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ORIGINAL ARTICLE

The effect of moderate-intensity combined exercise in decreasing inflammation in young obese women

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Abstract

Background and Study Aim: Obesity results from excessive lipid accumulation in adipose tissue, which causes low-grade inflammatory reactions. These reactions are characterized by the production of pro-inflammatory cytokines. Endurance-resistance combined exercise is believed to inhibit the activation of inflammatory pathways through several mechanisms. The aim of this study was to investigate the impact of endurance-resistance combined exercise on decreasing serum TNF-α and IL-6 levels in young obese women.

Material and Methods: A pre–post control group design was used with 16 obese women aged 20–30 years in Malang, Indonesia. Participants were randomly assigned to a control group (CG, n = 8) or a combined exercise group (EXG, n = 8). The combined exercise consisted of 20 sessions of treadmill exercise at 60–70% HRmax and circuit training at 60–70% 1RM intensity, performed over 4 weeks. Pre- and post-exercise blood samples were analyzed to measure serum TNF-α and IL-6 levels using the colorimetric assay method. Statistical analysis included independent and paired t-tests with a 5% significance threshold. Effect size was evaluated using Cohen's d, with d > 0.8 defined as large.

Results: Baseline characteristics showed no significant differences between groups. The combined exercise group demonstrated significant reductions in TNF-α (p = 0.010) and IL-6 (p = 0.018) compared to the control group, with large effect sizes for TNF-α (d = 1.23) and IL-6 (d = 1.00).

Conclusions: Moderate-intensity combined exercise significantly reduced pro-inflammatory cytokines, including TNF-α and IL-6, compared to the control group. The findings suggest that endurance-resistance combined exercise may serve as an effective therapeutic strategy for inflammatory diseases and can be recommended for obesity treatment.

Keywords: IL-6, TNF-α, combined exercise, obese women, cytokine

Introduction

Obesity represents a complex metabolic condition influenced by genetic, behavioral, and environmental factors. It is closely associated with chronic low-grade inflammation, which contributes to the development of various metabolic and cardiovascular disorders. The excessive accumulation of adipose tissue promotes the secretion of pro-inflammatory cytokines, leading to systemic inflammation and impaired metabolic homeostasis. The growing prevalence of obesity underscores the need to address its physiological consequences and health implications in different populations.

In this context, the incidence of obesity has consistently risen worldwide during recent decades. In 2022, the World Health Organization (WHO) stated that about 16% of people aged 18 years or older were obese, a figure that has doubled since 1990 [1]. The 2023 Indonesian Basic Health Research (Riskesdas) reported that the prevalence

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of obesity among individuals aged over 18 years was 23.4%, an increase from 21.8% in 2018 [2]. The prevalence of obesity among Indonesian women (31.2%) is almost twice that of men (15.7%) [2], which may be attributed to differences in adipose tissue distribution and hormonal influence [3]. Obesity is defined as excessive lipid accumulation that impairs health [1]. The increasing prevalence of obesity is a significant concern for both global and Indonesian public health because it contributes to metabolic disorders such as insulin resistance and cardiovascular disease [4].

The mechanism underlying obesity involves low-grade chronic inflammatory reactions in white adipose tissue (WAT). Hyperplasia and hypertrophy of WAT lead to decreased vascularization and eventually cause tissue necrosis [5]. The human body recognizes this injury and initiates inflammatory reactions. Immune cells involved in the reaction secrete inflammatory mediators, such as cytokines, to amplify the response. Examples of these mediators are tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) [6]. Furthermore, TNF-α impairs insulin signaling and promotes insulin resistance, contributing to the progression of metabolic syndrome [7]. While TNF-α shows only pro-inflammatory effects, IL-6 may act as both a pro-inflammatory and an anti-inflammatory cytokine, depending on the cell secreting it [6].

