INTERSECTORAL AND ECO-NUTRITIONAL APPROACHES TO RESOLVE PERSISTENT ANEMIA IN INDONESIA

Widjaja Lukito MD, PhD Mark L. Wahlqvist MD, FRACP, FAFPHM

INTERSECTORAL AND ECO-NUTRITIONAL APPROACHES TO RESOLVE PERSISTENT ANEMIA IN INDONESIA

Widjaja Lukito MD, PhD Mark L. Wahlqvist MD, FRACP, FAFPHM

INTRODUCTION

- 76 years of independence
- Anemia in Indonesia has not been resolved.
- Anemia is often perceived as nutritional anemia and iron-deficiency anemia (without knowing the parameter of iron deficiency itself)
- Comprehensive approaches through regional strengthening is needed

Prevalence of anemia in various at-risk people in Indonesia (2008, 2013, 2018)



Source: Basic Health Research 2008, 2013, 2018.

Prevalence of anemia group of urban Indonesian elderly,(Juguan dkk, 1999)



HEMOGLOBIN LEVELS TO DIAGNOSE ANEMIA AT SEA LEVEL (G/L)

	Non-anemia [†]	Anemia‡			
Population	Non-Greinig.	Milda	Moderate	Severe	
Children 6-59 months of age	≥ 100	100-109	70-99	< 70	
Children 5-11 years of age	≥ 115	110-114	80-109	< 80	
Children 12-14 years of age	≥ 120	110-119	80-109	< 80	
Non-pregnant women (≥ 15 years of age)	≥ 120	110-119	80-109	< 80	
Pregnant women	≥ 110	100-109	70-99	< 70	
Men (≥ 15 years of age)	≥ 130	110-129	80-109	< 80	

†Hemoglobin in grams per litre.

‡ "Mild" is a misnomer: iron deficiency is already advanced by the time anemia is detected.

The deficiency has consequences even when no anemia is clinically apparent.

MORPHOLOGIC ASSESSMENT OF ANEMIA, AND ITS POTENTIAL RISK FACTORS AND CAUSES

Morfologi Anemia	Μርν	Faktor Risiko dan Penyebab
Microcytic	MCV < 82 fL	Iron deficiency Anemia of inflammation (chronic disease) Thalassemias
Normocytic	MCV = 82-98 fL	Vitamin A deficiency Anemia of inflammation (chronic disease) Renal disease Bone marrow failure (aplastic anemia, leukemia)
Macrocytic	MCV > 98 fL	Folate deficiency Vitamin B12 deficiency

ANEMIA AND NUTRITIONAL ANEMIA

Anemia	Nutritional Anemia
 It is not generally defined but described by hematologic biomarkers: Low hemoglobin Low hematocrit concentrations Low red blood cell counts In Indonesian communities, anemia is often regarded as a health complaint 'kurang darah' (lack of blood) and 'pucat' (pale). 	 Associated with nutritional deprivation or requiring conjoint nutritional management. This may be evident with: Chronic energy deficiency (CED), Sub-optimal intakes and reduced bioavailabilities of hematinic nutrients (limited dietary diversity and food intake quality, vitamins, elements, essential fatty acids, and other bioactive food components), Excessive nutrient loss by way of the gut (malabsorption, intestinal parasitosis, atrophic gastritis), Reproductive tract (menstrual loss, lactation), Integument or intravascular hemolysis (inherited or acquired including malaria) with inflammatory diseases (including overfatness) and in association with a wide range of chronic diseases.

UNDER RECOGNITION OF OTHER CAUSES AND RISK FACTORS OF ANEMIA AND MISCONCEPTION OF NUTRITIONAL ANEMIA



• Iron-deficiency anemia

- Represents about half of nutritional anemia in developing countries including Indonesia.
- Iron supplementation with acceptable recipient compliance has improved hemoglobin concentrations and reduced morbidity and mortality related to IDA.
- Some reports indicate anemia associated with iron deficiency is much less than 50% in reproductive age women, especially in developing countries (prevalence may be >40%) with a high burden of infection and inflammation.





• Tuberculosis-associated anemia

- Related to inflammation as evidenced by high ferritin concentrations in TB-associated anemia, and adequate treatment of TB, not iron supplementation, to some extent, improve the hemoglobin status.
- Excess iron due to iron supplementation to active TB sufferers potentially leads to exacerbation of TB and worsen the outcome of TB.

Malaria-associated anemia

- In malaria endemic areas such as East Nusa Tenggara and Papua, anemia and iron/folate deficiency seem to protect individuals against malaria infection.
- However, available data also revealed iron supplementation to young children living in endemic area may increase the risk of malaria-related hospitalization and mortality. Morbidity among breast-fed infants given iron supplementals is dependent on hemoglobin concentration being greater when Hb was ≥110 g/L.
- Reticulocytosis stimulated by iron supplementation, with a younger and larger RBC population increases their susceptibility to the malarial parasite and may lead to overwhelming parasitosis, especially in infants.
- In pregnant women, malaria-associated anemia may lead to adverse pregnancy outcomes like low-birth weight due to preterm delivery and intra-uterine growth retardation, most likely caused by placental malaria.

ANEMIA AND THE COVID-19 PANDEMIC

• Anemia is an independent risk factor for adverse outcomes of community-acquired pneumonia, and this appears to apply with COVID-19 infection.





COVID-19 patients Hemoglobin Concentrations severe case < mild case



The relationships between iron deficiency and susceptibility to infection is

There is no evidence that iron supplementation in COVID-19 patients mitigates clinical progression of the disease. penyakit secara klinis.

THE NEED TO ADDRESS INTERSECTORAL AND ECO-NUTRITIONAL DESCRIPTION IN ANEMIA AND NUTRITIONAL ANEMIA

- One of the major weaknesses in many literatures on anemia and nutritional anemia of any forms is the lack of eco-nutritional description. Human biology is strongly associated with its ecosystem, and, any disturbances, potentially lead to ecosystem health disorders.
- Socio-cultural factors affect food habits and dietary patterns. In many cultural contexts with patrilineal and matrilineal systems, marginal income generation, intra-household food distribution is discriminatory, with women and children getting less nutritious foods at mealtime.
- Required food variety score to achieve dietary adequacy

Total food variety score	Dietary adequacy
30 or more per week	Very good
25-29 per week	Good
20-24 per week	Fair
Less than 20 per week	Poor
Less than 10 per week	Very poor

The concept of dietary adequacy embraces that of essential nutrient adequacy, but also take into account other food components and food properties.

