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Comparison of the Effects of Rapid, Moderate, and Slow Weight Loss Combined with a Low-Calorie Diet and Physical Activity on Inflammatory Factors in Obese Women

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A B S T R A C T

Objective: Obesity and overweight are defined as the excessive accumulation of fat in the body, which generally occurs when energy intake exceeds energy expenditure. Currently, obesity is considered one of the largest public health challenges worldwide and is inversely associated with various health outcomes. Obesity is often linked to inflammatory factors. The purpose of this study was to compare the effects of rapid, moderate, and slow weight loss combined with a low-calorie diet and physical activity on inflammatory markers in obese women.

Methods and Materials: In this study, 36 obese women (ages 20 to 45 years) with a body mass index (BMI) of 30 or higher were randomly divided into three groups: rapid weight loss (combined training with 30-35% caloric deficit, 12 weeks, 12 participants), moderate weight loss (combined training with 20-25% caloric deficit, 10 weeks, 12 participants), and slow weight loss (combined training with 15-20% caloric deficit, 15 weeks, 12 participants). Participants underwent interventions for rapid, moderate, or slow weight loss, which included exercise and nutritional programs. Aerobic exercise consisted of walking and jogging on a treadmill at an intensity of 50-65% of maximum heart rate, and resistance training at 40% of one-repetition maximum (1RM), including dumbbell cross movements, biceps curls, and triceps extensions. Inflammatory markers, including Interleukin-1 (IL-1) and high-sensitivity C-reactive protein (hs-CRP), were measured at the beginning and end of the study. Data analysis was performed using ANOVA, Shapiro-Wilk, Levene's test, and covariance analysis. Statistical analyses were conducted using SPSS version 23 at a significance level of 0.05.

Findings: Rapid, moderate, and slow weight loss combined with a low-calorie diet and physical activity did not have a significant effect on plasma IL-1 levels in obese women. However, significant differences were observed between the rapid weight loss group and the moderate and slow weight loss groups. Specifically, a 22.66% reduction in IL-1 levels was noted in the moderate weight loss group compared to

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the rapid weight loss group, and a 39.59% reduction was observed in the slow weight loss group compared to the rapid weight loss group. No significant difference was found between the moderate and slow weight loss groups. Similarly, rapid, moderate, and slow weight loss combined with a low-calorie diet and physical activity did not significantly affect plasma hs-CRP levels in obese women. However, a significant difference was observed between the rapid weight loss group and the slow weight loss group, with a 62.28% reduction in hs-CRP levels in the slow weight loss group compared to the rapid weight loss group. No significant differences were found between the other groups.

Conclusion: Rapid, moderate, and slow weight loss combined with a low-calorie diet and physical activity does not significantly impact inflammatory factors.

Keywords: *Weight loss, inflammatory factors, obese women.*

1. Introduction

In recent decades, the prevalence of obesity has been increasing, and today it is recognized as a public health issue worldwide. Obesity is associated with an increased risk of several metabolic syndromes and malignancies (1). Obesity is a complex chronic condition resulting from the interaction of biological, genetic, psychosocial, behavioral, and environmental factors, contributing to increased morbidity and mortality. Individuals with obesity often experience weight stigma and weight-based discrimination throughout their lives and in various environments (e.g., home, school, workplace, and healthcare settings), which independently of BMI contributes to reduced quality of life and increased morbidity and mortality (2-5). Chronic low-grade inflammation and immune system activation appear to play a role in the pathogenesis of obesity. Therefore, reducing obesity may improve the lipid profile of obese patients or prevent the development of related metabolic diseases (6). Given obesity's impact on individuals, families, and communities, a unified framework for obesity prevention and treatment is essential (7-9). Among the three options for weight management, bariatric surgery and pharmacotherapy are effective, but dietary strategies not requiring medical intervention offer advantages to the population. However, the weight loss and weight management diet market is extensive, projected to grow from $192.2 billion in 2019 to $295.3 billion by 2027 (10-12).

The World Health Organization (WHO) defines obesity as the abnormal or excessive accumulation of fat that poses a health risk. Body mass index (BMI), calculated by dividing body weight in kilograms by the square of height in meters, is a simple metric used to indicate overall body fat. Obesity is a critical health issue; in 2016, approximately 1.9 billion individuals worldwide were obese, with nearly every country experiencing this increase (13). According to the Global Obesity Atlas 2022, it is estimated that by 2030, 1 in 5 women and 1 in 7 men will be affected by obesity (BMI ≥ 30 kg/m²), equivalent to one billion people worldwide (14-16).

It is estimated that certain diseases, including hypertension, cardiovascular diseases, Alzheimer's disease, asthma, metabolic syndrome, fatty liver disease, gallbladder disease, osteoarthritis, obstructive sleep apnea, specific cancers, high cholesterol, musculoskeletal disorders (joint and muscle pain), and type 2 diabetes, have increased globally due to obesity (17-19). Evidence also suggests localized inflammation in adipose tissue, which, in turn, promotes systemic low-grade inflammation as a primary driver in the development of these pathologies. A better understanding of the underlying mechanisms behind obesity-induced adipose tissue inflammation is needed to develop effective therapeutic or preventive strategies (6). Furthermore, obesity alters the morphology and composition of adipose tissue, leading to changes in the production and secretion of proteins. Some of these secreted proteins, including several pro-inflammatory mediators, may be produced by macrophages residing in adipose tissue. Changes in the inflammatory status of adipose tissue and the liver associated with obesity have reinforced the understanding that obesity represents a state of chronic low-grade inflammation (10).