There are several modalities to treat obesity, targeting each step of its pathogenesis to either increase energy expenditure or decrease energy input. Physical exercise is known as an anti-obesity therapy that is less invasive while providing optimal results [8]. Exercise is also recognized for its anti-inflammatory effects [9]. The two types of exercise, endurance (aerobic) and resistance (anaerobic), have different mechanisms for reducing inflammation [10]. The WHO recommends that adults perform endurance training for at least 150 minutes per week at moderate intensity or 75 minutes per week at high intensity [11]. For resistance exercise, the American College of Sports Medicine (ACSM) suggests performing 8–10 sets weekly for different muscle groups, with each set containing 8–12 repetitions [11]. Among various exercise intensities, moderate intensity is recommended for reducing inflammation [12]. Combined exercise, which integrates endurance and resistance training in a single session, induces both anti-inflammatory mechanisms and is believed to produce better results in a shorter period [13]. However, previous studies have also shown that endurance exercise alone can reduce inflammation more effectively than combined exercise [9].

Combined exercise has been shown to decrease inflammation by reducing the secretion of pro-inflammatory cytokines. Previous studies that combined endurance exercise with resistance exercise on separate days, using low endurance frequency and moderate resistance frequency, showed significant reductions in TNF-α and IL-6 levels [14]. Meanwhile, the effect of performing endurance-resistance exercise on the same day with high frequency has not been extensively explored, especially regarding pro-inflammatory cytokines in obese women. Several studies have demonstrated that long-term exercise, performed over eight weeks, can significantly decrease pro-inflammatory cytokines [15]. However, evidence on the effects of shorter exercise periods remains limited. One study reported that two weeks of endurance exercise did not significantly reduce IL-6, while another study found increased TNF-α after three weeks of combined exercise [16, 17]. Based on this finding, the minimum duration of exercise required to produce an anti-inflammatory effect remains unclear. A meta-analysis in healthy subjects reported that a significant reduction in TNF-α levels was mainly observed in interventions with high exercise frequency (⩾3 times per week), while a significant reduction in IL-6 was more commonly reported in studies with low exercise frequency (<3 times per week). However, the analysis also showed a high level of heterogeneity among the studies, so the effectiveness of high-frequency exercise in reducing pro-inflammatory cytokines is still not fully understood and requires further investigation [18].

There is limited comparative evidence regarding circulating IL-6 concentrations between Southeast Asian and European women within a single study cohort. South Asian women have elevated circulating IL-6 levels, partly due to greater visceral fat and overall body fat percentages compared with European women [19]. Malay ethnicity, representing Southeast and South Asian populations, shows higher total and visceral adiposity compared to Chinese and Caucasian groups [20]. Therefore, South Asian women are more prone to developing type 2 diabetes than European women, and inflammation plays a central role in the development and progression of this disease [21]. These findings indicate that inflammatory-mediated diseases among Southeast Asian women should be carefully addressed in terms of their pathomechanisms and treatment approaches.

Analysis of research findings has shown that physical exercise, particularly the combination of endurance and resistance training, exerts measurable anti-inflammatory effects and contributes to the regulation of metabolic health in obesity. Researchers emphasize that exercise parameters such as frequency, duration, and intensity may differently influence cytokine responses, yet the physiological outcomes vary across populations and study designs. At the same time, variations in inflammatory markers among women of different ethnic backgrounds, as well as uncertainties regarding the optimal exercise duration and frequency, continue to limit the practical implementation of exercise-based interventions for inflammation control. These

considerations define the rationale for further investigation into how specific exercise modalities can modulate inflammatory responses in young obese women.

Although prior research has examined the effects of combined exercise on serum pro-inflammatory markers, the effectiveness of the combination method, exercise duration, and exercise frequency remains controversial. This study aims to investigate the impact of high-frequency, moderate-intensity combined exercise conducted over a four-week period on serum TNF-α and IL-6 levels in young healthy women with obesity, particularly within the Southeast Asian population. We hypothesize that moderate-intensity combined exercise performed five times per week for four weeks will decrease both TNF-α and IL-6 levels compared to the control group.