INTER-SECTORAL AND ECO-NUTRITIONAL APPROACHES

- The inter-sectoral and eco-nutritional approaches enable us to deliberate practical measures taken to recognize anaemia by symptomatology, food and nutrition surveys, screening (fingerpick blood), nutrition assessment, blood loss recognition (menstrual and faecal).
- It identifies vulnerable groups including premenopausal and pregnant women, children and adolescents, unwell adults and the dependent aged.
- Risk settings include food insecurity, infectious disease, non-communicable disease, inheritance and epigenetics and socioeconomic disadvantage.
- Underlying socio-ecological problems are livelihood, food systems, cultural habits, belief systems, and social networks and activities.

Conceptual Framework of Anemia in Indonesia

Recognition and Diagnosis	Food and nutrition surve Unapparent outcomes micronutrient intervention e.g. food fortification, In tablet supplementation	eys of ons ron n	Anemia screening (fingerprick blood) Increasing incidensce and prevalence of anemia		Nutrition Assesment Nutritional deprivation: Chronic energy deficiency (CED), sub-optimal intakes and reduced bioavailabilities of hematinic nutrients, reproductive tract, iron status		Assesment of Nutrient Loss Malabsorption syndrome, excessive nutrient loss by way of the gut, integument or intravascular hemolysis, inflammatory diseases		Chronic blood loss Faecal occult blood, menstrual irregularity	
Vulnerable Groups	Reproductive-age women	Ρ	Pregnant women Under-5 children School children Ur and adolescents ac		Unwell The depe adults age		The dependents aged			
Risk Factors and Causes	Food insecurity		Infectious disease & chronic e.g. pulmon tuberculosis, helm	es (acute) ary iinthiasis	Prevalen communica (NG e.g. an inflamatic	ce of non- ble diseases CDs) emia of n, malaria	Inł epigel	neritance and netics acquisition		Socioeconomic disanvantage e.g. education, envrironment
Underlying Socioecological Problems	Livelihood		Food syste	m	Culture	al habits	B	elief system		Social network and activity

POLICY RECOMMENDATIONS

Recognise that, currently, anemia in Indonesia remains endemic with an underlying societal and epigenetic persistence, and a co-existently high burden of TB, malaria, NCDs and other neglected diseases as barriers to its mitigation, which constitute an imprimatur for action. Recognise that the endemicity of malaria and linkage with anemia is greatest in the eastern part of Indonesia, where it is combined notably with inherited anemias, a situation which might be more effectively addressed by socioculturally enhanced interventions and governance.

Empower local government by encouraging intersectoral communication within and beyond the health and nutrition sectors.

Recognise that most health problems, including anemia, require a 'one package solution', albeit ecological and sociocultural. Mitigate underlying the root and multifactorial socioecological causes and risk factors for anemia in Indonesia. Establish an independent national authority to integrate evidencebased strategies to reduce the burden of anemia in Indonesia.

Be action-orientated, with vigilant monitoring and evaluation, and to support research in progress for better solutions. Action plans would take into account:

- Age and gender;
- Women who are adolescent, of reproductive-age, pregnant and lactating;
- The endemicity of infectious diseases (e.g., TB, malaria, helminthiasis);

 Biomarkers to allow the differential diagnosis of anemia would include serum ferritin to define not only iron-deficiency anemia, but also to provide an inflammatory marker together with C-reactive protein, and hepcidin, possibly in sub-samples of the target population.

NUTRITIONAL CONTRIBUTORS TO MATERNAL ANEMIA IN INDONESIA: CHRONIC ENERGY DEFICIENCY AND MICRONUTRIENTS

• Nur Indrawaty Lipoeto MD, PhD • Masrul MD, PhD • Ricvan Dana Nindrea MPH, PhD





Woman-Mother-Newborn-Young Child Continuum Of Care

Nutrition at Life Cycle Stages (Ahmed Dkk, 2013)



Weight Gain During Pregnancy (n: 529): Cohort Study In West Sumatra (Soltani et al, 2017)



ANEMIA IN PREGNANCY IN INDONESIA

The mitigation of anemia during pregnancy in Indonesia may be limited by the widespread assumption that anemia is primarily caused by iron deficiency despite its likely multifactorial etiology; therefore, it is managed using a single-micronutrient approach with iron supplements, excluding other contributors.

A meta-analysis of available reports in Indonesia might increase understanding on the putative multifactoriality of anemia in pregnancy and inform policies and strategic actions for its mitigation.

Meta-analysis of the Likelihood of Anemia in Pregnancy by Maternal and Child Clinical Metrics

A meta-analysis of reports on anemia during pregnancy in Indonesia from January 2001 to December 2019 in the PubMed and ProQuest databases was conducted.

Authors	Region	Study Type	Patients Characteristic	Sample Size	Risk Factors	NOS
Aji et al, 2020	Padang	Cross-sectional study	Women in early pregnancy	176	Socioeconomic, knowledge, pre- pregnancy BMI status, Fe tablets consumption	7
Seu et al, 2019	Kupang, NTB	Cross-sectional study	Pregnant women who visited antenatal care in PHC Facilities	102	Underweight / chronic energy deficiency	7
Diana et al, 2019	Madura	Cross-sectional study	Anemic pregnant women	252	Dietary diversity	7
Lestari et al, 2018	North Sumatra	Cross-sectional study	Not available	140	Knowledge, parity and chronic energy deficiency	7
Ani et al, 2018	Bali	Cross-sectional study	Women with a year postpartum period	163	Parity, chronic energy deficiency	7
Lisfi et al, 2017	Padang	Cross-sectional study	Mother's third trimester of pregnancy	44	Fe tablets consumption	6
Mariza et al, 2016	Lampung	Cross-sectional study	Pregnant women who visited independent Midwifery	102	Level of education, social and economic	7
Opitasari et al, 2015	2 hospital in Jakarta	Cross-sectional study	Mother's third trimester of pregnanacy	1,202	Parity, age	7
Ristica et al, 2013	Pekanbaru	Cross-sectional study	Pregnant women	212	Level of education, knowledge, Fe tablets consumption, chronic energy deficiency, age	7
Suega et al, 2002	Bali	Cross-sectional study	Not available	1,684	Educational background, Fe tablets consumption	7



RESULT OF META-ANALYSIS

Among the prospective determinants of anemia during pregnancy in Indonesia, chronic energy deficiency had the highest OR, followed by greater sparity, limited education, and limited knowledge.

