Review Article

Nutritional anemia in Indonesia children and adolescents: Diagnostic reliability for appropriate management

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Background: Nutritional anemia in Indonesian children and adolescents is generally regarded and treated as iron-deficient anemia, as it is in individuals in other age groups. **Objectives:** Yet, it remains a public health threat without comprehensive management or a sustained solution. **Methods:** This review seeks to improve understanding of impediments to its resolution. Relevant studies reported in the past 5 years were identified in PubMed, Science Direct, Crossreff, Google Scholar, and Directory of Open Access Journals databases. **Results:** In all, 12 studies in several Indonesian cities provided the basis for the review. Most were conducted in schools, indicating the potential of these institutions as targets for intervention but pointing to serious deficiencies in identification of the problem across the archipelago and in remote and rural areas. No study has evaluated coexistent anemia and malnutrition, which likely would have revealed the multi-factoriality of nutritional anemia. Data regarding nutrition education, food-based innovation, and supplementation, which may alleviate anemia in children and adolescents, are available, although study lengths and sample sizes have limited interpretation and comparison. **Conclusions:** Broadly, three intervention approaches to nutritional anemia have been undertaken, namely food-based interventions, nutrient supplementation, and nutrition education. Some progress has been made with these approaches, presumably through increases in iron intake. More information is needed regarding the underlying causality and pathogenesis, suboptimal food patterns, and comorbidities, any of which might limit the effectiveness of programs designed to resolve childhood and adolescent anemia in Indonesia.

Key Words: multifactorial anemia, adolescent, children, Indonesia, nutritional interventions

INTRODUCTION

Nutrition-related anemia places a burden on the global public health sector, including the health care system in Indonesia.[1,2] It affects 1.62 billion people worldwide, mostly children, adolescents, and women.[3,4] In Indonesia, the Ministry of Health reported increasing prevalence of nutrition-related anemia among pregnant women, from 37% in 2013 to 48.9% in 2018. More than 80% of women aged 15–24 years are affected.[5] Children and adolescents face the same problem. In 2013, according to the Basic Health Research survey, more than 50% of Indonesian children and adolescents were anemic, consisting of 28% of children under 5 years and 26% of children aged 5–14 years.[6] A smaller study of 645 Indonesian elementary students revealed similar findings, with 27% of them being anemic. Aside from anemia, 20% had stunted growth, 14% had low weight for height, and 14% were overweight or obese.[7] Anemia often coexists with malnutrition.[8] Children with stunted growth have a 2.3-times higher risk of anemia than those without stunted growth.[9] Alzain[10] also mentioned that anemia and body height have a significant association.

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Overcoming this problem is essential because anemia can have physical, cognitive, and emotional impacts. Pollitt[11] proposed that anemia can change cerebral function during infancy, affecting the ability to learn. Other studies have mentioned that anemia during childhood has long-lasting effects on neurodevelopment, including on the auditory and visual systems.[12,13] The condition is associated with other nutritional statuses. A study conducted in Vietnam determined that malnourished children, whether underweight or wasted or with stunted growth, were more likely to be anemic.[14] A study conducted in rural China indicated that improvement in anemia status increased the cognitive function of children.[15]

The WHO proposed iron and folic acid supplementation as a strategy to prevent anemia in adolescence.[16] In Indonesia, anemia management in pregnant and adolescent women is focused on iron supplementation, often independent of other approaches. These approaches might include understanding sociodemographic and lifestyle characteristics and managing community food systems, food pattern optimization, food fortification, nutrition education, probiotic administration, menstrual irregularities, comorbidities, and inter-current infections.[17-19]

This review gathers recent reports on the occurrence, prevention, and management of anemia among young Indonesians. The focus on children and adolescents reflects the greater prevalence of poor dietary practices in this age group, the risk of post-pubertal anemia in girls, and the propensity to infection.[16] Timely preventive strategies for anemia in early life have implications for future health. Pollitt[11] advocated conducting community-based trials to find effective ways of overcoming anemia. The present review seeks to identify current weaknesses and opportunities for governments, food and health systems, and community health workers attempting to reduce the burden of nutritional anemia among young Indonesians.

METHODS

This systematic review was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[20]

Inclusion and exclusion criteria

The authors determined the focus of the study by using the participant, intervention, comparison, outcome (PICO) approach summarized in Table 1

The eligibility criteria consisted of experimental studies carried out in Indonesia and related to the effects of nutritional interventions on anemia and malnutrition. Children and adolescents were regarded as the study population. The studies reviewed were limited to research conducted in Indonesia and published in English or Indonesian during 2015–2020. Articles that were not primary studies (such as reviews) or not published in a journal were excluded.

Table 1. PICO approach to study selection

Participants	Indonesian children or adolescent
Interventions	Nutrition intervention (nutrition education, food-based intervention, supplementation)
Comparisons	Indonesian children or adolescent who did not receive interventions
Outcomes	Hemoglobin level, knowledge, attitude

PICO: participants, interventions, comparisons, outcomes.

