Exploring the Synergistic Effects of Concurrent Exercise for Managing Type-II Diabetes Mellitus: A Meta-Analysis

Uroosa Amin, Qurat-Ul-Ain Adnan, Tauseef Ahmad and Sumaira Imran Farooqui

Department of Rehabilitation Sciences, Ziauddin University, Karachi, Pakistan

ABSTRACT

The effectiveness of concurrent exercise (CE) as an emerging approach for type-II diabetes mellitus (T2DM) patients was evaluated through a comprehensive search on Google Scholar, PubMed, Pedro, CINAHL, and Medline from 2015 to March 2023. Sixteen RCTs were selected which evaluated CE (aerobic + resistance in the same session) effects on a minimum of three days/week among T2DM patients, and the control group received usual care or no exercise. Studies that evaluated at least one glycaemic variable, i.e. HbA1C, fasting blood glucose level (FBGL), and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR), were eligible. Intervention with a follow-up period of ≥8 weeks, patients of any age and gender, and literature in the English language were included. A rigorous review was performed using the Cochrane Collaboration risk of bias tool (RoB 2) to minimise biases, which include the randomisation process, deviation from intended intervention, missing outcome data, outcome measurement, and selection bias. CE significantly improved HbA1C (95% CI of -0.654 to 0.363, I^2 = 84.92% moderate heterogeneity), FBGL (95% CI of -0.239 to 1.145, I^2 = 93.74% - high level of heterogeneity), and insulin resistance (HOMA-IR) (95% CI of -0.593 to 0.544, I^2 = 92.85% - high level of heterogeneity). Collectively, findings indicate the potential of CE as an intervention to impact glycaemic control in T2DM patients positively. However, the relatively high I^2 values suggest notable variability among studies, and further research to explore the factors contributing to this heterogeneity, exercise protocol along with progression, and duration of diabetes are needed, which is more challenging to determine a precise dose-response relationship. Therefore, more studies are required to provide thorough insights into these components for T2DM management.

Key Words: *Glycated haemoglobin, Glycaemic control, Insulin resistance, Physical exercise, Type-II diabetes mellitus.*

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INTRODUCTION

Type-II diabetes mellitus (T2DM) is an emerging health issue characterised as a chronic metabolic disorder that entails an array of metabolic dysfunctions attributed to hyperglycaemia and impaired insulin function. Statistically, it currently affects approximately 537 million people throughout the globe, which is predicted to rise to 783.2 million by 2045.[1] This alarming increase is comparatively higher in low- and middle-income countries that lead to disease-specific complications.[2,3] Furthermore, the duration of T2DM and physical inactivity are strongly associated with developing diabetes-associated complications.[4-8] Therefore, physical exercise and pharmacological treatment could be a preferred strategy to overcome the deleterious effects.[9] A central objective for managing T2DM is glycaemic control.[10-12] Glycated haemoglobin (HbA1c) is considered a reliable and valid measure for evaluation.[12,13]

Correspondence to: Dr. Qurat-Ul-Ain Adnan, Department of Rehabilitation Sciences, Ziauddin University, Karachi, Pakistan
E-mail: qurat.adnan@zu.edu.pk
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Therefore, physical activity is evident to improve glycaemic control, insulin sensitivity, lipid profile, blood pressure, and other cardiovascular risk factors in patients with T2DM.[14-16] Evidence has highlighted that lifestyle modifications, including diet and exercise, are the first-line therapy for managing T2DM.[10-14] Therefore, implementing a structured exercise programme can counteract various predisposing factors of metabolic dysfunction and minimise the T2DM-associated sequelae.[8] In this regard, the American Diabetes Association (ADA) currently recommends that the majority of patients with T2DM must engage in at least 150 minutes per week of moderate-to-vigorous intensity aerobic activity and two or more resistance training sessions per week.[17] Physiologically, skeletal muscle insulin resistance and mitochondrial dysfunction are some of the significant pathological defects involved in developing T2DM.[18-21] Furthermore, physical exercise can effectively improve mitochondrial function, modulate mitochondrial oxidative capacity, and reduce the production of reactive oxygen species.[20] Aerobic exercise accelerates mitochondrial oxidative enzymes that help improve insulin sensitivity.[22,23] Similar to ADA recommendations, a dose-dependent effect of supervised aerobic exercise exerts a significantly higher effect on HbA1c among T2DM patients, which is inversely proportional to exercise duration.[24] Furthermore, to clarify the dose of exercise, progressive aerobic exercise has more significant benefi-

