

Effectiveness of iron supplementation for children with iron deficiency anemia: Study in Purbalingga, Central Java

Tien Budi Febriani*¹, Emi Azmi Choironi¹, Latifah Hanum²

¹Department of paediatrics, Faculty of Medicine, Universitas Islam Indonesia, Yogyakarta, Indonesia

²Paediatrician in Purbalingga District Hospital, Purbalingga, Central Java, Indonesia

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ABSTRACT

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*Corresponding author:

tienbudifebriani@gmail.com

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Background: Iron Deficiency Anaemia (IDA) is one of major factors for human health, especially young children. Iron supplementation can indicate a good response in haemoglobin concentration.

Objective: This study is to observe prevalence of anaemia and effectiveness of iron supplementation for children in Purbalingga district, Central Java.

Methods: This study was a quasi-experimental study by measuring haemoglobin concentration before (pre) and after (post) treatment. Its participants were determined by a purposive sampling method. 64 children (less than 5 years old) were included in criteria of anaemia. Their blood samples were collected before the treatment to measure SI (Serum Iron) and TIBC (Total Iron Binding Capacity). Administering 4 mg of iron per kg of body weight per day was conducted for a month. Data of participants such as age, nutritional status, socio-demographic, and medical history were also collected. A paired t-test was used to analyse mean differences of haemoglobin levels before and after treatment.

Results: Among the 64 children with anaemia, 98.4% indicated Iron Deficiency (ID) with 59.4% of them indicating IDA based on level of SI and TIBC. Anaemia has more prevalence in group of 6 - <12 months of age. There was a statistically significant increase of haemoglobin level with a mean difference of 1.52 g/dL between the pre and post treatment (p=0.000).

Conclusion: The prevalence of IDA in children (less than 5 years old) in Purbalingga District Hospital was 59.4%. Adequately oral iron supplementation for a month indicated a statistically significant increase of haemoglobin levels.

Latar Belakang: Anemia Defisiensi Besi (ADB) adalah salah satu faktor utama dalam kesehatan manusia, terutama anak-anak. Suplementasi zat besi dapat menunjukkan respon yang baik terhadap konsentrasi hemoglobin.

Tujuan: Penelitian ini bertujuan untuk mengobservasi prevalensi anemia dan efektivitas pemberian zat besi untuk anak-anak di kabupaten Purbalingga, Jawa Tengah.

Metode: Penelitian ini adalah penelitian quasi-eksperimen yang mengukur jumlah konsentrasi hemoglobin sebelum (pra) dan setelah (pasca) perawatan. Para peserta yang menjadi subyek dalam penelitian ini ditentukan dengan metode purposive sampling. 64 anak-anak (di bawah 5 tahun) termasuk dalam kriteria anemia. Sampel darah mereka dikumpulkan sebelum perawatan dilaksanakan untuk mengukur Serum Iron (SI) dan Total Iron Binding Capacity (TIBC). Pemberian 4 mg zat besi per kg berat badan per hari dilakukan selama sebulan. Data peserta dalam penelitian ini seperti usia, status gizi, sosio-demografis, dan riwayat medis juga dikumpulkan. Uji t-berpasangan digunakan untuk menganalisa perbedaan rata-rata kadar

hemoglobin sebelum dan sesudah pengobatan.

Hasil: Diantara 64 anak dengan anemia, 98.4% menunjukkan kekurangan zat besi dan 59.4% dari mereka menunjukkan ADB berdasarkan tingkat SI dan TIBC. Anemia memiliki prevalensi lebih banyak pada kelompok usia 6-<12 bulan. Ada peningkatan kadar hemoglobin yang signifikan secara statistik dengan perbedaan rata-rata 1.52 g/dL ketika sebelum dan sesudah pengobatan ($p=0.000$).

Kesimpulan: Prevalensi ADB pada anak-anak (di bawah 5 tahun) di Rumah Sakit Kecamatan Purbalingga adalah 59.4%. Suplementasi zat besi secara oral yang cukup selama sebulan mengindikasikan peningkatan kadar hemoglobin yang signifikan secara statistik.

