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# Expression of Peroxisome Proliferator-Activated Receptor Gamma Coactivator 1α Increases After 8-Weeks of Endurance Training in Obese Females

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### ABSTRACT

This study aimed to prove the effect of moderate-intensity aerobic exercise on increasing Peroxisome proliferator-activated receptor-gamma coactivator-1alpha (PGC-1 $\alpha$ ) levels in obese women. A total of 12 women aged 20-25, with body mass index (BMI) of 25-30 kg/m2, normal systolic blood pressure, and normal resting heart rate as subjects in the study. Subjects were randomly divided into 2 groups, namely K1 (n=6; control without intervention) and K2 (n=6; aerobic exercise). The exercise was carried out with an intensity of 60% -70% HRmax, frequency 3x/week for 8 weeks. Pretest and posttest PGC-1 $\alpha$  levels were analyzed using the Enzyme-linked immunosorbent assay (ELISA) method. The data analysis technique uses the Paired Sample T-Test with a significant level of 5%. Based on the results of the study it was concluded that aerobic exercise with an intensity of 60% -70% HRmax with a frequency of 3x/week for 8 weeks affected increasing PGC-1 $\alpha$  levels in obese women.

Keywords: Physical Exercise; PGC-1a Levels; Myokine; Obesity; Metabolism.

# INTRODUCTION

Peroxisome proliferator-activated receptor-gamma coactivator  $1\alpha$  (PGC- $1\alpha$ ) was found to be low in obese individuals (Fang et al., 2019). Previous studies have also found lower levels of PGC- $1\alpha$  in obese individuals compared to normal-weight individuals (Lanzi et al., 2014; Vaccari et al., 2020). Another study also reported that PGC- $1\alpha$  levels were found to be lower in obese individuals compared to normal-weight individuals (Liu et al., 2015; Fang et al., 2019). Physical exercise has been believed to increase PGC- $1\alpha$  levels, but the right exercise to increase PGC- $1\alpha$  levels is still controversial.

Low PGC-1 $\alpha$  levels lead to decreased muscle oxidative metabolism (Jeong et al., 2016). Low metabolism leads to lipid accumulation, decreased muscle mass, and

triglyceride energy storage (Arhire et al., 2019). Low PGC-1α levels can also lead to insulin resistance (Balampanis et al., 2019). It, therefore, impacts the body's functional ability to alter the body's homeostasis, which results in the onset of metabolic syndrome diseases, such as type II diabetes mellitus, cardiovascular disease and hypertension (Lobstein & Jackson 2006; Lupita et al., 2020). Worse conditions can lead to premature death (Collison et al., 2010; Lupita et al., 2020).

Moderate-intensity exercise has been shown to increase PGC-1 $\alpha$  levels, both acutely and chronically (Dinas et al. 2017). Research by Shirvani & Arabzadeh (2020) showed that aerobic exercise can increase PGC-1 $\alpha$  levels. However, research from Pekkala et al. (2014) reported that low-intensity exercise did not increase PGC-1 $\alpha$  levels and research from Lim et al. (2019) also reported that weight training did not increase PGC-1 $\alpha$  levels. Based on the background, the researchers wanted to reveal the effect of aerobic exercise with moderate intensity on increasing PGC-1 $\alpha$  levels in obese women.

### METHOD

This study was a true experiment with the research design of the randomized pretest-posttest control group design (Rejeki et al., 2023). using 12 female adolescents aged 20-25, body mass index (BMI) 25-30 kg/m<sup>2</sup>, normal systolic blood pressure, normal resting heart rate, body fat percentage  $\geq$  30%, and divided into 2 groups randomly, namely the control group without intervention totalling 6 subjects and the exercise group given aerobic exercise intervention totalling 6 subjects.

Blood sampling from the cubital vein as much as 4 mL was carried out in the morning. Blood was taken twice for the pre-test and post-test. For 15 minutes the blood will be centrifuged at 3000 rpm then the serum was separated and will be stored at -80°C to be analyzed for PGC- 1 $\alpha$  levels the following day. The serum that has been obtained was then examined for PGC-1 $\alpha$  levels using the Enzyme Link Immunosorbent Assay (ELISA) kit method (Cat.No.: E-EL-H6017; Elabscience, Inc., USA) (Sugiharto et al., 2021).

