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Study of Hemoglobin and Ferritin Profile as Indicators in Children Hematology of 12-15 Years Provided Local Rice Fortification

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Abstract

Basic Health Research *(Riskesdas)* reported that in 2007 the prevalence of anemia was 12.8%, of which 70.1% was Iron Deficiency Anemia, increased to 21.7% in 20013. The purpose of this study was to describe the profile of hemoglobin and ferritin as an indicator of hematology at students aged 12-15 years who consume rice fortification. This study design was Randomized Controlled Trial (RCT) double-blind, on children students, conducted from May 2015 through March 2016.

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The total sample consisted of 64 students: 32 cases and 32 controls aged 12-15 years, both samples and controls were anemic. Samples were given intervention by consuming rice fortification for 6 months, rice fortified with 6 micronutrients (Fe, Zn, vitamin B1, vitamin B3, folic acid and vitamin B12. The intervention was done by providing 200 grams of rice in the morning and evening for 6 months. Blood sampling was performed to monitor the levels of hemoglobin (Hb), Ferritin for 3 times that at this stage of the baseline, midline and endline. Descriptive analysis was conducted to asses determinant levels of hemoglobin and ferritin levels of the age. The result shows thatBaseline phase: The intervention group gained an average of 11.80 g Hb/dL, ferritin 38.50 ug/L and the control group Hb 11.90 g/dL, ferritin 38.60 ug/L. Midline stage: The intervention group gained an average of 11.78 cases Hb g /dL, ferritin 78.28 ug/L, whereas the control Hb 12.08 g/dL, ferritin 54.56 ug/L.Endline stage: The intervention group gained an average of 12.21 g Hb/dL, ferritin 28.56 ug/L and the control group Hb of 12.6 g/dL, ferritin 39.37 ug/L.There is an increase in average levels of hemoglobin from baseline to the intervention group midline to the endline, particularly in the age group of 12-12 years and 14-14 years 11 months. There is an increase in the average levels of ferritin from baseline to the intervention group but decreased in the midline endline.

Keywords: Rice fortification; micronutrients; Hemoglobin and Ferriti.

1. Introduction

WHO reported that about 30% of the global population are anemic, approximately 25.4% are in school age children. More than half the population is classified as anemia iron deficiency anemia [1]. WHO Regional Office South East Asia Region Organization (SEARO) stated that in Southeast Asia 25-40% of young women suffer from Iron Deficiency Anemia (IDA) ranging from mild to severe levels. Basic Health Research *(Riskesdas)* data showed that in 2007, the national prevalence of anemia (in urban areas) is 12.8%, about 70.1% is IDA, increased to 21.7% in 20013. For school age children, there was 29.0% of anemic [2]. This study showed that the largest proportion of anemia is anemia less iron, while the number of patients with anemia in junior high school student in Karawang is equal to or exceeds 34.33% of the national average [3].

Anemia is a condition in which the dismantling and the use of erythrocytes more rapidly than erythropoiesis.Ngui, Lim [4] stated that anemia is a condition in which red blood cells are not able to provide enough oxygen to the body tissues, mostly due to iron deficiency. Iron deficiency can occur because of inadequate iron intake and absorption is less, increased iron requirements during growth, and loss of iron overload [5]. According to WHO iron deficiency anemia resulted in deaths [6]. Iron deficiency in school age can affect immunity [7, 8], growth [9, 10], the effect on intellectual performance, function neurological, intelligence [11, 12].

Hemoglobin is the oxygen-carrying protein to the target cell and Carbon dioxide into the lungs, globular-shaped, consisting of 95% globin (polypeptide) and 5% heme. Low levels of hemoglobin school children especially in early growth period spurth, will greatly affect the growth in adolescence. Ahmed, Khan [13] reported that supplementation MMN short, 2 times a week for 12 weeks, with the formula of the United Nations International Multiple Micronutrient Preparation (UNIMMAP), which contains iron and other micro-nutrients which is

equivalent to the dose (Recommended Dietary Allowances (RDA) may increase the concentration of hemoglobin in young women in urban Bangladesh. the results of another study reported by Hyder, Haseen [14], that the provision of drinks fortified with multiple micro-nutrient, can raise hemoglobin levels up can reduce anemia and may increase micronutrient status and growth in adolescent girls in urban Bangladesh.

