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# Changes in Serum Betatrophin Levels in Obese Women after Two-Weeks of Moderate-intensity Aerobic Exercise

**Nabila Ainaya Mubasyiroh[a], Sugiharto[b]*, Desiana Merawati[c], Nur Ezza Fazleen Mohd Fathil[d], Purwo Sri Rejeki[e], Fikri Sasongko Widyatama[f], Adi Pranoto[g]**

[a,b,c]Universitas Negeri Malang, Indonesia
[d]University Shah Alam, Malaysia
[e,f,g]Universitas Airlangga, Indonesia

**Correspondence:** sugiharto@um.ac.id
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**Abstract**

Obesity is associated with increased betatrophin levels, which can lead to fat metabolism disorders. Increased levels of betatrophin may inhibit the performance of the lipoprotein lipase (LPL) enzyme, making it difficult for triglycerides (TG) in the blood to be converted into energy and causing excessive fat accumulation in adipose tissue. Physical exercise has been reported to increase energy expenditure in obesity. This study aims to determine changes in betatrophin in obese women after moderate-intensity aerobic exercise. A total of twenty obese women aged 20-30 years took part in the study. The participants were administered into two groups: control ($K_1$) and moderate-intensity aerobic exercise ($K_2$). Moderate-intensity aerobic exercise (60-70% HRmax) was performed five times a week for two weeks. Pretest and posttest betatrophin levels were measured using the Enzyme-Linked Immunosorbent Assay (ELISA) Kit method. Data were analyzed using a paired samples t-test with a significance level of $p \leq 0.05$. The results showed the average pretest and posttest betatrophin levels in $K_1$ (0.44±0.14 vs 0.44±0.13 ng/mL; p=0.894), and $K_2$ (0.41±0.05 vs 0.31±0.03 ng/mL; p=0.000). According to the study's findings, moderate-intensity aerobic exercise (60-70% HRmax) performed five times per week for two weeks positively impacted alterations in betatrophin levels in obese women.

**Keywords:** Aerobic exercise; betatrophin levels; metabolic health; obese women

## 1. Introduction

Betatrophin was found to be high in obese individuals (Kugelberg, 2013). In previous research, betatrophin levels were found to be higher in obese individuals compared to individuals with normal body weight (Kugelberg, 2013). Other studies also show that serum betatrophin levels in obese people tend to be higher when compared to people of normal weight (Ye et al., 2019). High levels of betatrophin will have an impact on metabolic functions, such as lipid metabolism (Ye et al., 2019). Increased betatrophin will increase Triglyceride (TG) levels in the blood and cause excessive fat accumulation in adipose tissue (R. Zhang, 2016). High betatrophin also affects the production of pancreatic b cell proliferation so that when insulin needs cannot be met, insulin resistance occurs (Kugelberg, 2013).

Obesity occurs due to excessive fat accumulation in the body (Hruby & Hu, 2015). Excessive fat accumulation causes an increase in triglyceride levels and betatrophin secretion (Fu et al., 2014), which inhibits the performance of the lipoprotein lipase (LPL) enzyme (Chi et al., 2017). The inhibited LPL enzyme will make it difficult for triglycerides to be converted into energy (Xie et al., 2015). Therefore,

betatrophin secretion needs to be controlled, namely by training. Moderate-intensity aerobic exercise intervention requires the conversion of glucose into energy (Hall, 2016). A higher glucose absorption and conversion into energy can lower glucose in the blood, potentially decreasing betatrophin release (Fu et al., 2014). Thus, providing moderate-intensity aerobic exercise intervention can be used as an efficient strategy for lowering betatrophin levels (Abu-Farha et al., 2016).

