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The Challenges in Eradication of Iron Deficiency Anemia in Developing Countries

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ABSTRACT

Anemia causes losses of billions of dollars annually in terms of productivity among working women of the reproductive age; it affects both their cognitive and physical performance. In developing countries where many manual labor jobs exist, an iron supplementation program is the first choice for eradicating anemia. However, this program cannot sufficiently meet reduction targets, and this created a polemic among health experts. The purpose of this study was to explore how iron deficiency anemia may be eradicated in developing countries. The results showed that the main challenges for iron anemia deficiency eradication are as follows: low adherence, infection, hidden symptoms, comorbidities from other non-communicable diseases, micronutrient deficiencies, and lack of program monitoring. In terms of low adherence, the side effects of iron supplements become a major factor in taking medication. Conversely, parasites and worms cause most of the high infection cases. Poor access to facilities of healthcare centers are becoming the main factor for the absence of anemia eradication program evaluation in remote areas of developing countries. Therefore, breakthroughs are expected to be developed to reduce anemia significantly. These include increasing patient visits to a healthcare center, diagnosing anemia accurately and intensively, prioritizing infection control, fortifying food, and monitoring iron side effects.

Keywords: Anemia, developing country, iron deficiency, women of reproductive age

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INTRODUCTION

Generally, in the global context, anemia is becoming a public health burden. In 2015, the World Health Organization (WHO) reported that no country succeeded in the Sustainable Development Goals target of anemia reduction. An approximate annual average rate of 5.2% per year occurred from 2012 to 2025. The WHO released a guideline for countries to reduce the prevalence of anemia. The WHO's goal was to reduce the prevalence of anemia by 50% by 2025 (1). However, the diversity of each country's characteristics requires targeted handling. The baseline prevalence data in 2012 indicates that it requires continuous monitoring every year (2).

Anemia demonstrates a variety of causes. One of the most common cause is due to a lack of the ability of red blood cells to perform their function to transport oxygen and carbon dioxide in the body (3). Red blood cells contain hemoglobin, composed of heme and globin. In general, the shortage of iron, which is the main raw material for manufacturing hemoglobin, mostly causes anemia (4). The metabolism of iron absorption, distribution, and excretion, as well as iron's role in a human body, can be explained through the field of pharmacology (5).

Previous studies already discovered the underlying causes of developing anemia. Such causes include the following: blood loss (i.e., hemorrhage, heavy bleeding in woman's period) (6), increased demand for blood (i.e., in pregnancy) (7), decreased or low production of red blood cells (8), and hemolysis of red blood cells (i.e., in infection) (9). However, the prevalence of anemia prevalence can be a more complex problem, depending on the economic level (10), education level (11, 12), and culture of certain geographical regions (13). In developing countries with limited resources, these issues may produce more significant effects. The purpose of this study was to conduct a literature review on the challenges of iron supplementation for eradicating iron deficiency anemia in developing countries, especially for women of reproductive age (15–49 years of age) (14).

Anemia prevalence in developing countries

Anemia is becoming an important issue in developing countries where high anemia incidence rates exist and heavy manual labor occurs. Their cognitive and physical productivity losses are even higher (15). Due to anemia, a developing country loses around $0.232 per capita or 0.057% of its gross domestic product (GDP). Furthermore, South Asian countries experience a $4.2 billion loss in physical productivity. Median total losses (physical and cognitive) are $16.78 per capita, which is 4.05% of the present GDP (16-18). Countries with an anemia prevalence rate of more than 40%, especially among women reproductive of age between the ages of 15 and 49 years old, demonstrate a severe public health burden to provide for healthcare facilities and iron supplementation programs (19). Epidemiological studies about the causes of anemia, especially among pregnant women, are required because of the risk of congenital disabilities and maternal mortality. The anemia cases with prevalence rates of 20%–39.9% are categorized as moderate anemia. Meanwhile, 5% to 19.9% is categorized as mild anemia (20). This classification will help many countries to prioritize their target (21, 22). Anemia is closely related to cognitive development and national productivity (23-25). In

Table 1, published studies on the iron supplementation programs in countries can be found. These were performed to reduce the prevalence of anemia in the said lower-middle-income countries. Daily or weekly treatment for anemia depends on the causes and severity level. This shall take into consideration possible urogenital disorders, respiratory disorders, gastrointestinal disorders, pregnancies, and infections.

The challenges of iron supplementation in developing countries

Therapeutic options for anemia, including iron supplementation, food fortification, and micronutrient powder, were expended in developing countries. Conversely, developed countries use a more expensive option such as erythropoiesis-hormone therapy, intravenous injections, or blood transfusions (26).

In the country with severe anemia prevalence (>40%), an iron supplementation program is implemented as the first choice for patients with anemia. This is also being used as a preventive measure (27). The recommended composition of iron for both women in the reproductive age and young women is 30–60 mg of elemental iron. Such is equivalent to 150–300 mg in the form of ferrous sulfate heptahydrate, or 90–180 mg of ferrous fumarate, or 250–500 mg of ferrous gluconate. The supplements are administered once a day for three months in a year (28).

