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Original Research Articles

## The Differences of Lipoprotein-Associated Phospholipase A2, Apolipoprotein B, and Low-Density Lipoprotein in Obese and Lean Men

Yuliana Yuliana<sup>1\*</sup>, Purwanto Adipireno<sup>2</sup>, Edward Kurnia Setiawan Limijadi<sup>2</sup>, Nyoman Suci Widyastiti<sup>2,3</sup>, Dwi Retnoningrum<sup>2,4</sup>

<sup>1</sup>Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia

<sup>2</sup>Department of Clinical Pathology, Faculty of Medicine, Universitas Diponegoro, Semarang, Indonesia

<sup>3</sup>Department of Clinical Pathology, dr. Kariadi Hospital, Semarang, Indonesia

<sup>4</sup>Department of Clinical Pathology, Diponegoro National Hospital Semarang, Indonesia

### Article Info

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### Abstract

**Background:** An increase in fat accumulation in obesity has been suggested to link with an increase in inflammation. This inflammation may be associated with an elevated of Lipoprotein-Associated Phospholipase A2 (Lp-PLA2), Apolipoprotein B (Apo B), and Low-Density Lipoprotein (LDL), thereby associated with the risk of atherosclerosis.

**Objective:** To investigate the differences between Lp-PLA2, Apo B, and LDL levels in obese and lean men.

**Methods:** A cross-sectional study was conducted on 74 men (obese and lean) at the Faculty of Medicine, Universitas Diponegoro, Indonesia, in 2020. The concentration of LDL was measured using the homogenous enzymatic colourimetric method, whereas the levels of Lp-PLA2 and Apo B were determined using the ELISA method. Data were analyzed using an Independent t-test, setting statistical significance at  $p < 0.05$ .

**Results:** This study showed that Lp-PLA2 levels were significantly different between obese and lean men ( $p = 0.039$ ). Furthermore, LDL levels were also significantly different between obese and lean men ( $p = 0.002$ ). However, we did not find any differences in Apo B between obese and lean men ( $p = 0.640$ ).

**Conclusion:** Lp-PLA2 and LDL levels were slightly higher in obese compared to lean men, but no difference of Apo B.

**Keywords:** *Lp-PLA2, Apo B, LDL, Obesity, Men.*

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### INTRODUCTION

Obesity is a condition of excessive fat accumulation in adipose tissue.<sup>1</sup> This disease has reached an epidemic as the major causative factor for many metabolic disorders.<sup>2</sup> In 2014, World Health Organization (WHO) were estimated that more than 1,9 billion people are overweight, with the prevalence's of 39% classified as overweight and 13% classified as obese.<sup>3</sup>

Basic Health Research (RISKESDAS) report in 2013 and 2018 showed an increase in obese individuals from 14,8% to 21,8%.<sup>4</sup> Obesity in adults (> 18 years old), according to RISKESDAS, is defined by the body mass index (BMI) criteria of  $\geq 27$  kg/m<sup>2</sup>.<sup>4</sup> Obesity is associated with the risk factors contributing in developing atherosclerosis.<sup>5</sup>

Obesity has been characterized by inflammation both in adipose tissue and systemic.<sup>6</sup> This inflammation process may be associated with Lipoprotein-associated phospholipase A2 (Lp-PLA2). Although Lp-PLA2 is an enzyme specific in vascular inflammation, which has

\* Corresponding author:

E-mail: [yuliana040190@gmail.com](mailto:yuliana040190@gmail.com)  
(Yuliana)

been suggested not be affected by systemic inflammation,<sup>7</sup> Lp-PLA2 levels may be used as an accurate and precise diagnostic tool in detecting atherosclerosis.<sup>8</sup> Lipoprotein-associated phospholipase A2 was produced by inflammatory cells and circulate while binding to lipoprotein in an active form in plasma cells.<sup>9-11</sup> About 80% of Lp-PLA2 is bound to apolipoprotein B (Apo B) from low-density lipoprotein (LDL), mainly found in small dense LDL (sdLDL), while the rest is bound to high-density lipoprotein (HDL) and very-low-density lipoprotein (VLDL).<sup>11-13</sup>