Ferritin is a form of iron stores in the blood, where the amount of blood ferritin is directly linked to the amount of Fe that is stored in the body. The study expressed that the serum ferritin is an indicator of good iron stores, except in certain inflammatory disorders and malignancies [15]. Various studies also suggest that the nutrient supply through the menu lunches Fe school children, can significantly improve the levels of hemoglobin, serum ferritin, serum retinol. This is also the logic solution in reducing the prevalence of ID, IDA and VAD in school children in developing countries [16]. Food fortification is foodstuffs fortified with specific nutrients [17, 18]. Examples of food fortification iron that has been done is soy, fish sauce, flour and rice with iron in the Republic of China (PRC), wheat flour with iron in India, fortification of wheat flour with iron in the Philippines, noodles and rice with iron in Thailand, fish sauce with iron in Vietnam. All wheat flour and corn flour is fortified with iron in 20 countries in Latin America, and wheat flour with iron in Indonesia [19]. Food fortification should focus on the fortification of foodstuffs consumed locally, such as the type of fortification can be implemented in a sustainable manner on a large scale, enabling people to get more nutritional value [20, 21].

The aims of this research were to describe deployment of hemoglobin and ferritin levels, and to describe deployment of hemoglobin and ferritin levels by age.

2. Materials And Methods

a. Research site and time

Study has been conducted at Boarding Annihayah, Rawamerta Sub District, Karawang District, West Java Province, Indonesia. Location of this study was based on, for example, Boarding Annihayah has the highest number of son students among boarding schools in Karawang District, and Karawang District has the largest number of rice production in West Java, and even Indonesia. This study was conducted from May 2015 to March 2016.

b. Research Design

The study design in this efficacy study is a Double Blind Randomized Control Trial. The sample was selected randomly. Samples were grouped into two groups: the treatment group (given rice fortification) and the control group (given non-fortified rice). It all happens for 6 months. Giving rice fortification and non-fortification performed double blind in which all of the research team studied subject did not know whether they eat rice fortified or non-fortified.

c. Population and Sample

The population in this study was all students at the boarding school of Madrasah Annihayah, Rawamerta Sub

District, Karawang District. Total population was 603 people. The sample in this study was male students aged 12-15 years old (n=36). To anticipate Drop Out and other reasons, then the "n" simulated, up to n = 40 students per group. So the total samples for cases and controls were 80 persons. Sampling procedures:

1. Choosing schools that have students (male) 603 children
2. Screening anemia by measuring hemoglobin concentration of students selected
3. Make a list of students who had Hb concentrations> 8 mg% to <12 mg%.
4. Perform random allocation from a list of the students, who made the point (3) into two groups, each group consisted of 40 students.
5. Each group (40 students) of random allocation results incorporated into one class.

Inclusion and Exclusion Criteria

Inclusion Criteria:

1. Male gender
2. Aged 12-15 years
3. Having a blood Hb concentration:> 8 mg% to <12 mg
4. Expressed a willingness to be sampled, with signing informed consent.

Exclusion criteria:

1. Suffer from chronic infections eg Tuberculosis and Malaria
2. Suffering from non-infectious degenerative diseases such as heart disease vascular, cancer, chronic kidney and diabetes.
3. Suffering from acute and chronic bleeding.

Criteria Drop out:

1. Acute recurrent bleeding
2. The high and repetitive frequency and duration of diarrhea
3. Not willing to have blood drawn at the midline and endline

d. Data collection process

1. Conducting approach to the subject of research by explaining the intent and purpose of the study.
2. Each student does early diagnose, and is selected based on predetermined criteria.
3. Asking the willingness of potential respondents or samples for respondent.
4. Signing an informed consent if willing to become respondents.
5. Providing equipment and materials for research. The tools used in the study were gauges Hb, Ferritin. Intervention materials used are fortified rice.
6. Measuring the levels of Hb, Ferritin.