Only a few countries published data about the outcome of iron supplementation programs. In several low-income countries, the United Nations managed the iron supplementation program, especially for iron deficiency anemia for high-risk groups. These include pregnant women, women of the reproductive of age, and school children (29). Low-income countries such as Ethiopia (30-32), Nepal (33), Nigeria (34), Sierra Leone (35), Tanzania (36-38), and Uganda (39-41) published studies about iron supplementation for women. Independent researches were also performed, which focused on anemia issues in other developing countries such as Indonesia (42-44), the Philippines (45, 46), Papua New Guinea (47-49), Pakistan (50, 51), and Cote d'Ivoire (52, 53).

An iron supplementation program has been the first choice of anemia treatment in developing countries. However, many challenges to be able to increase the accomplishment of this program still exist.

a. Low adherence

Low adherence is mostly caused by a side effect of iron salt, a form of synthetic iron distributed and used in developing countries as a supplement. Free iron ions may cause side effects in iron supplementation. Such results from the breaking down of the non-heme form (synthetic iron as iron salt) before its absorption through an ion channel inside the epithelium layer of the intestine. These side effects include the following: nausea, stomach pain, and constipation. Because of these side effects, negative perceptions arise about consuming iron supplements again (54). The side effect will not happen if they consume heme iron form supplements or take an iron supplement with a sustained release. This is convenient to the stomach and to absorption, but it is rather very expensive (55).

In Ethiopia, the most common reason of low adherence is the side effect of the supplementation (63.3%) and not the missed dose (16.7%) (56). Nigeria and Kenya exhibit similar problems with low adherence, side effects of iron (41.7%), and non-heme forms (31%) (53, 54). Early education about the advantage of iron supplementation and regular visits to healthcare centers are good strategies for the prevention and treatment of anemia in pregnant women (57). Regular visits to healthcare facilities will increase adherence to the iron supplementation regimen [OR; 2,83.95% CI (1.46, 5.48)] of pregnant women. Visiting focused antenatal care (ANC), at least four times, is a significant strategy of monitoring, educating, and consulting about iron supplementation, iron fortification, and maintaining self-hygiene to avoid infection (58).

b. Uncontrolled infection

Different challenges exist in Nepal (59, 60), Nigeria (61), Sierra Leone, and Tanzania (62, 63). These countries are also experiencing an endemic of malaria (64), worms (65), schistosomiasis (66), and other parasites. These countries should concentrate on infection control actions before implementing an iron supplementation program. In 2018, Pasricha *et al.* found that controlling the infection will initiate the recovery of hemoglobin levels naturally by homeostasis. This is because no more blood loss caused by infection occurs if such infection is controlled (67).

In lower-middle-income countries, malaria infection significantly increases the burden. The most severe prevalence of anemia is in Papua New Guinea (89.7%) (68). In particular, Papua Island exhibits the most severe prevalence of anemia, compared to other Indonesian islands. In 2015, a local study found that 72.9% of anemia cases were among women of reproductive age in Teluk Bintuni Regency, West Papua Province, Indonesia. Apart from malaria, countries such as Cote d'Ivoire, Ghana, Indonesia, and Kenya also controlled other parasites like helminthes and schistosomiasis.

Iron supplementation cannot make a positive impact on hemoglobin levels if any infection was not cleaned from the body of the woman suffering from anemia (69). Countries with high infection burdens are found to exhibit 3 to 5 times milder anemia cases among women than those in moderate and low infection countries (70). Conversely, 50 mild anemic women (hemoglobin 11,0–11,9 g/dL) among 100 anemic women exist at all levels (hemoglobin below 12,0 g/dL). This is a public health sign that a high infection burden will exist, especially with mild anemic women. To detect what kind of infection exists in this area, the government must start infection screening (71). After all the infections are under control, medical checkups for the patients' hemoglobin levels and iron supplements for anemic women can be conducted (72).

Recent research already warned developing countries to prioritize handling and preventing infections (malaria, parasites, and viruses) in children (73). They also recommended these countries to provide iron supplements for children who suffer from infections, to reduce the risk of death (74); this does not apply to adult patients (75). Most

likely, this is because adults demonstrate stronger immune systems compared to children.

c. Hidden symptoms and comorbidities of another non-communicable disease

Signs and symptoms accompany anemia, but some conditions are asymptomatic or exhibit hidden symptoms (76). Symptoms of anemia are different for each person, depending on hemoglobin levels and personal sensitivity. A pale color of the skin because of the lack of red blood cells containing hemoglobin is an indication of anemia (77). Hemoglobin levels below 11.0 g /dL are more typical than the normal level for women, which is usually between 11.0 to 12.0 g/dL. The pale color or invisibility of fine lines in the arteries and capillaries in the inner eyelid manifests the severity of anemia. No further studies exist linking the oddity that occurs between hemoglobin levels and symptoms in detail because the response is still very diverse. Another constraint is caused by the highly subjective nature of the complaint (78).

