

Combined Effects of Aerobic Training and Vitamin D Supplementation on Inflammatory Markers and Metabolic Health in Overweight Middle-School Girls: A Randomized Controlled Trial

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Article Info	Abstract
Article type: Research Article Article history: Received 18 June 2026 Received in revised form 21 March 2026 Accepted 08 April 2026 Available online 29 June 2026 Keywords: Overweight, Exercise, Vitamin D, Inflammation, Insulin Resistance.	Introduction: Overweight during early adolescence is associated with chronic low-grade inflammation and increased cardiometabolic risk. School-based aerobic exercise is a practical strategy to improve metabolic health, and vitamin D may provide additional anti-inflammatory benefits. Objective: To examine the effects of aerobic training (AT) with or without vitamin D supplementation on inflammatory markers and metabolic outcomes in overweight middle-school girls. Method: In this 12-week, three-arm randomized controlled trial, overweight girls (11-14 years) were randomly assigned to AT plus vitamin D (AT+VitD), AT only (AT), or control (CON). The AT was conducted 3 sessions/week at moderate-to-vigorous intensity. The AT+VitD group received vitamin D (2000 IU/day). Fasting blood samples were collected at baseline and post-intervention to assess hs-CRP, IL-6, TNF-α, fasting glucose, insulin, HOMA-IR, HbA1c, and lipid profile. Anthropometrics, waist indices, and blood pressure were also measured. Data was analyzed using ANCOVA adjusted for baseline values. Results: After 12 weeks, hs-CRP, IL-6, and TNF-α showed significant group effects ($p < 0.05$), with the greatest reductions in AT+VitD, followed by AT, versus CON. Fasting insulin and HOMA-IR also improved significantly in both intervention groups, with larger changes in AT+VitD. Waist indices, systolic blood pressure, and lipid profile improved favorably, generally with the strongest effects in the combined group. Serum 25(OH)D increased significantly only in AT+VitD ($p < 0.05$), confirming supplementation effectiveness. Conclusions: Combining AT with vitamin D may be an effective, feasible strategy to reduce inflammation-related cardiometabolic risk during early adolescence. Cite this Article: Farhangi, N. (2026). Combined Effects of Aerobic Training and Vitamin D Supplementation on Inflammatory Markers and Metabolic Health in Overweight Middle-School Girls: A Randomized Controlled Trial. <i>Physical Activity in Children</i>, 3(1), 57-65. https://doi.org/10.22034/pach.2026.586887.1091

1. Introduction

Overweight and obesity during early adolescence represent a major and growing public health challenge (1,2). Excess adiposity emerging in the middle-school years is associated with adverse cardiometabolic trajectories, including progression toward insulin resistance, dyslipidemia, elevated blood pressure, and central fat accumulation (3,4). Beyond these established risk factors, increasing evidence indicates that overweight youth also exhibit a state of chronic low-grade inflammation, characterized by elevated circulating inflammatory biomarkers such as high-sensitivity C-reactive protein (hs-CRP) and pro-inflammatory cytokines (e.g., interleukin-6 [IL-6] and tumor necrosis factor-alpha [TNF- α]) (5,6). This inflammatory milieu is clinically relevant because it contributes to endothelial dysfunction, impaired insulin signaling, and early atherogenic processes, thereby linking excess adiposity in adolescence with an unfavorable cardiometabolic risk profile later in life.

Early adolescent girls may be particularly vulnerable to unfavorable changes in body composition and metabolic health due to pubertal

transitions, reduced physical activity, and psychosocial factors that can influence lifestyle behaviors (7,8). During puberty, girls typically experience increases in fat mass, alterations in body-fat distribution, and transient changes in insulin sensitivity, all of which may contribute to greater inflammatory activity and metabolic variability (9). In parallel, the transition from childhood to adolescence is often accompanied by declines in structured physical activity, increased sedentary behavior, and reduced cardiorespiratory fitness (10). Collectively, these changes highlight the importance of developing feasible, school-based interventions that can improve inflammatory and metabolic profiles in overweight middle-school girls.

Aerobic training (AT) is widely recommended as a first-line lifestyle strategy for improving cardiometabolic health in youth (11,12). Regular AT can reduce fat mass, improve cardiorespiratory fitness, enhance endothelial function, and improve insulin sensitivity through increased skeletal muscle glucose uptake and improved mitochondrial function (13,14). Importantly, AT may also exert anti-inflammatory effects, both directly and indirectly (15). Proposed



mechanisms include exercise-induced changes in cytokine signaling, improved immune regulation, and reductions in oxidative stress (16). Indirect mechanisms include reductions in visceral adiposity and improved metabolic flexibility, which decrease adipose tissue-driven inflammatory signaling (17). However, responses to AT can vary across individuals, and improvements in inflammatory markers are not always robust in pediatric populations, particularly when changes in adiposity are modest or baseline inflammation is low. Therefore, identifying complementary strategies that can enhance exercise-induced improvements in inflammation and metabolic health is of substantial interest.

One candidate adjunct is vitamin D supplementation. Vitamin D has functions beyond bone and mineral metabolism and is increasingly recognized for its roles in immune regulation and inflammatory control (18). The active vitamin D metabolite influences gene transcription through the vitamin D receptor, which is expressed in numerous tissues including immune cells (19). Mechanistically, vitamin D may modulate innate and adaptive immune responses, reduce production of pro-inflammatory cytokines, and promote anti-inflammatory signaling pathways (20). Observational studies in adolescents have frequently reported associations between low serum 25-hydroxyvitamin D [25(OH)D] concentrations and higher adiposity, poorer insulin sensitivity, and elevated inflammatory markers, including hs-CRP (21-23). Vitamin D insufficiency is also common in school-age youth, particularly among girls, due to reduced outdoor activity, limited sun exposure, and dietary inadequacy (24). These patterns make vitamin D a biologically plausible and practical intervention target in overweight middle-school girls.

