Review Article

Iron-Deficiency Anemia: Indonesia's Striving

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Background: The nutritional-deficiency anemia, particularly iron-deficiency anemia, remains endemic in Indonesia, based on the Basic Health Research surveys in 2013 and 2018. This is an enormous threat to Indonesia's public health and quality of life.

Objectives: This narrative review was written to evaluate the implementation of various population-level interventions in Indonesia to reduce the prevalence of iron-deficiency anemia.

Methods: Relevant studies in English and Bahasa Indonesia were analyzed in this review.

Results: Knowledge of causes, pathophysiology, signs, and symptoms, as well as clinical treatment of individual iron-deficiency anemia, are well known and established. However, the challenges lie in the population-level interventions to reduce the prevalence of iron-deficiency anemia in endemic areas. The government of Indonesia currently conducts eight relevant programs as a part of the National Strategy to Accelerate Stunting Prevention 2018–2024. Those programs range from providing iron-folic acid tablets for female adolescents and pregnant women, fortifying food for the general population, and deworming children. Each intervention targets different populations and is closely connected, indicating that all of them should be conducted simultaneously to remove the endemicity of iron-deficiency anemia from Indonesia effectively.

Conclusions: The Indonesian government is conducting multiple population-level interventions. The next Basic Health Research survey, presumably in 2023, would demonstrate whether those programs effectively minimize the prevalence of iron-deficiency anemia in Indonesia.

Keywords: iron deficiency, anemia, Indonesia, population-level interventions

INTRODUCTION

Iron deficiency and iron-deficiency anemia (IDA) are major health problems worldwide, contributing to the global disease burden. Body iron levels will decline if the iron intake is insufficient to fulfill the needs or to compensate for the physiological or pathological losses of the iron body.[1] Iron deficiency commonly occurs among children under five years old and women of reproductive age (particularly during pregnancy) in low- and middle-income countries, such as Indonesia.[2] Globally, iron deficiency is the primary cause of nutrition-deficient anemia (i.e., the IDA).[3] The World Health Organization (WHO) reported in 2019 that approximately 30% of pre-menopausal women and 40% of under five-year-old children are anemic. The predominant cause was presumed to be iron deficiency.[4] The IDA is associated with much-reduced health status and quality of life of those patients, denoting that diagnosis and management of IDA are urgently required.[4]

Clinical diagnosis and management of IDA are relatively straightforward, particularly in uncomplicated cases. The diagnosis is confirmed based on the established laboratory tests (**Table 1**).[3,5] The administration of iron supplementation, either orally or per injection, would effectively rescue those individuals from IDA.[3,6–8] However, population-level approaches would be required to control IDA in endemic areas, including in Indonesia.[9] Thorough understanding and management would create and execute population-level approaches that effectively reduce the prevalence of IDA. Therefore, this narrative review discussed the pathophysiology and treatment of iron-deficiency anemia and reviewed the current population-level programs in Indonesia to minimize the rate and impact of IDA.

Table 1. Laboratory tests to diagnose iron deficiency and iron-deficiency anemia.[1,3,5]

Parameter	Normal Value	Iron Deficiency	Iron-Deficiency Anemia
Iron (µmol/liter)	10–30	<10	<10
Transferrin Saturation (%)	>16 to <45	≥16	<16
Ferritin (µg/liter)	>30–60	<15–30	<15–30
Hemoglobin (g/dL)			
Children aged 6–59 months old	>11	>11 or low-normal	<11
Children aged 5–11 years old	>11.5	>11.5 or low-normal	<11.5
Children aged 12–14 years old	>12	>12 or low-normal	<12
Girls aged >15 years old	>12	>12 or low-normal	<12
Boys aged >15 years old	>13	>13 or low-normal	<13
Women	>12	>12 or low-normal	<12
Men	>13	>13 or low-normal	<13
Mean Corpuscular Volume (fL)	80–95	normal or reduced	<80
Mean Corpuscular Hemoglobin (pg)	27–34	normal or reduced	<27

fL, femtoliter. pg, picogram. µ,micro.