Search strategy

The articles were identified through a search on the following major electronic databases: PubMed, ScienceDirect, Crossref, Directory of Open Access Journals, and Google Scholar. Search terms used included "anemia AND (children OR adolescent OR infants) AND nutrition AND Indonesia AND intervention." The search strategy was adapted according to the database. Studies reported up until July 2020 were retrieved to be assessed for eligibility.

Study selection

The authors selected articles initially by reading titles and abstracts. Rayyan, a web application for systematic reviews (https://rayyan.qcri.org/), was used to review the articles. Subsequently, the authors independently read the full texts of the selected articles. Articles were included that met the eligibility criteria of this systematic review. Any disagreements that arose among the reviewers were resolved through discussion.

Data extraction and quality assessment

The following data were extracted for analysis: author name, year of publication, study location, sample size, type of nutrition intervention, data analysis method, and findings. The quality of the selected articles was assessed using the Cochrane risk of bias assessment tool.[21]

RESULTS

The study was conducted in two stages, initial research and article review. From the initial research, a total of 198 articles were obtained from various databases. During the initial review, 161 articles were excluded because they did not meet the inclusion criteria. Another was excluded during the full-text review due to a high score of potential bias. In the end, 12 studies were included; 6 were published in English and 6 were published in Indonesian (Figure 1).

All the research was conducted in Indonesia, namely in cities on Sumatra Island (3),[22-24] in Java (6),[25-30] in Madura (1),[31] in Kalimantan (1),[32] and on Sulawesi Island (1).[33] Six studies focused on anemia prevention in adolescents, and the others focused on anemia prevention in children. Specifically, three targeted children under 5 years of age. Of these studies, 75% were conducted at a school (either a primary or a junior or senior high school). This review offers perspectives on three anemia prevention approaches, namely food-based interventions, nutrition education, and supplementation. One food-based innovation made use of local foods such as *nagara* nut (*Vigna unguiculata* subsp. cylindrica) and *haruan* fish (*Channa striata*), which are rich in nutrition and easy to obtain.[32] Five studies tested the effects of a food-based intervention or supplementation combined with nutrition education.

No study reported the effect of the intervention on the coexistence of anemia and undernutrition among the individuals involved. The study by Budiana et al[28] tested the

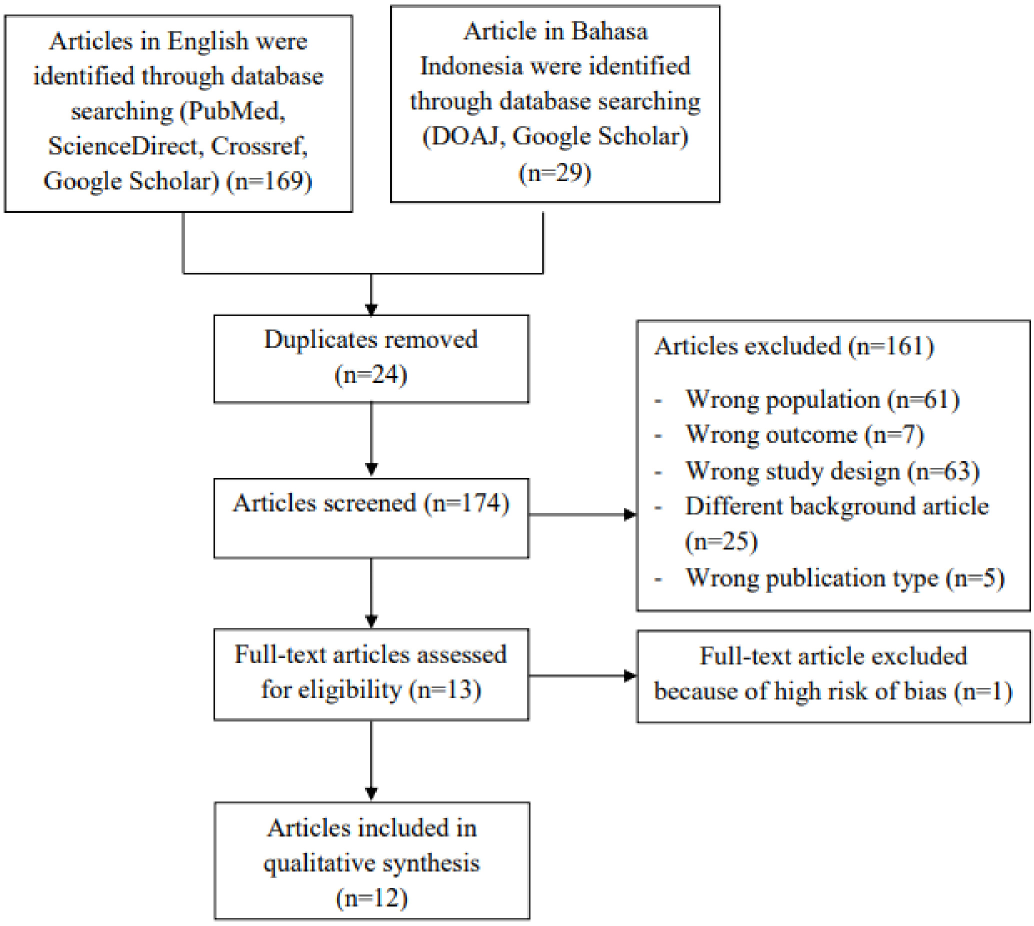

Figure 1. Information retrieval protocol.