Despite the plausibility of vitamin D as an anti-inflammatory and metabolic modulator, intervention findings in pediatric populations have been mixed. Some trials suggest that supplementation improves inflammatory markers or insulin resistance, while others report minimal effects, potentially due to differences in baseline vitamin D status, dosing regimens, intervention duration, adherence, and participant characteristics (25-27). It is also possible that vitamin D supplementation alone has limited impact unless combined with lifestyle modification that directly targets adiposity and fitness (28). In this context, a combined intervention pairing AT with vitamin D supplementation may be more effective than either strategy alone. AT could reduce adiposity-driven inflammation and improve metabolic function, while vitamin D may further support immune regulation and attenuate inflammatory signaling, potentially leading to larger improvements in inflammatory biomarkers and cardiometabolic outcomes.

From a feasibility standpoint, combining AT with vitamin D supplementation is attractive for school-based settings. AT can be delivered using accessible activities (e.g., running games, aerobic circuits, dance-based exercise) without specialized equipment. Vitamin D supplementation is inexpensive, easy to administer, and generally safe when used at standard doses and monitored appropriately. If effective, this combined approach could be implemented as part of school health initiatives to improve inflammatory and

metabolic markers associated with cardiometabolic health among girls at risk.

Therefore, the purpose of the present study was to examine the combined effects of a supervised AT program and vitamin D supplementation on inflammatory markers and metabolic health in overweight middle-school girls. It was hypothesized that (1) AT would improve inflammatory and metabolic outcomes compared with control, and (2) the combined intervention would produce greater improvements than AT alone.

2. Methods

2.1. Study design

This study was a three-arm, parallel-group randomized controlled trial.

2.2. Participants

Participants were overweight middle-school girls recruited from local schools through announcements and parent meetings. Overweight was defined as BMI-for-age between the 85th and 94th percentiles based on CDC growth charts. Participants were eligible for inclusion if they were middle-school girls aged 11-14 years with a BMI-for-age between the 85th and 94th percentiles, had not engaged in structured exercise training more than once per week during the previous 3 months, were free from acute illness and medically cleared for exercise participation, and provided written assent along with parental or guardian consent. Participants were excluded if they had diabetes, cardiovascular disease, chronic inflammatory disease, renal or hepatic disease, or any other major medical condition; were using medications or supplements known to affect inflammation, lipid metabolism, or glucose regulation; had known hypercalcemia, a history of kidney stones, or any contraindication to vitamin D supplementation; had musculoskeletal limitations that prevented exercise participation; or were unable to complete baseline blood sampling. Vitamin D insufficiency was defined as a 25(OH)D concentration <30 ng/mL (75 nmol/L), whereas vitamin D deficiency was defined as <20 ng/mL (50 nmol/L), according to established pediatric guidelines. Baseline vitamin D status was recorded for all participants prior to randomization. Sample size was estimated *a priori* to detect a moderate between-group difference in hs-CRP ($f = 0.25$) with 80% statistical power at $\alpha = 0.05$, allowing for an anticipated attrition rate of approximately 10-15%. The required sample size was estimated at 15 participants per group. Pubertal maturation was not formally assessed. After baseline testing, participants were randomized using a computer-generated random sequence prepared by an independent researcher. Allocation concealment was ensured using sequentially numbered, opaque, sealed envelopes. Due to the nature of the exercise intervention, participants and trainers were not blinded; however, laboratory staff and outcome assessors were blinded to group assignment where feasible.

2.3. Interventions

2.3.1. Aerobic training program

Participants in the AT+VitD and AT groups completed a supervised school-based AT program for 12

weeks, with three sessions per week lasting approximately 45–60 minutes each. Each session consisted of a 10-minute warm-up including light jogging or walking, dynamic mobility, and movement preparation, followed by a 30–40-minute main AT involving continuous and/or interval-based activities such as brisk walking, running games, aerobic circuits, and dance or aerobics, and concluded with a 5–10-minute cool-down of low-intensity walking and static stretching. Exercise intensity was prescribed using heart rate and perceived exertion, with participants exercising at 60–75% of age-predicted maximum heart rate during weeks 1–4 and progressing to 70–85% during weeks 5–12, where maximum heart rate was estimated as $220 - \text{age}$. Participants were encouraged to maintain a moderate-to-vigorous intensity corresponding to a rating of perceived exertion of approximately 12–16 on the Borg 6–20 scale. Heart rate was monitored during randomly selected training sessions using wearable heart-rate monitors to verify adherence to the prescribed intensity. Mean exercise intensity corresponded to approximately $74.8 \pm 5.6\%$ of age-predicted maximum heart rate across the intervention. Attendance was recorded at each session, and trainers supervised all sessions to ensure safety, appropriate progression, and participant engagement.

2.3.2. Vitamin D supplementation

Participants in the AT+VitD group received vitamin D3 (cholecalciferol) supplementation for 12 weeks using a daily oral dose of 2000 IU/day, consumed with the main meal. Vitamin D supplements were supplied in identical containers and distributed weekly by the research team. Supplement adherence was monitored using capsule counts and weekly compliance logs, and overall compliance was calculated as the percentage of prescribed capsules consumed.

2.3.3. Control group (CON)

Participants in CON were instructed to maintain usual daily activities and not begin new structured exercise or supplementation during the study. After study completion, general healthy lifestyle guidance was offered.

2.3.4. Diet and lifestyle control

All groups received standardized advice to maintain their habitual dietary intake and sleep routines throughout the intervention and to avoid initiating weight-loss programs. Dietary intake was monitored using 3-day food records (two weekdays and one weekend day) completed at baseline and again during the final week of the intervention. Dietary records were reviewed by the research team to identify major changes in total energy intake or macronutrient distribution. Participants were also asked to report any illness, medication changes, or additional supplement use throughout the study.