Materials and Methods

Participants

The sample size was determined using the Higgins and Kleinbaum formula, taking into account a confidence level of 95%, a margin of error of 5%, and an estimated proportion of 0.5. Based on these parameters, a minimum of sixteen participants was required. Sixteen women aged 20–30 years were included in the study. Their body mass index ranged from 25 to 35 kg/m^2 according to the Asia-Pacific criteria, and body fat percentage exceeded 40%, as measured using the Bioelectrical Impedance Analysis method. Participants had normal blood pressure (systolic 121.00 ± 10.64 mmHg, diastolic 72.13 ± 9.19 mmHg), fasting blood glucose, hemoglobin levels, resting heart rate, body temperature, and oxygen saturation. Each participant was medically certified as healthy through a clinical examination and a valid health certificate. None of the participants had a history of chronic illnesses such as heart disease, hypertension, diabetes mellitus, stroke, respiratory problems, cancer, fractures or trauma injuries, or digestive diseases. All were confirmed to have abstained from alcohol consumption, smoking, or any history of alcohol or tobacco use during the past five years.

Participant recruitment was conducted through an online registration form in June 2024 for women in Malang, Indonesia. Participants were selected using a consecutive sampling method and subsequently randomized into two groups: CG (control group; n = 8) and EXG (combined exercise group; n = 8). Randomization was performed using a computer-generated random number sequence. Allocation concealment was ensured through sequentially numbered, opaque, sealed envelopes prepared by an independent researcher who was not involved in participant recruitment or assessment. Due to the nature of the intervention, blinding of participants was not feasible; however, outcome assessors were blinded to group assignments. All study procedures received approval from the Health Research Ethics Commission, Faculty of Medicine, Universitas Airlangga (203/EC/KEPK/FKUA/2025).

Research Design

The endurance-resistance combined exercise program was performed five times weekly (Monday–Thursday and Saturday) over a four-week period for a total of 20 sessions. The exercise sessions were scheduled in the morning (06:00–10:00 a.m.), and both endurance and resistance exercises were completed on the same day. Each session followed a standardized sequence designed to optimize performance and recovery. It consisted of a warm-up, endurance exercise, resistance exercise, and cool-down phase. The warm-up and cool-down phases involved treadmill jogging using a Richter Treadmill. Endurance exercise included treadmill running at a speed of 1.5 mph and 5% inclination, at 60–70% HRmax for 30–40 minutes, measured and monitored with a Polar H7 Heart Rate Sensor. Individual HRmax was estimated using the Haskell and Fox formula (220 - age) [22, 23].

The resistance component followed circuit training that targeted both upper and lower body muscle groups. Exercises for the upper body included chest presses, overhead presses, and lat pull-downs. Exercises for the lower body consisted of hip abductions, leg presses, and leg curls. The intensity of resistance exercise was maintained at 60–70% of one-repetition maximum (1-RM), with four sets of 10–12 repetitions. Each set was followed by 30–60 seconds of active rest, and there was a 3–5 minute active rest between endurance and resistance components. The 1-RM was determined as the maximum amount of weight a participant could lift for one complete repetition of a specific exercise while maintaining proper form. Before testing, participants were provided sufficient rest to ensure optimal condition for the 1-RM test.

All exercise sessions were supervised and conducted by certified personal trainers from Atlas Sports Club Malang, maintaining a trainer-to-participant ratio ranging from 1:1 to 1:3 to ensure proper guidance and adherence to the protocol. Details of the specific endurance-resistance combined exercise program are presented in Table 1. Confounding variables in both groups were monitored using self-report questionnaires requiring participants to report their physical activity and dietary intake.