Global epidemiology and clinical presentation of iron deficiency

The WHO estimated in 2019 that approximately 39.8% of children aged 6–59 months old and 29.9% of women aged 15–49 years old were anemic worldwide.[4] It is well recognized that nutritional deficiencies, particularly iron, are the most common cause of anemia.[10] The Global Burden of Disease Study 2019 also reported that iron deficiency caused 1.1% of disability-adjusted life years across all ages.[11]

Iron-deficient individuals could be asymptomatic or symptomatic, as well as in the absence or presence of anemia. Clinical signs and symptoms of iron deficiency could include fatigue and lethargy, decreased concentration, dizziness, headache, tinnitus, pica, restless leg syndrome, pallor, alopecia, dry hair or skin, koilonychia, or atrophic glossitis.[1,12,13] Among children with iron deficiency, the symptoms could include irritability and poor feeding.[14] The IDA could exacerbate the clinical presentations of existing medical conditions, including heart disease, and worsen their prognosis as well.[1] Furthermore, IDA would cause substantial medical and social impacts globally, ranging from the adverse outcomes of pregnancy for both mothers and newborns, cognitive impairment in children, learning disabilities, declined physical capabilities in adults, and cognitive reduction in older adults.[15–18] Thus, it is prudent to understand the mechanism of iron homeostasis within the human body and prevent iron deficiency.

Iron homeostasis and its pathophysiology

Iron is crucial for various cellular functions, including DNA synthesis and repair, neurotransmitter production and function, enzymatic activity, and mitochondrial function.[19] However, the excess of cellular iron is toxic as it produces reactive oxygen species. Thus, the iron balance is tightly regulated by reutilizing the body iron (i.e., iron scavenged from senescent erythrocytes by reticuloendothelial macrophages) and limiting the environmental intake (i.e., iron absorbed from diet).[20] The iron recycling by reticuloendothelial macrophages contributes to body iron.[13] A smaller proportion of body iron comes from dietary iron intake, either as heme iron in animal products (which is efficiently absorbed and less susceptible to modulation by other dietary compounds) and non-heme iron in plants (which is less efficient to be absorbed and susceptible to the inhibitory presence of phytates, calcium, or tannins).[1] Of note, absorption of non-heme iron can be enhanced by the intake of meat, ascorbic acid, and citric acid.[21,22] The systemic iron homeostasis is controlled by hepcidin, a peptide hormone primarily synthesized in the liver. The iron content is maintained at around 40 mg/kg and 50 mg/kg in women and men, respectively.[23] Briefly, hepcidin negatively regulates the iron mobilization from macrophages and hepatocytes as well as the iron absorption by duodenal enterocytes through its interaction with ferroportin, a cellular iron-export protein. The iron channel would be occluded upon binding, and the iron-loaded ferroportin would be degraded, inhibiting iron efflux into the blood plasma.[24,25]

The cellular iron is primarily stored within hemoglobin (Hb) of erythrocytes (2,500 mg), enzymes (150 mg), and myoglobin (130 mg), with its surplus is stored in the liver.[1] Ferritin is the cellular storage protein for iron, in which the serum ferritin concentration correlates well with total-body iron stores. The measurement of serum ferritin is therefore commonly performed to diagnose disorders of iron metabolism.[23] In addition, approximately 0.1% of total-body iron within the plasma is bound to transferrin, which functions to relocate iron from enterocytes to tissues through its interaction with the transferrin receptor.[1]

Iron deficiency could be distinguished into functional and absolute iron deficiencies. The former condition occurs during inflammation as the elevated levels of hepcidin, and the declined transcription of ferroportin would restrict iron efflux into the plasma.[1,26] The latter condition is due to the imbalance between body iron's "supply and demand." This could be due to inadequate dietary iron intake, reduced iron absorption ("the supply"), blood loss, increased iron requirements ("the demand"), or both, as summarized in **Table 2**.