2.4. Measurements

All measurements were obtained at baseline and post-intervention under standardized conditions. Participants were asked to avoid vigorous activity for 48 hours and to fast overnight (10–12 hours) before blood sampling.

2.4.1. Inflammatory markers

Inflammatory markers were assessed using fasting venous blood samples. High-sensitivity hs-CRP, IL-6, and TNF- α were measured using commercially

available ELISA kits. All samples were analyzed in duplicate by laboratory personnel blinded to group allocation. Intra-assay and inter-assay coefficients of variation were maintained below 10% for all assays.

2.4.2. Metabolic health

Glycemic control / insulin resistance: Glycemic control and insulin resistance were evaluated using fasting glucose, fasting insulin, glycated hemoglobin (HbA1c), and the homeostasis model assessment of insulin resistance (HOMA-IR), which was calculated as:

$$\text{HOMA-IR} = \frac{\text{fasting insulin}(\mu\text{IU/mL}) \times \text{fasting glucose}(\text{mg/dL})}{405}$$

Lipid profile: The lipid profile was assessed by measuring total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and triglycerides (TG).

Vitamin D status: 25(OH)D concentrations were measured to characterize baseline vitamin D status and to confirm biological exposure and adherence to the supplementation intervention.

Blood pressure: Resting SBP/DBP measured after 5 minutes seated rest using an automated monitor; two readings were taken and averaged.

Anthropometry: Anthropometric measurements included height (stadiometer), body mass (calibrated scale), BMI and BMI-for-age percentile, waist circumference measured at the midpoint between the lowest rib and the iliac crest, and waist-to-height ratio (WtHR).

2.6. Statistical analysis

Data are presented as mean $\pm$ SD (or median [IQR] for skewed variables). Normality was evaluated using the Shapiro-Wilk test and visual inspection of distributions. Baseline differences were examined using one-way ANOVA for continuous variables and chi-square tests for categorical variables. Intervention effects were assessed using ANCOVA, with post-intervention values entered as dependent variables, group as the fixed factor, and baseline values included as covariates. Post hoc pairwise comparisons were performed using Bonferroni adjustment. Effect sizes were reported as partial eta-squared (η^2) for ANCOVA analyses and 95% confidence intervals were calculated for the primary outcome estimates to facilitate interpretation of treatment effects. Statistical significance was accepted at $p < 0.05$.

3. Results

3.1. Participant flow

A total of 93 participants were screened for eligibility, of whom 74 participants met the inclusion criteria and were randomized to the AT+VitD ($n = 25$), AT ($n = 24$), or CON ($n = 25$) groups. During intervention, five participants withdrew because of school absence, personal reasons, or incomplete post-intervention testing. Consequently, 69 participants completed the study and were included in the final analysis: AT+VitD ($n = 23$), AT ($n = 24$), and CON ($n = 22$) (Figure 1). Mean attendance at supervised exercise sessions was $88.4 \pm 6.7\%$ in the intervention groups. Supplement adherence in the AT+VitD group, assessed by capsule counts and weekly compliance logs, was 92.1%. Heart-rate monitoring performed during

randomly selected sessions confirmed that participants exercised at a mean intensity of $74.6 \pm 4.8\%$ of age-predicted maximum heart rate, consistent with

the prescribed training intensity. No serious adverse events were reported.

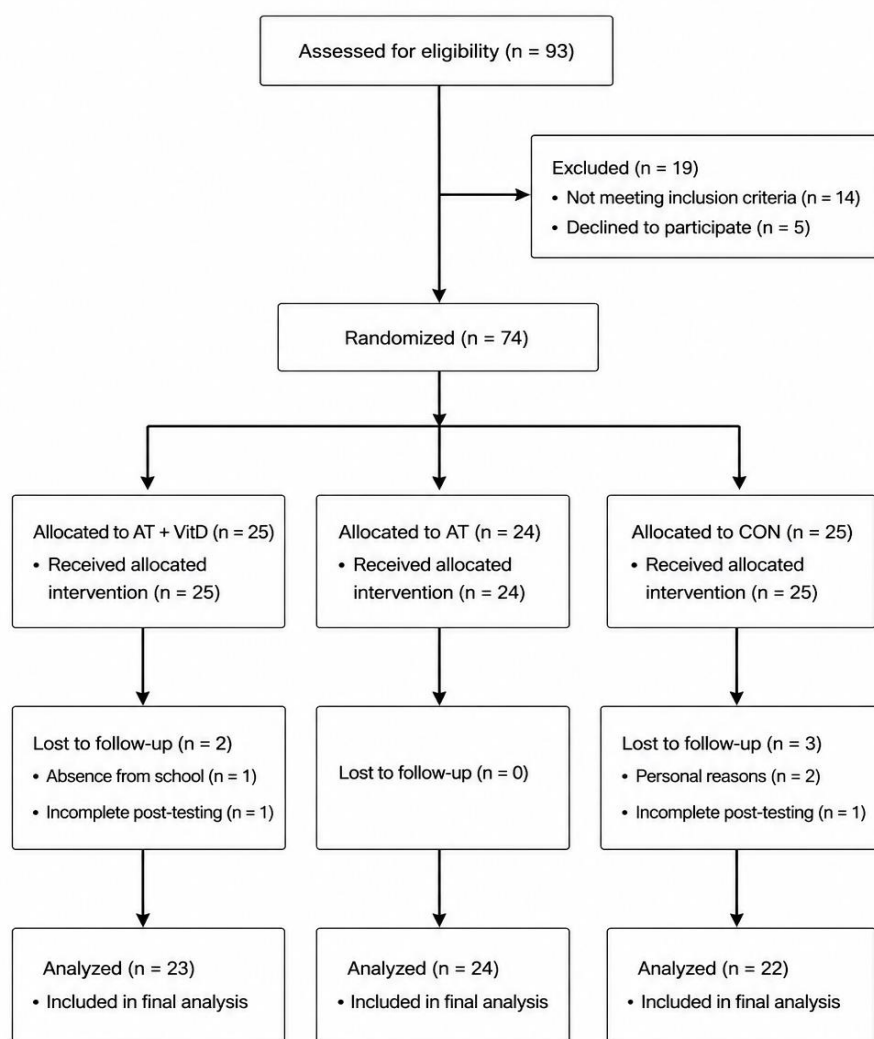


Figure 1. CONSORT Flow Diagram of Participant Recruitment, Randomization, Follow-up, and Analysis