INTRODUCTION

Anaemia is one of major problems in public health affecting for both developing and developed countries. It is estimated that almost 30% of world's population is anaemic, and half of them can indicate Iron Deficiency Anaemia. Prevalence of IDA in Indonesia is still high, especially in pregnant women, children less than five years old, children in school age and low-income workers.¹ Factors, which can lead to IDA in children, are lack of iron intake, increasing need, infections, and others. Indonesian Demographic and Health Survey in 2012 reported that incidence of IDA was 48.1% in a group below 5 years old and 47.3% in a group of school age.² Moreover, Basic Health Research (called RISKESDAS in Indonesia) in 2018 showed that 48.9% of pregnant women in Indonesia suffered the IDA, that could contribute to high incidence of anaemia in infants and children.³ It was also reported that 37% infants ageing 4-5 months in West Java, Central Java, and East Java had haemoglobin level of <10 g/dL, and 71% infants showed haemoglobin level of <11 g/dL.⁴

IDA refers to lack of iron stores that contribute to decrease of physiological capability of oxygen binding. This condition may be resulted from a decrease of iron absorption.⁵ Deficiency of iron can affect mental and intelligent development. Erythrocytes play an important role to transfer oxygen to all parts of the body especially brain; therefore, anaemic children can suffer less fulfilled oxygen in their brain.^{6,7} Consequently,

anaemic children can experience poor learning capability, low attention span, and low IQ test.⁸ Iron is also essential nutrient for development of the brain and immune system. Risks of infection can increase in IDA as a result of impaired function of immune system.⁹

A previous study in a rural in Central Java reported that daily oral supplementation of 10 mg ferrous sulphate per kilogram of body weight per day for 3 months can effectively increase haemoglobin (Hb) concentration and improve learning achievement among school-children.¹⁰ Muhilal et al. reported that a pilot program of daily oral iron supplementation of 3 mg/kg of body weight for 2.5 months could reduce 24% anaemia prevalence in pre-school children and 25% in school-children, respectively.¹¹ Indonesian Paediatric Society (IPS) recommends 4-6 mg of iron per kilogram of body weight per day to treat the IDA and to increase 1-2 mg/dl level of haemoglobin.¹² Therefore, a study on effectiveness of iron supplementation to increase haemoglobin concentration for children below 5 years old in Purbalingga need to be conducted.

METHODS

Study design and Subjects

This study used a quasi-experimental design located in Purbalingga District Hospital. Samples in this study were 64 children with anaemia below 5 years old, who were enrolled (between November 2016 and January 2017) and recruited from Paediatric Unit of Purbalingga District Hospital after getting an ethical agreement letter. All the participants were included in inclusion criteria of anaemia based on WHO criteria with haemoglobin level of <11.5 g/dL. They also had clinically severe diseases (severe infection, renal or autoimmune disease and malignancy) and other haematological disorders such as thalassemia, haemophilia, blood malignancy based on clinical manifestation (liver or spleen enlargement, node lymph enlargement, history of familial blood coagulation disorder, hamarthrosis) or supporting laboratory results (leucocytosis or leukopenia with anaemia or/ and thrombocytopenia) were excluded.

Measurement of haemoglobin concentration was conducted before and after treatment. Supplementation of 4-6 mg of elemental iron per kilogram of body weight per day was administered to each participant for a month. A daily monitoring questionnaire filled by parents was purposed to check subject's compliance during the treatment. A post-treatment evaluation was organized after the one-month treatment was finished. A nutritional status was determined based on growth chart curve, and body weight to length was based on z-score curve. Data was collected by using forms of study.

Socio-demographic data, medical and dietary history were obtained by interviewing participants' parents or caretakers by using a structured questionnaire that was conducted by a paediatrician. The paediatrician had no information about the SI and TIBC data.

Blood samples analysis

Laboratory observation in this study included complete blood count (Hb), SI and TIBC. Complete blood count was examined by using 2 cc EDTA blood, and SI and TIBC was examined by using specimen blood serum. Laboratory examination and measurement for the complete blood count, SI and TIBC applied a standard used in a private

laboratory in Purbalingga.

Blood samples were collected to measure the SI and TIBC. 5 ml venous blood sample was drawn from each participant into plain tubes without an added anticoagulant. The blood sample was drawn before an intervention.