Clinical treatment of IDA

The primary aim of treating iron deficiency is to replenish body iron levels, with an additional aim to normalize Hb concentrations among patients with IDA.[1,3] Uncomplicated IDA patients would be treated with oral iron administration as it is an effective and inexpensive method.[1,3] Various preparations of iron salts are available for this purpose, including ferrous sulfate, ferrous gluconate, and ferrous fumarate. The recommended daily dose is 100–200 mg of elementary iron for adults and 3–6 mg/kg of body weight of a liquid preparation for children.[3] Of note, as meat intake among infants and young children is generally low, and increasing consumption of meat or meat products without exceeding the daily recommendation would help to replenish body iron levels in children.[5,27]

Table 2. Multiple causes of absolute iron deficiency.[1,20]

Reduced Supply	Increased Demand
Inadequate iron intake: • Malnutrition; • Inadequate dietary iron content (e.g., low heme iron content, low iron content in the complementary diet, or low dietary diversity).	***Increased iron requirement:*** • Growth (infants, preschool children, or adolescents); • Pregnancy (second and third trimesters); • Erythropoiesis-stimulating treatment; • Physiological blood losses exceed dietary iron intake.
Decreased intestinal iron absorption: • Concomitant consumption of inhibitors of iron absorption (e.g., calcium or tea); • Inadequate stomach acidification (e.g., use of antacids or proton pump inhibitors or *Helicobacter pylori* infection); • Intestinal mucosal dysfunction; • Malabsorption syndrome; • Obesity; • Inappropriately increased hepcidicin concentrations (e.g., during chronic inflammation or *TMPRSS6* mutations).	***Blood loss:*** • Gastrointestinal bleeding; • Gynecological bleeding; • Urinary tract bleeding; • Respiratory bleeding; • Frequent blood donation; • Prolonged consumption of nonsteroidal anti-inflammatory drugs, corticosteroids, anticoagulants, or antiplatelets.

Multifactorial
Exercise:
• Reduced dietary iron intake, reduced iron absorption due to inflammation, increased losses in sweat, gastrointestinal bleeding, and hemolysis with hemoglobinuria.

TMPRSS6, transmembrane serine protease 6.

It is important to note that administration of iron salts in high doses (divided into two or three daily doses) is ineffective physiologically because therapeutic doses of iron salts would increase hepcidin concentrations, reducing iron absorption for the next 24 hours.[28] Thus, administering iron salts with intermediate doses and on alternate days is recommended in patients with mild IDA.[1] The usage of iron salts for oral supplementation is restricted, however, by the induced gastrointestinal adverse events, such as constipation, nausea, and diarrhea.[29] New oral preparations have been developed; therefore, ferric iron was combined with certain carriers (e.g., ferric maltol, sucrosomial iron, or iron hydroxide adipate tartrate) to enhance absorption and reduce gastrointestinal adverse events.[1]

Certain patients with IDA would require a faster therapeutic method to increase their Hb levels, such as patients with a failure of oral iron administration, patients with malabsorption, patients with chronic inflammation, or patients with chronic kidney disease.[3] Parenteral iron preparations (e.g., ferric gluconate, iron sucrose, low-molecular-weight iron dextran, ferumoxytol, ferric carboxymaltose or ferric derisomaltose) are effective for those patients. However, safety concerns and costs still restrict the intravenous administration of iron preparation.[1]

