PERBANDINGAN EFEK SUPLEMEN BESI PRA-HAMIL DAN SELAMA KEHAMILAN DALAM UPAYA MENURUNKAN ANEMIA DEFISIENSI BESI PADA WANITA HAMIL DENGAN ANEMIA RINGAN DI BALI

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ABSTRAK

Anemia defisiensi besi (ADB) masih merupakan masalah kesehatan wanita hamil terkait dengan tingginya prevalensi dan efek negatifnya terhadap kesehatan. Upaya pencegahan telah dilakukan dengan pemberian tablet besi selama kehamilan. Akan tetapi hasilnya belum memuaskan. Kegagalan ini mungkin diakibatkan oleh rendahnya bahkan kosongnya cadangan besi tubuh sewaktu pra-hamil, terutama di negara sedang berkembang. Oleh karena itu, suplemen besi yang hanya diberikan waktu kehamilan tidak cukup untuk mencegah terjadinya ADB. Oleh karena itu, dilakukan *a quasi experimental study* pada 99 pasangan baru yang belum hamil yang terdiri atas 47 group perlakuan dan 52 sebagai group kontrol. Tablet besi (200 mg ferrous sulfate) diberikan sejak periode sebelum hamil pada group perlakuan yang dilanjutkan sampai dengan 3 bulan kehamilan. Sementara, pada group kontrol diberikan tablet besi dimulai hanya pada kehamilan trimester pertama. ADB didasarkan atas konsentrasi hemoglobin dan serum feritin sesuai dengan criteria WHO dan keuntungan pemberian tablet besi didasarkan atas teknik BCR. Pada penelitian ini didapatkan bahwa pemberian tablet besi pada pra-hamil dapat menurunkan prevalensi ADB lebih tinggi dibandingkan dengan pemberian tablet besi yang dimulai saat kehamilan (0% vs 38.46%, $p<0.05$). Perbedaan yang signifikan juga pada rerata serum feritin pada akhir pengamatan yaitu 33.45±14.12 µg/dL pada group perlakuan dan 19.65±8.99 µg/dL pada group kontrol. Sementara itu, kadar hemoglobin adalah 12.25±1.20 g/dL pada group perlakuan dan 10.91±0.67 g/dL pada group kontrol ($p<0.05$). Analisis menunjukkan bahwa pemberian tablet besi yang dimulai saat pra-hamil adalah lebih menguntungkan dibandingkan dengan pemberian tablet besi mulai hanya pada kehamilan (*BCR* >1). Tidak terdapat perbedaan bermakna pada efek samping dan kepatuhan pada group perlakuan dan kontrol. Berdasarkan hasil-hasil ini dapatlah disimpulkan bahwa pemberian tablet besi yang dimulai masa pra-hamil adalah lebih baik dibandingkan dengan pemberian tablet besi yang diberikan hanya pada saat kehamilan. Program ini sangat mungkin diterapkan pada masyarakat karena kepatuhannya adalah baik.

Kata kunci: wanita hamil, anemia defisiensi besi, suplemen besi

PENDAHULUAN

Anemia defisiensi besi (ADB) masih merupakan masalah kesehatan yang penting terkait prevalenisnya yang tinggi dan efek sampingnya, terutama pada wanita hamil. Di berbagai negara termasuk Indonesia dilaporkan bahwa prevalensi tinggi ADB pada kehamilan dengan variasi yang lebar. Prevalesi ADB di negara maju sekitar 18%, sedangkan di Indonesia sekitar 63 % [(1)] dan di Bali dilaporkan 46,2% [(2)].

Tingginya prevalensi ADB pada wanita hamil memberikan efek negatif terhadap kesehatan dan ekonomi. Bebagai studi ADB pada wanita hamil dapat memberikan efek pada kehamilan, setelah kelahiran, anak-anak dan bahkan sampai masa dewasa. Salah satu efek ADB adalah kelahiran premature dimana hal ini berasosiasi dengan masalh baru seperti berat badan lahir rendah, defisiensi respon imun dan cenderung mendapat masalah psikologik dan pertumbuhan [(1)]. Apabila hal ini berlanjut maka hal ini berkorelasi dengan rendahnya IQ dan kemampuan belajar. Semua hal tersebut mengakibatkan rendahnya kualitas sumber daya manusia, produktivitas dan implikasi ekonomi [(3)]. Secara ekonomi, efek ADB pada ibu hamil dapat diestimasi dengan analisis *benefit-cost ratio* (BCR).