7. Conducting interviews semi-quantitative FFQ early in students before being given treatment and then every month.
8. Writing result of semi-quantitative FFQ questionnaire.

Respondents were asked about the frequency and amount of food eaten during this time (last 1 month), by referring to a list of questions in the questionnaire FFQ semi-quantitative, comprising: a staple food, side dishes, vegetables and fruits, snacks, drinks, consumption of processed foods , and the consumption of fast food with food aid picture. Foodstuffs in the list of the questionnaire are a food that is usually consumed and affordable by the respondent. Before administering rice, respondents were given worm medicine albendanzole.

Table 1: Composition of Rice Fortification and Nutrition needs numbers in accordance age

Variables		**Vitamin**				**Mineral**	
	Energy	**B1**	**B3**	**B9 (Folic)**	**B12**	**Fe**	**Zn**
		(mg)	**(mg)**	**(µg)**	**(mg)**	**(mg)**	**(mg)**
Rice fortification per (100 grm)	183	0,447	18	400	2,6	60	15
AKG males	2100	1,1	12	400	1,8	13	14
12-15 years old							

From beginning to end this intervention study, all of the sample of 80 people (40 cases and 40 controls) were given food fortified rice at every lunch and evening meal, as much as 200 grams, 2 times for 3 months. The process of weighing and delivery of rice fortification was done directly by field workers (8 persons). Each field worker supervised 10 students. Furthermore, field staff conducted observation and supervision so that students could eat well. Field personnel ensured that the rice fortification eaten directly by students and if there were leftovers, immediately do the weighing and recording the rest of the rice fortification, in order to know how much rice was consumed.

e. Analysis and presentation of data

Descriptive analysis was conducted to determine the profile picture of hemoglobin and ferritin as indicators of hematology at the students. The data were analyzed using SPSS and Microsoft Excel.

Table 2 shows the distribution of socio-economic characteristics of the respondents, whereas in the case group (intervention) 47.5% is a grade 1; 40.0% and 12.5% are grade 2 grade 3. In the non-intervention group (control) 60.0% of the class is grade 1; 30.0% and 10.0% are respectively grade 2 and grade 3. Most parents are sundanese. Mothers' occupation is mostly housewife both intervention group and non-intervention group. The parents' education is generally only senior high school.