3.2. Baseline characteristics

Baseline demographic, anthropometric, inflammatory, metabolic, and cardiovascular characteristics did not differ significantly among

groups (all $p > 0.05$), indicating successful randomization (Table 1). Baseline serum 25(OH)D concentrations indicated vitamin D insufficiency across all groups.

Table 1. Baseline Characteristics of Participants.

Variable	AT+VitD	AT	CON	p
Age (years)	12.6 $\pm$ 0.9	12.5 $\pm$ 0.8	12.7 $\pm$ 0.8	0.71
Height (cm)	153.4 $\pm$ 6.8	152.8 $\pm$ 6.5	154.1 $\pm$ 6.9	0.79
Body mass (kg)	58.7 $\pm$ 7.2	57.9 $\pm$ 6.8	59.1 $\pm$ 7.5	0.83
BMI (kg/m ²)	24.9 $\pm$ 1.8	24.8 $\pm$ 1.7	24.9 $\pm$ 1.9	0.97
BMI-for-age percentile	90.8 $\pm$ 2.6	90.5 $\pm$ 2.8	91.0 $\pm$ 2.4	0.76
Waist circumference (cm)	81.4 $\pm$ 4.9	80.9 $\pm$ 4.6	81.7 $\pm$ 5.1	0.84
WHtR	0.53 $\pm$ 0.03	0.53 $\pm$ 0.03	0.53 $\pm$ 0.03	0.92
Systolic BP (mmHg)	116.2 $\pm$ 7.5	115.8 $\pm$ 7.2	116.6 $\pm$ 7.8	0.89
Diastolic BP (mmHg)	72.9 $\pm$ 5.8	73.1 $\pm$ 5.4	73.4 $\pm$ 5.6	0.95
Serum 25(OH)D (ng/mL)	18.7 $\pm$ 4.1	19.1 $\pm$ 4.3	18.9 $\pm$ 4.0	0.93
hs-CRP (mg/L)	2.9 $\pm$ 0.9	2.8 $\pm$ 0.8	2.9 $\pm$ 0.9	0.88
IL-6 (pg/mL)	2.8 $\pm$ 0.7	2.7 $\pm$ 0.6	2.8 $\pm$ 0.7	0.84
TNF- α (pg/mL)	3.5 $\pm$ 0.8	3.4 $\pm$ 0.7	3.5 $\pm$ 0.8	0.87
Fasting glucose (mg/dL)	94.8 $\pm$ 6.2	94.1 $\pm$ 6.0	95.0 $\pm$ 6.3	0.89
Fasting insulin (μ U/mL)	17.6 $\pm$ 4.1	17.2 $\pm$ 3.9	17.8 $\pm$ 4.2	0.86
HOMA-IR	4.1 $\pm$ 1.1	4.0 $\pm$ 1.0	4.2 $\pm$ 1.1	0.82
HbA1c (%)	5.6 $\pm$ 0.3	5.6 $\pm$ 0.3	5.6 $\pm$ 0.3	0.99
TC (mg/dL)	176.4 $\pm$ 18.2	174.8 $\pm$ 17.6	177.0 $\pm$ 18.5	0.91
LDL-C (mg/dL)	108.9 $\pm$ 13.9	107.6 $\pm$ 13.1	109.4 $\pm$ 14.1	0.89
HDL-C (mg/dL)	43.6 $\pm$ 5.7	43.9 $\pm$ 5.5	43.4 $\pm$ 5.9	0.95
TG (mg/dL)	126.8 $\pm$ 21.6	124.9 $\pm$ 20.8	127.5 $\pm$ 22.1	0.91

3.3. Inflammatory markers

After adjustment for baseline values, ANCOVA demonstrated significant overall group effects for hs-CRP ($F_{2,65} = 15.17$, $p < 0.001$, $\eta^2 = 0.32$), IL-6 ($F_{2,65} = 6.84$, $p = 0.002$, $\eta^2 = 0.17$), and TNF- α ($F_{2,65} = 5.96$, $p = 0.004$, $\eta^2 = 0.16$). Post hoc Bonferroni-adjusted comparisons showed that hs-CRP decreased significantly more in the AT+VitD group than in both the AT and CON groups,

whereas the AT group also demonstrated greater reductions than CON. For IL-6 and TNF- α , significant reductions were observed in the AT+VitD group compared with CON, while differences between the AT and CON groups did not reach statistical significance. The estimated adjusted between-group difference in hs-CRP between AT+VitD and CON was -0.86 mg/L (95% CI: -1.28 to -0.44). Similar trends were observed for IL-6 and TNF- α (Table 2; Figure 2).

Table 2. Changes in Inflammatory Markers Outcomes After 12 Weeks.