Aerobic exercise was performed with a frequency of 3x/week for 8 weeks. Aerobic exercise was done by running on a treadmill with an intensity of 60-70% HRmax, with a 45-minute training volume consisting of 5 minutes of warm-up (50% HRmax), 35 minutes of core exercise (60-70% HRmax), closed with 5 minutes of cooling (50% HRmax) (Pranoto et al., 2023). The exercise was carried out every 6:00-10:00 WIB using a treadmill

(Richter Treadmill (4.0HP DC), Taipei, Taiwan, R.O.C) (Pranoto et al., 2023).

Data analysis technique using SPSS version 21.0. The normality test used the Shapiro-Wilk test, while to determine the difference in serum PGC-1 $\alpha$  levels between the pretest vs posttest in each using the Paired Sample T-Test test, while to determine the difference in serum PGC-1 $\alpha$  levels between groups using the Independent Samples T-Test with a significant level ( $p \le 0.05$ ).

### RESULTS

The results of descriptive analysis, from the characteristics of the research subjects can be seen in Table 1 below.

	•			-	-	-
Variable	n -	<b>K</b> 1		K2		<i></i>
		Mean	SD	Mean	SD	<i>p</i> -value
Usia (tahun)	6	22.67	1.75	22.17	1.47	0.604
TDS (mmHg)	6	110.60	6.84	124.58	21.39	0.178
TDD (mmHg)	6	70.83	3.63	74.50	6.35	0.254
TB (m)	6	157.75	4.41	154.95	3.88	0.271
BB (kg)	6	71.82	8.55	76.15	15.45	0.565
IMT $(kg/m^2)$	6	31.00	3.79	31.75	5.64	0.793
BFP (kg)	6	34.87	2.93	33.33	6.16	0.599
SM (kg)	6	26.32	2.40	26.40	3.05	0.959

 Table 1.

 Results of analysis of the characteristics of research subjects in both groups

**Description:** K1: Control group; K2: Aerobic exercise group.

Based on Table 1 descriptive analysis shows that the average data on subject characteristics has the same trend in both groups. The results of the Independent Samples T Test showed that there was no significant difference in the average data characteristics of the research subjects in the two groups (p>0.05). The results of the analysis of the average PGC- 1 $\alpha$  levels between the pretest and posttest in both groups are presented in the following subchapters.

Table 2.
Analysis results of pretest and posttest PGC-1 $\alpha$ levels in each group

Group	n	Pret	Pretest		Posttest	
	ш	Mean	SD	Mean	SD	- <i>p</i> -value
K1	6	1.21	0.97	1.26	0.71	0.851
K2	6	1.09	0.29	2.84	0.27	0.000**

**Description:** (\*\*) Indicates significant value with pretest ( $p \le 0.001$ ).

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**Figure 1.** Analysis results of pretest and posttest PGC-1 $\alpha$  levels in each group. (\*) Indicates significant values with pretest ( $p \le 0.001$ ).

Moderate-intensity aerobic exercise affected increasing PGC-1 $\alpha$  greater than the control group (Table 2). Further analysis showed differences in pretest and posttest PGC-1 $\alpha$  levels between the two groups (Table 3).

Table 3.	
Analysis results of pretest and posttest PGC-1 $\alpha$ levels in both grou	ıps

Observation	Group	n	Mean	SD	<i>p</i> -value
	K1	6	1.21	0.97	
Pretest	K2	6	1.09	0.29	0.796
	K1	6	1.26	0.71	
Posttest	K2	6	2.84	0.27	0.000**

**Description**: (\*\*) Indicates significant value with pretest ( $p \le 0.001$ ).

### Discussion

Based on the results of the study, it was reported that there was an effect on a significant increase in the average PGC-1 $\alpha$  levels between pretest and posttest in the aerobic exercise group (K2), while the control group (K1) did not show any significant differences. These results are in line with research conducted by de Souza-Teixeira et al. (2018) who reported that aerobic exercise affects increasing PGC-1 $\alpha$  levels in obesity. However, another study reported no effect on increasing PGC-1 $\alpha$  levels before and after exercise (Lim et al., 2019). This difference is because the previous study used male subjects who did not have musculoskeletal, cardiovascular, and respiratory system disorders while this study used obese female subjects who are likely if left unchecked can lead to metabolic syndrome such as type II diabetes mellitus, cardiovascular disease, hypertension,

musculoskeletal disorders, etc. Research from Pekkala et al. (2014) also reported that there was no effect on the average increase in PGC-1 $\alpha$  levels. However, this difference is because the previous study provided exercise interventions with low intensity, while this study provided exercise interventions with moderate intensity. Research by Hejazi et al., (2020) reported that exercise intensity has a positive relationship with increasing PGC-1 $\alpha$  levels, the higher the intensity performed, the greater the effect on increasing PGC-1 $\alpha$  levels.