The other non-communicable disease that is becoming an anemia comorbidity is hemoglobinopathies, a genetic disorder found in Cambodia (79) and the Philippines (80), and sickle cell diseases in Sierra Leone (81). Anemia can occur in both acute and chronic conditions. Multidimensional approaches are needed to control, prevent, and treat anemia among women of reproductive age in developing countries (82).

d. Micronutrient deficiency

In developing countries, eradication of iron deficiency anemia is carried out without specific diagnoses. Diagnosis of iron deficiency anemia can be seen through the results of blood plasma films, colorless blood plasma color, and lack of iron in bone marrow specimens. Inadequate laboratory infrastructure limits this diagnosis. In the end, after countries carried out iron supplementation programs, food fortification, and micronutrient powder for anemia patients in developing countries, they reported that a lack of complex nutrients is also found among the patients, and not just iron deficiency (83, 84).

Large scale food fortification programs for the undernourished in low and middle-income countries resulted in a 34% reduction in anemia rate ratio: 95% CI; 0.66 (0.59–0.74) (85), and the reason for this is a poor diet with minimal variety. Women who are busy with their activities often skip breakfast. Most of them take lunch at around 3 p.m–4 p.m. Thereafter, they eat again late at night. They are forced to fast because their lifestyles limit eating at night. Their diets consist mostly of ready-to-eat food, such as instant noodles, sardines, and fast food in Pakistan (86).

Women who experience puberty characterized by menstruation should be provided counseling and reproductive health education first. Thereafter, they must learn about the selection of food, especially micronutrient-fortified foods. This condition leads to an increased need for iron in growing genital tissues (including the compliance burden of menstrual blood deficiency every month). Hence, young women are more vulnerable to anemia than male adolescents, for whom worm infection treatment are also needed to be provided for in schools (87). Counseling and feeding supplementary nutrients such as meat, fish, protein, and iron-rich food according to local culture can help in anemia prevention among lactating women (88, 89).

Ethiopian women avoid certain foods when they are pregnant, according to their local culture. This contrasts with the usual daily habit of taking *Hibiscus Sabdariffa* plants (1.9 kg/day) to meet the iron needs of women and their babies. Similarly, randomized studies in Uganda reveal that providing micronutrient-fortified foods can reduce the prevalence of moderate to severe anemia in adolescent and adult women (90).

A low consumption of animal products as a heme iron form source, such as red meat, eggs, fish, and liver, can cause iron deficiency. Diagnostic laboratory data obtained a low iron content, but not all forms of iron deficiency are iron deficiency anemia (91). In addition to strengthening their short-term nutrition, the long-term recommendation of empowering partners to produce fish, poultry, and fresh meat is also fulfilled. However, if the area lacks a hygienic water source, or if it is in a dry area, then heme iron supplementation can be used (92).

e. Low monitoring and evaluation of the program

Pakistan and Cambodia demonstrate different issues regarding iron supplementation programs. In Pakistan, this program was successful (93). In support of the iron supplementation program, monitoring through regular health checkups also occurred, as well as an increase in the incomes of the mothers, variety in diets, health, sanitation, and education about anemia. They can decrease the prevalence of iron deficiency anemia among women of reproductive age from 90.5% (2008) to 50.4% (2011), as presented in Table 1. Bangladesh was also successful with monitoring and evaluating programs, as well as nutrient projects in the workplace (94).

The central government needs to support health departments in provinces, regencies, and district areas exposed to conditions such as different geography, social culture, low infrastructure, and policy. Short- and long-term programs, which are decided by health care providers and supported by the government, should be focused on the screening and evaluation for the leading cause of anemic conditions in women, especially pregnant women (95). In a short-term program, a health care provider needs to empower women to cook and eat varied diets, as well as to increase their consumption of red meat and liver. Furthermore, they need to educate them about how to recognize anemia symptoms in their bodies as the subject signal to feel, such as the pale color inside the lower eyelids, difficulty sleeping, fatigue, and insomnia. They typically have a caregiver, such as their partner or friend, to help them out during the process. The caregiver shall assist them from the diagnosis of the main cause of anemia, until the level of hemoglobin in anemic conditions increased (96). They shall also assist in changing the dosage form from oral administration to parenteral to whom cannot be tolerate the oral dosage form (97). In a long-term program, the government needs to invest in infrastructure (streets, transportations, bridges, and telecommunication) to handle the long distances between the

patients' homes to the health care providers (alleviating the transportation barrier). Indonesia is an archipelago with different geographic conditions and tribes divided by social culture. Indonesia still needs to increase transportation in the rural areas. The prevalence of anemia increased from 37.1%, in 2013 to 42% in 2016, and in 2018, it was already at 48.9%. (98, 99). It is in line with the World Bank's statement (100) that low-middle-income countries exhibit a greater burden of poverty than low-income countries. This is according to the population and income growth of the countries, as presented in Figure 1.

Anemia management in the future

a. Increase adherence by education and intermittent iron supplementation

Women (especially in reproductive age) should visit healthcare centers routinely to achieve proper diagnosis, education (101, 102), monitoring, and receive free iron supplements and micronutrient powder from health care providers. After screening their level of serum ferritin, anemic women who visit PHCs four or more times will exhibit higher adherence to consuming iron supplements (103) and better optimization of iron levels for pregnant women before delivery (104).