## MATERIALS AND METHODS

This was a cross-sectional study. The study was conducted in the Faculty of Medicine, Universitas Diponegoro, Semarang, during a time period from July to September 2020. Lp-PLA2 and Apo B measurements were carried out in the GAKI laboratory, Faculty of Medicine, Universitas Diponegoro, Semarang, while the LDL profile was measured at CITO Laboratory Semarang.

Subjects were gathered by consecutive sampling. The research sample was divided into obese men and lean

**Table 1.** Subject characteristic

Variable	Obese (n = 36)		Lean (n = 38)		p
	Mean±SD	Median (min-max)	Mean±SB	Median (min-max)	
Age (year)	30,64 ± 5,42	31 (21-43)	28,89 ± 5,22	30 (20-41)	0,163 †
Blood systolic pressure (mmHg)#	120,59 ± 7,33	120 (108-138)	118,08 ± 7,74	118 (108-138)	0,052 M
Blood diastolic pressure (mmHg)#	79,64 ± 6,42	80 (68-90)	78,82 ± 7,23	80 (67-90)	0,547 M
Weight (Kg)#	97,44 ± 14,72	91,5 (78-135)	63,37 ± 6,05	63,5 (50-76)	0,000* M
Height (cm)	171,58 ± 4,33	171,5 (162-180)	168,08 ± 5,27	167,5 (157-178)	0,003*†
BMI (kg/m2)#	33,08 ± 4,49	31,38 (27,36-47,36)	22,44 ± 1,63	22,85 (19,06-24,8)	0,000* M

SD, standard deviation; min, minimum; max, maximum; BMI, Body Mass Index; #Abnormal data distribution; \*significant ( $p < 0,05$ ); M Mann Whitney; † independent t-test.

**Table 2.** Difference of Lp-PLA2, Apo B and LDL level on obese and lean men

Variable	Obese (n = 36)		Lean (n = 38)		p
	Mean±SD	(min-max)	Mean±SD	(min-max)	
Lp-PLA2 (ng/mL)	147,09 ± 30,93	(74,3-200)	129,29 ± 40,77	(33 - 201)	0,039*
Apo B (mg/dL)	143,42 ± 87,86	(33-352)	143,24 ± 73,76	(48 - 328)	0,64
LDL (mg/dL)	135,17 ± 24,07	(93-193)	114,5 ± 30,48	(54 - 184)	0,002*

Data was analyzed by independent t-test.

SD, standard deviation; min, minimum; max, maximum; LDL, low density lipoprotein; Lp-PLA2, lipoprotein associated phospholipase A2; Apo-B, apolipoprotein B; \*, significant ( $p < 0,05$ ).

Apolipoprotein B (Apo B) is a large glycoprotein that plays a role in lipoprotein and lipid transport in humans.<sup>14</sup> Apo B levels are often used in estimating the number of atherogenic particles.<sup>15</sup>

Low-density lipoprotein (LDL) is the main cholesterol carrier in the blood, about 45% of all lipoprotein types.<sup>16</sup> The proportion of total cholesterol and LDL levels are factors contributing to developing atherosclerosis and its clinical manifestation, including coronary artery disease (CAD).<sup>17</sup> However, coronary artery disease can also occur in patients presenting with low LDL levels ( $<100$  mg/dL).<sup>18</sup> The mortality rate of patients with coronary artery disease with a total cholesterol level profile of  $<200$  mg/dL was 35%.<sup>19</sup>

Lp-PLA2 dan Apo B level measurement may help detect the possibility of atherosclerosis. Normal LDL profile will not guarantee and predict individual health. This study was conducted to analyze the differences in Lp-PLA2, Apo B, and LDL levels in obese and lean men.

men obtained in the Faculty of Medicine, Universitas Diponegoro, who met the inclusion and exclusion criteria. The inclusion criteria were as follows; obese men with BMI of  $27 \text{ kg/m}^2$ , lean men with BMI  $18.5 - <24.9 \text{ kg/m}^2$ , age 18-49 years, and not on a vegetarian diet. Exclusion criteria were alcohol drinkers, smokers, diabetes mellitus, liver disease, and kidney disease. A total of 74 samples was obtained.