Given the prevalence of obesity and the inflammation it causes, we decided to investigate the effects of weight loss intensity on inflammation levels in overweight and obese women. This study utilized a low-calorie diet and physical activity—two of the most common and essential strategies for obesity prevention and treatment. Previous studies have shown limitations. For example, research conducted in 2022 indicated that weight loss from energy-restricted diets or surgery is a determining factor in reducing pro-inflammatory marker levels in overweight and obese individuals. Low-calorie diets, regardless of their composition, have anti-inflammatory effects that may play a significant role in

preventing chronic diseases. However, the intensity of weight loss and the type of diet were not specified (13, 20). Another study showed that weight loss through a low-calorie diet reduces pro-inflammatory factors (IL-1β, IL-6, TNF-α, and hs-CRP) in patients with fatty liver disease over eight weeks. This effect was independent of gender, the extent of weight loss, and fatty liver grading (21).

One of the main benefits of weight loss is controlling inflammation levels. Research has shown that during weight loss, the unfavorable inflammatory profile associated with increased obesity can be improved, providing further evidence of the beneficial effects of weight loss in reducing the risk of comorbidities associated with overweight and obesity (L. Kirsty Forsythe et al., 2008). Studies on obese individuals have demonstrated a direct relationship between fat mass reduction and decreased inflammation. Caloric restriction alters cytokine gene expression, reduces IL-6 mRNA and IL-1β expression, improves insulin sensitivity, regulates gene expression in adipose tissue, and enhances mitochondrial function (17). Physical exercise can regulate inflammation by decreasing levels of inflammation-related cytokines in overweight/obese populations through various mechanisms. Regular exercise can reduce the production and secretion of pro-inflammatory adipokines by decreasing adipose tissue size. Additionally, exercise can enhance muscle tissue to produce anti-inflammatory myokines derived from muscle (13). These findings suggest that weight loss combined with a low-calorie diet and physical activity can affect inflammation caused by weight loss.

As obesity grows in human societies and presents numerous complications, nutritionists and sports science researchers strive to find ways to reduce its adverse effects. Evidence suggests that adipose tissue is responsible for generating inflammatory factors, which, in turn, contribute to many of these complications. Today, many overweight and obese individuals seek weight loss through gym training and strenuous exercises. Often, these individuals aim for rapid weight loss in a short period, which, in such cases, may have harmful physiological effects. Thus, extreme weight loss can have detrimental physiological effects and impact inflammatory factor levels. Therefore, the present study aimed to compare the effects of rapid, moderate, and slow weight loss with a low-calorie diet and physical activity on inflammatory markers in obese women. The results of this study are expected to highlight the effects of three weight loss intensities on inflammatory markers and propose a structured and scientifically sound method for weight reduction in obese individuals.

2. Methods and Materials

2.1 Study Design and Participants

This study was semi-experimental, utilizing a pre-test/post-test design with a control group. Given the involvement of human participants and the inability to control all influencing variables, the research was conducted to observe and measure the effects of various interventions.

The statistical population included obese adult women who visited weight control counseling centers in Qazvin in 2023. From a pool of 106 volunteers, 36 obese adult women were purposefully selected based on specific inclusion and exclusion criteria. Participants were divided into four groups: rapid weight loss, moderate weight loss, slow weight loss, and a control group, with 12 participants assigned to each group. Inclusion criteria required participants to be healthy women aged 20 to 45 years, have a BMI of over 30 kg/m², be inactive, and not have participated in regular physical activity or exercise for three months prior to the study. Participants were also required not to have experienced any weight loss due to dieting or exercise within the last three months. Exclusion criteria included any weight change greater than 3 kg in the three months preceding the study, adherence to a weight-loss diet in the same period, use of dietary supplements or medications, history of endocrine or metabolic disorders, chronic diseases, or a family history of early cardiac mortality and diabetes. Other exclusion criteria involved chronic or acute musculoskeletal, cardiovascular, or respiratory diseases, chronic headaches or migraines, mental health disorders, smoking, pregnancy or breastfeeding, and irregular participation in study-related programs. Participants who met these criteria and provided informed consent were included in the study.

Participants provided informed consent after being briefed about the research conditions and completed the Physical Activity Readiness Questionnaire to confirm eligibility. Before the pre-test, participants attended a session at the laboratory for body composition measurements. They recorded their food and drink intake before the first exercise test to ensure consistency in subsequent tests. Each participant adhered to the dietary regimen and physical activity dose prescribed for their group. The rapid weight loss group had a caloric intake set at 30-35% below the maintenance level, the moderate weight loss group at 20-25%, and the slow weight loss group at 15-20%. The goal was to achieve a weight loss of 7-10%. Height was measured using a SECA stadiometer (model 345, Germany) with a sensitivity of 1 mm, and weight was

measured using a SECA digital scale with a precision of 0.2 kg. Body fat percentage was assessed using the InBody 273 analyzer (South Korea) at the Dr. Irandoost Weight Control Clinic. Blood samples (5 mL) were collected twice: after 12 hours of fasting, 48 hours before the first session and 48 hours after the last session. Blood samples were drawn from the left arm vein while participants were seated and at rest. Plasma inflammatory markers, including Interleukin-1 (IL-1) and CRP, were analyzed using the sandwich ELISA method with kits from MyBioSource (San Diego, California), which had a sensitivity of 2.54 ng/mL, an intra-assay coefficient of variation below 4%, and an inter-assay coefficient of variation below 4.2%.

