Jurnal Kesehatan Ibu dan Anak
Vol.15, No.1, July 2021, pp. 18~24
10.29238/kia.v15i1.975

ISSN: 2599-3224 (Online)
ISSN: 2302-6014 (Print)

Suplementation of iron assosiated with increasing cholesterol levels in pregnant women

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ARTICLE INFO

Article history:

Received March 3rd, 2021
Revised December 14th, 2021
Accepted Month 16th, 2021

Keyword:

Cholesterol, Iron supplementation, Pregnant women

ABSTRACT

Iron supplementation is the most broadly utilized way to deal with controlling the worldwide issue of iron lack paleness. This study aimed to prove the effect of iron supplementation on cholesterol levels of pregnant women. This study was experimental study which type was 3 groups with the post-test only design was employed to determine the cholesterol level in pregnant women. The sample was the pregnant women in Kepuharjo Village, Yogyakarta, Indonesia who intake iron supplements. It's classified the intervention into 3 groups as no iron supplement use, iron supplement use ? 90 tablets and iron supplement use > 90 tablets. Each group included 30 pregnant women who fulfilled the inclusion and exclusion criteria. Cholesterol level were presented with mean and standard deviation. ANOVA with LSD were performed to compare cholesterol level from all groups to the respective iron supplement group. The results revealed that cholesterol level among no iron supplement use, iron supplement use ? 90 tablets and iron supplement use > 90 tablets were 152.53 (SD 34.67), 175.53 (SD 34.67) and 239.50 (SD 41.27), respectively. There was a significant difference among the mean cholesterol level on three groups. The post-hoc test showed the group of iron supplement use less than equal to 90 tablets and the group of iron supplement use > 90 tablets differed statistically significantly in term of their cholesterol level. Optimum iron supplement dosage should be considered for pregnant women.

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INTRODUCTION

Pregnancy is a physiological process in which anatomical, physiological and biochemical adaptations occur in line with gestational age. It is a critical time in a woman's life, when good nutrition can influence and improve her and her child's health. Unfortunately, almost **154 million women aged 20-49** are **underweight** and close to **613 million women of reproductive age (15-49 years)** are **anemic,** of whom approximately **35 million** are **pregnant women, globally[1].** As well as Indonesia that had 37% of pregnancy induced anemia in 2003[2]. Anemia are key risk factors for complications during pregnancy, delivery and poor birth outcomes, including preterm birth and low birth weight (LBW) babies.

Maternal anemia puts the mother at increased risk of death during and after childbirth, most likely due to hemorrhage[3]. Anemia at any point during pregnancy also increases the risk of poor neonatal outcomes[4]. Because of the hemodilution process during pregnancy results decrease in hemoglobin levels and increased iron requirements in pregnant women[5]. Iron requirements increases about 1000 mg compared with non-pregnant women[6,7]. Insufficient iron status during pregnancy can lead to changes in the formation of new blood vessels in the placenta, reducing the availability of nutrients and oxygen for the fetus; restricting its growth and resulting in a baby with low or insufficient birth weight[8]. Daily iron and folic acid (IFA) supplementation is commended by World Health Organization (WHO) to improve iron stores and prevent maternal anemia, puerperal sepsis, low birth weight, and preterm birth[9]. In 2018, Nutrition International supported national governments in Asia and Africa to reach an additional **1.2 million pregnant women** who consumed at least 90 IFA supplements. This improved the iron status of an estimated **185,000 pregnant women** and in turn averted approximately **56,000 cases** of **LBW.**

The Ministry of Health recommends that pregnant women in the second trimester take 60 mg iron and 0.25 mg folic acid daily for 90 d. Women obtain their IFA supplements from a variety of sources, including health care facilities, mainly from midwives when attending antenatal care checkups, through self-purchase over the counter from drug shops, or through trained traditional birth attendants[10]. While the study of Casanueva & Viteri showed that a dose of 60 mg / day during pregnancy in normal pregnant women caused hemoconcentration, decrease birth weight and increase prematurity[11]. According to Stoltz & Dreyfuss found iron supplementation should be done in the right case[12]. Iron supplements and increased iron reserved in blood was associated with complications in pregnant women and increased oxidative stress which causes an increasing in lipid peroxidase during pregnancy. Excessive iron is also reported to reduce placental perfusion so that it caused preeclampsia, low birth weight and preterm birth[13].