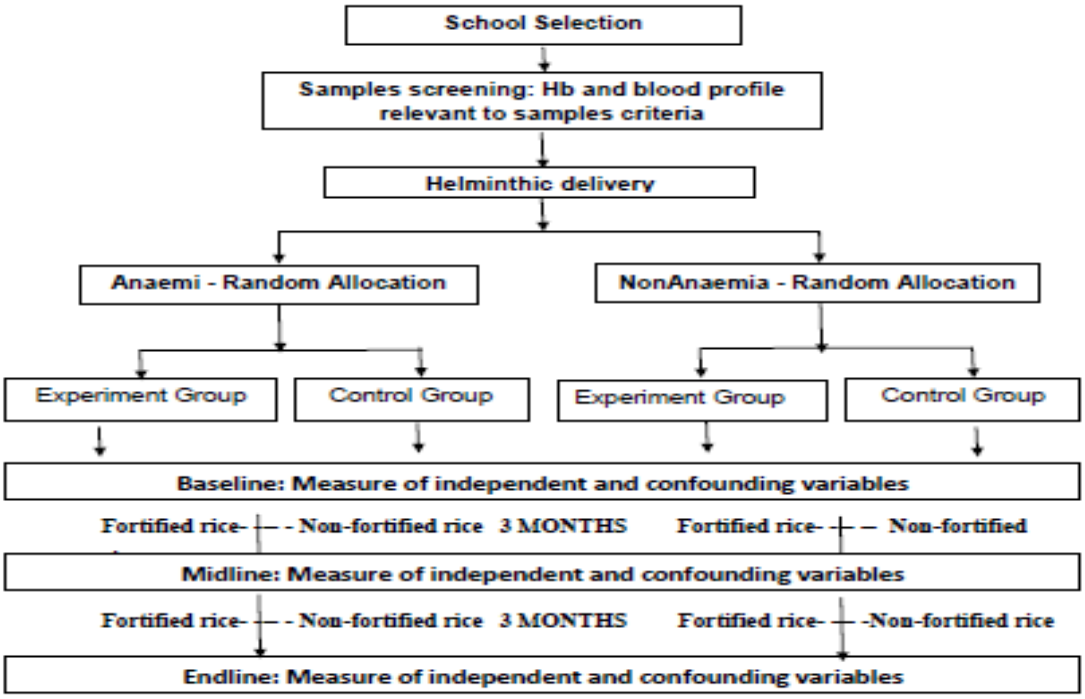

Figure 1: Flow of field activities

3. Results

a. Socioeconomic Characteristics of Respondents

Table 2: Distribution of Socioeconomic Characteristics of Respondents

Characteristics	Intervention group	Non-intervention group
Class, n (%):	n = 40	n = 40
1 (n=43)	19 (47.5)	24 (60.0)
2 (n=28)	16 (40.0)	12 (30.0)
3 (n=9)	5 (12.5)	4 (10.0)
Parents' tribe, n (%)		
Father, Sundanese (n=49)	22 (27.5)	27 (33.7)
Mother, Sundanese (n=58)	29 (36.2)	29 (36.2)
Parents' occupation, n (%)		
Father, entrepreneur (n=40)	24 (30.0)	16 (20.0)
Mother, housewife (n=58)	29 (36.2)	29 (36.2)
Parents' education, n (%)		
Ayah, SLTA (n=20)	14 (17.5)	6 (7.5)
Ibu, SLTA (n= 24)	16 (20.0)	8 (10.0)

b. Hemoglobin and Ferritin between cases and controls in the early baseline, midline and endline

Table 3: The average distribution of Hemoglobin and Feiritin between cases and controls in the early baseline, midline and endline

Characteristics	Baseline		Midline (3 months intervention)		Endline (6 months intervention)	
	Cases	**Controls**	**Cases**	**Controls**	**Cases**	**Controls**
Hemoglobin (g/dL)	11.80	11.90	11.78	12.08	12.21	12.60
Ferritin (µg/L)	38.50	38.60	78.28	54.56	28.56	39.37
Jumlah	32	32	32	32	32	32

Table 3 shows the distribution of haemoglobin and ferritin between cases and controls on baseline, midline and endline, as follows:

Baseline phase: The intervention group gained an average of 11.80 g Hb/dL, ferritin 38.50 ug/L and the control group Hb 11.90 g/dL, ferritin 38.60 ug/L.

Midline stage: The intervention group gained an average of 11.78 cases Hb g /dL, ferritin 78.28 ug/L, whereas the control Hb 12.08 g/dL, ferritin 54.56 ug/L.

Endline stage: The intervention group gained an average of 12.21 g Hb/dL, ferritin 28.56 ug/L and the control group Hb of 12.6 g/dL, ferritin 39.37 ug/L.

c. Hemoglobin and Ferritin Baseline by Age

Table 4: Distribution of Hemoglobin and Ferritin Baseline by age

Age group	Hemoglobin (g/dL)				Ferritin (µg/L)			
	Cases	**n**	**Controls**	**n**	**Cases**	**N**	**Controls**	**N**
(Years & months)								
12 years–12 years, 11 months	11.8	16	12.03	17	44.84	16	41.85	17
13 years–13 years, 11 months	11.65	11	11.87	13	37.13	11	46.15	13
14 years –14 years, 11 months	12.18	5	12.00	2	21.88	5	57.70	2
Total		32		32		32		32

Table 4 shows the average of hemoglobin, ferritin in the case and control groups according to age, the age group of 12-12 years and 11 months cases of hemoglobin 11.8 g/dL and control of 12.03 g/dL, aged 13-13 years, 11 months cases Hb 11.65 g/dL and control 11.87 g/dL, aged 14-14 years, 11 months cases of hemoglobin 12.18

g/dL and control 12.00 g/dL. The average ferritin cases and controls by age, for example, the age group of 12-12 years and 11 months cases of ferritin 44.84 ug/L and control 41.85 ug/L, aged 13-13 years, 11 months cases of ferritin 37.13 g/L and control 46.15 ug/L, aged 14-14 years, 11 months cases of ferritin 21.88 ug/L and control 57.70 ug/L.