2.2 Data Collection

To measure plasma inflammatory markers, blood samples were collected twice: 48 hours before the tests and 48 hours after the last session. Samples were collected between 9:00 and 10:00 AM while participants were seated and fasting. Plasma inflammatory markers, including Interleukin-1 (IL-1) and CRP, were measured using the sandwich ELISA method with MyBioSource kits. Sensitivity was set at 2.54 ng/mL, with intra-assay and inter-assay coefficients of variation below 4% and 4.2%, respectively. For anthropometric measurements, height was measured with participants standing barefoot and upright at the end of exhalation using a stadiometer. Body composition information was obtained using the InBody 273 analyzer. Participants stood barefoot on the device, entered their height and age, held the analyzer handles, and received a printout of their body composition data.

2.2.1 Exercise Protocol

The exercise protocol for the three experimental groups was designed as follows: the rapid weight loss group followed a 5-week program, the moderate weight loss group followed a 10-week program, and the slow weight loss group followed a 15-week program. Each training session started with a 10-minute warm-up consisting of 5 minutes of dynamic stretching and 5 minutes of jumping movements. Aerobic exercise included 45 minutes of walking or jogging on a treadmill, five days a week, at an intensity of 55-65% of maximum heart rate. The target heart rate was calculated using the Karvonen formula: Target Heart Rate = ((Maximum Heart Rate - Resting Heart Rate) × Intensity (50-65%)) + Resting Heart Rate. Heart rate was monitored using smartwatches or phone applications. Resistance training included three weekly sessions with 3-5 exercises at 40% of one-repetition maximum (1RM) for 12 repetitions and three sets, with 22-second rests between sets. Exercises included dumbbell flys, biceps curls, and triceps extensions, progressing to 50% of 1RM by the fifth week. The control group remained inactive during the 15-week period.

2.3 Nutritional Protocol

Participants followed the prescribed dietary regimens specific to their groups. The rapid weight loss group consumed 30-35% fewer calories than required for weight maintenance, the moderate weight loss group consumed 20-25% fewer calories, and the slow weight loss group consumed 15-20% fewer calories.

2.4 Data Analysis

For statistical analysis, descriptive statistics, including mean and standard deviation, were used alongside inferential statistics, including ANOVA, Shapiro-Wilk test, Levene's test, and covariance analysis. All statistical analyses were performed at a significance level of 0.05 using SPSS software version 23.

3. Results

The mean and standard deviation of anthropometric indices, including age, weight, body fat percentage, waist-to-hip ratio, and body mass index (BMI), as well as plasma inflammatory markers IL-1 and CRP, in the different study groups are presented in Table 1.

Table 1. Mean and Standard Deviation of Anthropometric and Inflammatory Indices in Different Study Groups

Study Groups	Measurement Times	Age (Years)	Height (cm)	Weight (kg)	Waist-to-Hip Ratio	Body Fat (%)	BMI (kg/m²)	IL-1 (pg/ml)	hs-CRP (mg/l)
Rapid Weight Loss	Pre-Test	36.75 ± 8.85	162.50 ± 3.03	83.72 ± 4.60	0.98 ± 0.02	41.03 ± 0.03	31.72 ± 1.83	8.04 ± 1.02	6.79 ± 3.00
	Post-Test	-	-	75.14 ± 5.28†	0.90 ± 0.03†	35.03 ± 0.02†	28.43 ± 1.40†	8.21 ± 0.87	7.29 ± 1.90
Moderate Weight Loss	Pre-Test	35.69 ± 7.53	162.15 ± 3.33	83.07 ± 3.93	0.99 ± 0.03	39.04 ± 0.04	31.61 ± 1.60	7.91 ± 0.82	6.99 ± 2.34

	Post-Test	-	-	74.97 ± 4.79†	0.90 ± 0.02†	32.03 ± 0.03†	28.50 ± 1.33†	6.35 ± 0.87	5.12 ± 2.67
Slow Weight Loss	Pre-Test	36.46 ± 6.91	161.23 ± 3.24	84.47 ± 2.93	0.98 ± 0.04	40.03 ± 0.03	32.53 ± 1.74	7.77 ± 1.07	6.29 ± 2.03
	Post-Test	-	-	75.63 ± 3.58†	0.87 ± 0.03†	31.03 ± 0.03†	29.13 ± 1.91†	4.96 ± 0.74	2.75 ± 1.27

According to the results presented in Table 1, weight changes in the post-test compared to the pre-test in all three groups (rapid, moderate, and slow weight loss) with a low-calorie diet and physical activity showed a significant decrease ($P < 0.000$), while there was no significant difference between groups ($P > 0.796$). A significant reduction in waist-to-hip ratio was observed in the post-test compared to the pre-test in all three weight loss groups ($P < 0.000$), with no significant difference between groups ($P > 0.124$). Similarly, BMI showed a significant decrease in all three groups after the intervention ($P < 0.000$), with no significant difference between the groups ($P > 0.339$).