Samples were taken after each individual underwent fasting for 8-10 hours before the examination, and the serum was examined. LDL levels were measured using the homogenous enzymatic colourimetric method, and the Lp-PLA2 and Apo B levels using the ELISA method. Data analysis includes descriptive analysis and hypothesis testing. The data for each variable was tested for normality of the data with the Shapiro Wilk test. Data were then analyzed using the Independent t-test, setting statistical significance at  $p < 0.05$ . The Medical Research Ethics Committee had approved the study at The Faculty of Medicine Universitas Diponegoro Semarang.

## RESULTS

Subjects of 74 were recruited divided into two groups of 36 (48,6%) obese men and 38 (51,45) lean men. The mean age of the study in the obese male group was older than the lean male group. The median BMI was 31,38 (27,36-47,36) kg/m<sup>2</sup> in obese male group, and 22,85 (19,06-24,8) kg/m<sup>2</sup> in lean male group (Table 1).

Data obtained and then analyzed are as follows (Table 2); Lp-PLA2, Apo B, and LDL on the obese and lean groups. Concentration of Lp-PLA2 was significantly different ( $p=0,039$ ). Furthermore, LDL levels were also significantly different ( $p=0,002$ ). However, there was no significant difference in Apo B values ( $p=0,64$ ).

## DISCUSSION

This study included 74 respondents consist of 36 (48,6%) obese men and 38 (51,4%) lean men. Our study showed that Lp-PLA2 levels were significantly different between obese and lean men. Furthermore, LDL levels were also significantly different between obese and lean men. However, we did not find any differences in Apo B between obese and lean men.

The results showed that the mean Lp-PLA2 level was higher in the obese male group of  $147.09 \pm 30.93$  ng/ml compared to the lean male group of  $129.29 \pm 40.77$  ng/ml. A study by Da Silva et al. showed that the Lp-PLA2 was positively correlated with obesity ( $p=0.003$ ).<sup>20</sup> The obtained analysis from the Independent t-test on Lp-PLA2 levels between obese men and lean men was a significant difference with the p-value of 0,039.

The difference in Lp-PLA2 levels between obese and lean men may partly be explained by fat accumulation within adipose tissue in obesity. Adipose tissue has the ability to enlarge and be elastic. Hypertrophic adipocytes are dysfunctional and lipolytic, which will produce excessive free fatty acids. As revealed by the spillover hypothesis, the limited ability of adipose tissue to expand causes free fatty acids spillover to non-adipose tissue to be excessive. According to the portal theory, the accumulation of fatty tissue in the central body that produces excessive free fatty acids will increase the amount of free fatty acid transfer to the liver through the portal vein<sup>22</sup>. A study by Jackisch et al. stated that adipocytes are a source of Lp-PLA2, and their capacity to influence oxLDL production contributes to obesity-mediated inflammation. In addition, Lp-PLA2 absorbs unfavorable circulating lipid profiles, including increased oxLDL and triacylglycerol.<sup>23</sup> Oxidized low-density lipoprotein may function as a chemoattractant for monocyte to migrate from the circulation to the sub endothelium space and differentiate into macrophages. Macrophages will then phagocytize the oxLDL in order for foam cells to be formed in the sub endothelium. Monocytes and macrophages may stimulate the synthesis of Lp-PLA2 enzyme in response to an increase in oxLDL (Shi et al.) in the sub endothelium, the substrate of the Lp-PLA2 enzyme<sup>24</sup> so that Lp-PLA2 levels in obesity are likely to be higher.