Variable	Time	AT+VitD	AT	CON	Group effect (p)	η^2
hs-CRP (mg/L)	Baseline	2.9±0.9	2.8±0.8	2.9±0.9	<0.001	0.32
	Post	1.9±0.6	2.3±0.7	2.8±0.9		
IL-6 (pg/mL)	Baseline	2.8±0.7	2.7±0.6	2.8±0.7	0.002	0.17
	Post	2.0±0.5	2.3±0.5	2.8±0.7		
TNF- α (pg/mL)	Baseline	3.5±0.8	3.4±0.7	3.5±0.8	0.004	0.16
	Post	2.8±0.6	3.1±0.6	3.5±0.8		

Data are mean $\pm$ SD. Group effects were tested using ANCOVA adjusted for baseline values.

3.4. Glycemic outcomes and insulin resistance

Significant overall group effects were observed for fasting glucose ($F_{2,65} = 3.68$, $p = 0.030$, $\eta^2 = 0.10$), fasting insulin ($F_{2,65} = 7.54$, $p < 0.001$, $\eta^2 = 0.19$), HOMA-IR ($F_{2,65} = 7.89$, $p < 0.001$, $\eta^2 = 0.21$), and HbA1c ($F_{2,65} = 7.74$, $p = 0.001$, $\eta^2 = 0.19$). Bonferroni-adjusted pairwise comparisons demonstrated that both intervention groups exhibited significantly lower fasting insulin and HOMA-IR values than the CON group, whereas the AT+VitD group achieved significantly greater improvements than the AT group. Changes in fasting glucose and HbA1c followed the same pattern but were smaller in magnitude. The adjusted mean difference in HOMA-IR between AT+VitD and CON was -1.08 (95% CI: -1.52 to -0.64), while the difference between AT+VitD and AT was -0.39 (95% CI: -0.74 to -0.04) (Table 3; Figure 2).

3.5. Lipid profile, anthropometric indices, and blood pressure

ANCOVA revealed significant overall group effects for TC ($F_{2,65} = 5.54$, $p = 0.006$, $\eta^2 = 0.15$), LDL-C ($F_{2,65} = 4.83$, $p = 0.010$, $\eta^2 = 0.13$), HDL-C ($F_{2,65} = 4.11$, $p = 0.020$, $\eta^2 = 0.11$), TG ($F_{2,65} = 6.11$, $p = 0.004$, $\eta^2 = 0.16$), body mass ($F_{2,65} = 3.11$, $p = 0.040$, $\eta^2 = 0.09$), BMI ($F_{2,65} = 3.68$, $p = 0.030$, $\eta^2 = 0.10$),

waist circumference ($F_{2,65} = 7.54$, $p < 0.001$, $\eta^2 = 0.19$), WHtR ($F_{2,65} = 6.84$, $p = 0.002$, $\eta^2 = 0.17$), and systolic blood pressure ($F_{2,65} = 7.74$, $p = 0.001$, $\eta^2 = 0.19$). HDL-C increased modestly in both intervention groups, with the largest improvement observed in the AT+VitD group. Likewise, reductions in waist circumference, WHtR, TG, LDL-C, and systolic blood pressure were greatest in the combined intervention group. Diastolic blood pressure showed a nonsignificant trend toward improvement ($F_{2,65} = 2.61$, $p = 0.080$).

3.6. Vitamin D status

After adjustment for baseline values, serum 25(OH)D concentrations differed significantly among groups ($F_{2,65} = 7.54$, $p < 0.001$, $\eta^2 = 0.19$). Post hoc analyses demonstrated that the AT+VitD group exhibited significantly higher post-intervention 25(OH)D concentrations than both the AT and CON groups, whereas no meaningful changes occurred in the AT or CON groups (Table 3; Figure 2). Dietary intake remained stable throughout the intervention. Analysis of 3-day food records showed no significant between-group differences in total energy intake or macronutrient composition at baseline or post-intervention (all $p > 0.05$).

Table 3. Changes in Glycemic Outcomes/Insulin Resistance, Lipid Profile, Anthropometry, Blood Pressure, and Vitamin D Status After 12 Weeks.