The Shapiro-Wilk test was used to evaluate the normality of data distribution. If the P-value exceeds 0.05, the data are considered normally distributed, warranting the use of parametric tests for analysis. If the P-value is below 0.05, the data are considered non-normally distributed, requiring non-parametric tests.

Table 2. Normality Test Results for Study Data

Variable	Study Group	P-Value	Z-Value
Age	Rapid Weight Loss	0.214	0.914
	Moderate Weight Loss	0.648	0.953
	Slow Weight Loss	0.151	0.904
Height	Rapid Weight Loss	0.153	0.899
	Moderate Weight Loss	0.055	0.855
	Slow Weight Loss	0.150	0.904
Weight	Rapid Weight Loss	0.136	0.895
	Moderate Weight Loss	0.497	0.943
	Slow Weight Loss	0.138	0.901

Based on the Shapiro-Wilk test results, all obtained data appear to have a normal distribution. Therefore, parametric statistical tests were used for data analysis.

Hypothesis 1: Rapid, moderate, and slow weight loss combined with a low-calorie diet and physical activity does not have a significant effect on plasma IL-1 levels in obese women.

Table 3. Two-Way ANOVA Results for Plasma IL-1 Levels

Variable	Statistical Factors	F-Value	P-Value	Eta Coefficient	Statistical Power
IL-1 (pg/ml)	Time	107.700	0.000	0.755	1.000
	Group	14.823	0.000	0.459	0.998
	Time × Group	40.452	0.000	0.698	1.000

Two-way ANOVA results showed significant differences for time ($P < 0.000$), group ($P < 0.000$), and the interaction of time and group ($P < 0.000$) in plasma IL-1 levels among the three groups. The null hypothesis of no significant difference between groups is rejected.

Table 4. Bonferroni Post-Hoc Test Results for Pairwise Group Comparisons

Study Groups	Mean Difference	P-Value	Percent Change (%)
Rapid vs. Moderate	-0.999	0.012	-22.66
Rapid vs. Slow	-1.763	0.000	-39.59
Moderate vs. Slow	-0.763	0.065	-21.89

Bonferroni results indicate significant differences between the rapid and moderate groups ($P < 0.012$) and the rapid and slow groups ($P < 0.000$), with IL-1 reductions of 22.66% and 39.59%, respectively. There was no significant

difference between the moderate and slow groups (P > 0.065).