> Meta-analysis of the Likelihood of Anemia in Pregnancy by Maternal and Child Clinical Metrics (Lipoeto dkk, 2020)



merepresentasikan 95% CI

Study details:

A total of 2,474 articles were appraised. Systematic review and meta-analysis were performed on 10 studies including 4,077 participants. Chronic energy deficiency had the highest OR for the risk of anemia (3.81 [95% CI: 2.36–6.14]) followed by greater parity (OR=2.66 [95% CI: 1.20–5.89]), low education level (OR=2.56 [95% CI: 1.04–6.28]), and limited health knowledge (OR=1.70 [95% CI: 1.17–2.49]), whereas older age and inadequate iron supplementation were not apparently associated with maternal anemia (p > 0.05).

KEY TAKEAWAYS



Limited knowledge among pregnant women on anemia prevention is evident in Indonesian

Basic Health Research reports (2013 & 2018)

40% pregnant women receive information on pregnancy complications

60% receive iron tablets (nevertheless, not all pregnant women consume them correctly)



Chronic energy deficiency in pregnant women

- May result from low quality awareness of the importance of dietary quantity and quality during pregnancy.
- •Chronic energy deficiency and anemia appear to be concurrent in pregnancy.



Iron deficiency may or may not be a cause of anemia in pregnant women.

The extent to which a woman's diet is sufficient, whether her iron bioavailability is questionable, and whether nutrient loss or comorbidities are present remain largely unknown, if not ignored.



Prenatal care should be personalized

to account for ethnicity, culture, education level, knowledge level on pregnancy, and diet.

FUTURE POLICIES AND STRATEGIC ACTIONS

STAKEHOLDER INVOLVEMENT

Involving community, mothers, and firstlevel health service facilities in increasing awareness of iron-deficiency anemia prevention in pregnant women and the health benefits for both pregnant women and babies as well as pregnancy outcomes

STRATEGIC COMMUNITY

Developing nutritional advocacy, communication, and mass mobilization by using clear and attractive messages tailored to specific age groups and enacting strategies that can be used by all stakeholders from the central level (Ministry of Health) to the community health level (first-level health facilities and midwives).

CAMPAIGN & COLLABORATION

 Campaigns to promote anemia prevention may include advertisements in various media.

• Collaboration with influential figures to promote prevention to the target audience and the wider community.

EMPOWERMENT

Increasing community-based social support through community empowerment activities to prevent maternal anemia e.g. increasing capacity and knowledge of health cadres and pregnant women.

NUTRITIONAL ANEMIA IN INDONESIAN CHILDREN AND ADOLESCENTS: DIAGNOSTIC RELIABILITY FOR APPROPRIATE MANAGEMENT

Mohammad Juffrie MD, PhD • Siti Helmyati DCN, PhD • Mohammad Hakimi MD, PhD

FACT AND FIGURE



Number of people affected by nutritional anemia, generally children, adolescents, and women

(McLean dkk , 2009; Deng dkk, 2020)



Risk of anemia in children with stunted growth. (Lipoeto et al, 2004; Al Qaoud et al, 2015)



Indonesian children and adolescent were anemic, consisting of 28% under-five children and 26% of children aged 5-14 years

(Basic Health, 2013)



3 interventions in Indonesia:

- 1. Food based
- 2. Nutritional supplementation
- 3. Nutrition education



Study of 654 elementary school children in Indonesia

(Utama dkk, 2018)

27% anemia

20% grow short

14% body weight for low height (W/BT)

leight (VV/BI)

14% excess body weight



In Indonesia, anemia management in pregnant and adolescent women is focused on iron supplementation,

often independent of other approaches (e.g., sociodemographic and lifestyle characteristics, community food systems, food pattern optimization, food fortification, nutrition education, probiotic administration, menstrual irregularities, comorbidities, and inter-current infections).

SYSTEMATIC REVIEW ON NUTRITIONAL ANEMIA IN INDONESIAN CHILDREN AND ADOLESCENTS

- **Subject:** incidence, prevention, and management of anemia in Indonesian children (adolescents, children, toddlers)
- Approach: PICO
- Year range: 2015-2020
- Total study: 12 studies
- Location: cities of Sumatra Islands (3), in Java (6), in Madura (1), in Kalimantan (1), and on Sulawesi Island (1).
- No study reported the effect of the intervention on the coexistence of anemia and undernutrition among the individuals involved.

PICO approach to study selection

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

Information retrieval protocol



CASE STUDIES ON INTERVENTION FOR ANEMIA PREVENTION AMONG YOUNG INDONESIANS

Bandar Lampung (Zuraida dkk, 2020a)



Subjects

Intervention: 55 female adolescents (mean age 15 y). Control: 47 female adolescents (mean age 15 y).



Intervention

Nutrition education in the form of an "anemia free club" for 12 weeks.



Results

- Hb levels were measured only pre-intervention.
- 41 individuals from the intervention group and 43 from the control group had low Hb levels (10.1-11.9 g/dL).

Bogor (Sekiyama dkk, 2017)



Subjects

68 elementary school students (boys and girls, mean age of 9 years).

Intervention

School lunch feeding for 1 month (lunchbox contained rice, vegetable, heme and nonheme protein dishes, and fruits).



Results

Hb (11.9 \pm 0.9 vs 11.2 \pm 0.9 g/dL) and Hct (34.0% \pm 2.7% vs 31.7% \pm 3.0%) levels were significantly increased after the intervention.

Majalengka (Budiana dkk, 2016)



Subjects

Intervention: 33 anemic wasting children aged 3-5 years.

Control: 33 anemic wasting children aged 3-5 years.



Intervention

The treatment group: Taburia + nutrition counseling over a 2-month period. **Control:** nutrition counseling.

The result did not differ by gender



Results

- 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).

Semarang (Kahayana dkk, 2016)



Intervention (P1): 30 children aged 10 months with normal nutrition status. **Control (C):** 30 children aged 10 months with

normal nutrition status.