cial effects in improving glycaemic control than non-progressive training, especially progressive volume and intensity of interventions.[25,26] On the other hand, resistance training reverses age-related degeneration in gene transcripts of myosin heavy-chain and increases muscle protein synthesis. Thus, the quality and function of skeletal muscle mass improve and lead to improving insulin sensitivity and glucose oxidation.[27,28] Therefore, to achieve good glycaemic control, resistance training might be recommended in the early stage of diabetes in a substantial amount to stimulate post-exercise glucose uptake.[29,30]

Aerobic and resistance exercises have distinctive positive effects in improving glycaemic variables.[22-30] An alternative emerging exercise approach termed concurrent exercise (CE) involves aerobic and resistance training in a single session for patients with T2DM to improve glycaemic control and insulin resistance more than aerobic or resistance training alone.[30,31] Various types and intensities of CE regulate the metabolic responses and physiological and molecular mechanisms.[32-34] However, due to physical inactivity, certain T2DM patients may have reduced activity tolerance and compromised exercise capacity, which may prohibit them from achieving the contemporary exercise-training goal.[6] In addition, many patients with T2DM struggle to adhere to the exercise prescription due to various factors, including lack of motivation, time constraints, and physical limitations.[7] To overcome these constraints, concurrent exercise training may be a time-efficient and convenient exercise approach for patients with T2DM.[30] Despite the potential benefits of CE training, this approach's optimal prescription and effectiveness for patients with T2DM are not well-established. Several RCTs have investigated the effects of concurrent exercise on glycaemic control, cardiovascular risk factors, and quality of life in patients with T2DM, but the results are controversial.[25-30] Therefore, a systematic review and meta-analysis of RCTs are warranted to synthesise the available evidence on the effectiveness of concurrent exercise training for patients with T2DM and to identify the optimal response of this approach on glycaemic variables, i.e. HbA1C, fasting blood glucose level (FBGL), and Homeostatic Model Assessment for Insulin Resistance (HOMA-IR). Hence, this meta-analysis aimed to evaluate the effectiveness of concurrent exercise training for patients with T2DM by focusing only on RCTs to address the gap in the literature and updated evidence for patients with T2DM.

METHODOLOGY

Following PRISMA's (preferred reporting items for systematic reviews and meta-analyses) standards, the systematic review and meta-analysis were carried out. An electronic search was generated by using keywords to identify the RCTs evaluating the effects of concurrent exercise training on HbA1C, FBGL, and HOMA-IR among patients with T2DM on various online sources; Google Scholar, PubMed (MeSH words), PEDro, Cochrane, and CINAHL from 2015 to March 2023. RCTs were prioritised if they followed certain criteria. RCTs evaluated the effects of concurrent exercise on glycaemic variables in patients with T2DM. The concurrent exercise group performed both aerobic and resistance exercises in the same session on at least three alternative days a week. The control group comprised patients receiving usual care or those not performing any exercises. Primary outcomes were glycaemic variables, including HbA1C, FBGL, and HOMA-IR. Studies that evaluated at least one of the above outcomes were eligible. Intervention was coupled with a follow-up period of ≥8 weeks and literature published in the English language. Studies were excluded if there were patients with type-I DM, single-arm studies, animal studies, *ex-vivo* or *in vitro* studies, reviews, retrospective studies, or case studies.