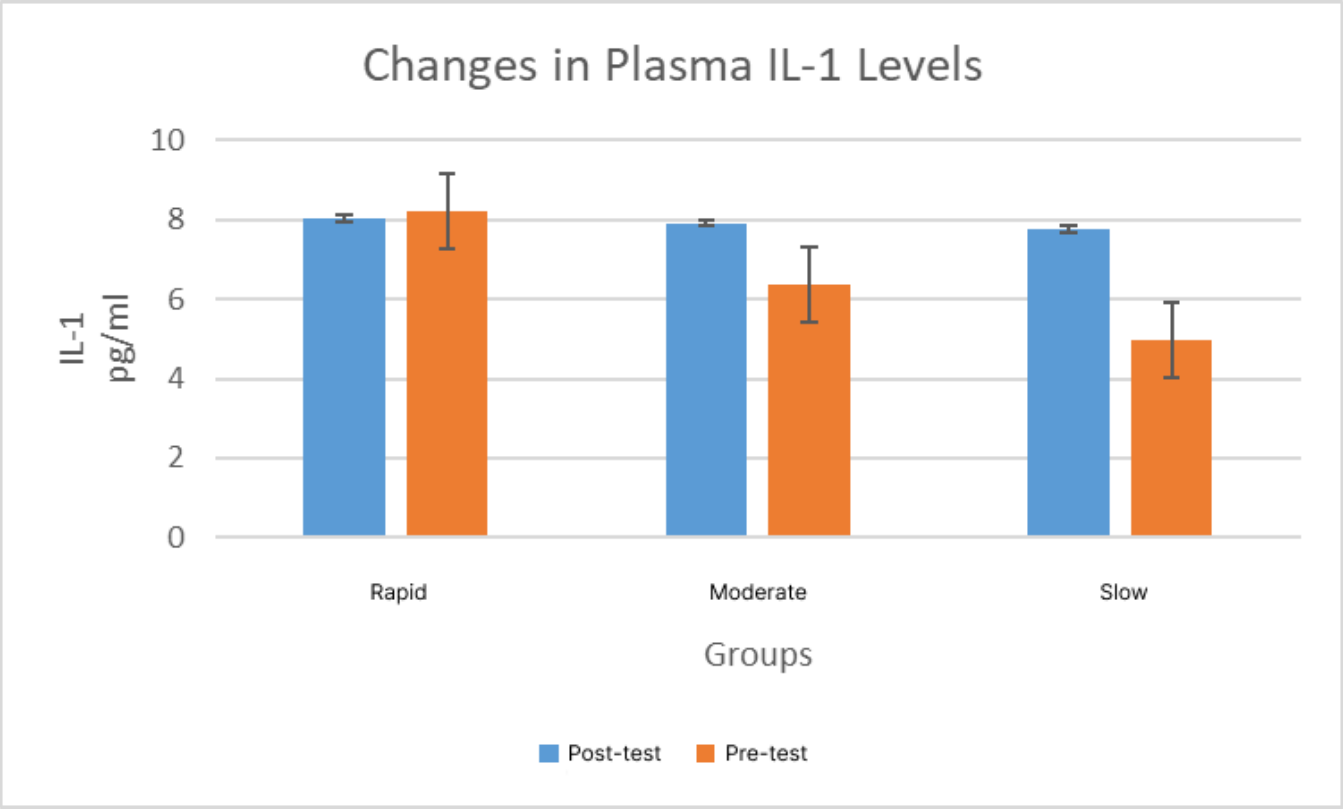

Figure 1. Changes in Plasma IL-1 Levels Across Different Time Points in the Study Groups

(*): Significance compared to post-test.
(†): Significance compared to the rapid weight loss group.

Hypothesis 2: Rapid, moderate, and slow weight loss combined with a low-calorie diet and physical activity does not have a significant effect on plasma hs-CRP levels in obese women.

Table 5. Two-Way ANOVA Results for Plasma hs-CRP Levels

Variable	Statistical Factors	F-Value	P-Value	Eta Coefficient	Statistical Power
hs-CRP (mg/l)	Time	19.817	0.000	0.362	0.991
	Group	5.256	0.010	0.231	0.800
	Time × Group	9.907	0.000	0.361	0.975

ANOVA results showed significant differences for time (P < 0.000), group (P < 0.010), and the interaction of time and group (P < 0.000) in plasma hs-CRP levels among the three groups.

Table 6. Bonferroni Post-Hoc Test Results for Pairwise Group Comparisons

Study Groups	Mean Difference	P-Value	Percent Change (%)
Rapid vs. Moderate	-0.986	0.655	-29.77
Rapid vs. Slow	-2.523	0.009	-62.28
Moderate vs. Slow	-1.536	0.162	-46.29

Post-hoc results indicate a significant difference between the rapid and slow groups (P < 0.009), with a 62.28%

reduction in hs-CRP in the slow group compared to the rapid group. No significant differences were found between the other groups ($P > 0.162$).

