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EFFECT OF BLOOD DONATION ON FERRITIN LEVELS AND LIPID PROFILE IN SUBJECTS WITH CENTRAL OBESITY

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ABSTRACT

Introduction. Several studies showed that inflammation is associated with the dyslipidemia. Ferritin is one of the inflammation marker which its level influenced by blood donation. Central Obesity in young adults may have benefit by blood donation because of this mechanism. Aim of this study was to compare the lipid profile between routine blood donation and non-routine blood donation subjects with central obesity.

Methods: Fourty-one appearantly health male obese subjects were enrolled in this study. To further investigate this topic, a lipid profile and ferritin level were evaluated in 21 routine blood donation male obese subjects and the other 20 non routine blood donation subjects as control. We use t-test to determine the difference of the mean level of Total Cholesterol, LDL, TG, and HDL.

Results. Mean level of Total Cholesterol in routine blood donation is lower than control group (198,2 vs 224,52; $p=0,011$). The LDL level was lower in routine blood donation than non routine group (130,10 vs 153,76; $p=0,013$), while Triglycerides level was significantly lower in this group (97,75 vs 137,38, $p=0,010$). In this study, mean level of HDL (46,75 vs 43,57; $p=0,276$) and Feritin (228,93 vs 269,4) was not significantly different between routine blood donation subjects as compare to control group.

Conclusion. Cholesterol, LDL, and TG level in routine blood donation subjects were significantly lower as compare to non-routine blood donation subjects.

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INTRODUCTION

Central obesity is a main component of metabolic syndrome that can cause cardiovascular complication. Pathogenesis of metabolic syndrome remains unclear, but recent study indicated there was oxidative stress catalysis. In addition, iron accumulation exceeding physiologic requirement can affect oxidative stress. Positive relation between iron reserve and insulin resistance/ diabetes has been known from several epidemiology studies. Serum ferritin level correlate with hypertension retinopathy and clinical hypertension characterized by increase prevalence of iron body excess. Ferritin and transferrin significantly correlate with presence of metabolic syndrome and its components and increase of ferritin level is a independent predictor of vascular damage in patient with Non-alcoholic Fatty Liver Disease (NAFLD) and metabolic syndrome¹

Similar thing has happened with new intervention that iron-chelation agent administration and blood donation can prevent diabetes in individual with iron excessive. Reduction of iron reserve in patient with type 2 DM with phlebotomy can increase insulin sensitivity in patient with diabetes. In recent study, repeat phlebotomy could reduce blood glucose and serum lipid level. In patient with steatohepatitis non-alcoholic, phlebotomy also can reduce insulin concentration. There was also report that low iron dietary positively influenced cardiovascular risk in patient with type 2 DM. In observational study of 15 patients with refractory essential hypertension with 3 regimens therapy has found that repeated phlebotomy followed by decline of blood pressure.^{2,3}

In recent studies, there was improvement of lipid profile in patient with metabolic syndrome underwent phlebotomy. These studies proved benefit of blood donor to donor's well-being. Most of these studies was done to subjects with metabolic syndrome and has never been done in Indonesia. It encourages authors to do this study.

METHODS

Study Population

Eligible patients were male aged 18-40 years, body weight more than 50 kg, waist circumference more than 90 cm, and agree to join this study and signed approval sheet after given informed consent. The Exclusion criteria included patient with kidney function impairment (eGFR reduction < 60 mL/min), anemia, acute infection, and consume statin.

Study design and procedures

This study was analytic descriptive with cross-sectional approach at Sam Ratulangi University. Total 41 subjects met research criteria were divided into two groups, 21 routine blood donation male obese subjects and the other 20 nonroutine blood donation subjects as control. They consecutively obtained as samples and underwent complete peripheral blood, ferritin, kidney function, and lipid profile test.