A lack of exercise may increase the risk of obesity (Pavilianingtyas, 2017; Hariyanto et al., 2023). Obesity raises the risk of noncommunicable diseases (NCDs) such as cardiovascular diseases, diabetes, and hypertension (Pavilianingtyas, 2017; Sholikhah & Tuah, 2021). Exercise is a non-pharmacological treatment that can reduce the development of obesity (Karaman et al., 2022). Other studies have demonstrated that moderate-intensity exercise coupled with slow-tempo music therapy is beneficial in lowering circulating betatrophin levels (Susanto et al., 2020). Similarly, anaerobic exercise improves glucose homeostasis by modulating betatrophin levels (Karaman et al., 2022). Several studies using obesity as subjects showed that treatment with modified exercise, diet, or a combination for three to twelve months showed lifestyle changes and reduced betatrophin concentrations (Abu-Farha et al., 2016). The study found that a short-duration exercise program reduced betatrophin concentrations in 62 obese persons from 82 non-obese participants who participated in a mix of strength training and moderate-intensity aerobic exercise (Abu-Farha et al., 2016). Long-term physical activity regimens can lower betatrophin concentrations in obese individuals (Abu-Farha et al., 2017). According to a previous study, moderate-intensity exercise had a positive effect on betatrophin levels in obese individuals (Susanto et al., 2023). However, based on the research report above, no one has yet revealed the effect of aerobic exercise at a dose of five times per week for two weeks on changes in betatrophin levels in obese women. Therefore, this study aims to determine changes in betatrophin levels in obese women after moderate-intensity aerobic exercise.

## 2. Method

This was a true-experimental study involving 20 obese women selected based on predetermined criteria. Then, twenty obese women were separated into two distinct groups: the control group ($K_1$) and the moderate-intensity aerobic exercise group ($K_2$). The Health Research Ethics Committee of the Faculty of Medicine, Universitas Airlangga, authorized all methods for this study under Ethical Clearance No. 42/EC/KEPK/FKUA2023.

The participant performed aerobic exercise by running on a treadmill for 40 minutes at a moderate effort, or 60-70% HRmax, five times weekly for two weeks. Blood samples for betatrophin were collected twice: before and after therapy. Four ml was taken from the cubital vein. The Human Betatrophin ELISA Kit (Cat. No. E3381Hu; BT-Laboratory, Inc., Shanghai, China P.R.) was used to analyze betatrophin levels.

The paired sample t-test and independent sample t-test were employed to detect differences in serum betatrophin levels before and after intervention in each group, as long as the data had a normal distribution and homogenous variance. All statistical studies employed a significance level ($p \leq 0.05$). All statistical analyses were performed using the Statistical Packet for Social Science (SPSS) software version 21.0.

## 3. Result

The findings between the control group ($K_1$) and the moderate-intensity aerobic exercise group ($K_2$), as shown in Table 1, reveal no feature variations. Meanwhile, Figures 1 and 2 show the differences in betatrophin level reduction between the two groups.

**Table 1. Results of analysis of research subject characteristics in both groups**

| Parameters | $K_1$ ($n$ = 10) | $K_2$ ($n$ = 10) | p-Value |
|---|---|---|---|
| Age, years | 23.20 ± 1.47 | 23.30 ± 1.70 | 0.890 |
| Systolic blood pressure, mmHg | 114.75 ± 4.99 | 115.25 ± 3.49 | 0.799 |
| Diastolic blood pressure, mmHg | 71.10 ± 6.49 | 72.65 ± 7.72 | 0.633 |
| Resting heart rate, bpm | 73.80 ± 5.73 | 75.80 ± 3.73 | 0.369 |
| Height, m | 1.54 ± 0.03 | 1.57 ± 0.05 | 0.153 |
| Weight, kg | 71.74 ± 4.05 | 72.72 ± 7.15 | 0.712 |
| Body mass index, kg/m² | 30.25 ± 1.54 | 29.41 ± 1.66 | 0.257 |