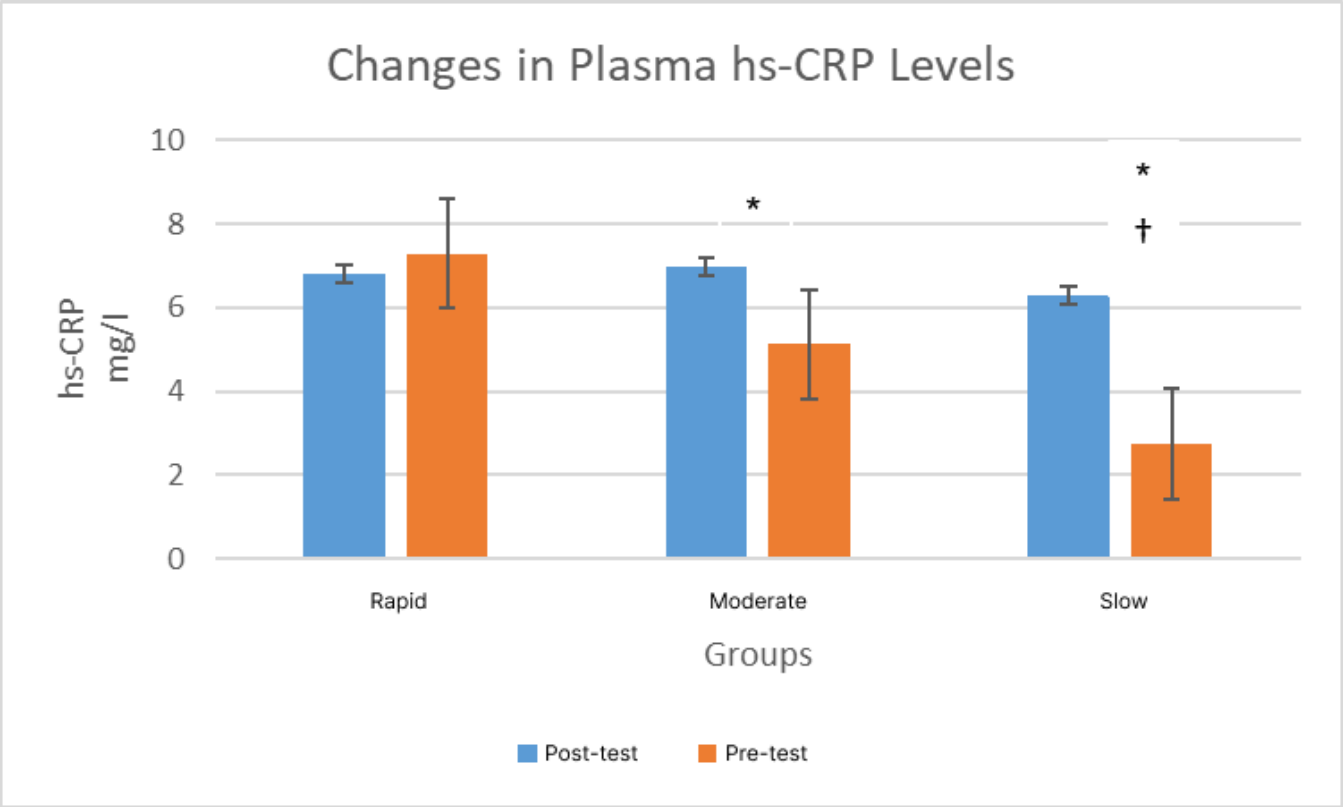

Figure 2. Changes in Plasma hs-CRP Levels Across Different Time Points in the Study Groups

(*): Significance compared to post-test.
(†): Significance compared to the rapid weight loss group.

4. Discussion and Conclusion

The purpose of this study was to compare the effects of rapid, moderate, and slow weight loss combined with a low-calorie diet and physical activity on inflammatory factors in obese women. To this end, 48 obese adult women aged 20 to 45 were purposefully selected from a weight control counseling center in Qazvin. Participants were voluntarily assigned to groups: rapid weight loss, moderate weight loss, slow weight loss, and a control group. This research employed a semi-experimental design with a pre-test/post-test framework and a control group. Following data analysis using SPSS software, the results were as follows:

According to the results concerning anthropometric indices, significant reductions in weight were observed in the post-test compared to the pre-test in all three groups (rapid, moderate, and slow weight loss) combined with a low-calorie diet and physical activity ($P < 0.000$), although no significant differences were found between the groups. Additionally, for the interleukin-1 (IL-1) index, pairwise comparisons revealed significant differences between the rapid weight loss group and both the moderate weight loss group ($P < 0.012$) and the slow weight loss group ($P < 0.000$). Specifically, IL-1 levels decreased by 22.66% in the moderate weight loss group and by 39.59% in the slow weight loss group compared to the rapid weight loss group. Moreover, rapid, moderate, and slow weight loss combined with a low-calorie diet and physical activity did not significantly affect plasma hs-CRP levels in obese women. However, a significant difference was found between the rapid and slow weight loss groups ($P < 0.009$), with a 62.28% reduction in hs-CRP levels in the slow weight loss group compared to the rapid weight loss group. No significant differences were observed between other groups ($P > 0.05$).

Significant differences were observed between the rapid and moderate weight loss groups ($P < 0.012$) as well as

between the rapid and slow weight loss groups ($P < 0.000$). Specifically, IL-1 levels decreased by 22.66% in the moderate weight loss group and by 39.59% in the slow weight loss group compared to the rapid weight loss group. No significant differences were found between the moderate and slow weight loss groups. Moreover, plasma IL-1 levels showed significant differences across all three groups. Moradian et al. (2022) examined the effects of an 8-week resistance circuit training program on inflammatory cytokines, blood pressure, and insulin resistance in obese women with pre-hypertension. Participants engaged in three 50-60 minute sessions per week (15 minutes of warm-up, 30 minutes of weightlifting, and 10 minutes of cooldown) with 40% 1RM for upper-body exercises and 60% 1RM for lower-body exercises. Their findings indicated no significant effect of resistance training on inflammatory cytokines such as IL-1β and TNF-α. The disparity may stem from the type of training chosen; resistance circuit training might not exert a strong anti-inflammatory effect compared to endurance or combined training (22). These findings conflict with the current study's results, which suggest significant reductions in IL-1β in the moderate and slow weight loss groups. The inconsistency could be due to differences in the duration, intensity, and type of interventions applied, as well as variations in participant demographics or baseline inflammatory status. Gielen et al. (2003) investigated the effects of endurance training on IL-1β levels in 20 obese men with stable chronic heart failure (CHF). Results showed that reductions in serum IL-1β due to endurance interventions correlated with improved cardiorespiratory fitness (CRF) and increased VO_2max (23). This aligns with the current study, where IL-1β reductions may also be attributed to improved physical fitness and reductions in fat mass following structured physical activity and dietary regimens. Najafi et al. (2023) allocated 44 obese men to four groups (control, low-intensity interval resistance training, moderate-intensity interval resistance training, and high-intensity interval resistance training) and observed significant reductions in IL-1β across all training intensity groups after 12 weeks of three weekly sessions. The study suggested that resistance training, particularly at moderate and high intensities, could be an effective method for reducing inflammation and managing obesity. These findings support the results of the current study, which demonstrated significant IL-1β reductions in moderate and slow weight loss groups (24). Balducci et al. (2010) examined the effects of aerobic and combined aerobic-resistance training on inflammatory biomarkers in 82 patients with type 2 diabetes. After 12 weeks of high-intensity and combined training, significant reductions in hs-CRP and IL-1β levels were observed (25). This is consistent with the current study, where slow and moderate weight loss interventions showed significant reductions in inflammatory markers, likely due to the comprehensive approach combining physical activity and dietary modifications.