Dalam upaya mengontrol ADB pada wanita hamil di Indonesia telah dilakukan program tablet besi dimana setiap wanita hamil diberikan 90 mg tablet besi sejak periode kehamilan. Hasil program ini belum memuaskan dimana prevalensi ADB masih tetap tinggi dan efeknya masih berlanjut seperti 10.2% abortus, 4.3% prematuritas dan 7.8% retardasi pertumbuhan [(4,5)]. Studi lainnya juga melaporkan bahwa risiko terjadinya abortus pada ADB yang diberikan tablet besi kombinasi dengan asam folat adalah tidak berbeda bermakna [(6)]. Pemebrian asam folat, vitamin B12 dan B6 kombinasi dengan tablet besi pada wanita hamil tidak meningkatkan kadar hemoglobin secara signifikan [(7)]. Demikian pula halnya, pemberian kombinasi tablet besi dan vitamin C [(8,9.10.11)]

Teori cadangan besi tubuh mungkin dapat menjelaskan sebab kegagalan program tablet besi tersebut dalam kaitannya dengan kontrol ADB pada wanita hamil [(12)]. Di negara sedang berkembang hal ini dapat diakibatkan oleh asupan besi yang tidak adekuat, rendahnya atau kosongnya cadangan besi tubuh sebelum hamil. Dalam kehamilan, terjadi peningkatan absorpsi dan kebutuhan besi dimana total besi yang dibutuhkan

adalah sekitar 1000 mg [13]. Kebutuhan yang tinggi dimana cadangan besi tbuh kosong maka hal ini tidak dapat dipenuhi melalui diet besi harian dan juga oleh besi suplemen. Menurut teori tersebut, supelemen besi seharusnya diberikan pada periode sebelum hamil untuk mengantisipasi rendahnya cadangan besi tubuh. Berdasarkan asumsi diatas, dilakukan studi eksperimental di lapangan dengan pemberian tablet besi mulai masa pra-hamil sebagai kelompok perlakuan. Sedangkan pemberian tablet besi yang hanya dimulai saat hamil sebagai kelompok kontrol. Tujuan studi ini adalah untuk mengetahui perbedaan efek suplemen tablet besi pada kelompok perlakuan dan kelompok kontrol dalam kaitannya dengan kadar hemoglobin, serum feritin dan prevalensi ADB.

MATERI DAN METODA

Studi *quasi experimental* with *randomized pre and post test control group design* dilakukan di Kecamatan Abiansemal, Kabupaten-Badung pada Mei 2006 - Januari 2007. opulasi adalah pasangan yang merencakan kehamilan dimana sampel adalah ibu dengan ADB ringan. Sejumlah 99 pasangan yang belum hamil terdiri atas 47 sebagai kelompok perlakuan dan 52 sebagai kelompok kontrol. Pada kedua kelompok dilakukan 3 kali pemeriksaan serum feritin dan kadar hemoglobin (Hb) yaitu pra-hamil, awal hamil dan 3 bulan hamil. Pada kelompok perlakuan diberikan tablet besi 66 mg ferrous sulfate per oral sejak pra-hamil sampai dengan 3 bulan kehamilan. Sementara, pada kelompok control diberikan tablet yang sama mulai saat hamil sampai dengan 3 bulan hamil. Data anamnesis tentang efek samping dan kepatuhan mengkonsumsi tablet besi dicatat khusus. Rasio beaya-keuntungan dianalisis dengan Cost-benefit ratio (BCR) [14].