An initial search was done on diabetes and exercise, which generated 44,300 searches on Google Scholar, 186 on PubMed, 8 on PEDro, and 944 on Medline. This search was followed by using T2DM and concurrent exercise filtered 15,416 studies on Google Scholar, which identified 608 records. After this, the identified records were further screened on the mentioned online sources for analysing the eligibility of studies. By following inclusion criteria and using different search strategies, such as T2DM, CE, HbA1c, fasting glucose, and HOMA-IR, which excluded review articles (n = 232), absence of outcome measures (n = 112), Type I and gestational diabetes (n = 68), intervention duration less than eight weeks (n = 62), studies other than RCTs (n = 84), conference abstract, editorial reports, correspondence and theses (n = 24), non-English papers (n = 6), and inaccessibility to full text (n = 10). Finally, 16 RCTs were included. During this complete screening process, the Cochrane tool of risk of bias (RoB2) was utilised for reviewing the level of bias among studies prior to inclusion in the present systematic review and meta-analysis.

Quantitatively, the data were analysed using MedCalc software by standardised mean difference (SMD) to estimate the pooled effect of the random effect model keeping I^2 at a 95% of confidence interval.[39] Continuous measure statistics formulated forest plot and the Cohen's rule of thumb measured effect size, i.e. values of 0.2^{small}, $0.5^{moderate}$, and 0.8^{large} for interpretation of SMD for each variable. Moreover, the percentile of heterogeneity and Cochrane Q were used to calculate the level of heterogeneity. If I^2 was >50%, random effect model was used, whereas if I^2 was <50% then fixed effect model was considered.[40] To estimate the level of significance, a p-value <0.05 is considered as significant. The first author conceived, designed, and analysed the data. For the interpretation of data, the first and second authors analysed the findings and revised them critically. For evaluation of the findings and documentation, the third author contributed as per the field specialist. Finally, the systematic review and meta-analysis were critically evaluated and approved by the professor (4^{th} author). All authors are accountable for all aspects of the work in ensuring the accuracy or integrity of work, along with evaluating the articles after team discussion.

RESULTS

Overall 16 RCTs evaluated the effectiveness of CE on glycaemic variables i.e. HbA1C, fasting blood glucose level (FBGL), and insulin resistance (HOMA-IR) among T2DM patients were included in this systematic review and meta-analysis, as presented in Table I.[41-50]

Table I: Characteristics of included randomised controlled trials.