Significant differences were observed between the rapid and slow weight loss groups, with a 62.28% reduction in hs-CRP levels in the slow weight loss group compared to the rapid weight loss group. No significant differences were found between the other groups. Additionally, plasma hs-CRP levels showed significant differences across all three groups. Beigrezayi et al. (2023) conducted a systematic review and meta-analysis of clinical trials to evaluate the effects of weight-loss diets combined with exercise compared to weight-loss diets alone on inflammatory biomarkers in adults. They found no significant additional effect of exercise combined with weight-loss diets compared to diet alone on reducing inflammatory markers (14). This discrepancy with the current study may be due to differences in study design, duration, or the specific inflammatory biomarkers analyzed. Justice (2011) investigated the additive effects of aerobic or resistance training to calorie restriction on hs-CRP compared to calorie restriction alone in obese individuals. Their 12-week intervention included calorie-restricted groups with or without aerobic or resistance training. While all groups showed significant weight and BMI reductions, hs-CRP levels remained unchanged across interventions (26). This contrasts with the present findings, which observed reductions in hs-CRP with combined weight loss and exercise, potentially due to differences in intervention intensity, duration, or baseline fitness levels of participants. Reljic et al. (2022) examined various exercise regimens, including high-intensity interval training (HIIT) and resistance training, in conjunction with calorie restriction. Their results indicated that resistance training required higher volumes to produce significant anti-inflammatory effects and should be combined with appropriate dietary modifications for optimal outcomes (27). In contrast, the current study observed significant hs-CRP reductions with slow weight loss, possibly due to differences in exercise modalities or the intensity of interventions. The inconsistent findings may arise from variations in exercise type, intensity, and duration across studies. Moreover, the combined effect of diet and exercise may differ based on participant characteristics, baseline inflammatory levels, or adherence to protocols. Studies showing no effect of

exercise on hs-CRP could reflect insufficient intensity or duration to elicit systemic anti-inflammatory changes. Kasraei et al. (2019) investigated the effects of combined resistance-aerobic exercise with and without dietary restriction on inflammatory markers such as CRP and TNF-α. They found that combined exercise with dietary restriction had greater effects on reducing CRP than dietary restriction or exercise alone (28), supporting the current study's findings that dietary and exercise interventions combined yield more significant reductions in inflammatory markers. McLaughlin et al. (2002) measured plasma CRP levels before and after three months of calorie restriction in obese women and found significant CRP reductions parallel to weight loss. These results align with the current study, where slow and sustained weight loss with a low-calorie diet effectively reduced hs-CRP levels, highlighting the role of dietary management in reducing inflammation (29). Selvin et al. (2007), in a systematic review, concluded that weight loss achieved through diet, exercise, or surgical interventions directly correlates with CRP reductions. For every 1 kg of weight loss, an average CRP reduction of 0.13 mg/L was observed (30). This relationship aligns with the current study's observation of significant reductions in hs-CRP following slow and steady weight loss. Oh et al. (2013) conducted a randomized controlled trial involving six months of lifestyle modifications, including diet, exercise, and health counseling. They reported significant reductions in hs-CRP levels in intervention groups compared to controls, demonstrating the efficacy of comprehensive programs in improving inflammatory profiles, consistent with the current findings (31). Ordenez et al. (2014) explored the effects of a 10-week aerobic training program on inflammatory markers in obese women with Down syndrome. Their results showed reductions in CRP, TNF-α, and IL-6 following long-term exercise, consistent with the current study's findings that exercise interventions reduce systemic inflammation (32). Mousa Khalafi et al. (2022) conducted a meta-analysis comparing the effects of exercise (EX) versus calorie restriction (CR) and combined EX+CR on inflammatory markers in overweight and obese individuals. They concluded that EX+CR was more effective than CR alone in reducing inflammatory cytokines and CRP, aligning with the current study's findings that combining exercise with calorie restriction optimizes anti-inflammatory effects. Brunelli et al. (2015) found that moderate-to-high-intensity combined training significantly reduced obesity-related subclinical inflammation, including CRP levels, over a 24-week period (33). These results parallel the current study, which showed that slow and sustained weight loss effectively reduces hs-CRP levels through combined interventions. Lopes et al. (2016) examined the impact of combined training without calorie restriction on inflammatory markers in overweight girls. Significant reductions in CRP and improvements in body composition were observed (34), consistent with the current findings that exercise interventions, even without strict calorie restriction, can significantly reduce systemic inflammation. Shariat Zadeh et al. (2017) demonstrated that high-intensity interval training significantly reduced inflammatory markers, including CRP, IL-6, and TNF-α, in both groups undergoing different exercise regimens (35). These results align with the current study, indicating the importance of structured exercise in reducing inflammation, particularly with higher-intensity interventions. Consistent findings across these studies reinforce the current study's conclusion that combining dietary and exercise interventions, particularly in a slow and steady weight loss framework, significantly reduces inflammatory markers such as hs-CRP. The alignment underscores the cumulative benefits of sustainable weight management strategies in mitigating systemic inflammation, with slow weight loss possibly allowing greater physiological adaptations and better compliance.