effects of *Taburia* (a multimicronutrient powder) on hemoglobin (Hb) levels in anemic and wasted children aged under 5 years. However, the study did not report its effect on their nutritional status, only anemia. Another noteworthy study carried out by Sekiyama et al[26] investigated how a sustainable school lunch program can affect the nutritional status of children. Of the 68 participants, 32% had stunted growth, 3% were underweight, and 17% were overweight. During the program, the children received food with significant increases in protein, fat, calcium, and vitamin C, which improved the nutritional status of undernourished children. The complete results are provided in Table 2

DISCUSSION

Anemia is a major public health problem in Indonesia. The Basic Health Research report did not specify the type of anemia. Many researchers assume that the most common type is iron deficiency anemia (IDA), following the WHO, which mentioned that IDA is the most prevalent type of anemia worldwide.[22,23,34,35] This is in accordance with the research of Yip (1994) in Khusun et al,[36] who argued that the incidence of iron deficiency increases with the prevalence of anemia in a country. However, anemia has more than a single cause.

Anemia may be multifactorial, on account of diet, blood loss, chronic infection, micronutrient, or inherited red cell or Hb abnormalities. This is not to suggest that it necessarily has a complex causality and pathogenesis. Notably, the primary cause may well be related not to diet but instead to blood loss resulting from menstrual irregularities such as menorrhagia in women during the reproductive years, intestinal helminthiasis such as ascariasis or hookworm, or, in later life, large bowel tumours;[37,38] alternatively, it may result from malabsorption (as in cases of celiac disease). Nutritional measures are generally required, regardless of whether dietary characteristics are the primary factors.[39] The notion that most Indonesian cases of anemia are due to iron deficiency should be reevaluated; this may not be true for many cases of anemia. Understanding the distribution and prevalence of types of anemia is critical to designing targeted interventions.

Few published reports on anemia in Indonesia have provided direct evidence of iron deficiency or other causes. Few studies of anemia have reported iron deficiency, inflammation, or other biomarkers such as serum transferrin receptor (sTfR), serum ferritin, High-sensitivity C-reactive Protein (HS-CRP), IL-6, alpha 1-acid glycoprotein, or hepcidin. In chronic disease or infection, inflammation can occur, which results in increased use of iron as an essential component in the transport system.[40] Of the publications considered in this review, only three used ferritin as a biomarker of anemia. The remaining nine only reported on Hb levels and not red cell morphology or iron status. Thus, the type of anemia cannot be specified. Ferritin may be an indicator of iron deficiency and iron stores without any change in hematocrit or serum iron due to its role in inflammatory response.[30] Some 20% of Indonesian children aged 48–59 months have anemia

Table 2. Interventions for anemia prevention among young Indonesians by study design, locale, age, gender, diet, use of supplements, and outcomes

First author, year	City	Number of individuals		Intervention	Anemia biomarkers	Dietary information	Supplement
		Intervention	Control				
Zuraida et al, 2020a	Bandar Lampung	55 female adolescents (mean age 15 y)	47 female adolescents (mean age 15 y)	Nutrition education in the form of an "anemia free club" for 12 weeks	• Hemoglobin (Hb) levels were measured only preintervention. • 41 individuals from the intervention group and 43 the from control group had low Hb levels (10.1–11.9 g/dL).	• Dietary intake was measured twice (pre-post) using a food-frequency questionnaire. • Postintervention, the intakes of energy, iron, protein, and fat by subjects were significantly higher (p<0.05) than in the control.	This study did not include subjects who consumed any supplements.
Zuraida et al, 2020b	Bandar Lampung	55 female adolescents	47 female adolescents	Nutrition education in the form of an "anemia free club" for 12 weeks	• Hb levels were measured. • The control group had a higher percentage of individuals with low Hb levels (10.1–11.9 g/dL) than the intervention group (91.49% and 74.55%, respectively).	No information.	No information.
Muslihah et al, 2017	Madura	Two intervention groups, each with 56 infants (aged 6-59 months)	56 infants	• The lipid nutrient supplement paste—small quantity (SQ-LNS) group received 20 g of SQ-LNS per sachet per day for 6 months • The biscuit *Makanan Pendamping-Air Susu Ibu* (MP-ASI or complementary foods) group received three 30-g biscuits per day for 6 months	• Hb levels were measured three times (preintervention, mid-intervention, and postintervention). • The Hb levels in the SQ-LNS group were significantly higher than those in the control and biscuit groups (10.47±1.09 vs 9.98±0.97 vs 10.07±0.60 g/dL).	No information.	• The effects of supplement in the form of SQ-LNS were compared with fortified biscuit and control. • SQ-LNS contained energy (118 kcal), protein, essential fatty acids, 22 vitamins and minerals.
Sari et al, 2018	Banyumas	31 female students from SMA (senior high school) Negeri 2 Banyumas	39 female students from SMA Negeri 4 Banyumas	Six nutrition education meetings about anemia prevention (presentations, games, and lectures)	• Hb levels were measured. • Hb levels were significantly increased (from 12.17±1.29 to 12.68±1.22 g/dL) in the intervention group after treatment but not in the control group.	No information.	No information.