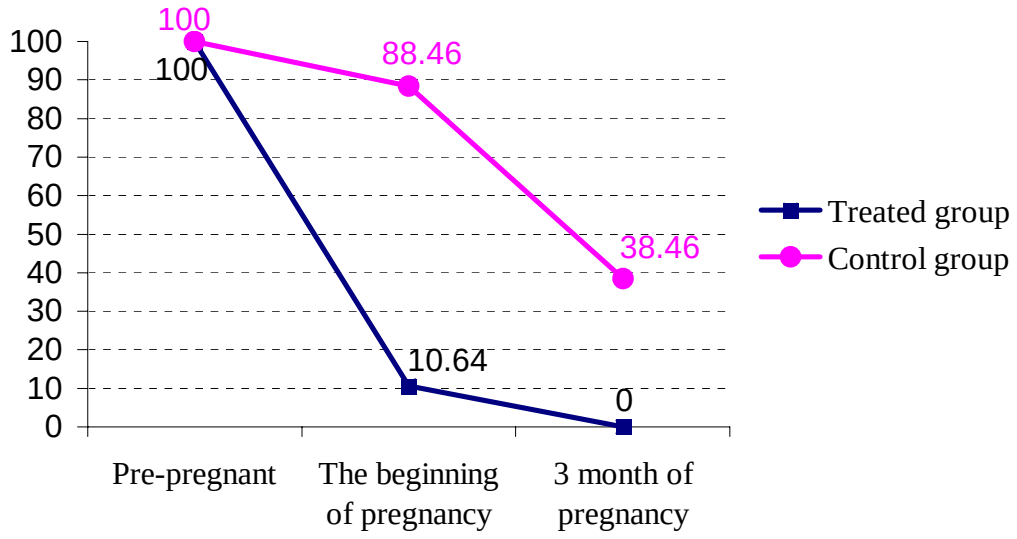
HASIL

Karakteristik sampel pada kedua kelompok untuk variabel umur, pendidikan dan pekerjaan adalah homogen. Pada kelompok perlakuan dan kelompok kontrol, rerata umur adalah 24.47±4.03 dan 25.71±3.81. Pendidikan sekolah dasar, sekolah menengah, dan akademi dimana terbanyak setingkat sekolah menegah atas adalah 25 (53.19%) pad kelompok perlakuan dan 23 (44.23%) pada kelompok kontrol. Terdapat variasi pekerjaan

pada sampel seperti petani, pedagang, buruh, swasta dan pegawai negeri sipil. Persentase pekerjaan yang paling tinggi adalah buruh yaitu 53.19% pada kelompok perlakuan dan 44.23% kelompok kontrol. Perbedaan ini dinyatakan tidak bermakna secara statistik ($p > 0.05$).

Pemberian tablet besi dari masa sebelum hamil (kelompok perlakuan) dapat mencegah ADB lebih banyak dibandingkan dengan pemberian tablet besi dimulai pada awal kehamilan (kelompok kontrol) (gambar 1). Pada kelompok perlakuan tidak ditemukan kasus ADB (0%), sedangkan pada kelompok kontrol prevalensi ADB adalah 38.46% pada akhir pengamatan. Perbedaan ini dinyatakan bermakna secara statistik ($p<0.05$).

Prevalensi ADB (%)



Gambar 1. Pengaruh pemberian tablet besi terhadap prevalensi ADB pada kelompok perlakuan dan kelompok kontrol

Perbedaan juga terlihat pada rerata kadar feritin serum dan hemoglobin. Rerata feritin serum kelompok perlakuan pada awal pengamatan, awal kehamilan dan tiga bulan usia kehamilan adalah 14,95±4,21 µg/dL, 25,68±9,0 µg/dL dan 33,45±14,12 µg/dL; sedangkan pada kelompok kontrol adalah 13,94±4,18 µg/dL, 13,32±4,25 µg/dL dan 19,65±8,99µg/dL. Rerata kadar hemoglobin pada kelompok perlakuan adalah 10,26±0,66

g/dL, 11,52±1,05 g/dL dan 12,25±1,20 g/dL; sedangkan pada kelompok kontrol adalah 10,19±0,63 g/dL, 10,23±0,55 g/dL, dan 10,91±0,67 g/dL. Perbedaan rerata serum ferritin dan hemoglobin pada kedua kelompok adalah berbeda bermakna secara statistic dengan p <0.05 (tabel 1).

Tabel 1. Distribusi rerata kadar serum feritin dan hemoglobin pada kelompok perlakuan dan kelompok kontrol

	Kelompok Perlakuan (N=47)		Kelompok Kontrol (N=52)		t	p
	Mean	SD	Mean	SD		
Feritin pada pra-hamil	14,95	4,21	13,94	4,18	1,193	0,230
Hb pada pra-hamil	10,26	0,66	10,19	0,63	0,477	0,060
Feritin pada awal hamil	25,68	9,00	13,32	4,25	9,088	0,000
Hb pada awal hamil	11,52	1,05	10,23	0,55	7,515	0,000
Feritin pad 3 bulan hamil	33,45	14,12	19,65	8,99	5,413	0,000
Hb pada 3 bulan hamil	12,25	1,20	10,91	0,67	6,462	0,000

SD = Standard deviation
Hemoglobin: g/dl
Serum ferritin: µg/dL

Efek samping tablet besi yang ditemukan adalah mual, dyspepsia dan konstipasi tetapi hal tersebut adalah minimal dan tidak terdapat perbedaan bermakna pada kedua kelompok. Kepatuhan sample untuk tindk lanjut adalah sangat baik dimana 44 dari 47 pada kelompok perlakuan dan 50 dari 52 pada kelompok kontrol dimana secara statistic tidak berbeda bermakna.