The anthropometric indices showed significant reductions in weight in the post-test compared to the pre-test across all three groups (rapid, moderate, and slow weight loss), combined with a low-calorie diet and physical activity. Park et al. (2022) observed improvements in inflammatory factors following short-term, moderate-intensity aerobic exercise in obese women, even before changes in body weight or fat mass occurred. This finding suggests that regular aerobic exercise can independently improve inflammation and oxidative stress, without the need for fat mass reduction. However, most studies indicate that fat mass reduction is essential for lowering pro-inflammatory cytokines and oxidative stress markers. This inconsistency with the current study might stem from the differing roles of exercise in improving inflammatory markers independent of weight loss. Koh et al. (2017) conducted a study on overweight and obese men, finding no significant changes in body weight, fat mass, CRP, or adiponectin after four weeks of aerobic exercise. However, the intervention reduced TNF-α levels, suggesting that physical activity may improve inflammation independently of fat mass reduction. The present study found significant weight loss-related changes, indicating that longer exercise periods combined with

weight reduction may be necessary to observe significant effects on markers like CRP and adiponectin. These findings differ from the current study, which emphasizes the role of significant weight reduction in improving anthropometric indices and inflammatory markers. Differences in study duration, exercise intensity, and participant demographics may explain the discrepancies. While the inconsistent studies suggest exercise can independently influence inflammation, the current study underlines the synergistic effect of diet and weight loss on anthropometric and inflammatory improvements. Bianchi et al. (2018) demonstrated that weight loss through a calorie-restricted diet significantly reduced plasma levels of inflammatory cytokines, including IL-1β and CRP. Their findings highlighted the importance of negative energy balance and lipolysis activation in reducing fat mass and improving metabolic and mitochondrial function (17). These results align with the current study, which shows that weight reduction is a determining factor in reducing pro-inflammatory cytokines. McLaughlin et al. (2002) found that three months of calorie restriction significantly reduced CRP levels in obese women. Their findings align with the current study, where a low-calorie diet coupled with exercise resulted in significant weight loss and CRP reduction (29). Selvin et al. (2007) concluded from a systematic review that weight loss, achieved through diet, exercise, or surgical intervention, directly correlated with reductions in CRP levels. For every kilogram of weight loss, CRP levels decreased by an average of 0.13 mg/L (30). This aligns with the current study, where significant weight reduction resulted in improvements in inflammation-related markersVarady et al. (2009) evaluated the effects of calorie-restricted diets aimed at a 5% initial weight loss. They found that weight loss below 5% was insufficient to produce significant reductions in chronic inflammation (36). These findings underscore the importance of achieving substantial weight loss, as seen in the current study, where weight reductions led to marked improvements in anthropometric indices. Aleman et al. (2017) reported that obese women achieved approximately 10% weight loss within 46 days through a calorie-restricted diet, leading to improved systemic inflammatory biomarkers, including hs-CRP and insulin resistance (37). These findings align with the current study's observation of significant reductions in hs-CRP levels with weight loss. These studies support the current findings by demonstrating that significant weight loss achieved through calorie restriction and exercise is crucial for improving anthropometric indices and reducing inflammation. The alignment underscores the importance of combining dietary and physical activity interventions to achieve meaningful health benefits. The consistent reductions in CRP, TNF-α, and IL-6 observed across these studies confirm the effectiveness of weight loss in mitigating systemic inflammation and improving overall metabolic health.

This study was limited by its focus on a single demographic group of obese women aged 20 to 45, excluding the potential effects of age-related hormonal changes, such as menopause, on inflammatory factors. The research also did not consider variations in dietary regimens, such as ketogenic or vegetarian diets, that could have influenced inflammatory markers in combination with exercise. Additionally, the exercise intensity was not varied systematically across low, moderate, and high levels, which might have provided deeper insights into the relationship between exercise intensity and inflammatory responses. Future studies should explore the effects of varying exercise intensities (low, moderate, and high) on inflammatory factors in obese women to identify optimal training protocols for reducing inflammation. It is also recommended to investigate the combined effects of different dietary regimens, such as ketogenic, vegetarian, or Mediterranean diets, with exercise on inflammatory markers in obese populations. Moreover, research should extend to other demographics, including obese men and children, to account for age and sex differences, especially in the context of hormonal changes and their influence on inflammation. Based on the findings of this study, which indicate that rapid weight loss is associated with higher levels of inflammatory factors compared to moderate or slow weight loss, individuals are advised to adopt a slower weight-loss approach combined with regular exercise. This strategy may not only improve long-term health outcomes but also minimize the inflammatory response associated with rapid weight reduction, promoting a safer and more sustainable pathway to achieving weight management goals.

Authors' Contributions

All authors equally contributed to this study.

Declaration

In order to correct and improve the academic writing of our paper, we have used the language model ChatGPT.

Transparency Statement

Data are available for research purposes upon reasonable request to the corresponding author.

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Declaration of Interest

The authors report no conflict of interest.

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Ethical Considerations

The study protocol adhered to the principles outlined in the Helsinki Declaration, which provides guidelines for ethical research involving human participants. "This research has been approved by the Ethics Committee under the code IR.UT.SPORT.REC.1402.111."

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