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The comparison of effects of iron supplementation since pre-pregnant and during pregnant period on reducing iron deficiency anemia in pregnant women with mild anemia in Bali

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ABSTRACT

Introduction: Iron deficiency anemia (IDA) is still a problem of pregnant women's health related to its high prevalence and its negative effects on health. Prevention efforts have been carried out through administration of oral iron tablets to women during their pregnancy; however, the expected results have not been satisfied yet. This failure is probably due to the assumption that, especially in developing countries, the iron store in pre-pregnant women is very low or may be empty, so that iron supplementation during pregnancy is not enough to prevent IDA. The aim of study is to know the difference of effect of iron supplementation in treated and control groups in terms of hemoglobin concentration, serum ferritin level and prevalence of IDA.

Method: A quasi-experimental study was conducted on 99 non-pregnant new couple women. Iron tablets were administered to the treated group from the beginning of pre-pregnant period, continuing until the first 3 months of pregnancy, while in the control group iron tablets were only given during the first 3 months of pregnancy. IDA was measured by serum ferritin and hemoglobin concentration using WHO's criteria, the benefit of iron tablet was measured by BCR technique.

Result: The administration of an oral iron tablet from the prepregnant period (treated group) could decrease prevalence of IDA higher than the administration of oral iron tablet during pregnancy only (control group) (0% vs 38.46%, $p<0.05$). A significant difference was also observed on mean serum ferritin concentration at the end of observation (the third month of pregnancy) 33.45±14.12 µg/dL in the treated group, and 19.65±8.99 µg/dL in the control group. This difference was statistically significant ($p<0.05$). Meanwhile, the hemoglobin concentration was 12.25±1.20 g/dL in the treated group and 10.91±0.67 g/dL in the control group. This difference was also statistically significant ($p<0.05$). Benefit analysis showed that administration of an oral iron tablet starting from pre-pregnancy is more advantageous (*BCR* >1) compared to oral administration of iron tablet during the pregnancy period only. There were no significant differences in side effects and compliance of the patient to consume iron pills in both treated and control groups.

Conclusion: The administration of oral iron tablets (iron supplementation) to pregnant women starting from pre-pregnant period results in a better effect compared to oral iron supplementation during pregnancy only. This program is feasible to be implemented in a community setting because its compliance is good.

Keywords: iron deficiency anemia, iron supplementation, pregnant woman.
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INTRODUCTION

Iron deficiency anemia (IDA) is still an important health problem, especially to pregnant women, related to its high prevalence and its negative effects. Many countries including Indonesia, reported high prevalence of IDA in pregnant women, nonetheless within a wide range. The prevalence in developed countries is lower: 18%, meanwhile the prevalence in Indonesia is around 63 %, and in Bali is reported to be 46,2%.[1,2]

The high prevalence of IDA in pregnant women, leads to negative impacts on health as well as on economic aspects. Many studies have reported that IDA in pregnant women give negative effects since pregnancy, after birth, children, and until adulthood. One of the earliest effects of IDA is premature labor. This condition will be associated with new problems for the baby such as low birth weight, immune-deficiency status, and tend to have physiological and growth-development disturbances[1]. If these conditions are correlated with low IQ, and decrease ability of learning. All these effects lead to impairment of quality of human beings, work productivity and economic implication[3]. Economically, the effect of IDA in pregnant women can be estimated with benefit-cost ratio (BCR) analysis.

To cope with the IDA problem in pregnant women an "iron pill program" was held by the government of Indonesia. In this program every pregnant woman will be given 90 iron pills from the beginning of pregnant period. The result of this program was not satisfying yet. The prevalence of IDA is still high and the effect of IDA on pregnant women continued: such as 10.2% abortion, 4.3% prematurity and 7.8% fetal growth retardation.[4,5] Another study also found the same result, there is no significant different on risk of abortion in pregnant women with IDA who were given oral iron tablet combined with folic acid.[6] Folic acid, vitamin B12 and B6 combined with oral iron tablet for treating anemia in pregnancy, does not increase hemoglobin concentration significantly.[7] Combination of oral iron tablet with vitamin C, does not increase hemoglobin concentration significantly, either.[8-11]

An iron store theory was developed to explain the failure of the iron pill program in controlling IDA in pregnant women.[12] In developing countries, due to inadequate iron intake, women had a low, or empty iron store before pregnancy. In pregnancy, iron requirements increase, abruptly, the total iron requirement during pregnancy is about 1000 mg.[13] This high requirement, in the setting of an empty iron store can not be fulfilled by iron neither from diet nor from iron supplementation. According to this theory, iron supplementation should be given before the pregnant period to overcome the low iron store.

Based on the above assumption, a field trial was held in which iron supplementation was given since pre-pregnant period, compared with a control group in which iron supplementation was given only during pregnancy. The aim of study is to know the difference of effect of iron supplementation in treated and control groups in terms of hemoglobin concentration, serum ferritin level and prevalence of IDA.