Data Collection Procedure

Blood samples (3 mL) were collected from the cubital vein before exercise (week 0) and after exercise (week 4). An 8-hour overnight fast was required before blood collection. Samples were centrifuged to separate serum, which was immediately analyzed for serum TNF-α and IL-6

levels using the Human Colorimetric Assay method at the laboratory. TNF-α levels were quantified using a Human TNF-α ELISA Kit (Catalog No. E-EL-H0109; Elabscience Biotechnology Inc., Houston, TX, USA) with a sensitivity of 4.69 pg/mL, a detection range of 7.81–500 pg/mL, and a coefficient of variation of less than 10%. IL-6 levels were measured using a Human IL-6 ELISA Kit (Catalog No. E-EL-H6156; Elabscience Biotechnology Inc., Houston, TX, USA) with a sensitivity of 0.94 pg/mL, a detection range of 1.56–100 pg/mL, and a coefficient of variation of less than 10%. Laboratory personnel who performed the ELISA analyses were blinded to the participant group assignments.

Statistical Analysis

Data analysis was performed using SPSS software version 25. The normality of the dataset was tested with the Shapiro–Wilk test. A paired-sample t-test was used to evaluate changes in cytokine levels (TNF-α and IL-6) within each group, whereas an independent-sample t-test was used for comparisons between groups. Alternatively, the Mann–Whitney U test was used to analyze data that were not normally distributed. Cohen's d was applied to evaluate effect size, with a value of $d > 0.8$ considered large. Analyses were regarded as statistically significant if $p < 0.05$.

Results

The dropout rate in this study was 0%, and the attendance rate was 100%. Baseline analysis revealed no significant differences between the control group (CG) and the exercise group (EXG) ($p > 0.05$), except for oxygen saturation. These results indicate that both groups had comparable baseline profiles, suggesting that the changes in cytokine levels were mainly attributed to the intervention. The results of the characteristics analysis are presented in Table 2.

Table 1. Details of the Combined Endurance-Resistance Training Protocol

Training Session	Combination Training			
	Type	**Intensity**	**Duration or Sets and Reps**	**Targeted Muscles**
1–10	Endurance	60% HRmax	30 minutes	-
	Resistance	60% 1-RM	4 set x 10 reps	Upper and lower extremities
11–20	Endurance	70% HRmax	40 minutes	-
	Resistance	70% 1-RM	4 set x 12 reps	Upper and lower extremities

Table 2. General Characteristics of the Study Subjects (n = 8 per group)

Parameters	Group	Mean ± SD	p-value
Age (years)	CG	23.38 ± 1.92	0.113[a]
	EXG	25.00 ± 1.93	
TDS (mmHg)	CG	124.88 ± 4.05	0.352[a]
	EXG	121.00 ± 10.64	
TDD (mmHg)	CG	72.13 ± 9.19	0.619[a]
	EXG	74.13±6.27	
DJI (bpm)	CG	93.38 ± 8.45	0.290[a]
	EXG	89.25 ± 6.43	
Suhu (°C)	CG	35.15 ± 1.14	0.111[b]
	EXG	35.86 ± 0.43	
GDP (mg/dL)	CG	101.13 ± 14.72	0.604[a]
	EXG	98.25 ± 4.23	
Hb (g/dL)	CG	14.43 ± 1.70	0.537[a]
	EXG	13.95 ± 1.27	
TB (m)	CG	1.56 ± 0.06	0.935[a]
	EXG	1.56 ± 0.06	
BB (kg)	CG	76.13 ± 9.55	0.778[a]
	EXG	77.94 ± 15.09	
BMI (kg/m^2)	CG	30.96 ± 2.91	0.672[a]
	EXG	31.80 ± 4.64	
Fat (%)	CG	46.34 ± 2.34	0.544[a]
	EXG	47.35 ± 3.96	

Note: CG = Control Group; EXG = Combined Exercise Group; SD = Standard Deviation; (a) = Independent t-test; (b) = Mann–Whitney U test; TDS = Systolic Blood Pressure; TDD = Diastolic Blood Pressure; DJI = Resting Heart Rate; GDP = Fasting Blood Glucose; Hb = Hemoglobin; TB = Height; BW = Body Weight; BMI = Body Mass Index.