Statistical methods

Research samples were members of research population who met inclusion and exclusion criteria. Sample size in this study was determined by Kirk formulation to evaluate hypothesis of comparative problems ≥ 2 groups. From this formula, kirk table it was obtained $n = 17$ participants/ groups. Minimal samples from 17 was fulfilled to 20 participants. Statistical analysis use t-test to determine the difference of the mean level of Total Cholesterol, LDL, TG, and HDL

Assesment

Central Obesity is defined with waist circumference measure. Waist circumference is measured with patient stand with feet shoulder width apart 25 to 30 cm without footwear. Examiner is beside subject. Waist circumference is measured horizontally circular from central point between the top of crista iliaca and bottom edge of last rib in media line. Central obesity is waist circumference ≥ 90 cm for men and ≥ 80 cm for women. Phlebotomy is a process to draw blood from cubital median vein. After aseptic and antiseptic technique is done in right or left arm area, cubital median vein is detained with cuff at 60 mmHg (or between systolic and diastolic pressure). Patient is asked to make a fist, then needle for donate is inserted to cubital median vein at 30° angle or less and blood is drawn to blood bag. Patient is asked to open and close the fist every 10-12 seconds, make sure blood flow smoothly, and release tourniquet when blood flow is stable or after 2 minutes. While this process occurs, observe subject to evaluate presence of sweat, pale, or dizziness. Phlebotomy is done while patient in supine position. After obtaining 300 cc, withdraw the needle. Press gauze pad onto puncture site, ask patient to elevate their arm while keep pressing the puncture site (Kolegium IPD, 2017). Frequent donor is subject frequently donate blood at least twice per year within previous two years. Infrequent donor is subject that has never been donated blood or once in more than previous year. Anemia: definition and classification of anemia are

determined based on WHO criteria hemoglobin level is less than 12 g/dL (7.5 mmol/L) in women and less than 13 g/dL (8.1 mmol/L) in men.

Iron status: show iron status in body with Serum Iron (SI), Total Iron Binding Capacity (TIBC), and Ferritin Serum (FS). Kidney Function Impairment is defined by measurement of estimated glomerulus filtration rate according to CKD-EPI.

RESULTS

The result shows there were 41 men with central obesity aged 22-39 years. From this number, 20 subjects frequently donated their blood and 21 subjects infrequently donated. All subjects had normal kidney function (creatinine less than 1.2). Table one show the characteristics subject.

Analysis difference of total cholesterol, ferritin serum, LDL level, HDL level, and TG level mean

between frequent donor group and infrequent donor group using unpaired t test are shown in table 2.

DISCUSSION

This study was aimed to evaluate ferritin level and lipid profile features in young adult men with central obesity frequently donating their blood. In addition, this study also compared ferritin level and lipid profile between frequent donor group blood (228.93 vs. and infrequent donor group as control. In this study, there was a difference in ferritin level it was due to in control group, some subjects had not too big waist circumference (91 cm), mean between subjects with central obesity frequently and infrequently donating indeed serum ferritin remained in normal range, even at minimal value of all groups. In contrast, in frequent donor group, there was a subject with larger waist circumference (> 110 cm) and higher serum ferritin level (> 600).

Table 1. Patients Characteristic.

Variable	N	Min	Max	Mean	SB
Age	41	22	39	30,09	5,001
Total Cholesterol	41	120	278	211,68	33,893
LDL	41	73	217	141,93	28,922
HDL	41	29	73	45,16	9,0825
Triglycerida	41	50	247	117,565	46,2505
Feritin	41	52,7	858	249,659	172,603
Creatinine	41	0,77	1,15	0,9390	0,11764

Table 2. Analysis Difference Of Total Cholesterol, Ferritin Serum, Ldl Level, Hdl Level, And Tg Level Mean Between Frequent Donor Group And Infrequent Donor Group.

Variable	Group	n	Mean	SB	p
Total cholesterol	Frequent donor	20	198,2	32,542	0,011
	Infrequent donor	21	224,52	30,602	
Feritin Serum	Frequent donor	20	228,93	135,62	0,196
	Infrequent donor	21	269,40	203,15	
LDL level	Frequent group	20	130,10	27,491	0,013
	Infrequent group	21	153,76	30,353	
HDL level	Frequent donor	20	46,75	7,833	0,276
	Infrequent donor	21	43,57	10,332	
TG level	Frequent donor	20	97,75	37,233	0,010
	Infrequent donor	21	137,38	55,268	

Abdullah SM did not found a significant difference in serum ferritin level between frequent donor group and infrequent donor group. Their research subjects were not limited to central obesity. They

involved subjects aged 19-50 years while our study involved subjects aged 18-40 years.⁴