The main barrier of poor transportation exists in developing and low-income countries that prevents anemic pregnant and non-pregnant women from visiting healthcare centers regularly. The collaboration of an anemia healthcare team and a health community must reach the patients from one village to another (105). All barriers from multiple sectors play roles in anemia prevention and treatment. For example, preventing recurrent anemia and increasing adherence to treatment with iron supplementation through the optimization of the iron availability in the blood, as well intermittent dosage to intake iron supplementation to avoid side effects (106).

b. Controlling infection is a priority for the endemic environment

The infection prevention program is carried out before the program for improving hemoglobin levels. Net bed insecticide, malaria drugs, fogging, and seasonal malaria chemoprevention help control the spread of malaria infection (107), as well as the infection of schistosomiasis and soil-transmitted helminthes (108). Treatment of seasonal malaria infection, combined with nutritional interventions, can reduce the prevalence of anemia in the population of North Nigeria (109). In malaria-endemic areas, high doses of folic acid should be avoided because they interfere with the effectiveness of antimalarial pyrimethamine sulfadoxine (110). A demand exists for more customized strategic planning in the future. However, this should be something that still follows the WHO guidelines. Information and protocols on handling an infected endemic environment need to be prioritized as well for the equivalent of anemia treatment to increase hemoglobin levels (111).

c. Diagnosing underlying causes of anemia intensively

Iron supplementation treatment cannot optimally reduce the prevalence of anemia in developing countries. This is because the program begins with the assumption that the main cause of anemia is iron deficiency (112). However, not all iron deficiencies are iron deficiency anemia. If an iron deficiency anemia program did not reduce the prevalence of anemia as expected in some countries, it turned out that, in Cambodia (113), a predictor of a disorder of hemoglobin E and pregnancy status was found. Moreover, in the Philippines, screening for causes of anemia in Manila revealed that 62.5% of the participants presented with hemoglobinopathy and other causes of iron deficiency. Infection of endemic areas, micronutrient deficits, pregnancy (114), cancer and tumor (115), HIV (116), genetic disorder (117), heavy exercises such as athletic exercise (118), urinary and genital infection (119), heart disorder (120), respiratory disorder (121), iron homeostasis (122), and other causes should also be identified as causes of anemia.

From a patient's perspective, anemia may exhibit no hidden symptoms until the hemoglobin level is very low. The team will be late to help such women with severe anemia with hidden symptoms because of their confusion about symptoms that have not appeared. Scientists should always investigate recurrent anemia, considering its underlying causes, and it requires intensive treatment in fragile and high-risk patients. Subjective feelings may lead women to avoid seeing a clinician or midwife. Proper diagnosis using laboratory screening from a health care provider should be conducted in areas where anemia is highly prevalent. Additionally, women in remote areas of developing countries tend to exhibit multivitamin and mineral/iron deficiency. Programs in developing countries should collaborate to find the main cause of anemia from each woman (123). The very complex nature of iron supplementation programs among anemic women in developing countries has been a challenge. A need for customized solutions for every person exists because many cases of anemia are caused by manifestations of acute or chronic diseases that must be addressed first so that doctors and scientists can cure anemia more easily.

d. Partnership collaboration

Healthcare teams should collect and prioritize treatments. The District Assessment Tool for Anemia (DATA) still needs to be modified according to the local culture in every country. For example, every anemic woman can use a special calendar to remind her when she should visit the PHC again, by receiving a checklist on the calendar during her iron supplementation therapy (124-126).

By approaching the government to facilitate the workshop between policymakers, the health care ministry, the agriculture ministry, and the education ministry, a non-government organization community leads in filling the DATA of anemia barriers and prioritizing the program outcome, integrity commitment, and evaluation team monitoring (127). Periodically, the teams disseminate the outcome of the public and patients in the program so that they can share it for helping other anemic women as well (128). The cost of a laboratory screening diagnosis to detect the causes of anemia is very high. Iron supplements are selected depending on what is considered more affordable by the government. Women in developing countries should be fully funded by health insurance to get diagnosed. They must

also be allowed to obtain specific and personal treatments, taking into consideration that not all types of iron deficiency are anemic (129). The partnership should be involved in anemia prevention and treatment from nutrition, disease control, reproductive health, water and sanitation, agriculture, and education.

e. Starting a pilot project area will be needed for broader area coverage

A pilot project of program innovation includes the following: performance monitoring to identify the constraints and equitable distribution, provision of a supplementary feeding program of iron and folic acid, monitoring pregnant women's visits for postnatal care and health care (130), evaluation of the efficiency of continuing the program, and the expansion to areas that were not yet covered. The Uganda anemia program, which started to build district capacity from a pilot project in three districts (two high and one moderate anemia prevalence), serves as a benchmark. Uganda used three strong foundations to build an anemia reduction program. This included policy environment, partnership approach, and building capacity. (131-133)

f. Increasing the variety of fortified food consumed and monitoring iron overdose

Women in developing countries tend to demonstrate little variety in their diets. They consume the same kind of food, even those without nutrition, just to fill their stomachs and avoid the feeling of starvation. Drug information about overdose is unavailable and women with poor cognition may misunderstand such information (134). Often, ignorance exists in developing countries regarding the deficiency about other nutrition besides. Fortified food or uptake of micronutrients and multivitamins can help them more, compared to when they just take iron supplementation only (135, 136). In hospital cases, delivering iron supplements by infusion might pose a higher risk of overdose than oral delivery. Other risks of iron supplementation include gastrointestinal side effects, thus resulting in low adherence (137).