Table 2. Interventions for anemia prevention among young Indonesians by study design, locale, age, gender, diet, use of supplements, and outcomes (cont.)

First author, year	City	Number of individuals		Intervention	Anemia biomarkers	Dietary information	Supplement
		Intervention	Control				
Sekiyama et al, 2017	Bogor	68 elementary school students (boys and girls, mean age of 9 years)	–	· School lunch feeding intervention for 1 month (lunchbox contained rice, a vegetable dish, heme and nonheme protein dishes, and fruits) · The results were not categorized by gender	· Hb and hematocrit (Hct) levels were measured twice (preintervention and postintervention). · Hb (11.9±0.9 vs 11.2±0.9 g/dL) and Hct (34.0%±2.7% vs 31.7%±3.0%) levels were significantly increased after the intervention (p<0.05).	· Intakes of protein (41.7 vs 36.7 g), calcium (240 vs 205 mg), and vitamin C (64 vs 12.5 mg) were higher during the intervention compared with before the intervention (p<0.05). · The intake of fat (36.6 vs 47.3 g) was lower during the intervention (p<0.05).	No information about supplement consumption.
Syahwal and Dewi, 2018	Banjarbaru	Two intervention groups (P1 and P2), each consisting of 15 anemic female adolescents	15 anemic female adolescents	· P1 was given a snack bar made of *nagara* nut flour and *haruan* fish and 12 iron supplements · P2 was given a snack bar made of *nagara* nut flour and *haruan* fish · The control group was given 12 iron supplements · Foods and/or supplements were administered thrice a week for 1 month	· Hb levels were measured. · All individuals were cured of anemia after the intervention (Hb >12 g/dL). · The Hb levels of P1 were significantly higher than those of P2 and the control after the intervention (p<0.05). · Hb levels of P2 and the control were not significantly different postintervention.	No information.	No information.
Rusdi et al, 2018	Padang Panjang	17 anemic female adolescents (no information about age)	17 anemic female adolescents (no information about age)	The treatment group was given 100 g of guava processed into juice, once per day for a week	· Hb and ferritin levels were measured twice (preintervention and postintervention). · Significant increases in Hb and ferritin levels were observed postintervention in each group (p<0.001). · After the intervention, Hb levels in the intervention group were higher than those preintervention (12.48±0.67 vs 10.50±1.04 g/dL). · After intervention, the ferritin levels of the intervention (36.63±8.09 vs 57.40±14.09 µg/L) and control groups (33.63±6.15 vs 40.35±6.80 µg/L) were higher than those preintervention. ·	No information.	No information.

Table 2. Interventions for anemia prevention among young Indonesians by study design, locale, age, gender, diet, use of supplements, and outcomes (cont.)

