacteria of dadiah pudding as food supplementation for pregnant women. *Open Access Macedonian Journal of Medical Sciences 9*(B), 1149–1155. https://doi.org/10.3889/oamjms.2021.6791

Utomo, R. T. N., Setianingrum, E. L. S., Kareri, D. G. R., & Lada, C. O. (2023). The relationship between sleep quality with hemoglobin levels and erythrocyte index of medical students at Universitas Nusa Cendana. *East African Scholars Journal of Medical Sciences*, *6*(02), 40–48. https://doi.org/10.36349/easms.2023.v06i02.003

Purnasari, P. W., Mayangsari, C. P., & Yuniarifa, C. (2021). Pengaruh Probiotik dan Zinc terhadap Kadar Hemoglobin Tikus Malnutrisi The Effects of Probiotic and Zinc on Hemoglobin Levels in Malnourished Rats. *Amerta Nutrition*, 341–346. https://doi.org/10.20473/amnt.v5i4.2021

Wardana, M. S., & Dinata, I. M. K. (2016). Tingkat stres siswa menjelang ujian akhir semester di SMAN 4 Denpasar. *Jurnal Medika*, *5*(9), 5–8. /https://ojs.unud.ac.id/index.php/eum/article/view/23478

Wong, C. (2017). Iron deficiency anaemia. *Paediatrics and Child Health (United Kingdom)*, *27*(11), 527–529. https://doi.org/10.1016/j.paed.2017.08.004

Wulandari, R. (2021). *Khasiat probiotik strain bakteri dan ragi pada pengobatan anak dengan besi*. http://repository.unhas.ac.id/id/eprint/13896/2/C105171005%201-2.pdf

Yani, M., Azhari, A., Al Rahmad, A., Bastian, F., Ilzana, T., Rahmi, C., Nora, A., Chanda, A., & Salsabila, S. (2023). The relationship between menarche and nutritional status in Junior High School students in Aceh Besar. A study from 30 years of armed conflict area, Aceh, Indonesia. *AcTion: Aceh Nutrition Journal, 8*(4), 635-641. http://dx.doi.org/10.30867/action.v8i4.1310

Yunita, M., Novela, V., & Mawardi. (2021). Faktor kejadian anemia pada remaja putri di SMA Negeri 3 Kota Bukittinggi tahun 2019. *Jurnal Public Health*, *7*(2), 55–63. https://ojs.fdk.ac.id/index.php/JPH/article/viewFile/1233/470