Lipid profiles in healthy women during pregnancy usually increase significantly. Total cholesterol, HDL and LDL increased by 25-50%, while triglycerides increased two to four times more than before pregnancy[14]. Hypercholesterolemia causes pervasive vascular reactivity which can affect the supply of oxygen and nutrients to the fetus through the placenta. Cholesterol is a very necessary source for fetal hormone synthesis. Although cholesterol is needed for normal fetal growth, excess cholesterol in pregnant women should be evaluated if it is a risk factor during pregnancy and fetal development[15]. A study showed LBW because of hypercholesterolemia, where hypercholesterolemia shows excessive accumulation of lipids in the placenta[16].

Kepuharjo Village, Klaten Regency is one of the villages with very good coverage of antenatal visits. The coverage of iron administration shows that 100% of pregnant women have iron supplementation, 62% consume iron regularly until the baby is born, 28% consume iron only until the third trimester and the amount is more than 90 tablets and 10% consume irregular iron and the number is less than 90 tablets during pregnancy. Iron overload is thought to be one of the causes of oxidative stress characterized by increased lipid peroxidase. Sullivan reports that increased iron levels are characterized by an increase in ferritin levels above 200, cholesterol levels also increase, especially low density lipoprotein (LDL) or bad cholesterol[17]. This increase was followed by increases in blood sugar, blood pressure and triglyceride levels while high density lipoprotein (HDL) or good cholesterol levels decreased[17].

Many studies in animals and humans prove the transfer of cholesterol through the trophoblast layer that carries HDL and LDL particles. The concentration of fat, lipoprotein and apolipoprotein increased significantly during pregnancy. Fat storage mainly takes place in the middle of pregnancy. This fat is available to be channeled through the placenta during the last trimester when the rate of fetal growth is maximal along with the need for essential fatty acids. It was necessary to study the effect iron supplementation on cholesterol levels

of pregnant women. Choi et al (2001) that total cholesterol levels insevere anemia group significantly lower in the other groups. Serum lipid concentrations in women with anemia was significantly higher after iron supplementation[18]. Coi & Pai (2000) reported that serum triglycerides, total cholesterol levels increase gradually during pregnancy[19]. Therefore, This study aimed to prove the effect of iron suplementation on cholesterol levels of pregnant women.

METHOD

An experimental study which type was 3 groups with post-test only design was employed to find the cholesterol level in pregnant women who consumed iron supplement. It classified the intervention into 3 groups as no iron supplement use, iron supplement use ≤ 90 tablets (iron supplement dosage 60 mg/tablet) and iron supplement use > 90 tablets (iron supplement dosage 60 mg/tablet). This research was through an ethical clearance from the health research ethics commission with the number 838/KEPK/VII/2018.

This research studied in Kepuharjo Village, Cangkringan, Indonesia on August 2018. Target population: pregnant women in Kepuharjo Village, Cangkringan, Indonesia. Pregnant women in the age group of 20-35 years were included in the study.

On the other hand, pregnant women with medical history of thyroid dysfunction and abnormal lipid profiles, chronic renal disease, malabsorption syndrome, and hypersensitivity to iron were excluded from the study. All the pregnant women who fulfilled the inclusion and exclusion criteria were recruited for this study after getting a written informed consent from them. Convenient sampling method was adopted. The selected 30 pregnant women did not receive oral iron supplement (control group), 30 pregnant women consumed ≤ 90 tablets (treatment I) and 30 pregnant women consumed substances iron > 90 tablets (treatment II). They were followed up for 9-month duration and at the end of the study period, the cholesterol level was assessed in the blood parameters.