Average of hemoglobin and ferritin levels midline (3 Months intervention) By Age

Table 5: Distribution of average of hemoglobin and ferritin levels midline (3 Months intervention) By Age

Age group	**Hemoglobin (g/dL)**				**Ferritin (µg/L)**			
	Cases	**n**	**Controls**	**N**	**Cases**	**n**	**Controls**	**N**
(Years & months)								
12 years–12 years, 11months	11.90	16	12.06	17	71.24	16	55.60	17
13 years–13 years, 11 months	11.43	11	11.90	13	91.80	11	49.88	13
14 years–14 years, 11 months	12.90	5	12.60	2	58.27	5	37.60	2
Total		32		32		32		32

Table 5 shows the average of hemoglobin, ferritin on cases and controls by age, for example, the age group of 12-12 years and 11 months cases of hemoglobin 11.9 g/dL and control 12.60 g/dL, aged 13-13 years, 11 months 11:43 Hb cases g/dL and controls 11.9 g / dL, aged 14-14 years, 11 months cases of hemoglobin 11.9 g/dL and control 12.60 g/dL. The average of ferritin cases and controls by age, for example, the age group of 12-12 years and 11 months cases of ferritin 71.24 ug/L and control 55.60 ug/L, aged 13-13 years, 11 months cases of ferritin 91.80 g/L and control 49.88 ug/L, aged 14-14 years, 11 months cases of ferritin 58.27 ug/L and control 37.60 ug/L.

d. Average of Hemoglobin and Ferritin Endline (6 months intervention) by age

Table 6: Distribution of average of Hemoglobin and Ferritin Endline (6 months intervention) by age

Age group	**Hemoglobin (g/dL)**				**Ferritin (µg/L)**			
	Cases	**n**	**Controls**	**n**	**Cases**	**n**	**Controls**	**N**
(years & months)								
12 years–12 years, 11 months	11.8	16	12.03	17	44.84	16	41.85	17
13 years–13 years, 11 months	11.65	11	11.87	13	37.13	11	46.15	13
14 years–14 years, 11 months	12.18	5	12.00	2	21.88	5	57.70	2
Total		32		32		32		32

Table 6 shows the average hemoglobin and ferritin in the case and control groups according to age, the age

group of 12-12 years and 11 months Hb case 12,18g/dL and control 12.59 g/dL, aged 13-13 years, 11 months cases of Hb 12.07 g/dL and control 12.50 g/dL, aged 14-14 years, 11 months cases of hemoglobin 12.60 g/dL and control 13.10 g/dL. The average ferritin cases and controls according to age were the age group 12-12 years, 11 months cases of ferritin 30.72 ug/L and control 41.74 ug/L, aged 13-13 years, 11 months cases of ferritin 27.48 ug/L and control 30.36 ug/L, aged 14-14 years, 11 months cases of ferritin 24.05 ug/L and control 57.20 ug/L.

e. Average of Hemoglobin by age: Baseline Midline and Endline

Table 7: Distribution of Average of Hemoglobin by age: Baseline Midline and Endline

Hemoglobin (g/dL) By age (years)	**Midline (before intervention)**		**Midline (3 months intervention)**		**Endline (6 months intervention)**	
	Cases (n)	**Control (n)**	**Cases (n)**	**Controls (n)**	**Cases (n)**	**Controls (n)**
< 13 years	11.80 (16)	12.03 (17)	11.90 (16)	12.06 (17)	12.18 (16)	12.06 (17)
< 14 years	11.65 (11)	11.78 (13)	11.43 (11)	11.90 (13)	12.07 (11)	12.50 (13)
< 15 years	12.18 (5)	12.00 [22]	12.60 (5)	12.60 [22]	12.90 (5)	13.10 [22]
Total	32	32	32	32	32	32