Intervention



Intervention (P1): 75 mg of vitamin C syrup during feeding time for 2 months. **Control (C):** Placebo.

Results

Serum iron $(45.70\pm17.4 \text{ vs } 44.06\pm18.16 \text{ µg/dL})$ and ferritin $(39.87\pm31.27 \text{ vs } 36.43\pm25.33 \text{ µg/L})$ levels of the intervention group were significantly increased after the intervention (p<0.05).

Banjarbaru (Syahwal dan Dewi, 2018)



Subjects

P1 & P2: each consisting of 15 anemic female adolescents.

C: 15 anemic female adolescents.



Intervention

P1: snack bar made of nagara nut flour and haruan fish + 12 iron supplements.
P2: snack bar made of nagara nut flour and haruan fish.
C: 12 iron supplements

C: 12 iron supplements.

Foods and/or supplements were given 3x a week for 1 month.



Results

- 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.

Madura (Muslihah dkk, 2017)



Intervention: 2 intervention groups, each with 56 infants (aged 6-59 months. **Control:** 56 infants.

Intervention



• The biscuit Makanan Pendamping-Air Susu Ibu (MP-ASI or complementary foods) group received three 30-g biscuits per day for 6 months.



Results

- 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).

KEY TAKEAWAYS

ANEMIA & SEX

- •Both men and women can experience anemia.
- •Women, especially adolescent girls, have a higher risk of anemia due to menstruation.
- Programs such as anemia related nutrition education and screening for boys as well as for girls are needed.

REEVALUATION OF THE NOTION THAT MOST INDONESIAN CASES OF ANEMIA ARE DUE TO IRON DEFICIENCY

- Understanding the distribution and prevalence of types of anemia is critical to designing targeted interventions.
- To be considered: nutritional problems (stunted growth, wasting, underweight), infectious diseases (e.g., malaria, tuberculosis, HIV).

ANEMIA BIOMARKER

Only 3 publications considered in the systematic review 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.

Classification of iron deficiency anemia (adapted from Lianos and Jose, 2016)

Stage	Hemoglobin	Feritin (ng/mL)	sTfR (ng/L)	Transferin (mg/dL)
Iron deficiency	Normal	< 20	< 5	360
lron-deficient erythropoiesis	Normal	< 12	> 5	> 380
Iron deficiency anemia	Lower	< 12	> 5	> 380

Notes:

- 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
- Often, it depends on contextual factors: geographical location, the burden of infectious disease, and coexistence with other types of nutritional anemia

POLICY DIRECTIONS ADDRESSING ANEMIA AMONG YOUNG POPULATIONS

Program suplementasi zat besi pada remaja putri dan perempuan usia subur

• Evaluation is required.

• 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 (Basic Health Research, 2018).

Program nasional suplementasi zat besi pada remaja dan anak

- 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 (e.g., malaria; high prevalence in some areas of Papua).
- A study on a population of pregnant women with malaria discovered that iron supplementation actually increased the risk of infants being born with malaria (Schumann and Solomons, 2013).

RECOMENDATION

- Identify the specific cause of anemia in a small area (e.g. city or province)
- Prevention of anemia in children and adolescents (nutrition education and screening)

NON-NUTRITIONAL ANEMIA: MALARIA, THALASSEMIA, G6PD DEFICIENCY, AND TUBERCULOSIS IN INDONESIA

Safarina G. Malik DVM, MS, PhD, Sukma Oktavianthi BSc, MBiomed, Mark L., Wahlqvist MD, FRACP, FAFPHM, FAIFST, FTSE Puji Budi Setia Asih PhD, Alida Harahap MD, PhD, Ari W. Satyagraha Dr.sc.hum, Din Syafruddin MD, PhD

ANEMIA AND MALARIA







Almost 50 % 50% of pregnant mothers in Indonesia are anemic.

Malaria is

belonging

to the genus Plasmodium.

a mosquito-borne

disease caused

by the parasite

Annual 6.3 pregnancies in Indonesia at MILLION risk of malaria infection.

Highly endemic in Eastern Indonesia

50

(The islands of

Papua and East

Nusa Tenggara).



Iron supplementation in handling anemia can exacerbate malaria, even to the point of overwhelming parasitosis.

Risk factors* for anemia in women living in Sumba and Papua 44



*Independent of nutritional status (determined by body mass index and mid-upper arm circumference).

ANEMIA AND THALASEMIA

The thalassemias—characterized by decreased Hb production—are the most common inherited hemoglobin disorders and also the most common human monogenic diseases. The two main types of thalassemia are α and β thalassemia, referring to the affected globin chains.

	Thalasemia α	Thalasemia β
Definition	An autosomal recessive hereditary RBC disorder due to mutations in the a-globin genes, causing a decrease in or absence of α -globin chain production	An autosomal recessive hereditary RBC disorder caused by mutations in the β-globin gene.
Characteristics	it is characterized by microcytic hypochromic anemia	It is characterized by the reduction in or absence of β-globin chain synthesis, resulting in reduced Hb, decreased RBC production, and anemia.

The prevalence of anemia (according to Hb concentration) in the population of Banjarmasin and Ternate was 11.4% (67/587; cutoff is <12 g/dL for women individuals and <13 g/dL for men individuals; according to the WHO criteria).

Even though thalassemia is closely associated with anemia, some of the hematologic features of the RBCs could appear normal in the thalassemia trait. • Clinical characteristics of individuals with and without anemia in the Banjarmasin and Ternate population