Variable	AT+VitD	AT	CON	Group effect (p)	η^2	Adjusted mean difference (95% CI)*
Vitamin D status						
Serum 25(OH)D (ng/mL)	18.7 $\pm$ 4.1 $\rightarrow$ 30.8 $\pm$ 5.2	19.1 $\pm$ 4.3 $\rightarrow$ 19.8 $\pm$ 4.4	18.9 $\pm$ 4.0 $\rightarrow$ 18.6 $\pm$ 4.2	<0.001	0.19	12.1 (9.3 to 14.9)
Glycemic outcomes / insulin resistance						
Fasting glucose (mg/dL)	94.8 $\pm$ 6.2 $\rightarrow$ 90.6 $\pm$ 5.4	94.1 $\pm$ 6.0 $\rightarrow$ 92.1 $\pm$ 5.6	95.0 $\pm$ 6.3 $\rightarrow$ 94.7 $\pm$ 6.1	0.030	0.10	-3.8 (-6.8 to -0.8)
Fasting insulin (μ U/mL)	17.6 $\pm$ 4.1 $\rightarrow$ 13.2 $\pm$ 3.1	17.2 $\pm$ 3.9 $\rightarrow$ 14.8 $\pm$ 3.3	17.8 $\pm$ 4.2 $\rightarrow$ 17.5 $\pm$ 4.0	<0.001	0.19	-4.1 (-5.9 to -2.3)
HOMA-IR	4.1 $\pm$ 1.1 $\rightarrow$ 2.9 $\pm$ 0.8	4.0 $\pm$ 1.0 $\rightarrow$ 3.3 $\pm$ 0.9	4.2 $\pm$ 1.1 $\rightarrow$ 4.1 $\pm$ 1.1	<0.001	0.21	-1.08 (-1.52 to -0.64)
HbA1c (%)	5.6 $\pm$ 0.3 $\rightarrow$ 5.3 $\pm$ 0.2	5.6 $\pm$ 0.3 $\rightarrow$ 5.4 $\pm$ 0.3	5.6 $\pm$ 0.3 $\rightarrow$ 5.6 $\pm$ 0.3	0.001	0.19	-0.28 (-0.41 to -0.15)
Lipid profile						
Total cholesterol (mg/dL)	176.4 $\pm$ 18.2 $\rightarrow$ 165.2 $\pm$ 16.1	174.8 $\pm$ 17.6 $\rightarrow$ 168.3 $\pm$ 16.8	177.0 $\pm$ 18.5 $\rightarrow$ 176.1 $\pm$ 18.0	0.006	0.15	-10.4 (-16.8 to -4.0)
LDL-C (mg/dL)	108.9 $\pm$ 13.9 $\rightarrow$ 99.2 $\pm$ 12.4	107.6 $\pm$ 13.1 $\rightarrow$ 101.8 $\pm$ 12.8	109.4 $\pm$ 14.1 $\rightarrow$ 109.0 $\pm$ 13.9	0.010	0.13	-9.1 (-14.8 to -3.4)
HDL-C (mg/dL)	43.6 $\pm$ 5.7 $\rightarrow$ 47.1 $\pm$ 5.8	43.9 $\pm$ 5.5 $\rightarrow$ 45.9 $\pm$ 5.4	43.4 $\pm$ 5.9 $\rightarrow$ 43.6 $\pm$ 5.8	0.020	0.11	3.4 (1.1 to 5.7)
Triglycerides (mg/dL)	126.8 $\pm$ 21.6 $\rightarrow$ 111.6 $\pm$ 18.9	124.9 $\pm$ 20.8 $\rightarrow$ 116.8 $\pm$ 19.5	127.5 $\pm$ 22.1 $\rightarrow$ 126.9 $\pm$ 21.8	0.004	0.16	-14.8 (-22.5 to -7.1)
Anthropometric variables						
Body mass (kg)	58.7 $\pm$ 7.2 $\rightarrow$ 57.2 $\pm$ 6.9	57.9 $\pm$ 6.8 $\rightarrow$ 57.0 $\pm$ 6.7	59.1 $\pm$ 7.5 $\rightarrow$ 59.4 $\pm$ 7.6	0.040	0.09	-1.7 (-3.1 to -0.3)
BMI (kg/m ²)	24.9 $\pm$ 1.8 $\rightarrow$ 24.1 $\pm$ 1.7	24.8 $\pm$ 1.7 $\rightarrow$ 24.3 $\pm$ 1.6	24.9 $\pm$ 1.9 $\rightarrow$ 25.0 $\pm$ 1.9	0.030	0.10	-0.83 (-1.39 to -0.27)
Waist circumference (cm)	81.4 $\pm$ 4.9 $\rightarrow$ 77.8 $\pm$ 4.2	80.9 $\pm$ 4.6 $\rightarrow$ 79.0 $\pm$ 4.4	81.7 $\pm$ 5.1 $\rightarrow$ 81.5 $\pm$ 5.0	<0.001	0.19	-3.6 (-5.1 to -2.1)
WHtR	0.53 $\pm$ 0.03 $\rightarrow$ 0.51 $\pm$ 0.03	0.53 $\pm$ 0.03 $\rightarrow$ 0.52 $\pm$ 0.03	0.53 $\pm$ 0.03 $\rightarrow$ 0.53 $\pm$ 0.03	0.002	0.17	-0.021 (-0.033 to -0.009)
Blood pressure						
Systolic BP (mmHg)	116.2 $\pm$ 7.5 $\rightarrow$ 110.3 $\pm$ 6.4	115.8 $\pm$ 7.2 $\rightarrow$ 112.4 $\pm$ 6.7	116.6 $\pm$ 7.8 $\rightarrow$ 116.1 $\pm$ 7.5	0.001	0.19	-5.5 (-8.2 to -2.8)
Diastolic BP (mmHg)	72.9 $\pm$ 5.8 $\rightarrow$ 70.4 $\pm$ 5.0	73.1 $\pm$ 5.4 $\rightarrow$ 71.5 $\pm$ 5.2	73.4 $\pm$ 5.6 $\rightarrow$ 73.0 $\pm$ 5.5	0.080	—	-2.2 (-4.8 to 0.4)

Note: Data are presented as mean $\pm$ SD (baseline $\rightarrow$ post-intervention).