Based on the distribution of data in Table 7, it appears that in the age group <13 years, an increase in the average case group Hb levels from baseline, midline to the endline. The same age in the control group did not show an increase. In the age group of 14 to <15 years, the case group was also an increase in Hb levels from baseline, midline to the endline. For the age group of 13 to <14 years of the cases there was an increase only in the midline to the endline. Except in the control group of the same age was no increase in hemoglobin concentration from baseline, midline to the endline.

f. Average of Ferritin by age: Baseline, Midline and Endline

Table 8: Distribution of Average of Ferritin by age: Baseline, Midline and Endline

Ferritin (µg/L) By age (years)	**Midline (before intervention)**		**Midline (3 months intervention)**		**Endline (6 months intervention)**	
	Cases (n)	**Controls (n)**	**Cases (n)**	**Controls (n)**	**Cases (n)**	**Controls (n)**
< 13 years	44.84 (16)	41.95 (17)	71.24 (16)	55.60 (17)	30.72 (16)	41.74 (17)
< 14 years	37.13 (11)	46.15 (13)	91.80 (11)	49.88 (13)	27.48 (11)	30.36 (13)
< 15 years	21.88 (5)	57.70	58.27 (5)	37.60 [22]	24.05 (5)	57.20 [22]
Total	32	32	32	32	32	32

Table 8 shows the average distribution rate of ferritin, which in the case group from baseline (44.84), up to the midline into (71.24), but decreased at baseline (41.74). The same thing occurred in the control group.

4. Discussion

The study examines the level of hemoglobin in children of students who suffer from anemia who eat rice fortification with six micronutrients (Fe, Zn, vitamin B1, vitamin B3, folic acid and vitamin B12 for 6 months, subsequently followed by taking blood to check hemoglobin levels and ferritin after 3 months and 6 months of the intervention. Although these studies have been carried out with great precision and very careful, appropriate procedures and protocols of existing studies, but less deliver maximum results. the results of blood tests as shown above indicate that the mean average increase in hemoglobin level only in the age group 13 years to 13 years 11 months and in the age group of 14 years to 14 years 11 months.

Rice is the main food in Indonesia so it has great potential for widely spread. In this study, the samples are given rice fortified with the six nutrients: vitamin B1, vitamin B3, vitamin B9, vitamin B12, iron and zinc. Indonesia since 2012 has developed a special rice fortification project for poor rice. To make this project as a policy and then to the intervention program to address the Iron Deficiency Anemia, it is necessary to provide a scientific evidence in the form of efficacy studies, followed by effectiveness studies. Several studies of rice fortification in school shows the change of the concentration of hemoglobin (Hb)[23, 24], Ferritin concentrations [16, 25] and the prevalence of anemia [20].

Body ferritin levels are always opposed to hemoglobin levels. However, ferritin is a positive acute phase protein response, where the levels are increased during inflammation, and thus no longer a reflex of the amount of iron deposits. This makes the interpretation of that normal or high levels of serum ferritin difficult to be used as an indicator in areas with infection and inflammation widespread [26]. Serum ferritin concentration was positively correlated with the amount of body iron stores in a state with no inflammation. Low levels of serum ferritin are a reflection of the low iron stores in the body [6]. Normal ferritin levels vary according to age and gender. The concentration will be high at birth, increased in the first 2 months of life and then decreased at the end of infancy [27]. Around the age of 1 year ferritin concentration started to rise again and continue to grow into adulthood. Since early adolescence ferritin levels begin to diverge, where men are taller than women. The mean peak increase in ferritin levels a number of men aged between 30-39 years, then settled until the age of 70 years. In some women the average ferritin levels are relatively low until menopause, and then increased [28].