First author, year	City	Number of individuals		Intervention	Anemia biomarkers	Dietary information	Supplement
		Intervention	Control				
Susanti et al, 2016	Tasikmalaya	P1: 59 and P2: 58 anemic female adolescents	58 anemic female adolescents	· P1: an iron supplement was given once a week and every day during menstruation · P2: an iron supplement was given once a week, accompanied by nutrition education · Control: an iron supplement was given once a week · The iron supplement consisted of 60 mg of elemental iron and 0.25 mg of folic acid · Nutrition education about anemia was provided through lectures, discussions, and pamphlets	· Hb levels were measured. · No significant differences in Hb levels after the intervention were observed between the three groups (ΔHb P1: 0.60; P2: 0.43; C: 0.52).	No information.	· Iron tablets (60 mg of elemental iron and 0.25 mg of folic acid). · The highest rate of compliance in taking supplements was observed for the P2 group (81.9%), and the lowest was observed for the P1 group (48.8%). · Iron supplementation in adolescents is better provided intermittently.
Budiana et al, 2016	Majalengka	33 anemic-wasting children aged 3–5 years	33 anemic-wasting children aged 3–5 years	· The treatment group was given *Taburia* (a sprinkle supplement) and nutrition counseling over a 2-month period · The control group received only nutrition counseling · The results did not differ by gender	· Hb levels were measured twice (postintervention and preintervention). · Hb levels were significantly increased postintervention in both the intervention (12.31 vs 11.14 g/dL) and control groups (11.8±0.53 vs 10.9±0.71 g/dL) (p<0.001). · The increase in Hb levels in the intervention group was significantly higher than that in the control group (1.55±0.98 vs 0.86±0.54 g/dL) (p<0.001).	· Dietary information was based on the percentage of adequacy of nutritional recommendations (no absolute number was reported). · Adequacy percentages of energy (94% vs 89%), protein (113% vs 106%), vitamin C (46% vs 40%), and Fe (74% vs 62%) were increased postintervention.	Supplementation in the form of *Taburia* (a sprinkle supplement) containing vitamin A, vitamin B complexes, vitamin D_3, vitamin E, vitamin K, vitamin C, folic acid, pantothenic acid, iron, iodine, zinc, and selenium.
Mulyantoro et al, 2015	Wonosobo	Three intervention groups (P1, P2, and P3), each consisting of 37 children aged 9–12 years	37 children aged 9–12 years	· P1 was given a supplement (840 µg iodine and 60 mg elemental iron) · P2 was given an iodine supplement (840 µg) · P3 was given an iron supplement (60 mg FeSO4) · The control was given a placebo · All supplements were given once a week for 13 weeks	· Ferritin levels in P1 (34.17 vs 51.19 µg/L) and P3 (36.85 vs 44.42 µg/L) were increased, whereas those in P2 were decreased (35.79 vs 33.52 µg/L). · The increase in ferritin levels in P1 and P2 (18.52 vs −2.63 µg/L) was significantly different (p<0.05).	No information.	Supplementation of iodine, iodine + iron, and iron was given to P1, P2, and P3.

Table 2. Interventions for anemia prevention among young Indonesians by study design, locale, age, gender, diet, use of supplements, and outcomes (cont.)

First author, year	City	Number of individuals		Intervention	Anemia biomarkers	Dietary information	Supplement
		Intervention	Control				
Kahayana et al, 2016	Semarang	P1: 30 children aged 10 months with normal nutritional status	30 children aged 10 months with normal nutritional status	· P1 was given 75 mg of vitamin C syrup during feeding time for 2 months · The control group was given a placebo	· Hb, serum iron, ferritin, total iron-binding capacity, and hepcidin levels were measured preintervention and postintervention. · Serum iron (45.70±17.4 vs 44.06±18.16 μg/dL) and ferritin (39.87±31.27 vs 36.43±25.33 μg/L) levels of the intervention group were significantly increased after the intervention ($p<0.05$). · No significant difference was noted for any biomarkers between the intervention and control groups either preintervention or postintervention.	Dietary information only compared the behavior of drinking formula milk, instant complementary food, and fruit consumption. No significant difference was observed between the two groups.	Supplementation in the form of vitamin C (75 mg) was compared with a placebo.
Manoppo et al, 2019	North Sulawesi	P1: 34 children aged 5–12 years with iron-deficient anemia	32 children aged 5–12 years with iron-deficient anemia	· P1 was given iron supplements with the addition of *L. reuteri* DSM 17938 · The control was given an iron supplement · The iron supplement was given in the form of 2 × 60 mg of elemental iron · *L. reuteri* DSM 17938 therapy was given as 3 × 108 CFU/day · The length of the intervention was 14 days	· Hb, hematocrit, and reticulocyte hemoglobin equivalent (Ret-He) levels were measured preintervention and postintervention. · Only Ret-He levels postintervention differed significantly between P1 (28.50 pg/L) and the control group (27.50 pg/L) ($p<0.05$).	No information.	Supplements in the form of 300 mg of sulfate ferrous (equivalent to 60 mg of elemental iron) were given.

Table 3. Classification of iron deficiency anemia

Stages	Hemoglobin	Ferritin (ng/mL)	sTfR (ng/L)	Transferrin (mg/dL)
Iron deficiency	Normal	<20	<5	360
Iron-deficient erythropoiesis	Normal	<12	>5	>380
Iron deficiency anemia	Lower	<12	>5	>380

sTfR: soluble transferrin receptor.
Adapted from Lianos and Jose with minor modification.[41]

according to their Hb levels, but only 12% have low ferritin.[41] Although Hb alone does not provide an indication of anemia causality, many Indonesian studies of anemia provide no further information.

Chronic iron deficiency is well-known as a common cause of anemia.[42-44] Naigamwalla et al[45] described three stages in IDA; iron deficiency, iron-deficient erythropoiesis, and finally IDA. Iron deficiency can occur for various reasons, one of which is the iron from dietary intake being too low for daily needs. Adolescent girls and women also lose iron due to blood loss during menstruation.[46] If an iron deficiency occurs latently, the body is not able to produce red blood cells properly. This causes the next stage, iron-deficient erythropoiesis, which is characterized by reduced heme synthesis and the formation of microcytic or hypochromic erythrocytes.[45] If this continues, it causes IDA. Lianos and Jose[42] described the characteristics of blood biomarkers according to the stages of anemia (Table 3).