The IDA treatment guidelines for pediatric and pregnant patients in Indonesia are consistent with the above recommendations. Pediatric patients would receive oral iron therapy (i.e., ferrous sulfate, ferrous gluconate, ferrous fumarate, or ferrous succinate) with a daily dose of 4–6 mg/kg of elemental iron.[30] The response will be evaluated after a month by measuring Hb concentration. The treatment will be extended for 1 to 2 more months if the Hb concentration increases by 2g/dL or more after one month.[30] In a rare circumstance that the Hb concentration is lower than 4 g/dL, a transfusion of packed red blood cells will be administered.[30] The IDA treatment in pediatric patients could be discontinued after achieving the recommended Hb according to the age group (**Table 1**). Similarly, pregnant patients with Hb <11 g/dL and Ferritin <15 □g/L would be treated with oral iron therapy of 80–100 mg/day.[31] If the anemia is worse, i.e., Hb <10 g/dL, the pregnant patients would be treated with an intravenous iron therapy of 200 mg/day, once or twice per week.[31] If the Hb is lower than 7 g/dL, pregnant patients will receive packed red blood cell transfusions.[31] Treatment of IDA in pregnant patients could be discontinued after achieving the target of Hb ≥11 g/dL and Ferritin >60 □g/L.[31]

Table 3. Current governmental interventions to prevent IDA in Indonesia[37]

Program	Target	Supporting Local Regulation
Provision of iron tablets and folic acid	Female adolescents and pregnant women	Peraturan Menteri Kesehatan No. 88/2014
Initiation of early breastfeeding and promotion of exclusive breastfeeding up to 6 months old	Lactating mothers and infants	Peraturan Pemerintah No. 33/2012
Provision of recommended feeding practices for infants and young children	Infants and young children	Peraturan Menteri Kesehatan No. 41/2014; Peraturan Menteri Kesehatan No. 25/2014; Peraturan Menteri Kesehatan No. 51/2016
Control and prevention of helminth infection	Children under five years old and children of school age	Peraturan Menteri Kesehatan No. 15/2017
Improvement of maternal healthcare services	Pregnant women	Peraturan Menteri Kesehatan No. 97/2014
Nutritional education for pregnant mothers	Pregnant women	Peraturan Menteri Kesehatan No. 97/2014
Promotion of a balanced diet	General population	Peraturan Menteri Kesehatan No. 28/2019; UU No. 18/2012
Fortification of diet	General population	Keputusan Menteri Perindustrian dan Perdagangan No. 153/2001; Peraturan Menteri Kesehatan No. 51/2016; UU No. 18/2012

IDA, iron-deficiency anemia.

Burden of IDA in Indonesia

As one of the low-to-middle income nations, the population of Indonesia is heavily affected by nutrition-related anemia, particularly IDA.[32] The Basic Health Research ("*Riset Kesehatan Dasar*") surveys by the Ministry of Health of the Republic of Indonesia in 2013 and 2018 reported an increased prevalence of anemia over time from

37.1% to 48.9% among pregnant women (with approximately 84.6% of pregnant women aged 15–24 years old suffered from anemia), from 28.1% to 38.5% among children under five years old, as well as from 18.4% to 32% among individuals aged 15–24 years old.[33–36] Of note, the anemia prevalence remained stable among children aged 5–14 years old, i.e., around 26%.[33,34] Collectively, these reinforce the statement that anemia, particularly IDA, remains a major challenge to the public health service in Indonesia.

The population-level programs to prevent IDA in Indonesia

The government of Indonesia is conducting multiple intervention programs at a population level to reduce the prevalence of IDA, as mentioned in our recent review.[37] Those programs, as depicted in **Table 3**, are parts of the National Strategy to Accelerate Stunting Prevention 2018–2024. It is important to emphasize that all programs are equally important (as they target different populations) and that the simultaneous implementation of all programs would create a synergistic effect in controlling IDA in Indonesia. Implementing those interventions was analyzed in this narrative review.

