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The Effect of Aerobic Exercise and Yoga on Serum Fetuin-A Levels in Obese Women with Type 2 Diabetes

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A B S T R A C T

Objective: Type 2 diabetes is a prevalent metabolic disorder strongly associated with obesity and physical inactivity and is often accompanied by alterations in hepatokines such as fetuin-A. While physical activity has been proposed as a potential modulator of fetuin-A, comparative evidence across different exercise modalities remains limited. This study aimed to compare the effects of twelve weeks of aerobic exercise and yoga on serum fetuin-A levels in obese women with type 2 diabetes.

Methods and Materials: In this quasi-experimental study with a pretest–posttest control group design, 30 middle-aged women with type 2 diabetes were randomly assigned to aerobic training, yoga, or control groups. The exercise interventions were performed three times per week for 12 weeks. Aerobic training was conducted at 60–70% of maximum heart rate, while the yoga program consisted of supervised postures, breathing exercises, and meditation. Fasting blood samples were collected before and after the intervention. Serum fetuin-A was defined as the primary outcome, while anthropometric indices, fasting blood glucose, and insulin resistance (HOMA-IR) were considered secondary outcomes.

Reaults: After 12 weeks, serum fetuin-A levels showed a modest reduction in both the aerobic exercise and yoga groups compared with the control group; however, these changes were not statistically significant (group × time interaction, $p > 0.05$). No significant between-group differences were observed for secondary outcomes, including body weight, body fat percentage, fasting glucose, or HOMA-IR.

Conclusion: 12 weeks of aerobic exercise or yoga did not produce statistically significant changes in serum fetuin-A or other metabolic markers in obese women with type 2 diabetes. Although a non-significant downward trend in fetuin-A was observed, these findings should be interpreted cautiously. Aerobic exercise and yoga appear to be safe and feasible lifestyle options, but larger and longer-term studies are required to determine whether these interventions can induce clinically meaningful metabolic adaptations.

Keywords: *Aerobic Exercise, Fetuin-A, Insulin Resistance, Type2 Diabetes, Yoga.*

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1. Introduction

Obesity and type 2 diabetes represent two of the most pressing global health burdens of the 21st century, driven largely by sedentary lifestyles and energy imbalance (1, 2). Beyond classical disturbances in glucose and lipid metabolism, recent research has highlighted the pathophysiological significance of hepatokines particularly fetuin-A as key modulators linking adiposity to systemic insulin resistance and cardiometabolic dysfunction (3, 4). Fetuin-A, a liver-derived glycoprotein abundantly circulating in plasma, has consistently been associated with elevated BMI, impaired glucose tolerance, type 2 diabetes, and increased cardiovascular risk (4).

Fetuin-A has been implicated in metabolic dysfunction primarily through its ability to interfere with insulin signaling and promote insulin resistance (5). Elevated circulating levels of fetuin-A are also associated with increased inflammatory activity and impaired metabolic regulation in insulin-sensitive tissues, particularly in the context of obesity and excess lipid availability (6, 7). Together, these effects position fetuin-A as an important mediator linking hepatic function, inflammation, and insulin resistance in obesity-related metabolic disorders.

Physical activity remains one of the most effective non-pharmacological interventions for improving metabolic health, with extensive evidence demonstrating its capacity to modulate inflammatory pathways and enhance insulin sensitivity (8-10). Aerobic exercise, through improvements in cardiorespiratory fitness and energy expenditure, has been shown to reduce fasting glucose, enhance insulin sensitivity, and improve lipid profile, while also exerting potential downregulating effects on fetuin-A (11-13). Resistance training, by increasing lean mass and augmenting basal metabolic rate, further contributes to improvements in glycemic control and body composition. Shabkhiz et al. (2021) demonstrated that resistance training can significantly reduce fetuin-A and FGF21 levels while improving insulin resistance (14). Combined aerobic–resistance protocols often elicit superior metabolic adaptations, including reductions in inflammatory markers and fetuin-A (15).