Data analysis was done by using a computer software. Quantitative data (age, Hb, RBC count, etc.) collected were presented with mean and standard deviation. One-way Analysis of Variance analysis (ANOVA) with least significant different (LSD) multiple comparison post-hoc test was performed in order to compare data from all groups to controls or to the respective iron supplement group. Values of $p < 0.05$ were considered statistically significant.

RESULTS

In this study the results of data analysis on the normality test were carried out using the Kolmogorov Smirnov test on ratio scale data, namely cholesterol levels in pregnant women. Based on the results of the Kolmogorov Simonov's test, it was found that the cholesterol data of each observation group showed a p-value of 0.200 which was greater than the significance level $\propto = 0.05$. So, the data has met the parametric prerequisite test, that is, the data proved to be normally distributed.

This study found that average cholesterol level in pregnant women with ≤ 90 tablet iron supplement intake, > 90 tablet iron supplement intake, and none (control group) were 175.53 (SD 34.67), 239.50 (SD 41.27) and 152.53 (SD 34.67), respectively. Levene's test for homogeneity of variances showed the variances in cholesterol level was the same for each of three groups (p= 0.132). There was a significant difference among the mean cholesterol level on three groups.

Table 1. Descriptive study of mean and SD of cholesterol levels between group in pregnant women

Groups of iron supplement	n	mean	SD
None	30	152.53	34.67
≤ 90 tablet	30	175.33	22.90
> 90 tablet	30	239.50	41.27

The post-hoc test for multiple compared mean of cholesterol level between pregnant women with ≤ 90 tablet iron supplement intake, > 90 tablet iron supplement intake, and none (control group). There was the statistically significant of the difference in term of their cholesterol level. (Table 2)

Table 2. One-way ANOVA with multiple comparison of cholesterol levels between group in pregnant women

Groups of iron supplement		**mean difference**	**SE**	**sig**
None	≤ 90 tablet	-35.333	10.910	0.002
	≤ 90 tablet	-86.967	10.910	0.000
≤ 90 tablet	None	35.333	10.910	0.002
	> 90 tablet	-51.633	10.910	0.000
> 90 tablet	None	86.967	10.910	0.000
	≤ 90 tablet	51.633	10.910	0,000

DISCUSSION

Based on the analysis of cholesterol levels in Table I, it was found that there was a significant increase in the mean cholesterol level from the control group to group P1, then there was an increase in P2. Cholesterol levels that increase with increasing doses describe conditions where there is excessive iron and can cause reactive oxygen speises (ROS) which causes cell damage. Provision of routine iron supplements without medical indications (Hb and low iron stores) can worsen the risk of oxidative stress[i]. In accordance with a study conducted by Sullivan that an increase in iron levels is characterized by an increase in ferritin levels along with an increase in cholesterol levels[17]. Increases especially LDL and triglyceride levels while HDL levels decrease[17]. Iron overload also causes increased levels of uric acid, triglycerides, very low-density lipoprotein (VLDL), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), urea and creatinine[ii].

The Turbino-Ribeiro's study that iron overload causes cellular damage and functional abnormalities in hepatocytes by the lipid peroxidation process[20]. The liver has an important role in maintaining lipid homeostasis so that excess iron can alter serum lipid concentrations which can reduce or increase the risk of atherosclerosis[20]. As a result of lipid peroxidation, the membranes in other cells also become damaged resulting in changes in important elements such as blood pressure and heart rate[20]. Increased LDL cholesterol, decreased HDL cholesterol and changes in systolic blood pressure have been shown to be risk factors for atherosclerosis and cardiovascular disease[20].