Authors	Target population	Group	n	Intervention	Outcome measures	Results	p-value
Hosaini *et al.*,[35] (2023)	T2DM	Training	15	3 times/week for 8 weeks RT (20 mins.) and ET (25 mins.-stationary bike at 50-80% of HRmax)	HOMA-IR	Significant	<0.05
		Control	15	No exercise			
Moghadam *et al.*,[36] (2022)	T2DM	Training	15	3 times/week for 12 weeks RT: (3 sets/ 6 exs./ 60–90sec rest interval, 60–80% of 1RM, 15–10 reps. AT: 10 mins. on a treadmill at 80–95% HRmax with 1 min. active rest at 40–60% HRmax.	FBGL, HOMA-IR, HbA1C	Significant	<0.001
		Control	15	No exercise			
Silveira-Rodrigues *et al.*,[37] (2021)	T2DM	Training	16	3 times/week for 8 weeks AT: 20-25 min, 100–110% v6MWT RT: 13–10reps, 2-3 sets	FBGL, HOMA-IR	Significant FBGL, Non-significant HOMA-IR	0.04, 0.09, resp.
		Control	15	maintain their life routine			
Rad *et al.*,[38] (2020)	T2DM	Training	15	3 times/week for 12 weeks RT: 3 sets, 15–8 reps., 40–80% of 1RM AT: (10 min) walking or running on a treadmill at 75–95% HRmax.	HbA1C	significant	<0.01
		Control	13	No exercise			
Da Silva *et al.*,[34] (2020)	T2DM	Training	13	3 times/week for 12 weeks (RT+MICT, 50 min; 60 - 70% of HRmax).	HbA1C and HOMA-IR	Non-significant	>0.05
		Control	13	without formal exercise			
Jeon *et al.*,[41] (2020)	T2DM	Training	30	3 times/week for 12 weeks AE + RT; 20 minutes. RPE scale (11 - 14). RT (rubber band exercises approximately 30 minutes) at RPE 11 - 14 or 70% of 1RM.	HbA1C, and HOMA-IR	Non-significant HbA1C Significant HOMA-IR	0.268, 0.041 resp.
		Control	15	No exercise			
Amanat *et al.*,[14] (2020)	MetS	Training	15	3 times/week for 12 weeks (60 mins.) AE: (60 - 75% HRmax); 20 min of treadmill walking, followed by 5 min rest. RE: (60 - 80% 1RM) 10 ex's	FBGL and HOMA-IR	Significant	<0.001
		Control	15	No exercise			
Alvarez *et al.*,[42] (2019)	T2DM	Training	20	3 times/week for 20 weeks ET and ST (50 min for RT and 30 min for ET)	Fasting glucose (FBGL).	Significant	0.019
		Control	20	No training			
Magalhaes *et al.*,[43] (2018)	T2DM	Training	28	3 times/week for 1 year ET + ST (150 min/week at 40-60% of HRR for AT and 1 set of 10–12 reps. for RT	fasting glucose (FG) and HbA1c	Non-significant	>0.05
		Control	27	Counseling			
Eskandary *et al.*,[44] (2017)	T2DM	Training	9	3 times/week for 8 weeks AT: treadmill, 60-65 % of HRmax, for 20-30 min/day. RT: 3 sets, 8-13 reps., 60-75% of 1 RM.	FBS, HOMA-IR, HbA1C	Significant	<0.05
		Control	10	No exercise			
AminiLari *et al.*,[45] (2017)	T2DM	Training	13	3 times/week for 12 weeks Average intensity - 5.5 MET into the first week and progressed to 7.1 METs.	HOMA-IR	Significant	0.002
		Control	15	No exercise			
Bassi *et al.*,[46] (2016)	T2DM	Training	21	3 times/week for 12 weeks, 1hr sessions AT (30 min at 60 - 80% vo2) and RT (30 min at 60 - 80 % of 1RM)	HbA1C, and HOMA-IR	Significant HBA1C, Non-significant HOMA-IR	0.03, 0.31 resp.
		Control	20	Sedentary			
Kang *et al.*,[47] (2016)	T2DM	Training	20	3 times/week for 12 weeks, 60 mins. AE: treadmill at 60% HRR for 30 mins. RE: 60–80% 1RM; 2 sets, 9 exs. by weight machines, 8–12 reps., 30 mins.	HOMA-IR, HbA1C	Significant	<0.001, <0.01, resp.
		Control	20	No exercise			
Lui *et al.*[48] (2015)	T2DM	Training	20	3 times/week for 12 weeks AE: 40 - 60 minutes (40-60% VO2 max); 20 min of treadmill walk-5 min rest. RE: (50-60% 1RM) 2–3 x/week. 8–10 reps., 2 sets by an elastic band (Thera-band).	FBS, HOMA-IR, HbA1C	Significant	<0.01
		Control	20	No exercise			
Byrkjeland *et al.*,[49] (2015)	T2DM + CAD	Training	20	3 times/week for 12 weeks - 60 mins. (2 sessions supervised and 1 home-based) (1) Circuit training: 10 A + R exs. (40 sec exercise, 20 sec rest); (2) interval training (5-6 sets for 3–4min); (3) interval step training (4-5 setds for 3-min) and RT; (4) spinning on bike and RT. RT (10-15 reps.) with free weights.	HOMA-IR, HbA1C	Significant	<0.005
		Control	20	No exercise			
Park *et al.*,[50] (2015)	T2DM	Training	20	3 times/week for 12 weeks - 60 mins. Circuit training (for 40 min); ST (20 min) & AT (20 min).	HbA1C	Significant	<0.01
		Control	20	No exercise			

Table II: Findings of concurrent exercise on HbA1C in patients with T2DM using the random effect model.