The increase in PGC-1 $\alpha$  in this study was thought to be influenced by the factor of increasing muscle mass. Muscle mass in the subject increased after giving moderateintensity aerobic exercise intervention for 8 weeks with a frequency of 3x/week. Muscle mass before the intervention amounted to (24.3 kg) and after the intervention increased to (25.2 kg) as measured using a Tanita tool. Increased muscle mass reduces fat levels in the body. Fat mass before the intervention showed a figure of (20.9 kg) and after the intervention showed a decrease to (19.3 kg). The decrease in fat mass is due to aerobic exercise which is carried out continuously giving the effect of increasing fat burners as a source of energy, so that the accumulation of fat in the body decreases and increases PGC-1 $\alpha$  and starts the formation of muscle mass. These results are in line with research conducted by Bae et al, (2018) reported that continuous muscle contraction through exercise induces an increase in PGC-1 $\alpha$  levels which increases the level of protein in muscle tissue.

Exercise increases muscle contraction which is a contributor to thermogenesis, induced by the activation of thermogenic genes, such as Uncoupling Protein-1 (UCP-1) (Knudsen et al., 2014; Sugiharto et al., 2021). Exercise increases the need for Adenosine Triphosphate (ATP) which will change the AMP/ATP ratio (Laurens et al., (2020); Sugiharto et al., 2021). The change in AMP/ATP ratio stimulates an increase in Peroxisome proliferator-activated receptor-gamma coactivator  $1\alpha$  (PGC- $1\alpha$ ) (Elizondo-Montemayor et al., 2019; Sugiharto et al., 2021) and Fibronectin Type III Domain Containing 5 (FNDC-5) which transforms into irisin molecules and is found in the blood circulation (Ikeda & Yamada., 2019; Sugiharto et al., 2021). Increased lipolysis causes the breakdown of triglyceride as an energy source to increase, increases energy expenditure through oxidation phosphorylation, and regulates glucose and lipid homeostasis, which has implications for metabolic health (Petridou et al., 2019; Sugiharto et al., 2012). This mechanism is in line with research conducted by Boström et al, (2012) reported that increased levels of PGC- $1\alpha$  in muscle cells induce the expression of type I membrane

protein FNDC-5, which is cleaved and secreted into the blood circulation. This signifies that thermogenic genes are interrelated and influence each other, with PGC-1 $\alpha$  as a key regulator of biogenesis (Halling & Pilegaard., 2020; Sugiharto et al., 2021). It is hypothesized that 24 hours after exercise, thermogenic genes are expected to remain active. These conditions are favourable and attractive for the browning process in maintaining homeostasis in response to a decreased AMP/ATP ratio and increased biogenesis in mitochondria (McKie & Wright., 2020; Sugiharto et al., 2021). The decrease in AMP/ATP ratio causes AMPK to activate, which is observed to occur 3 hours after exercise (Skovgaard et al., 2016; Sugiharto et al., 2021). AMPK activation triggers PGC- $1\alpha$  gene receptor activation stimulating an increase in FNDC-5, which then cleaves into circulating irisin to activate UCP-1 (Park et al., 2020; Sugiharto et al., 2021). Consequently, PGC-1α-induced activation of UCP-1 enhances browning (Otero-Díaz et al., 2020; Sugiharto et al., 2021). This process increases energy generation through oxidative phosphorylation and energy expenditure (Yang et al., 2020; Sugiharto et al., 2021). It also increases browning capacity, which can oxidize glucose and lipids as energy sources (Castro et al., 2020; Sugiharto et al., 2021).

# **CONCLUSIONS AND SUGGESTIONS**

#### Conclusions

Based on the results of the study, it was concluded that aerobic exercise with an intensity of 60%-70% HRmax with a frequency of 3x/week for 8 weeks affected increasing PGC-1 $\alpha$  levels in obese women.

#### Suggestion

Based on the results of the study, it can be suggested to do moderate-intensity aerobic exercise to increase PGC-1 $\alpha$  levels as a way to prevent an increase in obesity rates. In addition, it is also hoped that future research will involve obese subjects in men.

#### Announcement

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