Table 3. Differences in IL-6 and TNF-α levels before and after exercise in each group (n = 8 per group)

Group	Parameters	Mean ± SD	p-value
Control Group	Pre-exercise IL-6	2.52 ± 1.26	0.165
	Post-exercise IL-6	3.19 ± 1.50	
	Pre-exercise TNF-α	31.25 ± 19.34	0.187
	Post-exercise TNF-α	42.91 ± 23.95	
Combined Exercise Group	Pre-exercise IL-6	2.44 ± 0.87	0.018*
	Post-exercise IL-6	1.62 ± 0.77	
	Pre-exercise TNF-α	44.87 ± 20.43	0.010*
	Post-exercise TNF-α	28.67 ± 16.49	

Note: SD = Standard Deviation; * = statistically significant at $p < 0.05$ (paired-sample t-test).

Table 4. Effect size results for IL-6 and TNF-α levels (n = 8 per group)

Group	Parameters	Cohen's d
Combined Exercise Group	Pre-exercise IL-6	1.002
	Post-exercise IL-6	
	Pre-exercise TNF-α	1.230
	Post-exercise TNF-α	

Note: The effect size is considered large when Cohen's d > 0.8.

The results of cytokine analysis are summarized in Table 3, which presents the differences in IL-6 and TNF-α levels before and after the intervention in both groups.

Following the four-week training program, participants in the combined exercise group showed a clear downward trend in pro-inflammatory cytokine levels, whereas the control group did not exhibit notable changes. This tendency suggests that regular moderate-intensity endurance-resistance exercise contributed to a reduction in systemic inflammation. The results also demonstrate a consistent response pattern for both cytokines, reflecting an overall anti-inflammatory adaptation to the exercise protocol.

The results of the effect size analysis are presented in Table 4, which summarizes the magnitude of changes in IL-6 and TNF-α levels following the four-week combined exercise program.

The data indicate that both cytokines demonstrated large effect sizes, confirming a substantial physiological response to the intervention. These findings emphasize that the applied training protocol was not only statistically effective but also produced a meaningful practical impact on reducing inflammation among participants in the exercise group.

Discussion

This study aimed to examine the impact of moderate-intensity combined exercise on serum TNF-α and IL-6 levels in young healthy obese women. The results showed that a four-week endurance-resistance training program performed five times per week significantly reduced circulating concentrations of both cytokines. This finding suggests that moderate-intensity combined exercise may contribute to reducing inflammatory responses associated with obesity.

These outcomes are consistent with previous research highlighting the anti-inflammatory effects of physical activity. Moderate-intensity endurance-resistance programs have been reported to lower serum TNF-α and IL-6 levels after several weeks of training [14]. Other studies have also demonstrated that physical exercise plays an important role in suppressing pro-inflammatory cytokines and improving metabolic function, thereby contributing to better health outcomes in individuals with obesity [8, 9, 10, 12]. The observed reductions in inflammatory markers in this study align with these findings, reinforcing the evidence that combined exercise can effectively modulate inflammation and promote metabolic balance in overweight populations.

The decrease in serum TNF-α and IL-6 levels induced by endurance and resistance exercise involves different physiological mechanisms. The mechanism of endurance exercise in decreasing inflammation is related to increased insulin sensitivity. Hyperglycemic conditions cause oxidative stress, thereby promoting inflammation. AMP-activated protein kinase (AMPK), activated by insulin, translocates GLUT-4 from the cytosol to the skeletal muscle and adipocyte membranes, allowing more glucose to be taken up from the blood. Resistance exercise acts through a different mechanism, involving the secretion of myokines such as IL-6 by skeletal muscle, which antagonize pro-inflammatory cytokines. In addition, resistance exercise stimulates growth hormone (GH) activity

and enhances lipolysis. As a result of the lipolysis process, lipid storage in adipose tissue decreases, as does the inflammatory reaction. Combined exercise integrates both effects within a single training session, achieving more optimal results in a shorter duration.