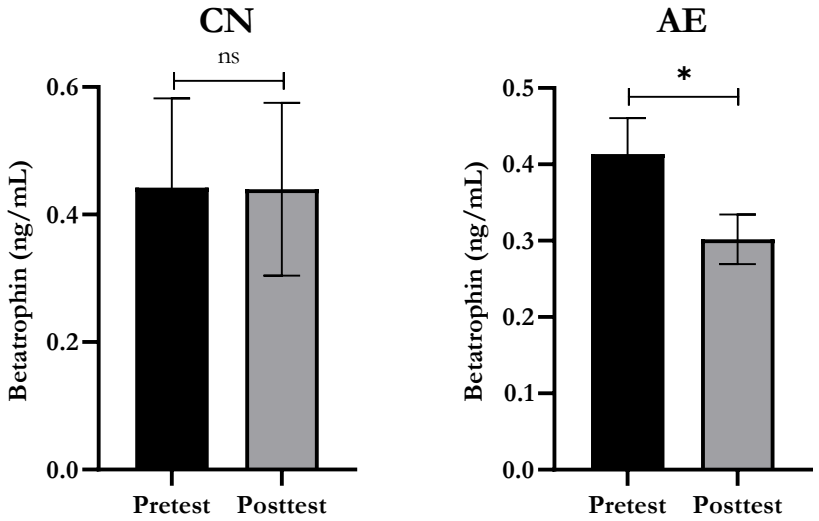


**Figure 1. Results of Betatrophin Levels Analysis in $K_1$ and $K_2$ (Pretest vs Posttest)**
**Description: (ns) Not significant (p ≥ 0.05). (*) Significant with pretest (p ≤ 0.05).**

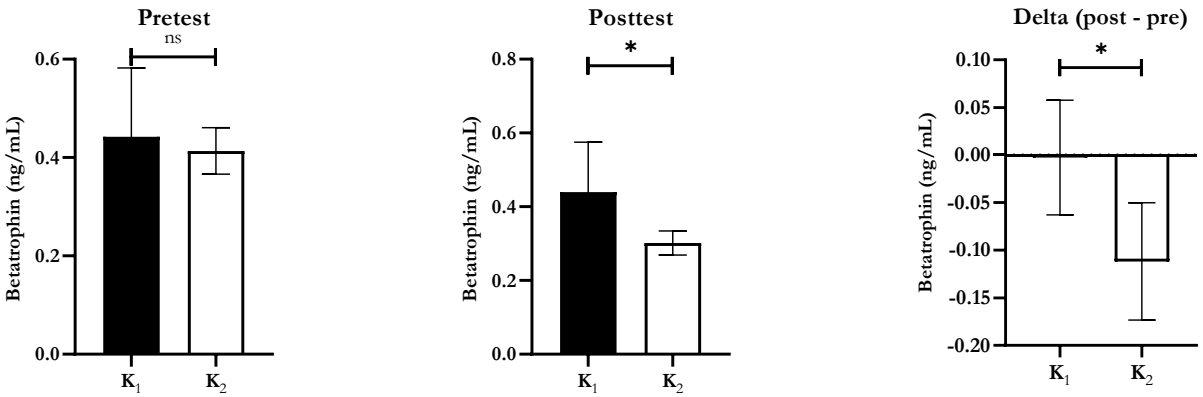


**Figure 2. Pretest, Posttest, and Delta Betatrophin Levels in Both Groups ($K_1$ vs $K_2$)**
**Description: (ns) Not significant (p ≥ 0.05). (*) Significant with a control group ($K_1$) (p ≤ 0.05).**