Beyond conventional exercise modalities, yoga integrating physical postures, controlled breathing, and meditative practices has gained recognition as a complementary therapeutic approach capable of modulating autonomic function (16, 17), reducing psychological stress (18), and influencing hormonal and metabolic pathways (19). Evidence suggests that structured yoga interventions can improve glycemic indices and lipid metabolism in individuals with type 2 diabetes (20).

Despite these findings, clear gaps persist in literature. No study to date has simultaneously examined aerobic exercise and yoga within a single comparative framework to determine their distinct or relative effects on serum fetuin-A, particularly in obese middle-aged women with type 2 diabetes, a group disproportionately vulnerable to metabolic deterioration due to chronic physical inactivity. Given the biological relevance of fetuin-A as a mechanistic marker of metabolic dysfunction, identifying exercise modalities capable of modulating its levels is of clinical value.

Therefore, the present study aims to systematically evaluate and compare the effects of a structured 12-week aerobic training program and a yoga intervention on serum fetuin-A levels in obese women with type 2

2. Methods and Materials

2.1 *Study Design*

This study was conducted as a randomized controlled trial with a pretest–posttest parallel-group design. Participants were randomly allocated to aerobic training, yoga, or control groups using a computerized block randomization procedure to ensure balanced group sizes. Although the study did not include allocation concealment or blinding, the randomized design was selected to reduce selection bias and allow comparison of intervention effects over time.

2.2 *Participants*

30 obese (BMI $\geq$ 25 kg/m^2), non-menopausal women aged over 40 years with a clinical diagnosis of type 2 diabetes were recruited from sports centers in Karaj. Diagnosis was confirmed according to ADA criteria. Inclusion criteria consisted of confirmed type 2 diabetes, overweight or obesity, absence of cardiovascular, hepatic, renal, or musculoskeletal diseases, and no engagement in regular exercise during the preceding six months. Exclusion criteria included acute illness, use of medications affecting metabolic status, and insufficient adherence to training sessions. Due to feasibility constraints, no priori sample size or power calculation was performed, and the sample size was determined pragmatically. Consequently, study should be considered exploratory in nature.

2.3 Randomization and Allocation

Eligible participants were randomly assigned to aerobic training (n = 10), yoga (n = 10), or control (n = 10) groups using block randomization generated by computer software. Group allocation was performed after baseline assessments.

2.4 Aerobic Training Protocol

The aerobic exercise intervention consisted of three supervised 60-minute sessions per week over 12 weeks. Sessions included a 15-minute warm-up period with light walking and dynamic stretching, followed by 30 minutes of structured aerobic movements targeting major muscle groups, and concluded with 15 minutes of cool-down stretching. Training intensity began at 60% of HRmax and progressively increased to 70%, with heart rate continuously monitored using a Polar telemetry system to ensure compliance with prescribed intensity.

2.5 Yoga Intervention

The yoga group also participated in three 60-minute supervised sessions per week for 12 weeks. Each session incorporated an opening prayer, muscle relaxation, Sun Salutation sequences, structured asana practice, kriya techniques, breathing exercises (pranayama), and guided meditation. Certified yoga instructors to ensure accuracy of technique and participant safety conducted sessions.

2.6 Control Group

Participants assigned to the control group were instructed to maintain their usual lifestyle and refrain from initiating any structured exercise program during the study period. Physical activity and lifestyle behaviors in the control group were not objectively monitored, which may have allowed unmeasured behavioral changes during the intervention period.

2.7 Dietary Intake and Confounding Factors

Participants in all groups were advised to maintain their habitual dietary patterns and avoid major lifestyle changes during the study. Dietary intake was not quantitatively assessed or controlled, and no standardized nutritional intervention was implemented. Consequently, variations in energy intake or macronutrient composition may have influenced metabolic outcomes.

2.8 Anthropometric and Physiological Measurements

All measurements were conducted at baseline and 48 hours after completion of the intervention to eliminate acute exercise effects. Height was measured using a stadiometer (0.1 cm accuracy), weight via a Seca digital scale (0.1 kg accuracy), and BMI subsequently calculated. Body circumferences (waist, hip, arm, and thigh) were assessed using standard anthropometric procedures. Body fat percentage was estimated using skinfold caliper measurements at the triceps, subscapular, and abdominal regions. Cardiorespiratory fitness was evaluated through a progressive treadmill exercise test to volitional exhaustion, conducted following American Heart Association guidelines. VO_2max was estimated using standard ACSM-based predictive formulas, with continuous heart rate monitoring throughout testing.