Patients educated and monitored by health care professionals will be able to recognize the symptoms of overdose, such as irregular heartbeat, by comparing it to their heartbeat in normal conditions. Furthermore, they also know how to handle the side effects of iron supplements (138, 139). Supervision by health care professionals is crucial to avoid the risk of an overdose of iron supplementation with routine administration, such as contraindications with malaria infection, increased hepcidin, cardiovascular symptoms due to excess iron, and other risks (140).

g. Evaluating the impact of an intervention to the quality of life of patients

Limited resources in developing countries mean only a few governments focus their attention on the handling of the problem of anemia and infection in their country. Detailed studies of anemia diagnosis and screening, such as complete examination of blood, hemoglobin status, ferritin serum, transferrin saturation, definitive diagnosis in the bone marrow should be evaluated in every program report. This will allow the determination of whether or not they fit in the population and whether or not they increase the quality of a patient's life (141, 142). Empowering the health care professionals by a hands-on practice workshop, knowledge in research, policy renewal, and improvement of the implementation strategies will help in alleviating the anemia burden program in low-income countries (143, 144).

Recent studies showed the need for evaluation of whether or not any change exists in Disability Adjusted Life Years from the intervention programs of iron supplementation (145). According to the WHO guidelines, when analyzing the change of clinical benefit for improving cognitive and psychological well-being, one must look into the early symptoms before and after the intervention (146), morbidity (147, 148), growth (149), economic productivity (150), and the quality condition of the mother and baby after birth (151). Adding the intervention program's effect on the quality of a patient's life is important in every evaluation and policy renewal (131, 152).

CONCLUSION

The eradication of iron deficiency anemia is influenced by five main factors. The most prominent factor is low adherence to iron supplementation due its side effects. The other factors include the following: infection because of parasites and worms, unnoticeable symptoms, micronutrient deficiency, and low monitoring or evaluation of the supplementation program due to the access and transportation to the healthcare facilities. Furthermore, the healthcare program should be improved such as health promotion and monitoring program to increase the adherence level, self-hygiene, balanced nutrition intake, and health environment.

CONFLICT OF INTEREST

All authors declare that there is no conflict of interest related to this study

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TABLES AND FIGURES

Table 1: Monitoring, prevention, treatment, and challenges of anemia in women in developing countries

Category	Countries (Anemia prevalence in 2016)	Monitoring	Prevention	Treatment	Challenges	Reference(s)
Low-income countries	Ethiopia (24.3%)	Pregnant women in eight rural districts of Ethiopia exhibited lower utilization of iron supplementation. The main reason for this is because of the iron supplementation's side effect (63.3% rather than 16.7%).	Early education about the function of iron supplementation for pregnant women, and frequent visits to ANC centers are good strategies to prevent anemia.	Iron supplementation in maternal anemia.	Nutrition deficiency, a side effect of iron supplementation to gastrointestinal organs.	(56)
		Frequent visits to four or more ANCs were positively associated with significant adherence to iron-folic acid supplementation.	Visiting four or more ANCs will increase compliance to iron-folic supplementation [AOR; 95% CI 2.83(1.46–5.48)]	Iron-folic acid supplementation among pregnant women in Eritrean refugee camps in Northern Ethiopia.	Women with lower education about anemia and those with only limited importance of iron-folic acid supplementation were negatively associated with significant adherence.	(103)
		Women who started ANC follow up early [AOR; 95% CI 2.43 (1.12–5.26)] demonstrated a more frequent number of ANC visits [AOR; 95% CI 2.73 (1.32–5.61)], took a small number of tablets per visit [AOR; 95% CI 3.0 (1.21–7.43)], presented with a history of anemia [AOR; 95% CI 1.9 (1.17–3.12)], were from the urban areas [AOR; 95% CI 2.2 (1.29–3.77)], and were more likely to conform to recommended iron-folic acid supplementation.	Anemia education and customized programs prescribed to individuals according to their backgrounds	Iron-folic acid supplementation among pregnant women in Tesfaye Molla, Northwest Ethiopia.	How to educate women to use food iron fortification, cook a variety of food, compliance to iron supplementation, and the avoidance of infection.	(30)