Beaya pemberian tablet besi sejak pra-hamil adalah Rp. 7.560 untuk kelompok perlakuan; sedangkan untuk kelompok kontrol adalah Rp. 3.240,-. Keuntungan yang diperoleh pada efek ADB (berat badan lahir rendah, prematuritas dan abortus spontan) dan harga suplementasi besi. Secara ekonomi, akibat yang ditimbulkan oleh pemberian tablet besi dihitung berdasarkan atas efek beaya rumah sakit yang ditimbulkan seperti

berat badan lahir rendah, prematuritas dan abortus [7] dimna kalkulasinya dapat dilihat pada tabel 2.

Tabel 2. Prakiraan rasio keuntungan pada pemberian tablet besi pada ibu hamil dengan ADB ringan terhadap berat badan lahir rendah, prematuritas dan abortus

Keuntungan		Kelompok Perlakuan	Kelompok Kontrol
		Proportion without IDA = 100%	Proportion without IDA = 61.54%
		Incidence without Low Birth Weight = 95%	Incidence without Low Birth Weight = 51.5%
1. Berat badan lahir rendah	Rp 135.934	Rp 129.137	Rp 43.081
		Incidence without Prematurity = 93%	Incidence without Prematurity = 76%
2. Prematuritas	Rp 276.346	Rp 257.001	Rp 129.248
		Incidence without Abortion = 90%	Incidence without Abortion = 70%
3. Abortus	Rp 317.021	Rp. 285.318	Rp. 136.566

Konskuensinya, nilai BCR dapat dihitung dengan membandingkan keuntungan dan beaya pada pemberian tablet besi pada kedua kelompok seperti yang terlihat pada tabel 3.

Table 3. CBR pada pemberian tablet besi pada kelompok perlakuan dan kelompok kontrol

Risiko	BCR	
	Kelompok Perlakuan	Kelompok Kontrol
Berat badan lahir rendah	7.4	3.2
Prematuritas	14.6	9.3
Abortus	16.3	10.2

Pada tabel 3 terlihat bahwa BCR pada berat badan lahir rendah, prematuritas dan abortus adalah lebih besar 1 yang artinya bahwa pemberian tablet besi sejak pra-hamil memberikan nilai ekonomis lebih tinggi dibandingkan pemberian tablet besi pada yang dimulai waktu hamil.

DISKUSI

Anemia defisiensi besi (ADB) masih merupakan masalah utama bagi kesehatan masyarakat di negara berkembang, termasuk Indonesia [1,11,14]. Wanita hamil dan anak-anak usia dibawah lima tahun adalah kelompok yang paling sering mengalami ADB. Faktor utama dalam masalah ini adalah rendahnya bioavibilitas besi diet harian dan tingginya kebutuhan besi bagi wanita hamil dan anak-anak selama masa pertumbuhan. WHO[14] menganjurkan program standar untuk mengontrol ADB pada wanita hamil, "*iron pills program*". Setiap wanita hamil akan diberikan 90 tablet besi (66 mg sulfas ferosus dikombinasikan dengan asam folat). Indonesia mengadopsi program WHO ini [7,10].Hasil dari program ini tidak memuaskan. Tidak ada penurunan ADB pada wanita hamil secara signifikan, termasuk di Indonesia [8,9,10,11]. Tidak ada penjelasan secara ilmiah untuk menjelaskan kesenjangan ini. Kesenjangan ini diasumsikan bahwa di negara berkembang, cadangan besi tubuh pada wanita hamil sangat rendah atau mungkin kosong sehingga program pemberian tablet besi tidak cukup untuk memenuhi cadangan besi tubuh selama masa kehamilan. Pemberian tablet besi sejaka masa prahamil dibutuhkan untuk mengisi cadangan besi dan memenuhi peningkatan kebutuhan besi selama kehamilan.[12]