2.9 Biochemical Measurements

Fasting venous blood samples (5 mL) were collected in the morning following a 12-hour overnight fast at both time points. Samples were centrifuged immediately to separate serum, which was stored at −80°C until analysis. Serum fetuin-A concentrations were measured using a commercial ELISA kit (manufacturer: [ZELLBIO], country: [Germany], catalog number: [ZB-11386C-H9648]), according to manufacturer instructions. Fasting glucose and insulin were determined via enzymatic and immunoassay techniques, respectively, and insulin resistance was calculated using the HOMA-IR formula. Participants were instructed to avoid vigorous physical activity for 48 hours prior to testing, abstain from caffeine, alcohol, and supplements during the study, maintain stable dietary habits, and obtain at least eight hours of sleep the night before assessments.

2.10 Handling of Missing Data

All participants completed baseline and post-intervention assessments. Therefore, no missing data or dropouts were observed, and all analyses were conducted on complete cases.

2.11 Statistical Analysis

Statistical analyses were conducted using SPSS version 20. The Shapiro–Wilk test was used to evaluate normality of variable distributions. Within-group differences were assessed using paired t-tests, while between-group variations over time were examined using two-way repeated-measures

ANOVA. Pearson's correlation coefficients were calculated to explore associations between biochemical and anthropometric variables. Given the exploratory nature of the study and limited sample size, no formal correction for multiple comparisons was applied, and results should be interpreted cautiously. Statistical significance was defined as $p < 0.05$.

3. Results

3.1 Key Findings

Overall, the results of this study showed that twelve weeks of aerobic exercise and yoga did not produce statistically significant changes in serum fetuin-A levels, fasting blood glucose (FBS), insulin resistance (HOMA-IR), or anthropometric indices in obese women with type 2 diabetes. No significant group × time interactions were observed for any of the primary or secondary outcomes ($p > 0.05$). Although modest numerical reductions in fetuin-A, body weight, and body fat percentage were observed in the intervention groups particularly in the yoga group, these changes did not reach statistical significance and were not different from those observed in the control group. The following sections present the descriptive and inferential results in detail.

3.2 Descriptive Characteristics of Participants

Table 1 presents the descriptive characteristics of participants, including mean ± standard deviation for age, height, weight, waist-to-hip ratio, body mass index (BMI), fasting blood glucose, and insulin resistance index (HOMA-IR) across the aerobic training, yoga, and control groups. At baseline, no significant differences were observed among the groups in any anthropometric or metabolic variables, indicating successful randomization and homogeneity of participants prior to the intervention.

Table 1. Descriptive characteristics of anthropometric and metabolic variables in the groups

Variable	Group	Pre Test Mean ± standard deviation	Post test Mean ± standard deviation
Weight (kg)	Yoga	6.72 ± 70.59	6.60 ± 69.92
	Aerobic	5.09 ± 70.92	5.01 ± 68.47
	Control	5.89 ± 70.98	7.61 ± 71.83
Body fat (%)	Yoga	3.59 ±39.88	3.80 ±39.67
	Aerobic	3.71 ± 41.04	3.78 ± 39.91
	Control	2.01 ±41.63	3.13±42.14
WHR	Yoga	0.04 ± 0.91	0.04 ±0.90
	Aerobic	0.04 ± 0.91	0.04 ± 0.91
	Control	0.05 ± 0.92	0.05 ± 0.92
BMI (W/H2)	Yoga	2.71 ± 27.75	2.73 ± 27.46
	Aerobic	2.43 ±28.08	2.44 ± 27.10
	Control	2.62 ±28.05	3.47 ± 28.41
FBS (mg/dl)	Yoga	51.06 ± 150.20	36.47 ± 140.30
	Aerobic	45.92 ± 182.50	34.59 ± 145.40
	Control	34.91 ±130.25	34.87 ± 133.50
HOMA-IR	Yoga	2.32 ±4.57	2.65 ± 5.55
	Aerobic	6.90 ±7.66	2.94 ±4.53
	Control	1.74 ± 3.06	4.53 ± 5.05