As Table 3 indicates, further tests are required to confirm that cases are truly anemia due to iron deficiency. This is crucial because iron supplementation is currently central to anemia prevention and management programs. Clearly, where the prevalence of infection and inflammation is high, iron deficiency is not the only reason for anemia.[47] Often, it depends on contextual factors such as geographical location, the burden of infectious disease, and coexistence with other types of nutritional anemia; thus, further research is required.[44]

Infection is closely related to causality in anemia. Malaria, an example of an acute infection, causes anemia as a result of red blood cell damage due to parasites.[48] Another study conducted in Bandung, Indonesia, revealed that 63% of adult patients with pulmonary tuberculosis had anemia.[49] Research on 400 school-aged children in Vietnam reported a prevalence of hookworm infection of 92%; 25% of the infected were anemic (Hb <11.5 g/dL), and 2% had iron deficiency (TfR >8.5 mg/L). More than 30% exhibited elevated levels of C-reactive protein (≥8 mg/L) and 80% exhibited elevated levels of immunoglobulin E (>90 IU/mL).[50] This reinforces the notion that anemia occurring in areas with high infection rates might not be due to iron deficiency.

Iron status assessment among Indonesian people is commonly based on food intake and the types of food consumed.[51] This has several weaknesses resulting in inaccurate data because the assessment of food intake is based on estimation. The Indonesian Food Consumption Survey of 2018 revealed that the consumption of heme iron was lower than that of nonheme iron (32.2% vs 67.8%, respectively).[52] Fitri et al determined that the consumption of meats, fruits, and lentils in Indonesia has remained low.[53]

Policy directions addressing anemia among young populations

Indonesia has focused on anemia prevention through a program of iron-folate supplementation in the form of iron (60 mg $FeSO_4$) and folic acid (0.25 mg), otherwise known as iron tablets or *Tablet Tambah Darah* (TTD).[54] This program, intended for women of childbearing age, began in 1997.[55,56] In 2016, the Indonesian government adopted the iron supplement program launched by the WHO in 2011, where iron tablets are administered once a week at school.[55] The Indonesian Basic Health Research initiative in 2018 determined that 76.2% of adolescent girls received TTD, 80.9% of them at school and 19.1% elsewhere.[5] By region, Bali had the highest rate of iron supplementation (92.6%), and West Kalimantan had the lowest (9.6%).[57] In the *Taburia* program, the micronutrient sprinkle contains vitamin A, vitamin B_1, vitamin B_2, vitamin B_3, vitamin B_6, vitamin B_{12}, vitamin D_3, vitamin E, vitamin K, vitamin C, folic acid, pantothenic acid, iron, iodine, zinc, and selenium.[54] This program is aimed at improving the overall nutritional status of children under 5 years of age and has improved Hb counts in children.[28,58,59]

Iron supplementation is at the core of anemia prevention programs. An iron supplementation program targeting female adolescents and women of childbearing age should be evaluated briefly. The Indonesian Basic Health Research 2018 report noted that 76.2% of young women had received iron tablets in the previous 12 months. However, only 3.7% received iron tablets of ≥52 grains, and only 1.4% consumed them.[5] Many studies have been conducted in Indonesia to determine the effect of iron supplements in increasing Hb levels, but few have actually tested their effect on serum iron status. In this review, six studies tested the effects of iron or multimicronutrient supplements.[27-31,33]

As a country with large geographic and cultural variations, the nationally established youth iron supplementation program is likely inappropriate. Certain areas in Indonesia are particularly prone to infectious diseases. An example is malaria, which has a high prevalence in some areas of Papua.[60] A study by Schumann and Solomons[61] on a population of pregnant women with malaria discovered that iron supplementation actually increased the risk of infants being born with malaria. These results are consistent with research by Indrawanti[62] in Papua, Indonesia, which identified that infants had a nine-times greater risk of developing malaria if the mother was infected with malaria. Furthermore, at 3 months of age, infants had a three-times greater risk of experiencing nutritional problems, including underweight, wasting, or stunted growth. Other infectious diseases are also present in Indonesia, such as tuberculosis, worms, and HIV. Indonesia has a helminth infection prevalence rate of 45%–65%,[63] and data suggest that in 2017, Indonesia became one of the top three countries for number of cases of tuberculosis, with 8% of total cases in the world.[64] Furthermore, approximately 0.3% of the population aged 15 years or over are HIV-positive.[65]