MATERIALS AND METHOD

This research was held at the district of Abiansemal, Badung Regency in May 2006 - January 2007. The research design was *quasi experimental* with *randomized pre and post test control group design* (field trial). The population were marriage women planning for pregnancy. The persons included in this study were married women with mild IDA. Samples are 99 married women and not pregnant yet, consisting of 52 control group and 47 treated groups. The two groups were checked for serum ferritin and hemoglobin concentration three times: at the beginning of observation (pre-pregnancy), at the beginning of pregnancy and at the third month of pregnancy (end of observation). On treated group iron tablets (66 mg ferrous sulfate) were given orally from the pre-pregnant period until the first 3 months of pregnancy, meanwhile on control group, oral iron tablets were given from the beginning of pregnancy until the first 3 months of pregnancy. Data on side effects and compliance to consume iron pills were collected by anamnesis on a special record. Cost-benefit ratio is assessed by BCR analysis.[14]

RESULTS

The characteristics of patients in the treated and control group were similar in regard to age, education and occupation. The mean age is 24.47±4.03 years among the treated group and 25.71±3.81 years among the control group. Educational status of samples consist of elementary school, junior high school, senior high school and undergraduate degree. The most frequent education status were senior high school 25 (53.19%) in the treated group and 23 (44.23%) in the control group. There were various occupations among samples, such as farmer, merchant, labor, private workers and state employees. The highest percentage of occupation was labor, 53.19% in the treated group and 44.23% in the control group. All the differences were not statistically significant ($p > 0.05$).

Iron supplementation from the pre-pregnant period (treated group) could prevent IDA more than iron supplementation from the beginning of pregnancy (control group) (Figure 1). There were no IDA cases in the treated group (0% prevalence), while in the control group the prevalence of IDA was 38.46% at the end of observation. This difference was statistically significant ($p<0.05$).

Differences were also seen on mean serum ferritin and hemoglobin concentration. The mean serum ferritin of treated group on the beginning of observation (pre-pregnant period), on the beginning of pregnant period and on the third month of pregnancy were 14.95±4.21 µg/dL, 25.68±9.0 µg/dL dan 33.45±14.12 µg/dL respectively in treated group; while in control group were 13.94±4.18 µg/dL, 13.32±4.25 µg/dL and 19.65±8.99µg/dL respectively. The mean hemoglobin concentration in treated group were 10.26±0.66 g/dL, 11.52±1.05 g/dL, and 12.25±1.20 g/dL; while in control group were 10.19±0.63 g/dL, 10.23±0.55 g/dL, and 10.91±0.67 g/dL respectively. Differences of the mean of serum ferritin and the hemoglobin concentration in treated and control groups were statistically significance ($p <0.05$) (Table 1).

Side effects of iron tablets found were nausea, stomach discomfort, and

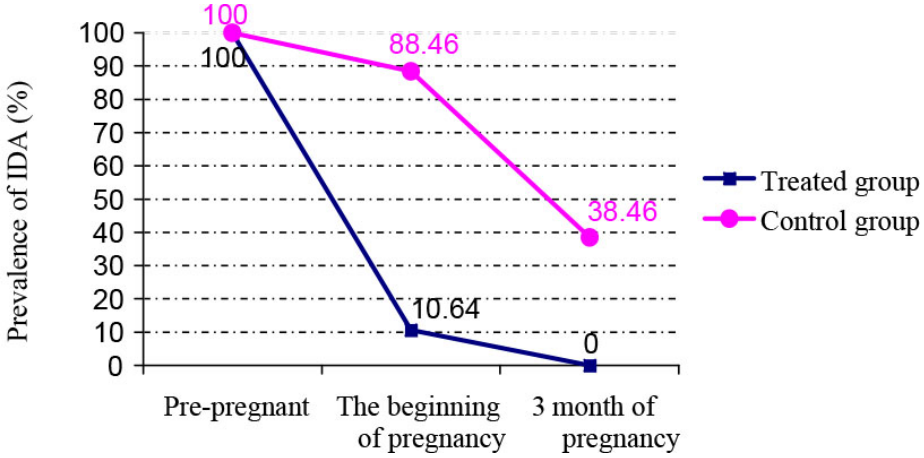

Figure 1. The effect of iron supplementation on the prevalence of IDA in treated and control group.

Table 1. Distribution mean of ferritin serum and hemoglobin concentration in women with IDA in treated and control groups.

Variable	Treated group (N=47)		Control group (N=52)		t	p
	Mean	SD	Mean	SD		
Ferritin at pre-pregnant period	14.95	4.21	13.94	4.18	1.193	0.230
Hb at pre-pregnant period	10.26	0.66	10.19	0.63	0.477	0.060
Ferritin at the beginning of pregnancy	25.68	9.00	13.32	4.25	9.088	0.000
Hb at the beginning of pregnancy	11.52	1.05	10,23	0,55	7.515	0.000
Ferritin at 3 month of pregnancy	33.45	14.12	19.65	8.99	5,413	0,000
Hb at 3 month of pregnancy	12.25	1.20	10.91	0.67	6.462	0.000

*Note: SD = Standard deviation; Hemoglobin (Hb): g/dl ; Ferritin serum: µg/dL

Table 2. The estimation of the benefit ratio of administration of iron tablets in pregnant women with mild IDA based on risk of low birth weight, prematurity, and abortion.