Hemoglobin is the protein carrier O2 and CO2 in the form of globular. Each molecule of hemoglobin contains heme-containing 5% iron and 95% globulin a polypeptide [29]. Hemoglobin contains four polypeptide chains and four heme prosthetic groups that have an iron atom in the form of ferrous (Fe +2). A part of protein is called globular consisting of two α chains and two β chains, each with 141 amino acid residues [30]. Structurally there are some minor variations on the different chain subunits of hemoglobin, depending on the composition of amino acids at the polypeptide, namely α β chain, ɣ and Δ. The most common form of hemoglobin in an adult is Hb A, a combination of 2 α chains and 2 β chains [31]. According to Sherwood [29] there are some reactions on hemoglobin, other than O2 namely: (1) CO2, Hb role of transporting gas from the tissues back to the lungs, [22]

Ion hydrogen acid (H2) of carbonic acid ionized , formed from CO2 at the network level. Hb participated supporting this acid, to a pH not very influential, (3) Carbon monoxide (CO), under normal conditions the gas was not contained in the blood, but if inhaled, the CO gas will occupy the binding site for O2 in Hb, to occur poisoning monoxide.

A study conducted by Allen, Rosado [21], that low levels of hemoglobin in response to the reduced iron is an indicator of chronic malnutrition and micronutrient deficiency in multi pre-school children. A study results are somewhat different, that the provision of MMN for 12 weeks, can significantly raise the status of micronutrients assessed but cannot be proven by supplementing with iron and folic acid alone in improving hemoglobin levels of anemia in adolescent girls [32]. This study presents only descriptive data, but the possibility of intervention effect on hemoglobin and serum ferritin.

5. Conclusions

There is an increase in average levels of hemoglobin from baseline to the intervention group midline to the endline, particularly in the age group of 12-12 years and 14-14 years 11 months. There is an increase in the average levels of ferritin from baseline to the intervention group but decreased in the midline endline. Further research is needed to extend the provision of rice fortification interventions.

Acknowledgment

This study is part of a research study on the efficacy of rice fortification to hemoglobin and ferritin levels and anemia prevalence in children students of the age group of 12-15 years.

References

[1] WHO, Worldwide Prevalence of Anaemia 1993-2005: Who Global Database On Anaemia. 2008, World Health Organization: Geneva.

[2] Kemenkes RI, Riset Kesehatan Dasar tahun 2007. 2007, Badan Penelitian dan Pengembangan Kesehatan, Kementerian Kesehatan RI: Jakarta.

[3] Dinkes Kab. Karawang, Profil Kesehatan Kabupaten Karawang. 2008, Dinas Kesehatan Kabupaten Karawang: Karawang.

[4] Ngui, R., et al., Association between anaemia, iron deficiency anaemia, neglected parasitic infections and socioeconomic factors in rural children of West Malaysia. PLoS Negl Trop Dis, 2012. 6(3): p. e1550.

[5] Pasricha, S.-R., et al., Control of iron deficiency anemia in low-and middle-income countries. Blood, 2013. 121(14): p. 2607-2617.

[6] WHO, Global Health Risks: Mortality and Burden of Disease Attributable to Selected Major Risks.

2009, World Health Organization: Geneva.

[7] Ekiz, C., et al., The effect of iron deficiency anemia on the function of the immune system. The Hematology Journal, 2005. 5(7): p. 579-583.

[8] Macdougall, L.G., et al., The immune response in iron-deficient children: Impaired cellular defense mechanisms with altered humoral components. The Journal of pediatrics, 1975. 86(6): p. 833-843.

[9] Chwang, L., A. Soemantri, and E. Pollitt, Iron supplementation and physical growth of rural Indonesian children. The American journal of clinical nutrition, 1988. 47(3): p. 496-501.

[10] Michaelsen, K., N.M. Thanh, and G. Samuelson, A longitudinal study of iron status in healthy Danish infants: effects of early iron status, growth velocity and dietary factors. Acta Paediatrica, 1995. 84(9): p. 1035-1044.

[11] Igbal, K., et al., Effect of Iron Deficiency Anemia on Intellectual Performance of Primary School Children in Islamabad, Pakistan. Tropical Journal of Pharmaceutical Research, 2015. 14(2): p. 287-291.

[12] Mesfin, F., Y. Berhane, and A. Worku, Anemia among primary school children in Eastern Ethiopia. PloS one, 2015. 10(4): p. e0123615.