(1) Provision of iron-folic acid tablets for female adolescents and pregnant women

Iron deficiency is presumed to be the main cause of nutrition-related anemia; hence an iron supplementation program, with a primary focus on female adolescents and pregnant women, is also conducted in Indonesia.[37] Female adolescents are one of the primary targets because of double risks of contracting anemia (i.e., rapid growth with expansion of erythrocyte mass and increased body iron requirements, accompanied by menstrual blood loss) among this population.[38] Pregnant women are chosen because iron supplementation for this population could reduce maternal morbidity, promote fetal health, and provide adequate iron store for newborns.[39] Indeed, a systematic review reported that weekly iron-folic acid supplementation prior the conception and within the first trimester of pregnancy could reduce the risk of anemia by 34%.[40]

Historically, the government of Indonesia has provided ferrous sulfate tablets to pregnant women since 1952.[41] In 1973, iron supplementation was incorporated into the program of Family Nutritional Improvement (*"Upaya Perbaikan Gizi Keluarga"*) by providing oral iron tablets to pregnant women for minimum of 90 days, accompanied by an educational training to identify nutritional resources and to recognize nutritional issues, such as anemia, deficiency of vitamin A, and diarrhea.[41,42] The government of Indonesia currently provides ferrous sulfate, comprising 60 mg elemental iron (in the form of ferrous fumarate) and 400 □g folic acid, to prevent IDA among women of reproductive age.[42,43] Of note, adding folic acid to the iron tablets follows the WHO guidance to reduce the prevalence of nutrition-deficiency anemia and improve the health status of mothers and neonates.[44]

The Basic Health Research survey in 2018 by the Ministry of Health reported, however, that the proportion of pregnant women receiving iron tablets was approximately only 73% and that the prevalence of IDA was increasing among pregnant women.[34] A recent national survey, i.e., Indonesia's Nutritional Status Study (*"Studi Status Gizi Indonesia"*) in 2021, reported that the proportion of pregnant women who had received iron tablets increased to 90.4%, with the lowest and highest proportions being 80.1% and 98.2% in the province of North Sumatra and West Sulawesi, respectively.[45] However, neither survey elucidated the individual adherence to taking iron tablets. The readers could not discern whether the female subjects routinely took iron-folic acid tablets based on the recommendation and whether the female subjects took iron-folic acid tablets for minimum 90 days. These findings challenge the implementation and effectiveness of iron-folic acid supplementation as a sole program.

Unfortunately, the low- or even non-adherence of pre-conceived and pregnant women to follow the dietary guidelines to take iron is a global phenomenon. One systematic review reported that pregnant women who did not meet their iron requirements were observed in 91% of analyzed studies.[46] The common reasons for the noncompliance were forgetting or feeling frustrated over routinely taking an iron-folic acid tablet, disliking the taste of iron-folic acid tablet, feeling nauseous upon taking the iron-folic acid tablet, and vomiting due to pregnancy.[34] One interesting observation from that review was that, nonetheless, higher the education level, higher the adherence,[46] suggesting that educational training on IDA and changing attitudes toward IDA would play important roles in maximizing the efficiency of iron-folic acid supplementation. Findings from two studies in Indonesia support this argument. First, the Ministry of Health of the Republic of Indonesia revised its national program for preventing and controlling the prevalence of anemia among female adolescents and women of reproductive age in 2016. The revision aimed to be more closely related to the WHO guideline of weekly iron-folic acid supplementation (WIFAS). This revised program recommended that the existing school health program ("*Usaha Kesehatan Sekolah/Madrasah*") should be utilized to deliver the iron-folic acid supplementation because approximately 86% of female adolescents are enrolled in secondary schools.[47] To demonstrate whether this school-based approach was feasible, a pilot study was conducted through a collaboration between the Ministry of Health and Nutrition International between 2015 and 2018, targeting secondary students at Cimahi and Purwakarta in West Java.[47] Three key learnings of this study were that the successfulness of the project depends on (i) increasing awareness of government officials and securing their commitments to the WIFAS project; (ii) improving the commodity's supply through capacity building of the Ministry of Health staff and strengthening the supply chain management systems; and (iii) increasing the need and acceptability of all stakeholders to the project.[47] This demonstrates the importance of multisectoral collaborations to ensure the school-based intervention could reach as many female adolescents as possible.