Anemia prevention among children and adolescents

The results of the present review indicate that the prevention of anemia in children and adolescents in Indonesia has been based principally on three approaches: food-based interventions, nutrition education, and micronutrient supplementation, independently or in combination. Three of the articles examined nutrition education as a strategy for preventing anemia in adolescents,[22,23,25] and two others combined nutrition education with micronutrient supplementation.[28,66] No changes in the anemia indices of hemoglobin (Hb) or hematocrit (Hct) were evident when nutrition education interventions alone were applied. Micronutrient supplementation accompanied by nutrition education had a greater impact on Hb levels than did supplementation or education alone.[28] Previous studies have shown, however, that education changes knowledge and attitudes as well as consumption patterns.[22,23,67,68] Several countries have adopted multiple dietary approaches that combine nutrition education and sufficiently improve dietary quality to prevent anemia.[69,70] These have inevitably identified advantageous non-iron food and food pattern factors. Likewise, comprehensive educational interventions combined with food supplementation that benefits the child's general health and nutritional status is of hematological benefit.[71,72]

Evidently, anemia prevention strategies in Indonesia mostly target school-aged children,[21-27,29,30,32,66] with only three of the twelve reports being on children under 5 years old.[28,30,31] The target population predicates the type of intervention, and nutrition education, school feeding programs, and iron supplementation (TTD) are seen as more suitable and feasible for school-aged children who can be managed independently at school without reliance on their caregiver. Needless to say, opportunity costs and ethical considerations arise in not involving caregivers. With children aged under 5 years, parents and caregivers have an obligatory, vital role, and their goals are made more achievable by an aid such as *Taburia*, a micronutrient sprinkle that is mixed into food.[28,58,59] Locally sustainable school lunch interventions with traditional Sundanese meals for students improve the quality of children's food intake, their Hb and Hct levels, and their nutritional status.[26] Experiences in other countries confirm that school program–based approaches to anemia prevention in children have merit.[73-76]

Current approaches compromise anemia prevention

The efficacy of interventions to reduce anemia has both educational and therapeutic dimensions.[77] The possible pathways of the role of nutrition education in anemia prevention are preceded by improvements in nutrition knowledge.[23,25,70,78] Understanding the concept of anemia prevention leads to positive changes in behavior as well as iron status,[79] and providing education to caregivers may improve their feeding practices.[69,71] Caregivers with improved knowledge, skills, and self-efficacy are more likely to practice better hygiene in food preparation as well as ensure the proper composition of complementary diets.[80] However, whether an educational intervention can affect behavior depends on how knowledge is transferred by field technicians and their skills in conducting community activities.[81] Anemia prevention using an education approach has been implemented in some developing countries as an alternative strategy in cases of limited access to iron-rich food/heme iron sources.[82,83]

The consensus of the UNICEF, United Nations University (UNU), WHO, and Micronutrient Initiative (MI) is that if the prevalence of anemia among pregnant women is higher than 40%, then the administration of iron–folic acid supplements should also be provided to female adolescents.[16] The provision of iron supplements from adolescence is cost effective and enables an iron store to be accumulated before pregnancy.[84-86] However, although it is theoretically effective, a refusal to consume iron supplements persists in some countries.[16,87] Tolkien et al[88] proved that it this is due to the side effects of iron supplementation, such as black stool, constipation, nausea, and iron aftertaste.

Rusdi et al[24] and Kahayana et al[30] reported that the serum ferritin levels of individuals after an intervention were increased compared with individuals who received a placebo. In an intervention with guava juice,[24] serum ferritin increased from 36.63±8.09 μg/L to 57.40±14.09 μg/L; vitamin C supplementation[30] increased it from 36.43±25.33 μg/L to 39.87±31.27 μg/L (p<0.05). This is probably a reflection of the form of the vitamin C, either as a supplement or in guava juice, with the juice increasing iron absorption. An increase in serum ferritin means an increase in iron reserves. Iron derived from plant foods is classified as nonheme iron, which is more difficult to absorb (only 1%–10% uptake).[89] Nonheme iron is also generally associated with phytate, dietary fiber, and calcium, which inhibit absorption. If it is consumed together with a source of vitamin C, however, much more iron will be absorbed.[90-93] Vitamin C has many roles, including acting as an antioxidant, promoting immune function, and increasing the absorption of nonheme iron. Vitamin C plays a role in iron kinetics and red blood cell formation. The WHO[16] recommends giving weekly iron supplements if high compliance is observed. This preventive program has been proven to be cost effective, with fewer side effects, easier management, and greater efficacy than daily iron supplementation. In Indonesia, national monitoring of compliance with iron supplementation among adolescent girls is rarely reported. A small study by Susanti et al[27] involving 117 Indonesian female students determined that providing nutrition education is more effective than iron supplementation only. Titaley et al reported similar findings[94]; better knowledge can increase the compliance of pregnant women in consuming iron–folic acid supplements.