		The results showed very low adherence because of low maternal and health education, supply during supplementation, early stage visit to clinics, and health education.	Unknown	Iron-folic acid supplementation among pregnant women in Asella Town, Southeast Ethiopia.	Very low adherence to the intake of iron supplementation.	(31)
		Compliance rate in this district is very low. The compliance rate was found only at 39.2%. Mothers' knowledge of anemia (AOR; 95% CI 4.451 (2.027–9.777)), knowledge of iron-folate supplementation (AOR; 95% CI 3.509(1.442–8.537)), and counseling on iron-folate supplementation (AOR; 95% CI 4.093(2.002–8.368)) were significantly associated with compliance to iron-folate supplementation.	Studies showed that providing clear information about supplementation intake and education about the benefit of supplementation will increase the compliance rate.	Iron-folic acid supplementation among pregnant women in Misha District, South Ethiopia.	Very low adherence to the intake of iron supplementation.	(32)
	Nepal (40 %)	Multi-sectoral efforts using DATA Sanitation, and mid-day meal monitoring, fund establishment and mobilization of pregnant women, monitoring and supervision by the district development committee.	Disease control: Malaria prevention, proper hygiene and washing, access to clean water, improved latrines, family planning; Agricultural: Increase in family income, production of crops rich in iron, home food production; Education: Deworming in school and hygiene education.	Reduction of Infections: Malaria and deworming in pregnant women; Nutrition: Micronutrient supplementation.	1. Language barriers in bilingual conversations and different languages between campaign materials and local communications; 2. Multi-causes of anemia need multi-sectoral efforts; 3. No tools to measure the impact of intervention programs exist; 4.The barrier to the prevention are the lack of public awareness; 5. The coverage of deworming is high, but hygiene education in schools or/and community is low; 6. Difficulty in accessing the data entry health system.	(4, 33, 50, 60)

	Nigeria (58.7 %)	Screening the low level of serum ferritin in pregnant women before their babies' delivery.	Infection control of malaria, schistosomiasis and soil-transmitted helminth; Micronutrient uptake for pregnant women prevented anemia.	More than 90 days uptake of micronutrient; Traditional herbal management of sickle cell anemia; Routine iron supplementation among pregnant women.	The distance of the health center from their homes reduced compliance of pregnant women to uptake micronutrients. Optimization of hemoglobin levels of pregnant women before delivery; Gastrointestinal side effect of iron supplementation (41.7% in Enugu, Southeastern Nigeria) reduces compliance.	(66, 81, 104, 136, 153)
	Sierra Leone (55.9 %)	Sierra Leone exhibits the highest prevalence of anemia in the world at around 48% (2013). Multi-sectoral monitoring by the United Nations (UN) team in charge of this country because of poverty. National-District coordination.	Infection control programs: Intermittent preventive treatment, control of Malaria-helminth-schistosomiasis.	Insecticide treated net; Fortified food and micronutrient supplementation, vitamin A, iron folate, micronutrient powder, intervention for short and long terms; Promoting women's empowerment efforts in education and literacy, family planning, and spacing between births; water sanitation, Hygiene intervention for general inflammation.	Different with another countries; Sierra Leone has a low prevalence of iron deficiency anemia. A paper-based tests for Sickle Cell Diseases –is conducted in August 2019 in this country.	(35)
	Tanzania (48 %)	By comparing the studies and results of anemia prevalence in different years. A decrease in prevalence exists between 2012 and 2018, from 47.4% to only 18%.	Infection control such as Malaria chemoprophylaxis by mosquito nets, HIV, and deworming.	Iron supplementation; government strengthened the ANC to serve pregnant women.	Prevalence anemia is a mild problem of the public health sector in North Tanzania (18%). Low education in pregnant women is an independent factor associated with anemia in women.	(36-38, 62-64, 110)

	Uganda (34.3 %)	Monitoring indicators of anemia: research of cost-effectiveness between two channels. The facility health worker and the village health team to deliver vitamins and mineral powder It has been found that the village health team is more effective than the facility health workers.	Fortified food from production, regulation, and consumption (i.e., vitamin A-fortified banana.)	In Uganda, three strong foundations to reducing anemia are present: 1. policy environment, 2. partnership approach, 3. Building capacity. This is similar with all programs applied the UN to other countries in Africa, such as the following: fortified food, vitamin and mineral powder, micronutrients, controlling infections, campaign awareness for anemia, education of local	1. A multi-sectoral collaborative process needs regular coordination in the national and district scale. 2. Spreading contribution to all sectors by the increased understanding of anemia from the health sector to all non-health sectors (i.e., agriculture, education, industrial, and economic departments). 3. Three diverse contexts in accordance to the need to build district capacity to start the pilot project: Namutumba (high anemia prevalence), Arua (high anemia prevalence), Amuria (moderate anemia prevalence)	(39-41, 91, 131-133, 154)
Low-Middle-income countries	Cambodia (55.8 %)	Multi-sectors play a role in the problem of anemia.	An alternative way to prevent anemia exists. In 2017, Cambodia's anemia problem in women was solved through the use of an iron fish-shape for the uptake of iron elementals in cook. This was done in a span of 6–12 months. But, a low impact to their anemia condition exists.	Weekly iron supplementation (60 mg) and folic acid (2.8 mg).	The high prevalence of anemia in Cambodian women (43%) cannot be explained by micronutrient deficiency. The predictors of hemoglobin concentration are as follows: disorder of hemoglobin E homozygous and pregnancy status. Poor compliance occurs, and an issue about the distribution and procurement of supplement supply exists.	(79, 80, 113)
	Cote d'Ivoire (59.3 %)	Monitoring iron stores according to iron deficiency related inflammation anemia and HIV among women with ART.	Control malaria and gastrointestinal helminthes infection using herb medicine.	Traditional medicine using herbs to treat anemia. The highest iron content in Tectona	This is a country with high infection burdens. The prevalence of mild anemia was 3 to 5 times more than the infection countries. 50% of mild	(49, 53)