Secondly, another study was conducted among female adolescents and their parents in East Java and East Nusa Tenggara, focusing on their awareness and acceptance of the WIFAS.[48] Twenty and ten focused group discussions were conducted for female adolescents and their parents, respectively. Neither group perceived anemia as a high-risk health condition, and their parental opinions influenced the female adolescents' acceptance of iron-folic acid tablets. This reinforces the importance of educating all relevant stakeholders (and not only the target population) and modifying public attitudes in accepting the WIFAS. The iron-folic acid supplementation would only effectively reduce the prevalence of IDA among female adolescents and pregnant women in Indonesia if this program is integrated with the educational provision and attitude changes.

In line with this argument, the government of Indonesia collaborated with UNICEF to initiate an integrative program called "*Aksi Bergizi*" in 2017, targeting both female and male adolescents. This integrative program consisted of iron supplementation, nutritional education, and engagement for attitude changes. A pilot study was conducted at Klaten, Central Java, and West Lombok, West Nusa Tenggara, with total subjects of 540 from 60 different schools. It reported an increment from 55% to almost 90% of female adolescents participating in the WIFAS after the intervention.[49] The next Basic Health Research survey, presumably in 2023, would demonstrate whether this kind of integrative intervention could be well implemented and reduce the IDA prevalence in Indonesia.

Another crucial factor in this initiative's success is ensuring the government's ability to plan, purchase, and distribute the iron-folic acid tablets. However, the availability of iron-folic acid tablets in 2017 only reached 75% of the total requirement in Indonesia due to budget efficiency measures.[42] The Directorate of Community Nutrition's 2018 Budget Realization Report indicated that only 92.47% of the total budget (i.e., IDR 6,283,713,000) was utilized to purchase iron-folic acid tablets.[50] Furthermore, the Audit Board of the Republic of Indonesia concluded that in 2018, the Ministry of Health was inefficient in planning, purchasing, and distributing iron-folic acid tablets to regions across Indonesia, resulting in IDR 6.13 billion worth of iron-folic acid and vitamin A tablets been wasted.[42] This becomes a substantial task for the Ministry of Health as it needs to plan the procurement and distribution adequately, prepare health service providers and communicate with mothers, ensure quality control and product's traceability, and conduct intensive monitoring and supervision.[42]

(2) Initiation and promotion of exclusive breastfeeding up to 6 months of age and provision of recommended feeding practices for infants & young children

Exclusive breastfeeding up to 6 months of age is strongly recommended as human breastmilk contains all necessary nutrients for adequate growth and development of newborns. In addition, exclusively breastfed infants have a reduced risk of gastrointestinal infection.[51] In Indonesia, governmental regulation and a recommendation from the pediatric society exist to support the practice of exclusive breastfeeding. In 2020, however, the proportion of Indonesian infants under 6 months old who received exclusive breastfeeding was only 66.1%,[52] indicating a large gap in implementing this policy. This finding was reinforced by the results of Indonesia's Nutritional Status Study in 2021, which reported that only 52.5% of Indonesian infants under 6 months old received exclusive breastfeeding.[45] Political support (e.g., establishing a longer maternal leave) and community support (e.g., creating an environment that fully facilitates lactating mothers) would be required to increase this proportion.