To examine the assumption of equality of variances, Levene's test was performed. The results showed that the significance level for all variables exceeded 0.05, confirming the homogeneity of variances across the study groups and supporting the use of ANOVA. The two-way ANOVA results indicated that there was no significant difference between the two training programs (aerobic and yoga) in their effect on serum fetuin-A levels in obese women with type 2 diabetes ($p = 0.95$). Moreover, the main effect of time was not significant ($p = 0.37$), meaning that changes in fetuin-A levels over the 12-week intervention period were not statistically different regardless of group allocation. Additionally, the interaction effect of group × time was also non-significant ($p = 0.69$), suggesting that the pattern of changes in fetuin-A across the three groups was similar.

Despite the lack of statistical significance, inspection of mean scores showed a downward trend in fetuin-A levels in both training groups particularly in the yoga group, following the intervention, whereas no notable change was observed in the control group. Although these reductions did not reach statistical significance, they may indicate a potential positive tendency of exercise interventions to improve the target metabolic marker.

Overall, the findings revealed that twelve weeks of aerobic training and yoga reduced fetuin-A levels, yet these changes did not achieve statistical significance. Table 2 presents the mean serum fetuin-A levels of obese women with type 2 diabetes before and after the interventions in the aerobic, yoga, and control groups.

Table 2. Mean Serum Fetuin-A Level in the Groups

Variable	Group	Pre Test Mean ± standard deviation	Post test Mean ± standard deviation
Fetuin_a (mg/L)	Yoga	458/88 ± 138/55	414/27 ± 73/37
	Aerobic	435/21 ± 56/19	429/01 ± 75/64
	Control	443/03 ± 27/92	436/37 ± 38/59

The changes in serum fetuin-A levels of obese women with type 2 diabetes in the aerobic, yoga, and control groups across the pre-test and post-test stages are illustrated in Figure 1.

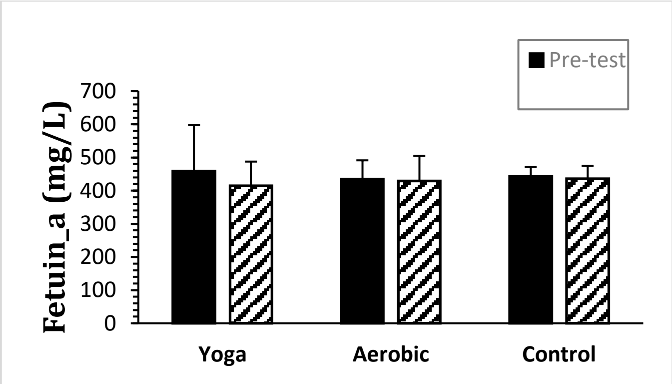

Figure 1. Comparison of Changes in Serum Fetuin-A Levels Across the Study Groups

The percentage changes in serum fetuin-A levels of obese women with type 2 diabetes in the different study groups, relative to the pre-test stage, are presented in Figure 2.

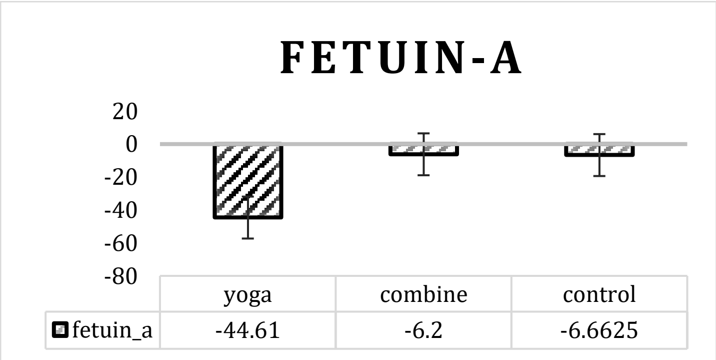

Figure 2. Percentage Changes in Serum Fetuin-A Levels in Obese Women with Type 2 Diabetes

The examination of anthropometric indices showed that although weight and body fat percentage decreased in both training groups following the intervention, these changes were not statistically significant when compared across groups. Likewise, fasting blood glucose (FBS) levels in obese women with type 2 diabetes did not differ significantly among the aerobic, yoga, and control groups (Figure 3).