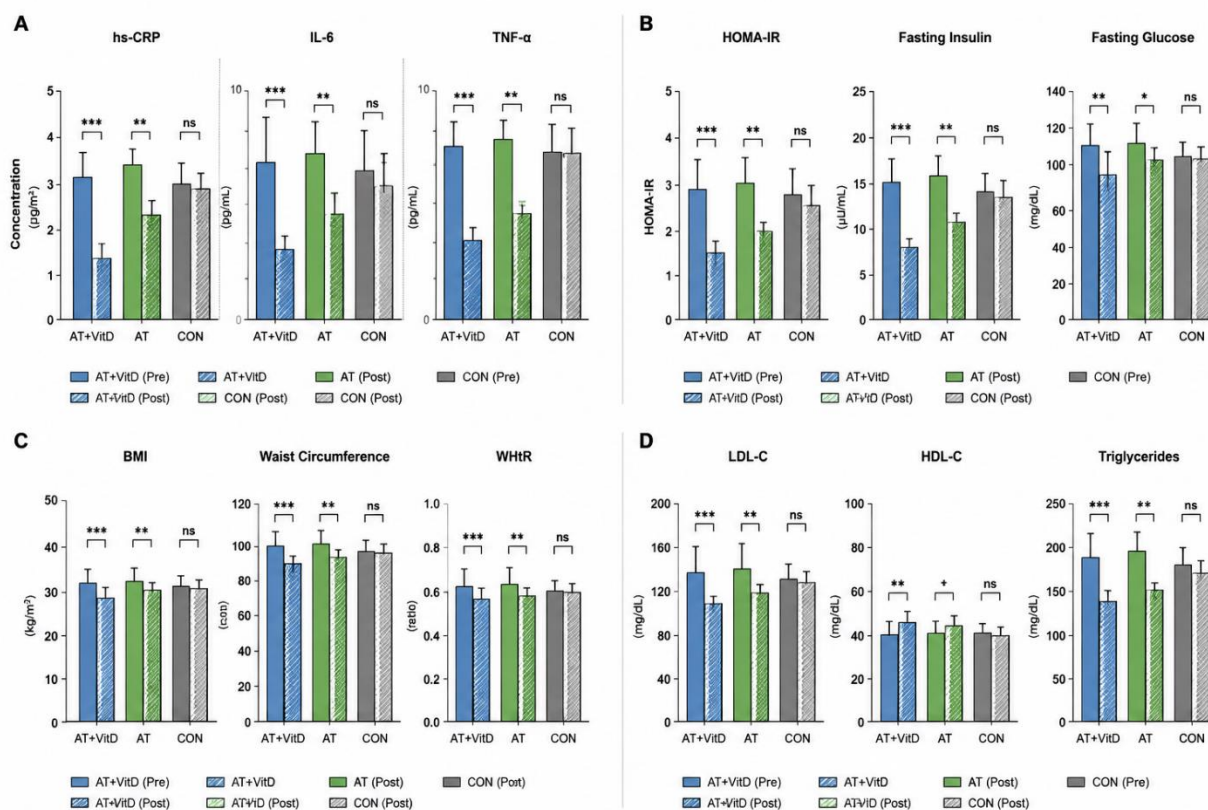


Figure 2. Effects of aerobic training program with or without vitamin D supplementation on inflammatory, metabolic, and cardiometabolic risk markers in overweight adolescent girls. Data are expressed as mean $\pm$ SD.

4. Discussion

The present study examined the effects of a 12-week school-based AT program, with or without vitamin D supplementation, on inflammatory markers and metabolic health in overweight middle-school girls. The main findings were that: (1) AT elicited significant improvements in systemic inflammation and cardiometabolic risk factors compared with a non-exercise control condition; and (2) combining AT with vitamin D supplementation produced the most consistent and pronounced benefits, particularly for hs-CRP, IL-6, TNF- α , insulin resistance indices (fasting insulin and HOMA-IR), abdominal adiposity markers, and selected lipid outcomes. Collectively, these results support the utility of feasible school-based AT for improving inflammatory and metabolic health in overweight girls and demonstrate that the combined intervention produced greater improvements than AT alone. Although this pattern is consistent with a possible additive benefit of vitamin D supplementation, the present study was not designed to establish true biological synergy or determine the underlying mechanisms.

Low-grade inflammation is increasingly recognized as a key mechanistic link between adolescent overweight and later cardiometabolic disease. In this study, both exercise groups demonstrated reductions in hs-CRP and pro-inflammatory cytokines, indicating that 12 weeks of structured AT was sufficient to improve inflammatory status in this population. These findings align with pediatric exercise literature (11,14,17), showing that regular AT can reduce inflammatory burden through improvements in body composition,

enhanced endothelial function, and favorable changes in immune regulation. From a physiological perspective, repeated aerobic bouts may attenuate adipose tissue-driven inflammatory signaling by reducing central fat and improving adipocyte function, while also promoting anti-inflammatory myokine responses and potentially reducing oxidative stress (29).

Importantly, the combined intervention induced greater reductions in hs-CRP, IL-6, and TNF- α than AT alone, indicating greater efficacy of the combined intervention. Although the present study was not designed to investigate mechanistic pathways, several biologically plausible explanations have been proposed in previous literature. Vitamin D has been suggested to enhance inflammatory regulation by modulating immune cell activity and cytokine production via vitamin D receptor signaling (21,22). Experimental studies have suggested that adequate vitamin D status may downregulate pro-inflammatory pathways and promote a more balanced immune response, potentially complementing the anti-inflammatory adaptations induced by regular AT (19,21). The marked increase in serum 25(OH)D in the supplemented group confirms that the intervention achieved meaningful biological exposure; however, because inflammatory signaling pathways were not directly assessed, the present findings cannot confirm that these mechanisms were responsible for the additional improvements observed.

Insulin resistance is common in overweight youth and is closely linked to both adiposity and inflammatory activity. In the present study, fasting

insulin and HOMA-IR improved significantly in both exercise groups, with the largest reductions occurring in AT+VitD. AT likely improved insulin sensitivity by increasing skeletal muscle glucose transporter activity, improving mitochondrial function and substrate oxidation, and reducing ectopic lipid accumulation (30,31). Even modest reductions in central adiposity can substantially improve insulin signaling in adolescents, which may explain the observed changes in HOMA-IR.

The greater improvements in insulin resistance indices in AT+VitD may also reflect the proposed role of vitamin D in glucose metabolism. Vitamin D has been proposed to influence insulin secretion and sensitivity through effects on pancreatic β -cell function, calcium handling, and inflammatory regulation (32,33). Since inflammation can impair insulin signaling, the greater reductions in inflammatory markers observed in the combined intervention may have contributed indirectly to improvements in HOMA-IR; however, these pathways were not directly evaluated in the present study. The modest improvement in HbA1c further supports a favorable shift in overall glycemic exposure across the intervention period, although HbA1c changes in youth may be small over 12 weeks, especially when baseline values are within normal ranges.

AT produced favorable changes in lipids, including reductions in TG and LDL-C and increases in HDL-C, with stronger effects generally observed in the combined group. These results are consistent with the established impact of AT on lipid metabolism through enhanced lipoprotein lipase activity, improved hepatic lipid handling, increased fatty acid oxidation, and reduced adiposity (12,13,34,35). Although lipid responses in adolescents can vary depending on baseline dyslipidemia severity and dietary intake, the overall pattern observed here supports AT as an effective approach for improving lipid-related cardiometabolic risk in overweight girls.