Human breast milk contains little iron. As long as the maternal iron store during pregnancy is adequate, the gestational age of newborns is adequate, and the clamping of the umbilical cord is delayed, the iron stores in many newborns are likely to be sufficient for the first 6 months.[53] It means infants under six months old would not rely on iron concentration in breast milk with an adequate iron store. This also reinforces the importance of providing iron-folic acid supplementation for pregnant women. In addition, a systematic review reported that in low- and middle-income countries where newborns' iron stores might be inadequate, the practice of exclusive breastfeeding for 6 months or beyond could have an adverse impact on the hematological status of those infants.[51]

Infants over six months old would need appropriate complementary feeding to meet their nutritional requirements, including iron. Indeed, the complementary foods would fulfill 90% of the iron requirement during this period,[54] indicating that the first-introduced complementary foods around 6 months old should be rich in iron, such as meat or iron-fortified foods.[55] Meat intake could supplant the iron requirement as it is enriched of bioavailable heme iron,[55,56] with a reminder that protein intake (e.g., from meat) up to 2 years old should not exceed more than 15% of the total energy intake to prevent childhood obesity.[57] A local study reported that commercial fortified complementary food was better than homemade complementary food in preventing iron deficiency and IDA.[58] This finding is not surprising because the commercial fortified food would have standardized and sufficient iron concentrations. Next, the government of Indonesia is conducting a supplementation program called "*Taburia,"* improving the nutritional status and Hb concentration among infants aged 6–50 months old with inadequate body weight (weight/age <−2 standard deviations). In this program, infants would receive micronutrient sprinkle comprising vitamin A, vitamin B1, vitamin B2, vitamin B3, pantothenic acid, vitamin B6, folic acid, vitamin B12, vitamin C, vitamin D3, vitamin E, vitamin K, iron, iodine, zinc, and selenium.[59] The overall effectiveness of this program requires further verification. Nonetheless, two local studies demonstrated that *Taburia* supplementation increased the Hb levels of the participating infants,[60,61] suggesting a likelihood that this intervention could work.

(3) Control and prevention of helminth infection among under five-year-old and school-age children

This intervention follows the WHO guideline, which recommends regular deworming in endemic areas with helminth infections.[62] Hookworms (*Ancylostoma duodenale* and *Necator americanus*) reside in the small intestines of infected humans, in which the worms attach to the intestinal mucosa and withdraw blood from the host.[63] This would result in iron deficiency and IDA. A systematic review reported that the prevalence of IDA was strongly associated with the severity of hookworm infection and that a combination of albendazole and praziquantel was the optimum choice for deworming.[63]

The prevalence of those soil-transmitted helminths in Indonesia was high due to its tropical climate and overall low-to-middle socioeconomic status.[64] The Ministry of Health issued its decree in 2017 to conduct a national surveillance program and sustain the deworming program ("*Pemberian Obat Pencegahan Massal Cacingan*") for hookworms and other soil-transmitted helminths in Indonesia. This population-level program prescribed albendazole to children aged 1–12 years old, bi-annually in high-endemic areas and once annually in moderate-endemic areas.[65] According to the regulation, the evaluation would be performed after five years of implementing the deworming program.[65] Thus, the upcoming Basic Health Research survey would demonstrate the implementation and the effectiveness of this deworming program to reduce the prevalence of IDA.

(4) Improvement of maternal healthcare services and nutritional education for pregnant women

The Ministry of Health issued its decree in 2014 to improve healthcare services and provide nutrition education for pregnant women.[66] Both interventions should be an integral part of the provision of iron-folic acid supplementation, particularly to modify socio-cultural factors predisposing women to develop iron deficiency and IDA. For example, the household food distribution in several societies is discriminatory as women and children receive less nutritious foods than adult men.[67] Another prevalent socio-cultural factor is the practice of various food avoidance during pregnancy, predisposing pregnant women to develop IDA.[67] Through concurrent and synergistic interventions in providing healthcare services and modifying socio-cultural factors (i.e., changing attitude), it is anticipated that the next Basic Health Research survey could demonstrate a reduction of IDA among pregnant women.