Populasi	Variabel	Non-anemia	Anemia	<i>p</i>
Banjarmasin		(N=179)	(N=19)	
	Usia [tahun, median (IQR)]	20.0 (19.0-21.0)	19.0 (19.0-20.0)	0.175
	Jenis kelamin [n (%)]			
	Pria	74 (41.7)	1 (5.3)	0.002
	Wanita	105 (58.3)	18 (94.7)	
	Hb [mg/dL, median (IQR]	14.1 (13.3-15.2)	10.8 (10.6-11.7)	< 0.001
	MCV [fL, median (IQR)]	84.7 (82.3-87.5)	80.0 (71.4-82.7)	< 0.001
	MCH [pg, median (IQR)]	28.3 (27.4-29.2)	24.4 (21.4-26.1)	< 0.001
	MCHC [g/dL, median (IQR)]	33.2 (32.5-33.8)	31.2 (30.6-32.2)	< 0.001
	RDW [n (%)]	13.4 (13.0-13.9)	15.7 (14.7-17.0)	< 0.001
	HbA2 [n (%)]	2.8 (2.7-2.9)	2.6 (2.5-2.9)	0.021
	HbF [n (%)]	0.3 (0-0.5)	0.0 (0.0-0.4)	0.281
	HbE [n (%)]	2 (1.0)	0 (0.0)	1.000
Ternate		(N=341)	(N=48)	
	Usia [tahun, median (IQR)]	20.0 (17.0-21.0)	19.5 (18.8-20.0)	0.185
	Jenis kelamin [n (%)]			
	Pria	146 (42.8)	1 (2.1)	< 0.001
	Wanita	195 (57.2)	47 (97.9)	
	Hb [mg/dL, median (IQR]	14.0 (13.1-15.6)	11.2 (9.6-11.6)	< 0.001
	MCV [fL, median (IQR)]	82.9 (80.4-85.2)	74.6 (66.6-79.2)	< 0.001
	MCH [pg, median (IQR)]	28.2 (26.9-29.3)	23.4 (19.9-25.4)	< 0.001
	MCHC [g/dL, median (IQR)]	33.8 (32.9-34.9)	31.4 (29.5-32.4)	< 0.001
	RDW [n (%)]	13.6 (13.1-14.3)	15.7 (14.8-19.2)	< 0.001
	HbA2 [n (%)]	2.8 (2.6-2.9)	2.5 (2.3-2.7)	< 0.001
	HbF [n (%)]	0.3 (0.2-1.0)	0.2 (0.0-0.9)	0.030
	HbE [n (%)]	4 (1.2)	2 (4.2)	0.162

Hb: hemoglobin; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; RDW: red cell distribution width; HbA2: hemoglobin subunit alpha 2; HbF: fetal hemoglobin; HbE hemoglobin E. World Health Organization anemia criteria were employed: hemoglobin <12 mg/dL for women or hemoglobin <13 mg/ dL for men. P value were calculated using Wilcoxon-Mann Whitney U test for continuous variabels or Fisher's exact test for categorical variables. Significant P values are in bold (p<0.05). Unpublished data, Eijkman Institute.

ANEMIA AND GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY (G6PD)

- G6PD deficiency (G6PDd) is a common RBC enzyme disorder worldwide, affecting approximately 400 million people.
- The clinical manifestations of G6PDd
 - Ranging from asymptomatic to acute hemolytic anemia, renal failure, and death.
 - Result from mutations in the G6PD gene that cause instability in the produced enzyme.
- In Indonesia, G6PDd do not exhibit any symptoms unless exposed to exogenous agents that trigger oxidative stress resulting in acute hemolytic anemia.

Predictors of anemia in G6PD deficiency



Crude OR (95% CI) Adjusted OR(95% CI)



Age Older age increases the risk of getting anemia by 3%.



Sex Being a male reduces the risk of getting anemia by 70% or 73%.*



G6PD activity

13% People with G6PD deficiency are at risk of getting anemia by 13% or 31%.*



Malaria

People with malaria are at risk of getting anemia by 57% or a 2.68-fold risk increase.*sebesar 57% atau 2.68 kali peningkatan risiko.*

Notes: *adjusted OR (CI)



ANEMIA AND TUBERCULOSIS



Iron deficiency anemia was associated with a 99% increased incidence of tuberculosis. (Chu K A dkk, 2019)



Patients with active pulmonary tuberculosis are more anemic with poor nutritional status as compared to healthy subjects (Karyadi et al, 2000).

Indonesia is ranked second as the biggest contributor to the global increase of newly diagnosed tuberculosis.



Iron supplementation may exacerbate tuberculosis, since the tuberculosis causative pathogen, Mycobacterium tuberculosis, requires iron for essential metabolic pathways.

CONCLUSION

The Role of Malaria, Thalassemia, G6PD Deficiency, and Tuberculosis in Anemia in Indonesia

Effects of anemia

- In children: irreversible neurological damage that may affect the quality and global competitiveness of future human resources.
- In adults: limit the quality of people's work and their productivity.

Management of anemia in the Indonesian population

- Necessary to conduct complete blood count screening, Hb analysis, and iron status examination as anemia could be due to either chronic infection or genetic disorders.
- Requires a knowledge of local pathogens, as well as nutritional factors, especially since iron supplementation may otherwise worsen infectious disease such outcomes as in malaria and tuberculosis.



NON-NUTRITIONAL AND DISEASE-RELATED ANEMIA IN INDONESIA: A SYSTEMATIC REVIEW

Agussalim Bukhari MD, MMed, PhD, Firdaus Hamid MD, PhD, Rahmawati Minhajat MD, PhD, Nathania Sheryl Sutisna MD, Caroline Prisila Marsella MD



Anemia remains a major public health problem in Indonesia.

A possible reason for the failure of anemia intervention to reduce anemia prevalence is that the causes of underlying anemia are not only nutritional but also nonnutritional.

FACT



Anemia of inflammation (AI), the most common type of non-nutritional anemia, is associated with chronic diseases and NCDs.



Iron deficiency anemia can also coexist in patients with chronic AI.

ANEMIA OF INFLAMMATION

 Al is typically associated with chronic systemic inflammatory diseases including TB, malaria HIV, acquired immunodeficiency syndrome (AIDS), immune-mediated diseases (e.g., systemic lupus erythematosus), cancerous and hematological malignancies, obesity, T2DM, anemia in elderly persons, anemia in critical illness, congestive heart failure, CKD, and chronic pulmonary diseases.

Prevalence of infectious diseases in Indonesia (Basic Health Research, 2018)



• Differences in IDA and AI biomarkers

	Iron deficiency anemia (IDA)	Anemia of Inflammation
Mean corpuscular volume	Low	Normal
Mean hemoglobin volume	Low	Normal
Reticulocyte hemoglobin content	Low	Normal
Serum transferrin	High	Low
Serum transferrin receptor	High	Normal
Serum ferritin	Low	High
Serum hepcidin	Low	High

ANEMIA IN CHRONIC AND METABOLIC DISEASE

• Noncommunicable diseases (NCDs) or chronic diseases result from a combination of factors including those that are genetic, behavioral, and environmental.