Study	N1	N2	Forest plot	SMD	95% CI	Weight (%)
Moghadam *et al.*,[36] (2022)	15	15		1.908	1.023 to 2.794	8.45%
Da Silva *et al.*,[34] (2020)	13	13		0.081	-0.703 to 0.866	8.93%
Jeon *et al.*,[41] (2020)	30	15		-0.098	-0.725 to 0.529	9.54%
Rad *et al.*,[38] (2020)	15	13		-1.482	-2.341 to -0.623	8.59%
Magalhaes *et al.*,[43] (2018)	28	27		-0.060	-0.594 to 0.473	9.91%
Eskandary *et al.*,[44] (2017)	9	10		-0.902	-1.878 to 0.0737	8.17%
Bassi *et al.*,[46] (2016)	21	20		-0.947	-1.602 to -0.292	9.43%
Kang *et al.*,[47] (2016)	8	8		-0.856	-1.920 to 0.209	7.86%
Byrkjeland *et al.*,[49] (2015)	52	62		-0.030	-0.400 to 0.340	10.46%
Park *et al.*,[50] (2015)	27	15		-0.683	-1.339 to -0.0273	9.42%
Lui *et al.*,[48] (2015)	20	20		1.367	0.667 to 2.066	9.24%
Total (fixed effects)	238	218	-3 -2 -1 0 1 2 3 Standardised Mean Difference	-0.114	-0.304 to 0.0759	100.00
Total (random effects)	238	218		-0.146	-0.654 to 0.363	100.00

Table III: Findings of concurrent exercise on FBGL in patients with T2DM using the random effect model.

Study	N1	N2	Forest plot	SMD	95% CI	Weight (%)
Moghaddam *et al.*,[36] (2022)	15	15		3.321	2.18 to 4.46	11.95
Silveria-Rodeigues *et al.*,[37] (2021)	16	15		0.378	-0.34 to 1.10	14.57
Amanat *et al.*,[14] (2020)	15	14		-0.258	-1.00 to 0.48	14.45
Alvarez *et al.*,[42] (2019)	20	20		-0.479	-1.11 to 0.15	15.03
Magalhaes *et al.*,[43] (2018)	28	27		0.256	-0.28 to 0.79	15.55
Eskandary *et al.*,[44] (2017)	9	10		-0.236	-1.16 to 0.69	13.47
Lui Y *et al.*,[48] (2015)	20	20		0.684	0.04 to 1.33	14.97
Total (fixed effects)	123	121	-2 -1 0 1 2 3 4 5 Standardised Mean Difference	0.276	0.02 to 0.53	100
Total (random effects)	123	121		0.453	-0.24 to 1.14	100

Table IV: Findings of concurrent exercise on HOMA-IR in patients with T2DM using the random effect model.

Study	N1	N2	Forest plot	SMD	95% CI	Weight (%)
Hosaini *et al.*,[35] (2023)	15	15		-0.33	-1.07 to 0.39	8.77
Moghaddam *et al.*,[36] (2022)	15	15		7.78	5.60 to 9.97	4.27
Silveiria-Rodrigue *et al.*,[37] (2021)	16	15		-0.69	-1.43 to 0.05	8.75
Da Silva *et al.*,[34] (2020)	13	13		-0.097	-0.88 to 0.69	8.62
Joen *et al.*,[41] (2020)	30	15		-0.23	-0.85 to 0.40	9.07
Amanat *et al.*,[14] (2020)	15	14		0.04	-0.70 to 0.78	8.75
Eskandary *et al.*,[44] (2017)	9	10		-1.41	-2.45 to -0.36	7.82
AminiLari *et al.*,[45] (2017)	13	15		-1.40	-2.25 to -0.55	8.40
Bassi *et al.*,[46] (2016)	21	20		-0.04	-0.66 to 0.57	9.10
Kang *et al.*,[47] (2016)	8	8		-1.03	-2.12 to 0.055	7.73
Byrkjeland *et al.*,[49] (2015)	52	62		0.06	-0.31 to 0.43	9.72
Lui *et al.*,[48] (2015)	20	20		0.72	0.069 to 1.37	9.01
Total (fixed effects)	227	222	-4 -2 0 2 4 6 8 10 Standardised Mean Difference	-0.13	-0.32 to 0.063	100.0
Total (random effects)	227	222		-0.02	-0.59 to 0.54	100.0