[13] Ahmed, F., et al., Long-term intermittent multiple micronutrient supplementation enhances hemoglobin and micronutrient status more than iron+ folic acid supplementation in Bangladeshi rural adolescent girls with nutritional anemia. The Journal of nutrition, 2010. 140(10): p. 1879-1886.

[14] Hyder, S.Z., et al., A multiple-micronutrient-fortified beverage affects hemoglobin, iron, and vitamin A status and growth in adolescent girls in rural Bangladesh. The Journal of nutrition, 2007. 137(9): p. 2147-2153.

[15] Losen Adnyan, I.W., et al., Hubungan Feritin Serum dengan Kadar Il-2 Pada Penderita Anemia Defisiensi Besi. Journal of Internal Medicine, 2007. 8(1).

[16] Hussain, S.Z., B. Singh, and A. Rather, Efficacy of Micronutrient fortified Extruded Rice in Improving the Iron and Vitamin A status in Indian Schoolchildren. International Journal of Agriculture and Food Science Technology, 2014. 3(3): p. 227-238.

[17] Gera, T., H.S. Sachdev, and E. Boy, Effect of iron-fortified foods on hematologic and biological outcomes: systematic review of randomized controlled trials. The American journal of clinical nutrition, 2012. 96(2): p. 309-324.

[18] Muthayya, S., et al., Iron fortification of whole wheat flour reduces iron deficiency and iron deficiency anemia and increases body iron stores in Indian school-aged children. The Journal of nutrition, 2012.

142(11): p. 1997-2003.

[19] KFI Indonesia. Makanan yang Dapat Difortifikasi. 2011 [cited 2011 12 Maret]; Available from: http://www.kfindonesia.org/index.php?pgid=11&contentid=13.

[20] Nogueira Arcanjo, F., P. Santos, and S. Segall, Ferric pyrophosphate fortified rice given once weekly does not increase hemoglobin levels in preschoolers. J Rice Res, 2013. 1(2): p. 1-6.

[21] Allen, L.H., et al., Lack of hemoglobin response to iron supplementation in anemic Mexican preschoolers with multiple micronutrient deficiencies. The American journal of clinical nutrition, 2000. 71(6): p. 1485-1494.

[22] Soliman, A.T., V.D. Sanctis, and S. Kalra2, Anemia and Growth. Anemia and growth. Indian Journal of Endocrinology and Metabolism, 2014. 18: p. S1–S5.

[23] Pinkaew, S., et al., Triple-fortified rice containing vitamin A reduced marginal vitamin A deficiency and increased vitamin A liver stores in school-aged Thai children. The Journal of nutrition, 2014. 144(4): p. 519-524.

[24] Pinkaew, S., et al., Extruded rice grains fortified with zinc, iron, and vitamin A increase zinc status of Thai school children when incorporated into a school lunch program. The Journal of nutrition, 2013. 143(3): p. 362-368.

[25] Angeles-Agdeppa, et al., Efficacy of iron-fortified rice in reducing anemia among schoolchildren in the Philippines. International journal for vitamin and nutrition research, 2008. 78(2): p. 74-86.

[26] WHO, UNICEF, and UNU, Iron Deficiency Anaemia: Assessment, Prevention And Control, a Guide For Programme Managers. 2001, World Health Organization: Genewa.

[27] Domellöf, M., et al., The diagnostic criteria for iron deficiency in infants should be reevaluated. The Journal of nutrition, 2002. 132(12): p. 3680-3686.

[28] Gibson, R.S., Principles of Nutritional Assessment. 2005, New York: Oxford University Press.

[29] Sherwood, L.L., Fisiologi Manusia dari Sel ke Sistem. 2001, Jakarta: ECG.

[30] Marieb, E.N. and K. Hoehn, Human Anatomy & Physiology. 2007, San Fransisco: Pearson Education.

[31] Guyton, A.C. and J.E. Hall, Textbook of Medical Physiology. 1997, EGC: Jakarta.

[32] Ahmed, F., et al., Efficacy of twice-weekly multiple micronutrient supplementation for improving the hemoglobin and micronutrient status of anemic adolescent schoolgirls in Bangladesh. The American journal of clinical nutrition, 2005. 82(4): p. 829-835.