## 4. Discussion

This study found that betatrophin levels decreased significantly in the exercise group but not in the control group. Susanto et al. (2023) found that moderate-intensity exercise improves betatrophin levels in obese patients. According to Abu-Farha et al. (2016), a combination of 30 minutes of moderate-intensity aerobic exercise and 10 minutes of strength training on a treadmill or cycling can dramatically lower betatrophin levels in obese individuals. The study of Rejeki et al. (2022) found that moderate-intensity aerobic exercise improved betatrophin levels in obese people. Similarly, Susanto et al. (2020) found that moderate-intensity aerobic exercise might considerably lower betatrophin levels in non-professional athlete volunteers. The intervention of moderate-intensity aerobic exercise caused a reduction in betatrophin levels. Exercise intervention increased energy needs derived from blood glucose, resulting in a drop in blood glucose levels (Rejeki et al., 2022). Other studies suggest that moderate-intensity aerobic exercise can reduce blood glucose and enhance glycemic management (Zheng et al., 2020). Van Dijk et al. (2013) found that offering moderate-intensity aerobic exercise intervention to obese patients resulted in considerable blood glucose reduction. A drop in blood glucose might lead to a decrease in betatrophin production (Fu et al., 2022). Obese people with high blood glucose levels secrete more betatrophin in their livers (Zhang & Abou-Samra, 2014). Other studies have shown that glycemic management can minimize betatrophin release in addition to preventing hypoglycemia and hyperglycemia (Gusarova et al., 2014). Exercise reduces betatrophin production via activating p38MAPK, which regulates PGC-1α and stimulates irisin secretion via FNDC5 expression. The released irisin then acts on WAT, activating UCP-1, inducing betatrophin production, b cell renewal, and decreasing insulin secretion (Sanchis-Gomar & Perez-Quilis, 2014). Betatrophin knockdown can increase biogenesis beiging and mitochondria in WAT through activation of the AMPK pathway (Liao et al., 2020).

A moderate-intensity aerobic exercise intervention requires glucose to be converted into energy (Hall, 2016). Improved glucose absorption, which is transformed into energy, will lower blood glucose levels and betatrophin release (Fu et al., 2014). Thus, moderate-intensity aerobic exercise interventions can reduce betatrophin levels more efficiently (Abu-Farha et al., 2016). Exercise improves insulin sensitivity in obese people and improves the absorption of glucose by boosting the phosphorylation process of the Akt substrate AS160 in skeletal muscle (Zheng & Liu, 2015). Exercise triggers muscle contractions, which stimulate myokines. This interaction between skeletal muscle and fat is important in determining metabolic health by decreasing inflammation and enhancing lipid oxidation, thermogenesis, browning, and insulin sensitivity (Leal et al., 2018). Irisin is a key myokine involved in "cross-talk" between skeletal muscle and adipose tissue (Leal et al., 2018). Irisin, a peroxisome proliferator, stimulates PGC-1α (Boström et al., 2012). PGC-1α expression leads to increased FNDC5 expression and irisin secretion, which stimulates betatrophin expression in adipose tissue (Y. Zhang et al., 2014).

According to the information above, exercise may be used to prevent, treat, and rehabilitate a variety of conditions, including diabetes and cardiovascular disease (Demeco et al., 2022). Exercise can help persons with diabetes maintain their blood glucose levels and enhance their overall health (Palermi et al., 2022). Several factors, such as diabetics' lifestyles and behaviors, must be examined to optimize diabetes therapy (Rejeki et al., 2022). Exercise that is done appropriately and effectively is safe and useful for cardiovascular patients (Palermi et al., 2022).

The limitations of this study include the small sample size, the fact that only one parameter was measured, and the fact that the research was conducted only on obese women. This study only used a small sample size, namely, 20 obese female subjects. Therefore, future research should include more subjects on obese women. Furthermore, this study only used one parameter to restore fat metabolic function, namely using betatrophin. Thus, in future research, it is hoped that thorough research will be carried out on other parameters so that the mechanism of change in each parameter can be known specifically. Only obese female individuals were employed in this study, allowing the findings to be

generalized across genders. It is envisaged that the outcomes of this study will bring advantages and become an appropriate training model to produce changes in betatrophin levels and lower obesity rates in the future.

## 5. Conclusion and Recommendation

Based on the discussion and findings of the data analysis, it can be concluded that moderate-intensity aerobic exercise (60%-70% HRmax) with a frequency of five times per week for two weeks has a positive effect on lowering betatrophin levels in obese women.

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