According to the Cohen's rule of thumb, 11 out of 16 studies on an aggregate of 456 patients for HbA1C demonstrated a small effect size. Table II shows the impact of CE through SMD on patients with T2DM, with a value of -0.146 (95% CI, -0.654 to 0.363) with a 95% confidence interval for the random effect model, as shown in the forest plot. I^2 was applied to calculate the heterogeneity percentage. However, Cochrane Q was used to compute the percentages of discrepancies between the SMD of the included research revealed I^2 = 84.92% (95% CI of 74.68 to 91.02) with Q = 66.2992.

Seven studies out of 16 on an array of 244 individuals with T2DM were selected to explore the impact of concurrent exercise training on the FBGL (fasting blood glucose level). These studies showed a substantial improvement over the control group. As shown in Table III, the pooled impact of concurrent exercise training had an SMD of 0.453 (95% CI of -0.239 to 1.145) in the random effect model, indicating a modest effect size per Cohen's rule of thumb. The Forest plot shows a growing trend in the scores of fasting glucose levels, which makes these results even more intriguing. To calculate the statistical heterogeneity, the Q and I^2 test showed Q = 47.9571 and I^2 = 93.74% with a 95% confidence interval.

Twelve out of 16 studies with a total of 449 individuals with T2DM were examined to determine the impact of concurrent exercise training on the HOMA-IR, which showed a substantial improvement over the control group. Ultimately, as shown in Table IV, the pooled impact of concurrent exercise training had an SMD of -0.0242 (95% CI of -0.593 to 0.544) in the random effect model, which is considered to have a small effect size by Cohen's rule of thumb and forest plot, showing an increasing trend in the scores of HOMA-IR by performing concurrent exercises. Q and I^2 test was applied in order to estimate the statistical heterogeneity. Q = 55.9802 and I^2 = 92.85% in the random effect model on a 95% confidence interval.

The search articles have been reviewed and included studies with minimum risk of biasness based on the outcome or treatment were used in that study. For evaluating the risk of biasness for studies included in systematic review and meta-analysis, the Cochrane Collaboration risk of bias tool (RoB 2) is presented in Table V.

DISCUSSION

This meta-analysis intended to objectively analyse the therapeutic effects of concurrent exercise training on glycaemic variables such as HbA1C, FBGL, and HOMA-IR among patients with T2DM. Five hundred and sixty-three individuals from 16 RCTs who performed resistance and aerobic exercise in the same session were recruited. The main findings suggested significant improvement of glycaemic parameters that can induce beneficial changes among T2DM patients, which supports the clinical guidelines from the American diabetes association for enhancing glucose homeostasis by increasing physical activity levels.
Evidence from the multidisciplinary, quickly growing field of exercise suggests that the type and intensity of concurrent exercise influences several metabolic, physiological, and molecular pathways.[23] Every 30 minutes/week of moderate-vigorous intensity aerobic exercise can lower HbA1c by 0.22%, which is inversely proportional to exercise duration, based on a meta-analysis of 26 trials on the dose-dependent effect of supervised aerobic exercise on HbA1c. Exercise sessions exceeding 100 minutes per week do not contribute to afterwards reductions.

Table V: Risk of bias for analysis.