Lipoprotein-associated phospholipase A2 (Lp-PLA2) is an enzyme specific in vascular inflammation which will not be affected by systemic inflammation.<sup>7</sup> This enzyme may aid the identification of atherosclerosis.<sup>8</sup> Atherosclerotic plaques, especially the lipid core and

macrophages in the fibrous capsule of the rupture-prone lesion, express Lp-PLA2. This indicates that Lp-PLA2 may apply as a marker of plaque destabilization before the rupture of arterial plaque.<sup>25-27</sup> In our study, the mean Lp-PLA2 levels in both groups were within the reference value of <200 ng/ml, however, in these findings, the occurrence of the might rupture plaque probably has not occurred yet. Histopathological studies have shown that the elevation of Lp-PLA2 levels are prone to occur in unstable plaques with thin fibrous caps and large lipid cores, which indicates the Lp-PLA2 is more likely related to plaque quality than their dimensions.<sup>28</sup>

Obesity indeed causes impairment of lipoprotein metabolism, especially LDL. This began with the overproduction of VLDL by the liver due to ectopic fat accumulation in the liver. An elevated VLDL production leads to an increased LDL concentration.<sup>29</sup> This part in line with the result from our study, which showed that the mean LDL level was higher in the obese male group of  $135.17 \pm 24.07$  mg/dl than the lean male group of  $114.50 \pm 30.48$  mg/dl. These results are in accordance with the study of Khan et al., which found significantly higher LDL levels in obese men compared to non-obese men ( $p<0.05$ ).<sup>30</sup> Aljaffar's research (2018) also found significantly higher LDL levels in the obese group compared to the non-obese group ( $p\leq 0.05$ ).<sup>31</sup> Research by Kanwar et al. found that there was a significant difference in LDL in the obese compared to non-obese groups with  $p < 0.0001$ .<sup>32</sup> Kaniawati et al. reported there was no significant difference between obese male adolescents and non-obese male adolescents ( $p=0,105$ ).<sup>15</sup> Results from the Independent t-test analysis reports that the LDL value between obese and norm weight men obtained  $p=0,002$ , indicating the significant difference between obese and lean men.

The results showed Apo B levels in obese men were approximately  $143.42 \pm 87.86$  mg/dl, while in lean men, it was  $143.24 \pm 73.76$  mg/dl. The obtained analysis using an Independent t-test on Apo B levels between obese and lean men result in no significant difference in Apo B with  $p=0,64$ . A study by Da Silva et al. showed no significant difference in Apo B levels between obese and non-obese adolescents (0,533).<sup>20</sup> However, in a study by Kaniawati et al. found significant differences in Apo B profile in obese male adolescents than non-obese male adolescents ( $p=0,04$ ).<sup>15</sup> A study reported by Sakka et al. also found significantly higher Apo B levels in obese male children than lean men-children ( $p < 0,001$ ).<sup>21</sup>

Obese individuals are frequently characterized by having a high accumulation of triglycerides profiles deposits under the skin. Triglycerides are the main component of VLDL formation in the liver so that obesity may be the result of the elevation of total cholesterol level, VLDL, and LDL.<sup>33</sup> Apolipoprotein B is a marker of a number of atherogenic particles. Apo B is present in every atherogenic lipoprotein particle, including LDL, sdLDL, IDL, and VLDL<sup>14</sup>. LDL cholesterol measurement does not give an accurate impression of the patient's higher *small dense* LDL proportions than cholesterol LDL, which indicates that Apo B measurement is a better marker than LDL overall.<sup>34</sup> Our study showed no significant difference in Apo B levels between the two groups. These findings may be influenced by VLDL, IDL, and sdLDL proportions

because our study did not measure these levels, which is a limitation of this study.

## CONCLUSION

There were differences in Lp-PLA2 and LDL levels, while no difference in the Apo B levels between obese and lean men.

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