(5) Promotion of a balanced diet and diet fortification for the general population

The Ministry of Health issued its decree in 2019 to stipulate the recommended dietary allowances (RDAs) ("*Angka Kecukupan Gizi*") for Indonesians, as stratified by age categories.[68] The RDAs refer to the recommended concentration of intake of essential nutrients, including iron, to meet the nutrient needs of all healthy individuals.[69] In order to meet the RDAs stipulated by the government of Indonesia, nutritional interventions should utilize balanced diets that are healthy and diversified.[70] Dietary diversification, particularly with local nutrient-dense foods, would indeed facilitate better access for the general population to meet their micronutrient adequacy, particularly the iron.[27,67,71]

Next, micronutrient fortification of highly consumed foods has been widely implemented to meet the RDAs of essential nutrients because the food fortification is considered cheaper and more effective than supplementation.[27,42,72] Food fortification began Indonesia in 1927 through iodization of salt used in various districts in Java[73] (for an interesting history on food fortification in Indonesia, please read [74]). Regarding iron fortification, the government of Indonesia issued a mandatory regulation in 2001 for wheat flour to be fortified with iron, folic acid, zinc, vitamins B1 and B2 (i.e., to meet the Indonesian National Standard ["*Standar Nasional Indonesia*"] for wheat flour). The government withdrew, however, the mandatory wheat flour fortification program in February 2008 in order to brake a dramatic increase in staple food prices.[42,74] Fortunately, the government revoked its decision by re-implementing the wheat flour fortification program.[42,74] In 2019, the WHO recommended that Indonesia change electrolytic iron to a higher bioavailable iron compound (e.g., 30 ppm of ferrous fumarate or 20 ppm of NaFeEDTA) for food fortification.[75] The evaluation of the wheat flour fortification in Indonesia, however, has not been performed thus far. Nonetheless, a systematic review on 10 studies of iron fortification in Indonesia suggested a promising result in reducing iron deficiency.[76]

Next, the fortification of rice should be prioritized in Indonesia as rice is the main staple food in this nation.[42] In 1952, the Philippines government has established laws on rice fortification with vitamin B1, vitamin B3 and iron,[42] hence its experience could be studied by the government of Indonesia. A pilot project started in 2015 by the government of Indonesia and the Asian Development Bank to fortify rice with iron and folic acid.[42,74] It has been reported that consumers well accepted the fortified rice because the fortification did not alter its color, taste, and smell.[42] In parallel, the Indonesian Bureau of Logistics has marketed fortified rice since 2019, in which 100 g of rice contained 4 mg of iron, 6 mg of zinc, 195 □g of vitamin A, 650 □g of vitamin B1, 9.1 mg of vitamin B3, 780 □g of vitamin B6 and 169 □g of vitamin B9.[77] This fortified rice is branded Fortivit. It would be sold for IDR 20,000 per kg and IDR 12,000 per kg under the premium and medium categories, respectively.[77] With the average price of rice is around IDR 10,000 per kg in Indonesia. However, the higher price of fortified rice could be an obstacle to being well received by the wider population across Indonesia.

CONCLUSIONS

Causes, pathophysiology, clinical presentation, and treatment of individuals with IDA are established. However, prevention and management of IDA at the population level in endemic areas require a holistic approach. The government of Indonesia is currently implementing various interventions for this purpose, which are part of the National Strategy to Accelerate Stunting Prevention 2018–2024. Those interventions target various groups of the population, in which they should be performed simultaneously to create a widespread, synergistic effect. The upcoming Basic Health Research survey in 2023 would demonstrate whether those interventions, as a whole, are sufficient to reduce the prevalence of IDA in Indonesia.

Abbreviation

Hb, hemoglobin. IDA, iron-deficiency anemia. RDAs, recommended dietary allowances. WHO, world health organization. WIFAS, weekly iron-folic acid supplementation.

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Conflict of interest

R.W.B. and C.D. are employees of Danone Specialized Nutrition Indonesia. All other authors have no conflict of interest.

Author contributions

RS, NAW, NRMM, JJ, RWB, and CD discussed and wrote the manuscript. All authors critically reviewed the manuscript and approved the final manuscript.

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