Bias						
Study	**Randomisation process**	**Deviation from intended intervention**	**Missing outcome data**	**Measurement of outcome**	**Selection of reported results**	**Overall**
Hosaini *et al.*,[35] (2023)	a	a	a	a	a	a
Moghadam *et al.*,[36] (2022)	a	a	a	a	a	a
Silveira-Rodrigues *et al.*,[37] (2021)	a	a	a	a	a	a
Amanat *et al.*,[14] (2020)	a	a	a	a	a	a
Rad *et al.*,[38] (2020)	a	a	a	a	Ä	a
Da Silva *et al.*,[34] (2020)	a	a	a	a	a	a
Jeon *et al.*,[41] (2020)	a	a	a	a	a	a
Alvarez *et al.*,[42] (2019)	a	a	a	a	a	a
Magalhaes *et al.*,[43] (2018)	a	a	a	a	Ä	a
Eskandary *et al.*,[44] (2017)	a	a	a	a	a	a
AminiLari *et al.*,[45] (2017)	a	a	a	a	a	a
Bassi *et al.*,[46] (2016)	a	a	a	a	a	a
Kang *et al.*,[47] (2016)	a	a	a	a	a	a
Lui *et al.*,[48] (2015)	a	a	a	a	a	a
Bykjeland *et al.*,[49] (2015)	a	a	a	a	a	a
Park *et al.*,[50] (2015)	a	a	a	a	a	a

Low risk: a, High risk: Ä, Some concerns: ~

Additionally, aerobic exercise reduced anti-diabetic medication consumption by 13%, according to a meta-analysis of seven T2DM trials.[24] Similarly, a distinct meta-analysis revealed that aerobic exercise of light to moderate intensity considerably enhanced glycaemic control.[25] A subsequent meta-analysis on glycaemic control found that progressive aerobic exercise significantly improved glycaemic control (0.84%) compared to non-progressive exercise (0.45%). By progressing exercise volume, HbA1c levels were reduced to 0.94%.[51] Additionally, mixed protocol and walking or running both reduced HbA1C levels by 1.12% and 0.69%, respectively.[51] Accordingly, twelve-week or longer aerobic exercise programmes improve glycaemic management in individuals with T2DM. However, longer or more intensive interventions do not have any further benefits for HbA1c.[52]A thorough network meta-analysis on 106 trials mentioned that supervised aerobic exercise could lower HbA1c levels compared to unsupervised sessions. Additionally, moderately specific evidence shows that combining resistance and aerobic training led to significant but dramatic decreases in HbA1c levels.[53] Meanwhile, resistance training promotes the synthesis of muscle protein, which enhances the quality and functionality of skeletal muscle mass. It also reverses the age-related decline in myosin heavy-chain gene transcripts.[54] A meta-analysis of twelve trials found that aerobic exercise significantly reduced HbA1c levels more than resistance training (difference of 0.18% or 1.97 mmol/mol).[55] These results may be constrained by variations in the exercise duration, which ranged from 8 weeks to 6 months, and by inconsistencies in methodology in seven trials. When multiple sets (21 *vs.* 21) were performed in one training bout and when participants with relatively short duration of diabetes (6 *vs*. 6 years) or baseline HbA1c of 7.5% (58 mmol/mol) than 7.5%, a meta-analysis that included 23 studies reported large pooled effect size.[30] Resistance training may, therefore, be suggested for patients with early-stage diabetes who have relatively poor glycaemic control in order to enhance post-exercise glucose absorption, albeit the dose dependency was not made clear.[30]

Due to the fundamental physiological pathways connected to both exercise types, concurrent exercise (CE) that interacts with aerobic and resistance training can boost them. In a meta-analysis that covered 37 T2DM trials, it was revealed that both exercise types significantly decreased HbA1c by 0.30%.[56] Additionally, supervised aerobic exercise was more effective than unsupervised (0.53%) in lowering fasting plasma glucose by 9.38 mg/dl and HbA1c by 0.60%. In conclusion, the combined exercise demonstrated a more noticeable reduction in HbA1c levels.[56] Another meta-analysis of 106 RCTs obtained similar results.[53] CE volume and intensity are key mediators of insulin sensitivity.[54,57] Multiple studies using lower intensities support the paucity of effects on insulin sensitivity with concurrent training because lower exercise intensities physiologically limit mitochondrial oxidative enzymatic capacity, which reduces skeletal muscle glucose uptake and increases plasmatic glucose. These adverse consequences promote adipocyte glucose deposition while lowering insulin sensitivity.[54] Conversely, a high intensity may reverse this process, increasing insulin sensitivity and lowering blood glucose levels. Clinically, these findings have a considerable impact on CVD regression, primarily by lowering many metabolic T2DM indicators.[58]