Prevalence of anemia in chronic diseases at RS Wahidin Sudirohusodo, Makassar



ANEMIA IN OBESITY IN INDONESIA

In four studies including obese individuals, the average anemia incidence was 14,85% (range 6,9%-30%). However, not all studies mentioned the anemia type.

Wijayanti dkk, 2018



Population 50 obesity patients. No non-obesity controls.



Study Design Cross-sectional study.



Anemia Prevalence (%) 12%

Heryati dkk, 2014



Population

38 elementary students with overweight and obesity.

62 elémentary students with normal nutritional status.



Study Design Cross-sectional study.



Anemia Prevalence (%) 10.5% pada siswa obesitas 21% pada siswa dengan status gizi normal

Sukarno, Marunduh, Pangemanan, 2018



Population 29 subjects with BMI > 25 kg/m2. 31 subjects with BMI < 25 kg/m2.



Study Design Cross-sectional study.



Anemia Prevalence (%) 6.9% pada subyek obesitas. 15.7% pada IMT <18.5. 8.33% pada IMT.

Nisa, Nissa, Probosari, 2018



Population

30 obesity and 30 non-obesity (based on BMI over age) patients age 15-18 years old.



Study Design Cross-sectional study.



Anemia Prevalence (%) 30% pada pasien obesitas. 30% pada pasien non-obesitas.

ANEMIA PADA DIABETES MELITUS TIPE 2 (DMT2) DI INDONESIA

Studi anemia pada DMT2 secara umum berfokus pada pasien yang memiliki riwayat komplikasi pada ginjal sehingga anemia yang terjadi merupakan kombinasi antara inflamasi dan gangguan produksi eritropoietin. Berdasarkan penelitian di Indonesia, ratarata prevalensi anemia pada DMT2 adalah 49,2%.

Wijaya dkk, 2015



Population

46 patients with T2DM with mildly to severely impaired renal GFR (data from the medical records).



Study Design Cross-sectional study.



Anemia Prevalence (%)

80.4% total anemia, 26.1%, 39.1%, 15.2% in mildly, moderately, and severely impaired GFR, respectively.

Wijaya dkk, 2014



Population

192 T2DM patients in RSUP Sanglah Hospital, Bali (Data from the medical record).



Study Design Cross-sectional study.



Anemia Prevalence (%)

Total anemia 41.67%, mild anemia 76.25%, moderate 21.25%, severe anemia 2.5%.

Balela, Arifin, Noor, 2014



Population 78 T2DM patients



Study Design Cross-sectional study.



Anemia Prevalence (%) 57% in patients with T2DM < 5 years. 86% in patients with T2DM \geq 5 years.



ANEMIA IN CHRONIC KIDNEY DISEASE (CKD) IN INDONESIA

Inflammation increases hepcidin synthesis, promotes erythrophagocytosis, suppresses erythropoiesis in the bone marrow, and reduces erythropoietin production in the kidney.

Adiatma DC dkk, 2014



Population

35 CKD patients with hemodialysis stage 1-14 CKD 29%, stage 5 CKD 71%.



Study Design Cross-sectional study.



Anemia Prevalence (%)

Total anemia: 86%, anemia of chronic disease 80%, IDA 10%, hemolytic anemia 3.3%, posthemorrhagic anemia 6.7%.

Aisara S, Azmi S, Yanni M, 2018



Population 104 CKD patients with HD



Study Design Observational-descriptive study.



Anemia Prevalence (%) Hb < 7: 6.7% Hb 7-10: 68.3% Hb > 10: 25%

Minhajat, 2016



130 CKD patients. Stage 3b (2 pts), stage 4 (8 pts), stage 5 (120 pts), 43% with HD in RSUP dr. Wahidin Sudirohusodo Makassar.



Study Design Cross-sectional study.



Anemia Prevalence (%)

Total anemia: 95.38% (88.56% in stage 5) Normocytic normochrom: 66.13% Microcytic hypochromic: 13.71%

PERNEFRI, 11th Report of Indonesian Renal Registry, 2018



Population

87,710 chronic kidney disease patients.



Study Design Registry.



Anemia Prevalence (%) Hb < 10: 78%. Hb >10: 22%.

ANEMIA PADA PENYAKIT GINJAL KRONIS (PGK) DI INDONESIA

Suega K, Bakta M, Dharmayudha TG dkk, 2005



Population 26 CKD-dialytic patients. 26 CKD-predialysis patients.



Study Design Cross-sectional study.



Anemia Prevalence (%) 96.2% in dialytic group. 30.8% in predialysis group.

Note:

CKD: Chronic Kidney Disease; IDA: Iron Deficiency Anemia; HD: Hemodialysis; RSUP: Rumah Sakit Umum Pusat (Central General Hospital); PERNEFRI: Perhimpunan Nefrologi Indonesia (Indonesian Nephrology Association); Hb: Hemoglobin.

ANEMIA IN CARDIOVASCULAR DISEASE (CVD) IN INDONESIA

Prevalence of anemia in CVD (including heart failure and myocardial infarction) (A study in Dr. Wahidin Sudirohusodo Hospital)

Of the 105 patients admitted to the cardiovascular ward, 65 (62%) patients had anemia



67,7%

(44 patient) normocytic normochromic anemia

Therefore, in CVD, the predominant type of anemia was normocytic and normochromic consistent with the characteristics of AI.

*Including heart failure and myocardial infarction

ANEMIA IN CANCER

• In cancer, anemia can occur independently due to chemotherapy, typically as a consequence of chronic inflammation, and its features can resemble those of anemia in chronic inflammatory diseases.

Prevalence of Anemia in Cancer Study Case: Hidayati dan Arifah, 2020



47.8°

of the four hematology and lymphoma malignancy cases had anemia.

of patients with

anemia

solid cancer had



Radiotherapy significantly influences hemoglobin concentration:

29,4% (Dose < 60 Gy)

57,6% Dose >60 Gy)

Prevalence of Anemia in Cancer in Dr. Wahidin Sudirohusodo Hospital



Of 92 patients with malignancy, 81 patients had anemia with different types as follow:

The prevalence of cancer anemia in Dr. Wahidin Sudirohusodo Hospital. by type of anemia (n=92)



ANEMIA IN TUBERCULOSIS

50-70%5,8-54,8%47-81,48%The average
prevalence of anemia
in pulmonary TBAnemia normositik
normokromik*Anemia mikrositik
hipokromik*

* Based on 12 literatures that discuss anemia in pulmonary TB patients

Prevalence of anemia in pulmonary TB at RS Wahidin Sudirohusodo



Of 28 patients with pulmonary TB, 19 (67,9%) had anemia with different types

Prevalence of anemia in pulmonary TB at RS Wahidin Sudirohusodo based on the type of anemia



ANEMIA RELATED TO HIV-AIDS



Rata-rata prevalensi anemia pada HIV/AIDS berdasarkan 4 studi di Indonesia



Prevalence of anemia in HIV/AIDS at RS Wahidin Sudirohusodo*

*High prevalence might be due to the generally high disease severity among referral hospital's patients.