Tiwari *et al* noticed modifications in the lipid profiles in iron inadequate pregnant pallid ladies[21]. The grouping of absolute lipid, complete cholesterol and phospholipid were discovered to be fundamentally diminished in pregnant frail ladies[21]. The decrease of lipids might be corresponded with the iron insufficiency pallor instigated expanded lipid peroxidation[21]. These outcomes are like those revealed before in pre-eclampsic pregnant ladies[20]. It very well might be recommended that an overabundance of ROS in iron lacking patients caused the oxidative debasement of RBC lipids bringing about diminished degree of lipids in these patients[22]. The RBC is a significant wellspring of oxygenrelated revolutionaries in iron lack pallor (IDA). Notwithstanding, IDA, RBCs produces more prominent amounts of $O2^{\cdot-}$, H2O2 and OH° than do ordinary RBC[23]. Additionally, iron lack frailty, RBCs display expanded degrees of thiobarbituric corrosive responsive substances, recommending that they are targets for oxidative pressure[24]. During deoxygenation of

hemoglobin, there is an exchange of electrons between iron iota and O2 prompting the creation of $O2^{\cdot-}$. Physiological auto-oxidation of hemoglobin likewise prompts the creation of free extremists. Inside the RBC, one of the focuses of oxidant harm is the plasma layer[23]. In the presence of $O2^{\cdot-}$generating framework, iron (III) is diminished to iron (II) with resulting development of OH˚ and H2O2[24]. The hydroxyl extremist oxidizes unsaturated esterified film lipids, bringing about changes in smoothness of the bilayer[25]. Cholesterol in RBC layer regularly[26]. These results are reliable with the reports of examiners, exhibiting that dietary iron supplementation expands plasma lipids in iron inadequate young ladies and in rodents[27,28]. Ohira *et al* found that all out cholesterol fixations were raised after an increment in hemoglobin levels by bonding and iron treatment[29]. They likewise revealed that the grouping of red platelets may influence cholesterol combination or its assembly from tissue to plasma[29].

Fatty substances were discovered to be raised in iron insufficient frail ladies as contrasted and the controls and further expanded after oral iron treatment[21]. The increment in serum TG might be because of hypoactivity of lipoprotein lipase in veins that separates TG[29].The grouping of HDL was discovered to be diminished after iron inadequacy weakness and after iron supplementation[21]. Expanded degrees of LPO or VLDL and LDL in pre treated patients and even greatest augmentation of these lipoproteins in charge and gentle post regarded subjects as contrast with moderate and serious pallid patients are known to be cytotoxic to cells and tissues[21]. As of late it has been stressed that hyperlipemic β-lipoproteins are cytotoxic to cells and tissues probably because of upgraded levels of related LPO[30]. Lipids assume huge part in different issues like cardiovascular, hyperlipidemia greasy liver. It alters the piece, structure, and steadiness of cell films. Abundance lipid in the blood is considered to quicken the improvement of arteriosclerosis[30]. An adjusted lipid digestion can modify the cardiovascular capacity by changing the properties of heart cell layer and these progressions may add to the cell passing[30]. Late reports demonstrate that cytotoxicity incited by LDL and VLDL can result from lipoprotein oxidation[30]. Eventually demonstrated by the general measure of MDA counterparts or thiobarbituric corrosive responding substances (Ski lifts) living on the lipoprotein[31]. Opposite the consequences of Salonen et al., which would propose that people with iron insufficiency ought not be treated with supplements because of conceivable unfavorable occasions, the consequences of the present test study showed that proportions of oxidative pressure were influenced by a helpful portion of iron in ladies with low iron status[32].

CONCLUSION

This study showed significant increase cholesterol levels with higher consumption of iron in pregnant women. The group of iron supplement use ≤ 90 tablets and the group of iron supplement use > 90 tablets differed statistically significantly in term of their cholesterol level.

Suplementation of iron should consider the status and needs of iron in pregnant women. This procedure can be used as a screening for iron needs in pregnant women so that it does not cause iron overload which will cause various impacts on the iron homeostatis in the body.

ACKNOWLEDGEMENTS

We sincerely thank all my subjects for participated in this study. Special thanks go to all the health staffs of Primary Health Center Cangkringan for supporting to collect the data smoothly. Moreover, another special thanks to Higher Education Service Institution Region V Yogyakarta for funding this research.

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