Statistical analysis

Data were processed and analysed statistically to compare mean differences between the pre and post treatment of haemoglobin concentration. Mean differences of SI and TIBC between ID, IDA, and non-ID group were compared by using student's t-test. Chi square test was used to determine significant differences of prevalence between ID, IDA and non-ID group in nominal data (sex, level of parental education and economy, history of iron supplementation, nutritional status). Differences of mean and prevalence among the groups were considered statistically significant if $p < 0.05$.

RESULTS

64 children below five years old were enrolled in this study. Age of the participants ranged from 2-58 months, and their mean of age was 16.1 months. Characteristics of them were portrayed in Table 1.

Table 1. Participant Characteristics

Characteristics	Mean	N	%
Age (month)	16.1		
Hb level (pre-treatment)	9.88 (7.0-10.9)		
Age group (month)			
0 - <6		6	9.4
6 - <12		24	37.5
12- <24		23	35.9
24- <60		11	17.2
Sex			
Male		36	56.3
Female		28	43.8
Nutritional status			
Normoweight		13	81.3
Underweight		2	12.5
Severely underweight		1	6.3

Percentage of anaemia was highest in age 6 - <12 months compared to other groups based on their age. Families with low-middle economy and educational status had the highest prevalence among the participants, but most participants were normoweight. According to the level of iron status, 98.4% anaemic children indicated iron deficiency; however, only 59.4% of the participants suffered IDA. Then 40.6% of them was still in iron deficiency phase, either iron depletion or iron deficiency

erythropoietin phase. Table. 2 illustrates levels of iron deficiency based on iron status. It was also found that serum iron and transferrin saturation between ID and IDA group had significant mean differences ($p < 0.05$, student's t test, Table 3). Administering 4-6 mg of oral elemental iron per kilogram of body weight per day for a month showed a statistically significant increase of haemoglobin levels, with mean differences of 1.68 ($p < 0.008$, Table 4).

Table 2. Classification of anaemia based on iron status

Classification of Anaemia	N (%)
Iron depletion/storage iron deficiency	18 (28.1)
Iron deficient erythropoietin	7 (10.9)
Iron deficiency anaemia	38 (59.4)
Iron overload	1 (1.6)
Total	64 (100.0)

Table 3. Mean comparison of serum iron, TIBC, ID and IDA

Iron Status	IDA (SD)	ID (SD)	p
Serum iron (ug/dL)	22.57 (9.76)	72.69 (2.69)	0.000
TIBC (ug/dL)	345.44 (71.52)	317.19 (63.02)	0.109

* $p < 0.05$

Tabel 4. Mean difference of haemoglobin before and after an month treatment

	Pre treatment	Post treatment	p
Mean Hb level (g/dL)	9.88	11.56	0.008

DISCUSSION

Based on analysis of this study, the mean difference of haemoglobin before and after the oral iron treatment indicated a significance difference. This is consistent with an assumption suggesting that adequately oral iron treatment for a month can show a statistically significant increase of haemoglobin levels. Global trend of IDA prevalence has declined since the last decades; it is still a substantial problem in developing countries, such as Indonesia. Widjaja et al. reported that prevalence of anaemia in Malinau, East Kalimantan was 53.9%, and its IDA prevalence based on Mentzer index in age

groups of 6-59 months, 5-11.9 years old and 12-18 years old was 26.5%, 13.6%, and 13.2%, respectively.¹³ However, in this study, the IDA prevalence among all anaemia cases based on iron status was 59.4%. This is in accordance to a report by Widiaskara et al. that prevalence of IDA was 65.3% among hospitalized children due to other diagnoses in District Hospital of Wangaya, Denpasar.¹⁴

An recent study also found that IDA was more common in age of 6 - <12 months (37.5%). This result is supported by a previous study reporting that anaemia in children ageing 6-11 months was 37.3%.¹⁴ Results of Household

Health Survey (SKRT) in 2014 also pointed that prevalence of IDA in infants ageing 6-12 months was the highest (64.8%), compared to the infant ageing 0-6 months (61.3%) and children below five years old (48,1%).¹⁵ In our study, the SI level was significantly lower in the IDA group than in the ID group. However, there was no significantly difference of TIBC between the two groups. It might because most participants in this study were patients with illness or post illness. Therefore, aetiology of ID was not only IDA but also combination of anaemia with chronic diseases.