Of all 58 patients with HIV/AIDS, 52 had anemia with different types

Prevalence of anemia in pulmonary HIV/AIDS at RS Wahidin Sudirohusodo based on the type of anemia



ANEMIA IN PREGNANCY

• Prevalence of anemia in pregnancy (Basic Health Research, 2018)

Prevalence of anemia in pregnancy in Indonesia (1997-2018)



ANEMIA IN HELMINTHIASIS



Prevalence of anemia in helminthiasis in Indonesia from several studies

North Pontianak, West Kalimantan (Puspita et al, 2020)





Prevalence: 55% **Methode:** Kato-Katz thick smear, blood tests

Mimika, Papua (Burdam dkk, 2016)



Subject:

60 students from

five grade 3 and

4 elementary school

Subject: 629 children aged 1-59 months from 800 households



Prevalence:

24,5%

Methode: Katokatz method, Hb by electronic coulter counter (Hb <10 gr/dL = anemia)

OTHER CAUSES OF NON-NUTRITIONAL ANEMIA

GENETIC FACTORS:

- Genetic abnormalities in the metal divalent transporter-1 gene (MDT1); notable in patients with microcytic anemia, low serum ferritin levels, and liver iron overload.
- Disturbed DNA synthesis, which results in morphologic and functional changes in erythrocytes, leukocytes, platelets, and their precursors in the blood and bone marrow; megaloblastic anemia

IATROGENIC ANEMIA:

Туре	Causes	Triggering Drugs
Immuno-hemolytic anemia	Destruction caused by the reaction between antibodies and antigens in the erythrocyte membrane.	Penicilins, cephalosporins
Nonimmune hemolytic anemia	Side effects of drugs; glucose-6-phosphate dehydrogenase deficiency is common.	Primaquine and nitrofurantoin
Methemoglobinemia	Excessive methemoglobin production; induced by several drugs that oxidize hemoglobin.	Phenazopyridine, dapsone, local anesthetics
Megaloblastic anemia	Vitamin B-12 with or without folic acid deficiencies induced by drugs.	Trimethoprim, pyrimethamine, sulfasalazine, phenytoin, and antiretrovirals.
Sideroblastic anemia	heme biosynthesis being interfered by drugs.	Isoniazid, chloramphenicol, and linezolid.
Aplastic anemia	failure to produce blood cells	Drugs that can suppress bone marrow function.
Pure red cell aplasia	Induced by drugs.	Azathioprine and other immunosuppressants, linezoid, isoniazid, rimfapin, chloroquine, etc.





NUTRITIONAL ANEMIA: LIMITATIONS AND CONSEQUENCES OF INDONESIAN INTERVENTION POLICY RESTRICTED TO IRON FOLIC ACID

Nadiyah MSc, CSRS, Lintang Purwara Dewanti MSc, Erry Yudhya Mulyani PhD, Idrus Jus'at PhD



ANEMIA PREVALENCE



Global Nutrition Target (2025) = 50% decreased anemia in WUS

*World Bank Global Health Observatory Data Repository/World Health Statistic

**WHO World Health Organization Global targets 2021 to improve maternal, infant, and young child nutrition Geneva: WHO

CURRENT POLICY AND IMPLEMENTATION IN INDONESIA

• Iron fortification

- Management of major nutrition deficiency in Indonesia, including nutritional anemia, is an important part of the effort to reduce infant and toddler mortality.
- Relevant regulations

Permenkes RI Number 88 of 2014 on Iron Folic Acid Tablets Standard for Reproductive Women and Pregnant Mothers

- Technical specification for iron folic acid (IFA) tablets, with the aim of increasing the effectiveness of IFA tablet administration.
- Each IFA tablet consists of ferrous fumarate iron equal to 60 mg elemental iron and 0,400 mg folic acid.

Permenkes RI Number 51 of 2016 on Standard Nutritional Supplementation Product

• For iron and folic acid tablets, iron is added in the form of a ferrous fumarate compound to increase the effectiveness of IFA tablet administration Fe-fumarate IFA tablets had reduced compliance among pregnant mothers in Yogyakarta, whereas commercial IFA tablets had higher compliance rates because of their preferable flavor, smaller size, and fewer side effects (Sudargo et al, 2020). Consumption of IFA tablets among female adolescents (12-18 years) and pregnant woman:



Percentage of pregnant women who received 90 IFA tablets during pregnancy (2015-2018)



Source: Performance Report of the Directorate of Community Nutrition, MoH

 Summary of IFA tablet supplementation program evaluation in various areas in Indonesia



The quality of antenatal was low.







IFA tablet program implementation did not correspond to the SOP.



Analyses, follow-up, and feedback were lacking in IFA tablet program reports.



Facilities and infrastructure were insufficient.







Counseling material, information media, and IFA tablet supply were insufficient.

• Report by the Audit Board of the Republic of Indonesia (BPK RI) concluded that the Ministry of Health was not effective in managing funds for 2018 (Rp 6,13 billion). Some of IFA tablets remained undistributed throughout 2018 until the expiration date in 2019.

• Iron fortification

• Relevant regulations

Decree of the Minister of Industry Trade Number 153 of 2001 on Indonesian National Standard (SNI) for wheat flour fortification.

• Wheat flour fortification with iron, zinc, folic acid, vitamin B-1, and B-2 became mandatory.

Permenperin No. 1 of 2021 SNI 3751:2018

 Fortificant in the form of Fe Fumarat/Fe Sulphate/Fe-Na-EDTA in flour (effective commencing August 4, 2021). Decree of the Minister of Health Number 1452 of 2003 on additional requirements for fortificant addition to wheat flour.