Regarding insulin resistance (HOMA-IR), the findings indicated that changes in this variable were not statistically significant either between groups ($p = 0.67$) or overtime ($p = 0.18$) (Figure 4).

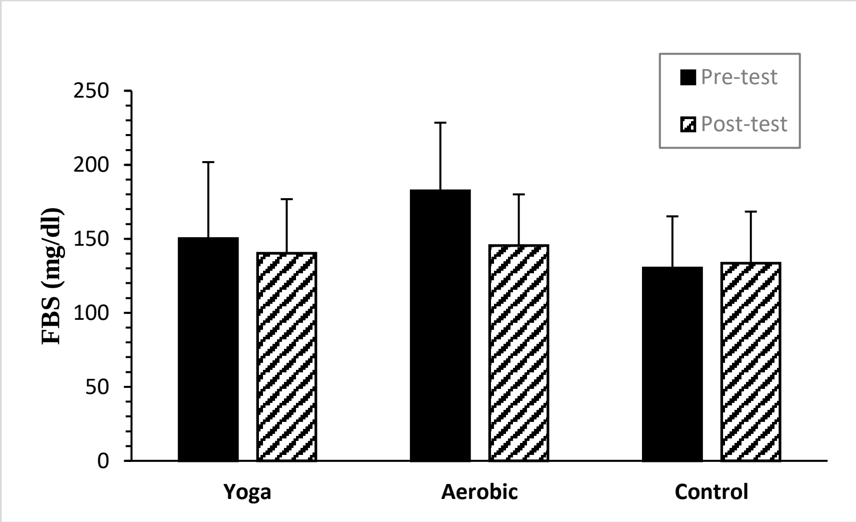

Figure 3. Comparison of Changes in Fasting Blood Glucose Levels across the Study Groups

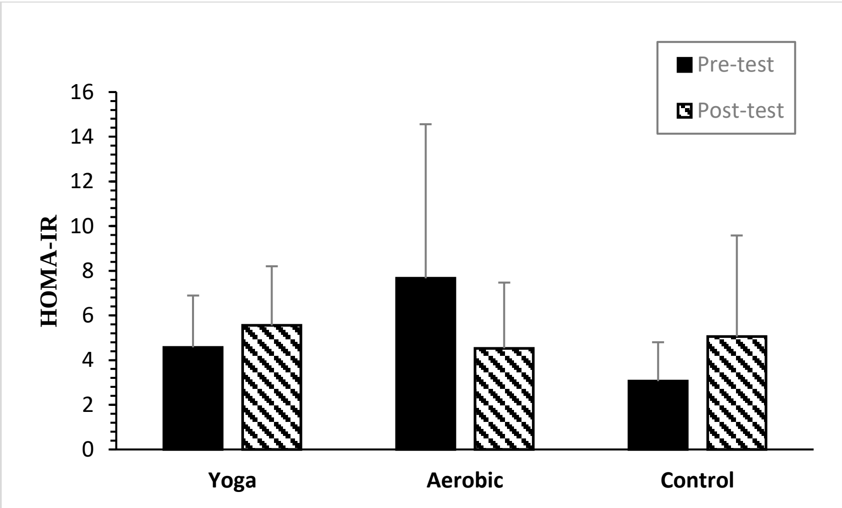

Figure 4. Comparison of Changes in Insulin Resistance (HOMA-IR) across the Study Groups