Hasil dari penelitian ini mendukung asumsi. Pemberian tablet besi sejak masa prahamil dapat meningkatkan kadar feritin serum dan hemoglobin dan mencegah ADB pada wanita hamil dengan anemia defisiensi besi derajat ringan. Cadangan besi dapat meningkat menjadi 33 µg/dL, melebihi *cut off point* (20 µg/dL), sedangkan cadangan besi pada kelompok kontrol hanya 19,65 µg/dL, masih lebih rendah dari *cut off point.*

Dampak positif dari program ini diperoleh dari analisis rasio antara manfaat dan biaya (BCR). Nilai BCR lebih dari 1, dapat disimpulkan bahwa program ini sangat bermanfaat. Program ini sangat feasible karena efek samping pemberian tablet besi rendah dan kepatuhan pasien tinggi. Beberapa studi lapangan yang terkait di berbagai demografi dan geografi yang berbeda dibutuhkan untuk konfirmasi hasil penelitian ini sebelum diterapkan secara formal.

KESIMPULAN

Pemberian tablet besi sejak masa pra-hamil pada wanita hamil memberikan hasil lebih baik dibandingkan dengan pemberian tablet besi syang dimulai pada awal kehamilan. Hal ini didukung dengan penemuan kadar rerata feritin serum dan kadar hemoglobin, rerata keduanya lebih tinggi pada kelompok perlakuan dibandingkan dengan kelompok kontrol. Program ini juga lebih efektif dalam pencegahan ADB pada wanita hamil serta sangat mungkin di implementasikan pada masyarakat.

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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

Iron deficiency anemia (IDA) is still to be a problem of pregnant women health related to its high prevalence and its negative effects on health. Prevention efforts have been carried out through administration of oral iron tablet 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. To test this hypothesis, a quasi experimental study was conducted on 99 non-pregnant new couple women consisting of 47 women in treated group and 52 in control group. Iron tablet (200 mg ferrous sulfate) was administrated to treated group from the beginning of pre-pregnant period, continued until the first 3 months of pregnancy, while in control group iron tablet was 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. The research result showed that administration of oral iron tablet since pre-pregnant 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 significance difference was also observed on mean serum feritin concentration at the end of observation (the third month of pregnancy) 33.45±14.12 µg/dL on treated group, and 19.65±8.99 µg/dL on control group. This difference was statistically significant ($p<0.05$). Meanwhile, the hemoglobin concentration was 12.25±1.20 g/dL on treated group and 10.91±0.67 g/dL on control group. This difference was also statistically significant ($p<0.05$). Benefit analysis showed that administration of oral iron tablet starting from pre-pregnancy is more advantage (*BCR* >1) compared to oral administration of iron tablet during pregnant period only. There were no significant difference on side effect and compliance of the patient to consume iron pills in both treated and control group. Based on these results, it can be concluded that administration of oral iron tablet (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: pregnant woman, iron deficiency anemia, iron supplementation.

INTRODUCTION

Iron deficiency anemia (IDA) is still to be 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 %,[1] and in Bali is reported to be 46,2% .[2]

The high prevalence of IDA in pregnant women, leads to negative impacts on health as well as on economic aspect. 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 this conditions it will correlated with low IQ, and decrease ability of learning. All these effect, lead to impairment of quality of human being, 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 "ironpill 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. [8,9.10.11]

An iron store theory was developed to explain the failure of iron pill program in controlling IDA in pregnant women.[12] In developing countries, due to inadequate of iron intake, women had a low, or empty iron store before pregnancy. In pregnancy, iron requirement increase, abruptly, the total iron requirement during pregnancy is about 1000 mg.[13] This high requirement, in the setting of 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 above assumption, a field trial was held in which iron supplementation was given since pre-pregnant period, compared with 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 group in term of hemoglobin concentration, serum ferritin level and prevalence of IDA.

MATERIALS AND METHOD

This research was held at the district of Abiansemal, Badung Regency on 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 marriage women with mild IDA. Samples are 99 marriage women and not pregnancy yet, consist of 52 control group and 47 treated group. 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 third month of pregnancy (end of observation). On treated group iron tablet (66 mg ferrous sulfate) were given orally since pre-pregnant period until the first 3 months of pregnancy, meanwhile on control group, oral iron tablet were given from the beginning of pregnancy until the first 3 months of pregnancy. Data on side effects and compliance to consume iron pill were collected by anamnesis on a special record. Cost-benefit ratio is assessed by BCR analysis.[14]

RESULTS

The characteristic of patients in treated and control group were similar in regard of age, education and occupation. The mean age are 24.47±4.03 years among treated group and 25.71±3.81 years among 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 treated group and 23 (44.23%) in control group. There were various occupation among samples, such as farmer, merchant, labor, private workers and state employee. The highest percentage of occupation was labor, 53.19% in treated group and 44.23% in control group. All the differences were not statistically significant ($p > 0.05$).