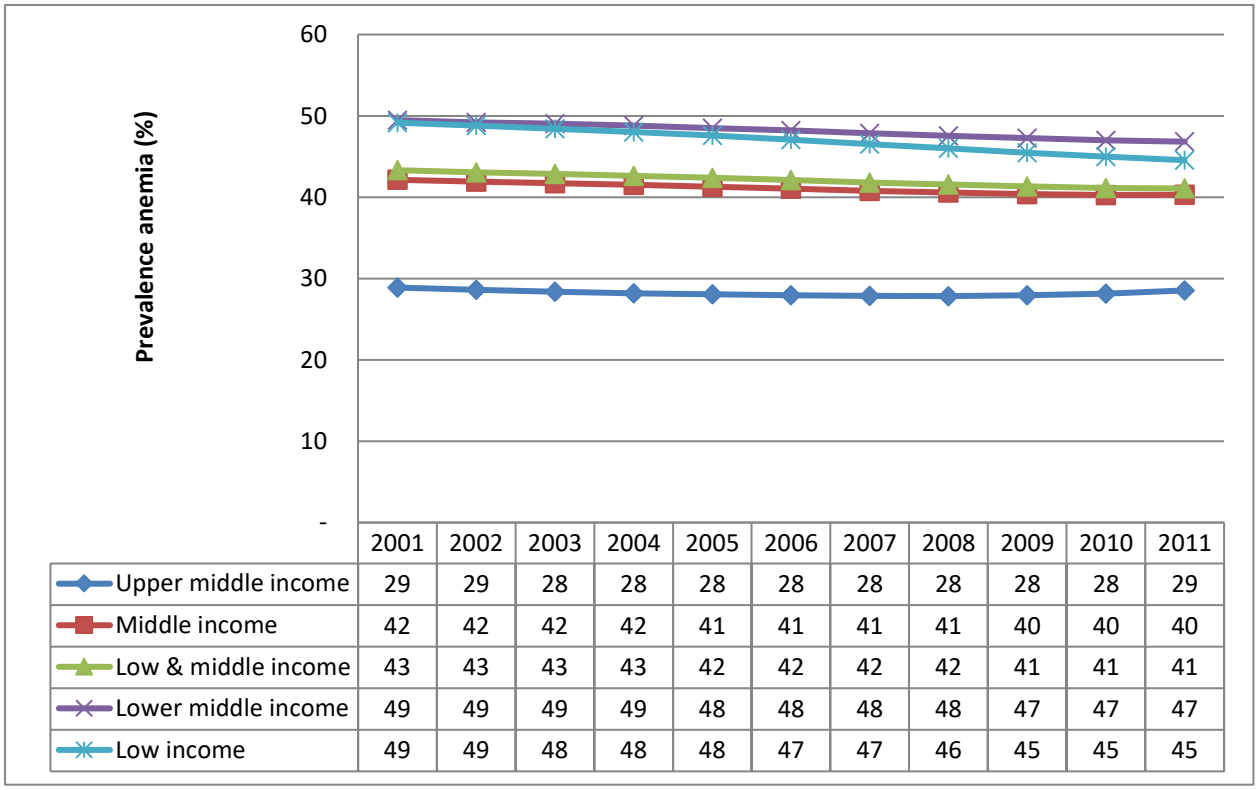
				grandis (266.6 mg/100 g), Amaranthus spinosus (236.6 mg/100 g), and Stylosanthes erecta (206.6 mg/100 g).	anemia cases come from infection countries.	
	Ghana (54.3 %)	Tracking the progress of anemia related programs. Infection control diseases (Malaria, Deworming, and HIV). Insecticide treated nets, indoor residual spraying, intermittent preventive treatment of pregnant women (IPTp), and diagnosis and treatment of malaria with artemisinin-based combination therapy.	Water sanitation facilitates (i.e., toilet improvement), family planning, fortified foods such vegetable oils with vitamin A, and wheat flour fortification with multiple micronutrients.	Treatment by iron-folic supplementation and by managing anemia. This includes malaria prevention, diagnosis, and treatment; helminthes prevention and control; and nutrition-related interventions. For example, Iron-folate Supplementation, Complementary feeding, Micronutrient powder.	High prevalence 42% in women of reproductive age (2014). Challenges to the main risk factors for anemia in Ghana are malaria, helminth infections, and micronutrient deficiencies. No recent national survey data exist on micronutrient deficiencies or helminthes infections.	(90, 155-157)
	Indonesia (42 %)	Infection of Malaria and helminthes control.	Health education and social behavior, traditional medicine, access to health centers, healthy environment, bio-medic parameter such as blood glucose, hemoglobin, cholesterol.	Iron-folic supplementation, nutrition improvement, and intermittent iron supplementation to adolescents in schools (once a week). Industrial food fortification, such as that in oil and instant noodles.	The anemia prevalence reached a severe level among the public health of pregnant women in Indonesia. It is now at 48.9% (2018), increasing from 37.1% (2013). The East Kalimantan is at 53.9% (2014) for children and adolescents. Education of health was an important risk factor for non-compliance to uptake iron supplementation in Bali. In Ciamis and Tasikmalaya, West Java, 9.6 % of anemia cases were concerning women of reproductive age. Indonesia exhibits varying cultures and	(98, 99)