Benefit		Treated group	Control group
		Proportion without IDA = 100%	Proportion without IDA = 61.54%
1. Low Birth Weight	Rp 135.934	Incidence without Low Birth Weight = 95% Rp 129.137	Incidence without Low Birth Weight = 51.5% Rp 43.081
2. Prematurity	Rp 276.346	Incidence without Prematurity = 93% Rp 257.001	Incidence without Prematurity = 76% Rp 129.248
3. Abortion	Rp 317.021	Incidence without Abortion = 90% Rp. 285.318	Incidence without Abortion = 70% Rp. 136.566

Table 3. The Cost- Benefit Ratio of administration of iron tablets in treated and control groups.

Risk	BCR	
	Treated group	Control group
Low Birth Weight	7.4	3.2
Prematurity	14.6	9.3
Abortion	16.3	10.2

constipation, but these side effects were very mild, both in the treated and control group. The difference of side effects between treated and control group was not statistically significant. The compliance of patients to follow this program is very good. Good compliance to consume iron pills was found in 44 among 47 subjects in the treated group, and 50 among 52 subjects of the control group. This difference was not statistically significant.

The spending cost for administration of iron tablets started in the pre-pregnant period was Rp. 7.560,- (treated group), while the spending cost of administration of iron tablets started on pregnancy was Rp. 3.240,-. The benefit appears in the difference between cost to overcome the impact of IDA (low birth weight, prematurity abortion) and the expenditure for iron supplementation. Economically, the effect caused by administration of iron tablets is calculated from the cost of hospitals such as low birth weight, prematurity and abortion. [7] The calculation of benefit ratio can be seen on table 2. Subsequently, the BCR value can be determined by comparing the benefit with the cost of administration of iron tablets between the two groups, as shown on table 3.

As shown on table 3, the BCR of low birth weight, prematurity, and abortion were all more than 1. These mean that the administration of iron pills since pre-pregnant period, economically gives better impact compared with administration of iron pills just after the beginning of pregnancy.

DISCUSSION

Iron deficiency anemia (IDA) is still a major public health problem in developing countries, including Indonesia.[1,11,14] The pregnant women and children under five are the most vulnerable groups. The major determinant of this problem is a low bioavailability of iron on daily diet and high requirement of iron in pregnant women and children during growth. WHO[14] proposed a standard control program for IDA in pregnant women, "iron pills program". Every pregnant woman will be given 90 iron pills (66 mg ferrous sulfate, combined with folic acid). Indonesia adopted this WHO's program.[7,10] The result of this program is not satisfactory. There is no significant decrease of IDA in pregnant women, including in Indonesia.[8,9,10,11] No exact explanation to justify this gap. It is assumed that, in developing countries, iron stores of pregnant women are very low, or may be empty, so the "iron pills program" is not enough to restore the iron store during the pregnancy period. Iron supplementation from pre-pregnant period is needed to restore the iron store and to fulfill the increase of iron requirement during pregnancy.[12,15-20]

The results of this study support this assumption. Iron supplementation from the prepregnant period could increase serum ferritin and hemoglobin levels, and prevent IDA in pregnant women with mild IDA. Iron stores can increase to 33 µg/dL, more than the cut off point (20 µg/dL), while in the control group the iron store is only 19.65 µg/dL, still below the cut off point.

The positive impact of this program is proved from benefit-risk ratio analysis. There is more than one BCR, so it can be concluded that this program is very useful. This program is very feasible because the side effect of iron supplementation is low and the compliance of the patient is high. More field studies in different demographic and geographical contexts are needed to confirm the result of this study, before it can be transformed into a formal program.

CONCLUSION

Administration of iron tablets from the pre-pregnant period in pregnant women gives better results compared with administration of iron tablets started just at the beginning of pregnancy. It is supported by the findings on mean serum ferritin and hemoglobin level; both were higher in the treated group compared with the control group. This program is also more effective in preventing IDA in pregnant women, with a good feasibility in its implementation in the community.

CONFLICT OF INTERESTS

All the authors declare that they have no conflict of interests.

AUTHORS' CONTRIBUTIONS

All authors contributed to this study's conception and design, data analysis and interpretation, article drafting, critical revision, final approval, and data collection.

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None.

ETHICAL CLEARANCE

This research has obtained an ethical feasibility permit number: 1053/UN14.2.2.VII.14/LT/2006 by the ethics commission of the Medical Faculty of Udayana University/Sanglah Hospital.

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