Iron supplements are rarely given to Indonesian children under 12 years old. In 1999, the UNICEF/WHO proposed that iron supplementation is necessary in children aged 6–18 months if the prevalence of anemia in children exceeds 40%.[95] However, the WHO also warned against iron supplementation in children who have an infectious disease because of the potential adverse effects.[96] Iannotti et al[97] explained that the administration of large amounts of iron can increase the number of pathogens and thus increase the risk of infection. A study of 478 Indonesian 4-month-old infants proved that iron supplementation effectively reduces the incidence of anemia but is inadequate for supporting their growth.[98] In the present review, the only study targeting Indonesian infants made use of food fortification to address anemia.[31]

In the past 5 years, 9 of the 12 studies on anemia prevention were carried out in schools. Schools are a potential environment for health promotion.[99] Moreover, a 12-year compulsory education program is in place; thus, children and adolescents spend most of their time in school.[100] In Indonesia, approximately 147,500 elementary schools, 37,000 junior secondary schools, and 25,300 senior secondary schools exist.[101] Despite their potential, collaboration between the education and health sectors is lacking. Research on school health promotion policies in the United States revealed that program implementation has been suboptimal due to the weakness of existing policies.[102]

Many health promotion programs for anemia prevention can be implemented in schools. In this review, three studies recommended nutrition education in schools for the prevention of anemia in adolescents.[22,23,25] One study recommended implementing a school lunch program,[26] two recommended a food-based approach,[24,32] and one recommended a supplementary intervention.[27]

The School Lunch Program proposed by Sekiyama et al[26] has not become a national program yet because of the wide variability of school characteristics in Indonesia. This is in contrast to several other countries, including Japan, which has had a national policy in place since 1954, governed by the School Lunch Act, to improve student health.[103] A study among 627 vulnerable households in Uganda reported substantial improvements in anemia status; the prevalence of anemia was significantly reduced in 25.7% of adolescent girls after they participated in a school feeding program.[104] Similar results were reported by Krämer et al[105] regarding the provision of iron-fortified salt in a school feeding program in India.

Anemia prevention studies in school settings had small sample sizes compared to Indonesia's total population of school-aged children. This makes generalizing the results difficult. The School Lunch Program carried out by Sekiyama et al,[26] although yielding good results, only involved 68 students. Not much research on anemia prevention in Indonesia has been conducted with large samples.

Anemia and sex

Both men and women can experience anemia. Various studies have shown that women, especially adolescent girls, have a higher risk of developing anemia due to menstruation.[16,27,37,42] Research by Susanti et al[27] on iron supplementation in adolescent girls revealed that taking a supplement once a week and every day during menstruation led to low adherence (48.8%) compared with the combination of once-weekly supplement consumption with nutrition education (81.9%).

In the reviewed studies, six included boys, either children or infants.[26,28-31,33] However, none stratified anemia based on gender. In research by Faiqah and Irmayani[106] on data for children under 5 years, reported by the 2013 Indonesian Basic Health Research, gender was significantly ($p<0.001$) associated with anemia. Of the 39,706 anemic children aged under 5 years, 57.9% were girls and 42% were boys. Another study of 712 Indonesian adolescents also discovered a significant relationship ($p<0.001$) between gender and incidence of anemia. Women and teenage boy account for up to 30% and 20% of anemia cases, reespectively.[107] No information regarding the types or causes of anemia has been provided. However, the results indicate that boys also experience anemia. Unfortunately, they have not been targeted for anemia prevention programs. Childhood and adolescence is a key phase for growth and development for both male and female individuals in which health status, including anemia, plays an essential role.[11,12,13,42] A need exists for programs such as anemia-related nutrition education and screening for boys as well as for girls.

Future directions

Anemia, like other public health problems, is multifactorial. The United States Agency for International Development[108] recommended an anemia prevention framework for children. This framework was based on the need to strengthen leadership, capacity, and policy in implementing various concordant programs in agriculture and health sectors. The authors suggested a need to identify the specific causes of anemia in smaller areas (such as cities/regions or provinces) and recommend preventive measures accordingly. Anemia in Indonesian children and adolescents may not be due to iron deficiency alone. Iron supplementation without understanding the exact underlying causes can lead to ineffective and inefficient programs.[109-111]

This review had several limitations. First, research only from the last 5 years was reviewed. Second, a meta-analysis was not feasible because of the low number of anemia intervention studies in Indonesia. Third, a major limitation is that the reports reflected the prevailing view among nutritionists and health policymakers that the causes of anemia are solely related to nutrition. This view does not take into account the likely multifactoriality of anemia and socioeconomic development. This entrenched approach has been fostered by an often commercial product–prescriptive approach with supplements rather than one in which food and health systems are informed and community-engaged. To say that anemia is strictly caused by iron deficiency, even if this is partly the case, blinds the intervener to the more complex causality and pathogenesis that may be involved and to the solutions actually required.

Conclusions

Despite the limitations identified in this review of studies on anemia among children and adolescents in Indonesian cities, progress has been made in these locations in terms of prevention and mitigation through food-based approaches, nutrition education, and nutrient supplementation (often unduly restricted to iron). These three types of intervention have ameliorated anemia among young people. Interventions across the Indonesian archipelago with attention to underlying causality and pathogenesis, socioculturally sensitive education, more optimal food patterns, and integrated embedment in local food and health systems would further alleviate the burdens of disorder and disease among young Indonesians.

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The authors have no conflicts of interest to declare.

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