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

Prevalence of IDA (%)

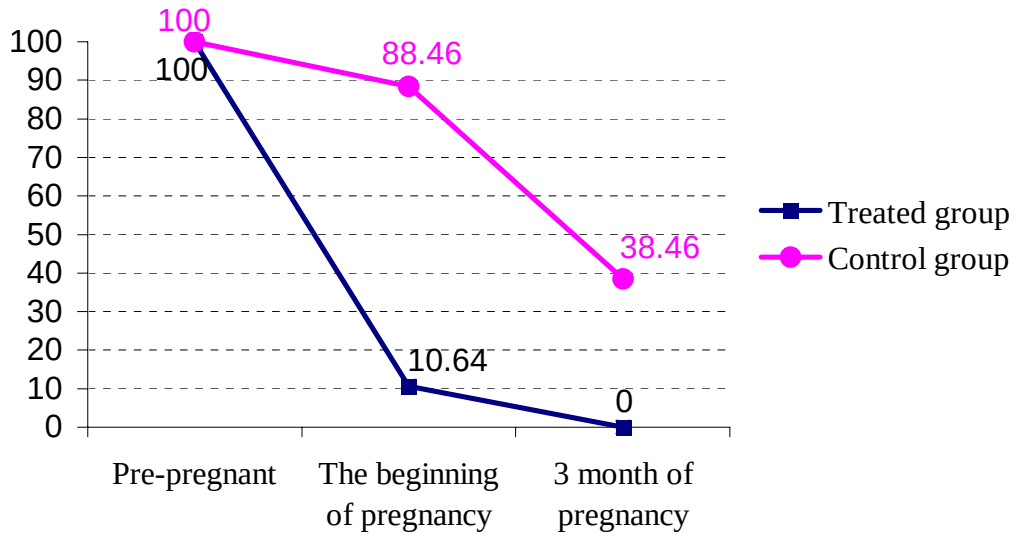

Figure 1.
The effect of iron supplementation on the prevalence of IDA in treated and control group

Differences were also seen on mean of 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)

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

SD = Standard deviation
Hemoglobin: g/dl
Ferritin serum: µg/dL

Side effects of iron tablet found were nausea, stomach discomfort, and constipation, but these side effects were very mild, both in 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 pill was found in 44 among 47 subjects in treated group, and 50 among 52 subjects of control group. This difference was not statistically significant.

The spending cost for administration of iron tablet started in pre-pregnant period was Rp. 7.560,- (treated group), while the spending cost of administration of iron tablet 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 iron tablet is calculated from the cost of hospital such as low birth weight, prematurity and abortion. [7] The calculation of benefit ratio can be seen on table 2.

Table 2
The estimation of benefit ratio of administration of iron tablet 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%
		Incidence without Low Birth Weight = 95%	Incidence without Low Birth Weight = 51.5%
1. Low Birth Weight	Rp 135.934	Rp 129.137	Rp 43.081
		Incidence without Prematurity = 93%	Incidence without Prematurity = 76%
2. Prematurity	Rp 276.346	Rp 257.001	Rp 129.248
		Incidence without Abortion = 90%	Incidence without Abortion = 70%
3. Abortion	Rp 317.021	Rp. 285.318	Rp. 136.566

Subsequently, the BCR value can be determined by comparing the benefit with cost of administration of iron tablet between the two groups, as shown on table 3.

Table 3
The Cost- Benefit Ratio of administration of iron tablet in treted 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

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 give 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 country, iron store of pregnant women is very low, or may be empty, so the "iron pills program" is not enough to restore the iron store during pregnant 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]

The result of this study support this assumption. Iron supplementation since pre-pregnant period could increase serum ferritin and hemoglobin level, and prevent IDA in pregnant women with mild IDA. Iron store can increase to 33 µg/dL, more than cut off point (20 µg/dL), while in 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. The BCR is more than one; 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 demographical 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 tablet from pre-pregnant period in pregnant women gives better result compared with administration of iron tablet started just on the beginning of pregnancy. It is supported by the findings on mean serum ferritin and hemoglobin level; both were higher in treated group compared with control group. This program is also more effective in preventing IDA in pregnant women, with a good feasibility in its implementation in the community.

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