Serum ferritin level shows balance between secretion and clearance, mainly in liver. Ferritin is also originated from adipocyte formed by macrophage

entering adipose tissue.⁵ Recent study in Korea found increase of serum ferritin level in young adult men with central obesity compared with non-central obesity subject⁶ Phlebotomy (blood donate) is expected to reduce ferritin level within body. Study by Adams et al. found reduction of ferritin level in patient with non-alcoholic fatty liver disease undergoing phlebotomy, even though there was no a significant correlation between serum ferritin level with LED, CRP, or liver inflammation degree according to biopsy.⁷ There was other study that found a significant difference of ferritin level mean ($p < 0.001$) in subjects with metabolic syndrome after phlebotomy.⁸

In this study, it were also found significant differences in total cholesterol, LDL, and trigliserida between frequent donor group compared with infrequent donor group. In frequent donor group, total cholesterol mean was 198.2 compared with 224.52 in control group ($p = 0.011$). Comparison of LDL level mean was 130.10 vs 153.76 ($p = 0.013$), and comparison of trigliserida level mean was 97.75 vs. 137.38 ($p = 0.010$) in frequent donor group and infrequent donor group, respectively. HDL level in subjects with central obesity frequently donating their blood was higher compared to subject infrequently donating blood (46.75 vs. 43.57, respectively) even it was no statistically significant ($p = 0.276$). It was different with study by Veeravich J et al. that found significantly increase of HDL level in subjects underwent phlebotomy.⁹

Other study in Nigeria by Uche et al. involved 52 voluntary donors (case group) and 30 not regularly donors (control group) evaluated lipid profile from both groups. Uche et al. found significantly lower lipid profile in case group compared with control group. They concluded that blood donate regularly might give protection to cardiovascular disease as shown by significantly lower total cholesterol level and LDL cholesterol in regular donor group.¹⁰

Veeravich J et al. evaluating subjects with non-alcoholic fatty liver disease found significantly reduction of trigliserida, HOMA-IR, and SGOT and SGPT level after phlebotomy.⁹

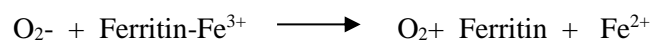
Improvement of lipid profile in subjects with central obesity frequently donating blood mainly correlates with inflammation status and ferritin level change in body. Higher ferritin level in body leads easily oxidize of LDL to oxLDL.¹¹ Ferritin level mean in subjects frequently donating blood was lower compared to subjects infrequently donating blood, even though it was no statistically significant.

Central obesity is a risk factor for dyslipidemia and chronic inflammation within body. With excessive

body weight, there will be increase of adipose tissue, lipid, and blood volume. Adipose tissue in its inflammation response will secrete IL-6 and TNF- α . Excessive of body weight is followed with increase of blood volume and its component, including ferritin.¹²

Every day, there is approximately 10,000 cells breakdown, mainly DNA and many enzymes, due to oxidative stress from superoxide. Most of the oxidative damage is caused by iron mobilization from feritin form and also caused by involvement of free iron in redox reaction.

Ferro ion formed in redox reaction reacts to lipid peroxide (e.g. oxidized LDL) and inducing oxidative chain reaction in phospholipid membrane.



This oxidation process plays a role in development of atherosclerosis heart disease and stroke.¹³ Solanen et al. reviewed cohort Kupio Ischaemic Heart Disease Risk Factor Study in 2,862 men aged 42-60 years in 1984 to 1995 found that frequent loss of blood in blood donation might correlate with reduce of acute myocardium infarct risk in men with middle age. That result supported animal experimental hypothesis that iron overload promoted atherosclerosis and impaired of myocardium.¹⁴

Ascherio et al. in 1992 found other result, that there was no a significant correlation between blood donor frequency with risk of myocardium infarct.¹⁵ Cross sectional study from R.S. Bharadwaj in India involved 157 voluntary donors found there was a very significantly difference in lipid profile between group donating blood in previous 2 years and group donating blood within 1 last year. Bharadwaj also concluded that voluntary donors would got more benefit if frequently donated blood, at least once in a year.¹⁶ Study in Nigeria by Adias et al. involving 150 subjects frequently donating blood and 90 initially donating blood has found a significantly difference reduction of total cholesterol in frequently donor group compared with subjects initially donating blood. Adias concluded that repeated blood donor could reduce lipid profile.¹⁷

CONCLUSION

In Conclusion Cholesterol, LDL, and TG level in routine blood donation subjects were significantly lower as compare to non-routine blood donation subjects Frequent blood donate improve lipid profile in men with central obesity aged 18-40 years. As a recommendation

socialization about blood donation benefit in lipid profile donors with central obesity is needed

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