Vitamin D supplementation may have contributed to additional lipid improvements through indirect mechanisms, such as reductions in inflammation and improvements in insulin sensitivity, rather than through direct lipid-lowering effects (15–17). Although evidence regarding vitamin D supplementation and lipid metabolism remains inconsistent, an improved inflammatory and metabolic environment could plausibly facilitate healthier lipid transport and utilization when combined with regular exercise.

Both exercise groups demonstrated reductions in body mass, BMI, waist circumference, and WHtR compared with controls, with the largest improvements in AT+VitD. Abdominal adiposity is particularly relevant in adolescents because it is closely tied to insulin resistance and inflammatory cytokine production (21,30). Therefore, reductions in waist-related indices likely contributed meaningfully to improvements in both inflammation and metabolic outcomes. The observed reduction in systolic blood pressure further supports improved cardiometabolic health and may reflect improved vascular function, reduced sympathetic activation, and better endothelial responsiveness induced by regular AT.

Although vitamin D is not primarily a weight-loss supplement, the combined group's greater improvements may reflect enhanced responsiveness to

exercise or improved metabolic regulation associated with improved vitamin D status. Another possible explanation is that improved vitamin D status may support muscle function and exercise performance, potentially allowing participants to maintain higher-quality training throughout the intervention (36). However, because physical performance and muscle function were not directly assessed, this explanation remains speculative.

A key strength of this trial is its school-based implementation, which enhances ecological validity and supports real-world feasibility. Middle-school settings offer a scalable platform for structured AT, and vitamin D supplementation is relatively low-cost and easy to administer with appropriate oversight. Given the high prevalence of vitamin D insufficiency among adolescent girls in many regions, the present findings provide a practical rationale for combined lifestyle strategies aimed at reducing inflammation and improving metabolic health early in life. Importantly, changes were observed over a relatively short period (12 weeks), suggesting that measurable cardiometabolic benefits can be achieved within a school term.

Several limitations should be considered. First, although dietary intake and sunlight exposure were monitored throughout the intervention, neither variable was experimentally controlled; therefore, residual confounding cannot be excluded. Second, the study duration was limited to 12 weeks, and longer follow-up is necessary to determine whether benefits are sustained. Third, although laboratory personnel and outcome assessors were blinded where feasible, participants and exercise instructors could not be blinded because of the nature of the intervention. Fourth, pubertal maturation was not formally assessed. Because pubertal stage influences insulin sensitivity, inflammatory responses, body composition, and hormonal status, residual confounding related to biological maturation cannot be excluded despite randomization. Finally, the findings are specific to overweight middle-school girls and may not generalize to boys, other age groups, or adolescents with obesity or chronic disease.

Future studies should examine whether baseline vitamin D status moderates responsiveness to combined exercise and supplementation, as individuals with vitamin D insufficiency may derive the greatest benefit. Additional mechanistic outcomes, including adipokines (e.g., leptin and adiponectin), oxidative stress biomarkers, endothelial function, and objectively measured physical activity and sedentary behavior, should also be evaluated. Longer-term interventions and follow-up studies are warranted to determine the sustainability of the observed improvements and to establish optimal supplementation strategies for improving inflammatory and metabolic markers associated with cardiometabolic risk during adolescence.

4.1. Conclusion

This study demonstrated that a 12-week school-based AT program improved systemic inflammation and metabolic health in overweight middle-school girls. While AT alone produced favorable changes in inflammatory markers, insulin resistance indices, abdominal adiposity, and selected lipid parameters,

the combined intervention yielded the largest and most consistent improvements, particularly for hs-CRP, IL-6, TNF- α , fasting insulin, and HOMA-IR. These findings demonstrate that adding vitamin D supplementation to AT resulted in greater improvements than AT alone, although the present study cannot determine the biological mechanisms responsible for these additional benefits. Overall, the findings support the feasibility of integrating structured AT with vitamin D supplementation as a practical school-based strategy for improving inflammatory and metabolic markers associated with cardiometabolic risk during early adolescence.

Authors' Contribution: The author was responsible for the conception and design of the study, development and implementation of the intervention, participant recruitment and assessment, data collection, statistical analysis, interpretation of the findings, and preparation and revision of the manuscript.

Funding Support: This study was conducted without financial support from governmental, institutional, commercial, or private funding sources.

Declaration of Generative AI and AI-Assisted Technologies in the Writing Process: The author declares that no generative artificial intelligence or AI-assisted technology was used in the preparation, writing, editing, or revision of this manuscript. The author takes full responsibility for the accuracy, originality, integrity, and overall content of the published work.

Ethical Considerations: The study was conducted in accordance with the ethical principles of the Declaration of Helsinki. Throughout participant recruitment, aerobic exercise sessions, vitamin D supplementation, biological sample collection, physical assessments, and data management, appropriate measures were taken to protect the participants' rights, privacy, safety, dignity, and well-being. Written informed consent was obtained from the parents or legal guardians of all participating girls before enrollment. The participants were provided with age-appropriate information about the study procedures, and their voluntary participation was respected.

Data Availability: The data underlying the findings of this study are available from the corresponding author upon reasonable request, subject to applicable ethical, privacy, and confidentiality requirements.

Acknowledgments: The author gratefully acknowledges the participating girls, their parents or legal guardians, and the school personnel and research staff who contributed to the successful completion of the study. The author also thanks the anonymous reviewers for their constructive feedback and valuable suggestions, which contributed to improving the manuscript.

Conflicts of Interest: The author declares that there are no financial, personal, or professional conflicts of interest related to this study.

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