Being a biphasic cytokine, the mechanism of IL-6 in reducing inflammation is determined by the type and duration of exercise. During acute moderate-intensity exercise, resistance exercise is more effective in increasing serum IL-6 myokines compared with endurance exercise [24]. Myokine IL-6 binds to the mIL6-R/gp130 receptor and activates the phosphoinositide-3-kinase/Akt (PI3K-Akt) pathway. PI3K-Akt signaling activates the mammalian target of rapamycin complex 1 (mTORC1) and enhances glucose uptake. The mTORC1 protein complex induces ribosome biogenesis and increases mRNA translational efficiency, resulting in skeletal muscle hypertrophy [25]. Skeletal muscle hypertrophy increases resting metabolic rate (RMR), which enhances energy expenditure [26]. In turn, chronic moderate-intensity endurance exercise significantly reduces serum IL-6 levels more than resistance exercise [14]. Energy expenditure during moderate-intensity endurance exercise predominantly relies on fatty acid oxidation, with a smaller contribution from glucose oxidation [27]. Fatty acids are obtained through the lipolysis of triacylglycerol, which is dominant in white adipose tissue as the main lipid storage organ [28]. This process reduces the accumulation of adipocyte–macrophage M1 tissue, leading to decreased IL-6 cytokine secretion [14, 29].

Our study demonstrated that combined exercise can significantly reduce inflammation. However, previous comparative studies have reported significant reductions in pro-inflammatory cytokines with other types of exercise. Khalafi et al. conducted a systematic review and meta-analysis indicating that only endurance exercise reduced TNF-α levels [30]. The difference in findings is likely due to variations in participant age, as our study included young adult women (20–30 years old), while Khalafi et al. examined subjects aged 65 years and older. The principle of resistance exercise involves inducing muscle damage to stimulate an acute inflammatory response. With aging, muscle cells undergo degeneration and exhibit inflammatory reactions even without exercise-induced stimulation [31, 32].

Moderate intensity is considered the most optimal level for reducing inflammation. A systematic review by Cerqueira et al. reported increased TNF-α levels only in groups exposed to high-intensity exercise [12]. High-intensity exercise may cause exercise-induced muscle injury due to excessive mechanical stress [33]. Sarcomere overstretching leads to the opening of stretch-activated calcium channels. The resulting calcium influx promotes degradation of contractile proteins, which the body recognizes as tissue injury, thereby initiating inflammatory responses [34].

In summary, the findings of this study confirm that moderate-intensity combined exercise effectively reduces pro-inflammatory cytokines such as TNF-α and IL-6 in young obese women. The results align with previous studies demonstrating that combined endurance-resistance training produces measurable anti-inflammatory effects through mechanisms linked to improved insulin sensitivity, activation of AMPK, and increased myokine secretion. These physiological adaptations jointly contribute to reduced systemic inflammation and enhanced metabolic regulation. Overall, the present study adds to the growing evidence that moderate-intensity combined exercise is an efficient and practical approach to reducing inflammation associated with obesity. The findings support the importance of incorporating both endurance and resistance components into structured training programs to achieve meaningful metabolic and anti-inflammatory benefits within a relatively short intervention period.

Study Limitations

Several limitations in this study should be considered when interpreting the findings. This study did not compare combined exercise with endurance or resistance exercise performed independently. Within the same age group, different exercise modalities can produce different outcomes. Moreover, variations in exercise intensity and duration may influence physiological responses and adaptation; however, these factors were not compared in this research. Future studies should include more diverse interventions, varying in type, intensity, frequency, and duration, to develop comprehensive exercise recommendations for specific age and sex groups.

In addition, several variables other than obesity may affect pro-inflammatory cytokine levels, including dietary intake, stress, smoking habits, menstrual cycle, and medication use. Although controlling all such factors in human studies is challenging, future research should monitor and account for these variables to minimize potential bias.

Conclusions

This study confirms that moderate-intensity combined exercise can be applied as an effective method for controlling inflammation related to obesity in young women. The physiological effects observed during the intervention demonstrate the practical value of combining endurance and resistance elements within a single training

program. The results emphasize the importance of structured physical exercise as a component of health management for individuals with obesity.

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Conflict of interests

The authors declare that there is no conflict of interests.

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