Based on this study, anaemia with chronic diseases was excluded. Anaemia with chronic diseases may be accompanied by IDA as a result of decrease of iron mobilization activity from reticuloendothelial system into plasma activity, whereas transferrin saturation may decrease due to transferrin degradation. Iron is bound to transferrin in the plasma. TIBC is a direct measure of transferrin level, so anaemia with chronic diseases may indicate a decrease or normal TIBC level, a distinct condition except those in the IDA. Serum ferritin level is also useful to distinguish between those two types of anaemia. In IDA, the level of serum ferritin is low contrasting to the serum ferritin in anaemia with chronic diseases.¹⁶ A limitation of our study is unable to determine the levels of serum ferritin because of limited cost of this study.

Nevertheless, our study reported a statistically significant increase of haemoglobin levels after treatment. This result is in accordance to high prevalence of iron deficiency in this region with more than 95%. An increase of haemoglobin level 1-2 g/dL within one month following adequate iron therapy is one of diagnostic tools in area with minimum facilities to measure iron status.¹²

There is three phases of iron deficiency. The first phase is iron depletion or storage iron deficiency; the second phase is iron deficient erythropoietin or iron limited erythropoiesis; and the final phase is IDA. The subsequent phases consist of decrease of iron storage, decrease of serum ferritin, decrease of iron

serum with increase of serum transferrin, increase of Red cell Distribution Width (RDW), decrease of Mean Corpuscular Volume (MCV), and decrease of haemoglobin level.¹⁷

Socio-economic and parental education as well as acute and chronic infections are widely known as important factors in IDA. Paternal schooling is closely associated to family income. Lower income family can relate to IDA due to inability to get iron-rich foods, poor sanitation leading to infection, and misinformation of iron supplementation.¹⁸ In this study, more than half participants were from family with low and middle income and with low and middle parental education level. Further investigation is necessary to explore relationship among factors contributing to the IDA.

Young children are more susceptible to iron deficiency because of rapid growth that requires high iron. On the contrary, lack of iron content in complementary foods and frequent episodes of infection. Breast milk contains relatively low levels of iron but it is simply absorbable and sufficient for infants until six months of age. Therefore, extra iron is required from six months to future age, either from complementary food or from some supplements. Unfortunately, common complementary food given to infants ageing 6 months in Indonesia are bananas or rice flour mixed with breast milk. This food provides many calories but contains low bioavailable iron, low protein and zinc, and high phytate. The amount of iron provided by a banana is 0.3 mg of iron, whereas 28 g of rice flour contains only 0.1 mg of iron. This condition is insufficient based on Recommended Daily Intake (RDI) stating that children ageing 6-12 months need 11 mg per day.¹⁹

This study was conducted as well as possible, but it still has some limitations. The guideline for the IDA is administering 4-6 mg of orally elemental iron per kilogram of body weight per day for one until two months. Daily iron supplementation is a preventive strategy that can be implemented at a population level.

Almost 50% of pregnant women in

Indonesia suffer IDA that contributes to the high incidence of anaemia in infants and children. To keep public health, Indonesian Paediatrics Society has recommended giving daily iron supplementation for infants and children ageing 6-23 month. Iron is a micronutrient that the body needs to make haemoglobin.

If the clinicians found a clinical manifestation of anaemia, supplementation of iron needs to be prescribed. Then the clinicians should check a response treatment after 1 until 1.5 months. If there is no response (below 1.0 g/dL of increase in haemoglobin or <3 unit of increase in haematocrit), despite what appears to be good compliance, the clinician should determine the serum ferritin concentration and consider other causes of anaemia. If there is a response resulting from the iron supplementation, it should be continued until the haemoglobin concentration becomes 12.0 g/dL. And after which iron can be decreased to a maintenance level of about 30 mg of iron per day for 4 months and then discontinued.¹⁵

Alteration of diet may retard the development of the IDA and avoid the need for supplemental iron in children. Further investigation is necessary to explore relationships among the factors contributing to the IDA in children.

CONCLUSION

This study found that Purbalingga had high prevalence of iron deficiency with more than 95%. Administering 4-6 mg of orally elemental iron per kilogram of body weight per day for a month could make the haemoglobin levels increase.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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