- Produced, imported, or circulated wheat flour in Indonesia should be fortified to contain iron at a minimum of 50 mg/ kg, zinc at a minimum of 30 mg/kg, vitamin B-1 (thiamine) at a minimum of 2,5 mg/kg
- Vitamin B-2 (riboflavin) at a minimum of 4 mg/kg,
 Folic acid at a minimum of 2 mg/kg.

 Consumption pattern of cereal groups by Indonesian population (Indonesian Total Diet Study, 2014)



• Estimated iron content (mg) in wheat flour and its derivative products (Nadiyah et al, 2020)





Flour 8,8 - 13,2 mg





Instan Noodle 1,2 – 9,9 mg



Biscuit 0,88 - 4,4 mg Electrolytic iron is not recommended when the average consumption of wheat flour is below 75 g/day because high levels of electrolytic iron could negatively affect the sensory properties of fortified flour (WHO, 2018).

Iron fortification evaluation:



- Iron fortification of rice
 - Should be considered as it is widely consumed by the Indonesian population (97,7%), with an average consumption as high as 203,1 g per capita per day.

Rice Fortification Projects in Indonesia



- Fortification of cooking oil
 - Fortification of cooking oil may be an alternative method of increasing vitamin A intake in mothers and children, especially in rural communities.



• Food-based approach

- Four Healthy Five Perfect (Empat Sehat Lima Sempurna/ESLS)
 - The slogan developed by Prof. Poerwo Soedarmo was aimed to educate people about the importance of nutrition
 - In the subsequent 25 years, ESLS became preferred in nutritional education and is widely known, especially among school-age children.
 - ESLS, which unintentionally provided a higher value for milk, produced a problematic situation for the governments of developing nations because of the unavailability of milk locally and its high price.lokal dan harga yang mahal.

- The Guide to a Balanced Diet (1993))
 - The guidelines were developed based on the results of research by the Nutrition Center for Research and Development, MoH. The guide has 13 messages.
 - In 2014, PUGS was revised to PGS (Guidelines for Balanced Nutrition) by the Directorate of Nutrition Development of the Ministry of Health of the Republic of Indonesia. PGS has 4 pillars which are described in the Balanced Nutrition Tumpeng.



Balanced Nutrition Tumpeng





Regulation

(1995)PUGS byMoHformally>>> regulation on nutrition&REPELITA /lprogram.

PUGS no. 6: consume foods high in [.]on.



Implementation

Average protein consumption = 64,64 g (> 57 g/cap/day(AKP 2018). Dominated by grains(30%).

Indonesian animal protein consumption= 8% << Malaysia (28%), Filipina (21%) & Thailand (20%).

Less consumption of vegetables/fruits = 95,5%



Obstacle

Low level of income>> low protein consumption.

Inequal access to foods (by the rule of balanced nutrition) in Indonesia.

Uneven distribution of animal protein supply, availability, and distribution throughout the region.



Recommendation

Aside from staple food, food assistance policy should also consider the choice of meat, poultry/ fish according to regional potential and capacity.

Improvement of livestock sector in each region through local wisdom.



POLICY RECOMMENDATIONS



Recognise that, currently, anemia in Indonesia remains endemic with an underlying societal and epigenetic persistence, and a coexistently high burden of TB, malaria, NCDs and other neglected diseases as barriers to its mitigation, which constitute an imprimatur for action.



Recognise that the endemicity of malaria and linkage with anemia is greatest in the eastern part of Indonesia, where it is combined notably with inherited anemias, a situation which might be more effectively addressed by socioculturally enhanced interventions and governance.



Empower local government by encouraging intersectoral communication within and beyond the health and nutrition sectors.



Recognise that most health problems, including anemia, require a 'one package solution', albeit ecological and socio-cultural.



Mitigate underlying the root and multifactorial socio-ecological causes and risk factors for anemia in Indonesia.



Establish an independent national authority to integrate evidence-based strategies to reduce the burden of anemia in Indonesia.



Be action-orientated, with vigilant monitoring and evaluation, and to support research in progress for better solutions. Action plans would take into account:

- Age and gender
- Women who are adolescent, of reproductiveage, pregnant and lactating
- The endemicity of infectious diseases (e.g. TB, malaria, helminthiasis)
- Biomarkers to allow the differential diagnosis of anemia would include serum ferritin to define not only iron-deficiency anemia, but also to provide an inflammatory marker together with C-reactive protein, and hepcidin, possibly in sub-samples of the target population.

REFERENCES

- Lukito W, Wahlqvist ML. Intersectoral and econutritional approaches to resolve persistent anemia in Indonesia. Asia Pac J Clin Nutr. 2020;29(Suppl 1):S1-S8. doi: 10.6133/apjcn. 202012_29(S1).01.
- Lipoeto NI, Masrul, Nindrea RD. Nutritional contributors to maternal anemia in Indonesia: chronic energy deficiency and micronutrients. Asia Pac J Clin Nutr. 2020;29(Suppl 1):S9-S17. doi: 10.6133/apjcn.202012_29(S1).02.
- Juffrie M, Helmyati S, Hakimi M. Nutritional anemia in Indonesian children and adolescents: Diagnostic reliability for appropriate management. Asia Pac J Clin Nutr. 2020;29(Suppl 1):S18-S31. doi: 10.6133/ apjcn.202012_29(S1).03.
- 4. Malik SG, Oktavianthi S, Asih PBS, Harahap A, Satyagraha AW, Syafruddin D. Nonnutritional anemia: malaria, thalassemia, and G6PD deficiency in Indonesia. Asia Pac J Clin Nutr.

2020;29(Suppl 1):S32-S40. doi: 10.6133/ apjcn.202012_29(S1).04.

- Bukhari A, Hamid F, Minhajat R, Sheryl N, Marsella CP. Non-nutritional and diseaserelated anemia in Indonesia: inflammation and helminthiasis. Asia Pac J Clin Nutr. 2020; 29(Suppl 1):S41-S54. doi: 10.6133/ apjcn.202012_29(S1).05.
- Nadiyah, Dewanti LP, Mulyani EY, Jus'at I. Nutritional anemia: limitations and consequences of Indonesian intervention policy restricted to iron and folic acid. Asia Pac J Clin Nutr. 2020;29(Suppl 1):S55-S73. doi: 10.6133/ apjcn.202012_29(S1).06.