4. Discussion

The present study showed that a 12-week program of aerobic exercise or yoga did not produce statistically significant changes in serum fetuin-A levels in obese women with type 2 diabetes. Although mean values tended to decrease in both intervention groups, these changes were small and should not be interpreted as evidence of a clear metabolic effect. A direct comparison between the two exercise modalities revealed no meaningful differences between aerobic training and yoga. While the yoga group demonstrated a slightly greater numerical reduction in fetuin-A, this difference was not statistically significant and therefore cannot be considered indicative of a modality-specific advantage. Within the context of the present study, both interventions appeared to exert comparable and limited effects on this outcome. Previous research has reported reductions in fetuin-A following structured exercise interventions; however, findings across studies remain heterogeneous. For example, the systematic review and meta-analysis by Ramírez-Vélez et al. (2019) reported that exercise training may be associated with lower fetuin-A levels in individuals with obesity or diabetes, although effect sizes varied considerably depending on exercise modality, intensity, and participant characteristics (11). Similarly, Zhang et al. (2018) observed reductions in fetuin-A following a 12-week aerobic training program in individuals with type 2 diabetes (13). Keihanian et al. (2019) also reported decreases in serum fetuin-A after both aerobic and resistance training interventions in men with type 2 diabetes (21).

In contrast, the present findings suggest that comparable interventions may not elicit statistically detectable changes in obese middle-aged women, highlighting potential population-specific responses. Several factors may explain the absence of statistically significant effects in the current study. The relatively small sample size likely limited statistical power, reducing the likelihood of detecting modest intervention-related changes. In addition, the 12-week duration may have been insufficient to induce sustained alterations in hepatokine regulation. Inter-individual variability in metabolic responsiveness to exercise may have further contributed to the observed null findings. Although previous studies have linked exercise-related reductions in fetuin-A to improvements in insulin signaling or inflammatory regulation (11, 22), such mechanisms were not directly assessed in the present investigation. Consequently, interpretations involving autonomic regulation, hypothalamic–pituitary–adrenal axis activity, cortisol modulation, or changes in hepatic fat content remain speculative and cannot be substantiated by the current data (23-25).

Consistent with the fetuin-A findings, no statistically significant changes were observed in anthropometric measures, fasting blood glucose, or insulin resistance across groups. Taken together, these results suggest that while the applied exercise programs were safe and well tolerated, they did not induce measurable metabolic adaptations within the timeframe studied.

4.1 Limitations

Several limitations warrant consideration. First, the modest sample size and the absence of a priori power calculation limit confidence in the interpretation of null findings. Second, dietary intake was not objectively monitored, and unmeasured variation in energy or macronutrient consumption may have influenced metabolic outcomes. Third, participants were recruited from a single center, which may restrict the generalizability of the results. Finally, the lack of long-term follow-up prevents conclusions regarding the persistence of any potential exercise-related effects. Future studies should incorporate standardized dietary monitoring or controlled nutritional interventions to better isolate the effects of exercise on metabolic markers.

5. Conclusion

In this study, twelve weeks of aerobic exercise and yoga were not associated with statistically significant changes in serum fetuin-A levels, glycemic markers, or anthropometric indices in obese women with type 2 diabetes. Although both exercise programs showed a modest, non-significant tendency toward lower fetuin-A levels, this finding should be interpreted cautiously and cannot be considered evidence of a definitive metabolic effect. The lack of significant changes may be attributed to the relatively small sample size, the limited intervention duration, and inter-individual variability in responses to exercise. In addition, dietary intake and habitual lifestyle behaviors were not strictly controlled, which may have further attenuated detectable effects. Importantly, no adverse events were reported, indicating that both aerobic exercise and yoga are safe and feasible for women with type 2 diabetes. From a practical perspective, these activities may serve as low-risk, supportive lifestyle options alongside standard medical care, even when measurable improvements in metabolic markers are not observed. Future studies with larger samples, longer follow-up periods, and more rigorous control of confounding factors are needed to clarify the potential long-term effects of structured exercise on fetuin-A and related metabolic outcomes.

Authors' Contributions

S.R. contributed to the study design, data collection, exercise supervision, and drafting of the manuscript.

P.P. assisted with data analysis, interpretation of results, and critical revision of the manuscript.

R.S. conceived and supervised the study, contributed to the study design, interpretation of findings, and final approval of the manuscript.

All authors read and approved the final version of the manuscript.

Declaration

None.

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 research protocol was approved by the relevant institutional review board under the reference number IR.UT.PSYEDU.REC.1403.077. All participants were fully informed about study procedures, potential risks, and their right to withdraw at any time, and subsequently provided written informed consent, in accordance with the principles of the Declaration of Helsinki.

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