					demographics between islands. Rare recent publications study the anemia prevalence from every island in Indonesia.	
	Kenya (38.2 %)	Control infection of malaria, intestinal worms, and other parasites, which reduces the bioavailability of iron in the body.	The increase in knowledge about anemia, nutrition education (learning to avoid food which inhibits iron absorption and learning to consume food which enhance the iron absorption in the body), dietary diversification, home gardening, food processing technique.	Iron-folic supplementation (tablets and syrup).	Low adherence in iron-folic supplementation. Coverage was only at 53%, with 31% being pregnant women. Malnutrition estimate in 2010–2030. Only 20% of the Kenyan land is suitable for farming.	(59, 158)
	Pakistan (51.3 %)	By regular health checkups.	Anemia can be prevented and treated by the guidance and awareness obtained from education. This can be done by providing awareness and counseling through education and the media.	Iron supplementation in women who are of the reproductive age because in stunted children may be anemic if they have an anemic mother as well. Increased income of the mother, various diets, health sanitation, and education about anemia will support iron supplementation programs.	Prevalence of iron deficiency anemia is severe at 50.4% (source data 2011) in women of reproductive age and 90.5% in pregnant women (2008). Poor economic status, low literacy, awareness of nutrition and minerals cause such prevalence. Income growth and understanding of the relative rule of various diets, health, sanitation, and education factors in the local context.	(50, 51, 57, 86, 93, 143)
	Papua New Guinea (30.3 %)	Control high infection rates of malaria.	Anemia prevalence was approximately at 40% in countries with a high infection burden, and 12% in countries with moderate infection	Iron-folic acid supplementation, micronutrients.	Prevalence of anemia is at 89.7%; hence, the country is included in the severe category. The country is facing a malaria endemic as well.	(47-49)

			burden, and 7% in countries with low infection burdens.			
	Philippines (44.8 %)	Population screening is needed to determine the real causes of anemia. Hemoglobinophaty was found (genetic disorder).	Assessment of the distribution and consumption of tablet iron-folic acid supplementation in ANC.	Iron-folic acid supplementation, since the research found that Single Nucleotide polymorphisms in *TMPRSS6* and *TF* are potential genetic risks factors for anemia ID, and IDA the treatment are more specific with changes.	Prevalence of anemia in women is at 15.7 % (2016). This decreased from 38.3 % (1990), with pregnant women's rates at 25.2% (2015). In 2018, screened anemia cases in Manila result in a rate of 62.5% from hemoglobinopathies and other cause than iron deficiency. Different causes of anemia require different treatments. Screening programs of anemia causes need to be implemented before the actual treatment of the anemia itself.	(25, 45, 46, 80)

Table 2: Symptoms and the hemoglobin level of anemia in women

Severity anemia in woman	Hemoglobin (mg/dL)	Symptoms felt by patients
Normal	12.0 or more	No specific symptoms
Normal (Pregnant)	10.0 or more	
Mild	11.0–11.9	Eyes: the lower eyelids are still clearly visible with, also with the presence of capillary arteries
Mild (pregnant)	10.0–10.9	Brain: often feeling sleepy because the brain lacks oxygen supply
Moderate	8.0–10.9	Eyes: pale yellowish cornea Skin: cold temperature, pale yellowish color
Moderate (pregnant)	7.0–9.9	Lungs: shortness of breath. Muscle: weak Colon Feces: stool changes color
		Brain: tired, dizzy Blood vessels: low pressure
		Heart: pulse rhythm changes, palpitations, rapid pulses Spleen: swelling occurs
Severe	< 8.0	Brain: fainting Heart: left chest pain, angina, heart attack
Severe (pregnant)	< 7.0	



	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011
Upper middle income	29	29	28	28	28	28	28	28	28	28	29
Middle income	42	42	42	42	41	41	41	41	40	40	40
Low & middle income	43	43	43	43	42	42	42	42	41	41	41
Lower middle income	49	49	49	49	48	48	48	48	47	47	47
Low income	49	49	48	48	48	47	47	46	45	45	45

Note: Income rises, but the population means that a double workload is present in the low-middle-income group (purple line X), so the line position is more than the low-income group (blue line X). This happens because workers engaged in manual labor exhibit a greater burden to generate income/GDP, compared to low-income countries where no increase in income exists. Indonesia is in between the lower-middle-income and the middle and low classification, meaning that income rose rapidly. However, technology, road infrastructure, and other similar innovations were not ready yet (under construction). Therefore, the country relied a lot on human power. This is the opposite of what happens in middle-income countries. Middle-income countries exhibit more stable infrastructure and technology.

Figure 1: Anemia profile among pregnant women in the world