In the current analysis, HbA1c was analysed by using eleven out of sixteen studies on 456 patients with T2DM.[14,35-49] Results of eight studies showed significant findings, whereas only three showed non-significant improvements. However, the significance of the effect of concurrent training on HbA1c in these studies may have been obscured by differences in the level of HbA1c at the time of enrollment, unsupervised nutritional status, non-progressive exercise training as per the linear prescription model, and proportion of insulin taken by patients.[39-42] Another meta-analysis of 26 trials supported this specific study and found that exercise significantly reduced patients' HbA1c levels. The HbA1c level used as an enrollment criterion in the included studies varied and was either HbA1c 6.5, HbA1c 7-10, HbA1c 6.4-7, HbA1c 7.2-9, HbA1c 10-11, or HbA1c 6.5-11. In the present research, researchers assumed that individuals with higher HbA1c levels than those with lower HbA1c levels had a higher likelihood of experiencing a decline in HbA1c.[26] Seven out of sixteen studies examined 244 T2DM patients to analyse FBGL. Results from six investigations showed a noticeable improvement. In contrast, only one study had non-significant findings because of variations in dietary status, inter-individual variability, exercise volume, frequency, or type, behavioural or environmental barriers, meal timing, or the impact of pharmacological medications (such as switching from oral to injectable insulin therapy).[42] A meta-analysis of 26 trials confirmed the therapeutic benefit of exercise by finding a substantial decrease in FBGL in this study as well.[26]

A considerable pathophysiologic role for T2DM is played by insulin resistance, which is also a risk factor for cardiovascular disease.[59] A comprehensive study and meta-analysis of the impact of structured exercise training on HOMA-IR revealed that people with T2DM may see an even more notable increase in their insulin sensitivity.[59] Twelve out of sixteen studies investigated 449 T2DM individuals to interpret HOMA-IR in this meta-analysis. Nine research findings demonstrated a substantial increase in insulin sensitivity; however, three trials' findings were insignificant. These results could not mean much because the exercise training's ability to reduce fasting glucose was not given enough time during the intervention.[37-40,60]

There are several limitations when interpreting these findings, which include significant differences in the duration of exercise programmes (8 weeks to 6 months), which could have an impact on the study's conclusions. The results' generalisability may be impacted by heterogeneity introduced by the variation in the intervention period. Furthermore, methodological inconsistencies were found, which could impact the conclusions.

Additionally, the analysis showed that some factors were not consistently addressed in the included studies, such as the number of sets performed in a single training session, the duration of diabetes, different baseline HbA1c levels, unsupervised nutritional status, and non-progressive exercise training. These differences in participant characteristics, exercise parameters, and environmental factors could create confounding variables that make it more challenging to determine a precise dose-response relationship. Furthermore, the effects of pharmacological drugs (shifting from oral to injectable insulin therapy) and the meal pattern may influence the impact of exercise training on fasting glucose levels. Therefore, more studies are required to provide more thorough insights into these components of glycaemic control and to determine the efficiency of CE for T2DM management.

CONCLUSION

Concurrent exercise training has moderate effectiveness in improving the fasting blood glucose level but has a mild effect on HbA1C and HOMA-IR among T2DM patients. However, due to limited data, heterogeneity in the intervention duration, and discriminations of baseline values, more trials must be conducted with different intensities and longer duration for better outcomes and to clarify the exercise dosage for prevention and management of disease-associated complications.

COMPETING INTEREST:
The authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
UA: Substantial contribution to the conception or design of the work, or the acquisition, analysis, and interpretation of data for the work, and drafting of the work.
QAA: Substantial contribution to the interpretation of data for the work and revising the manuscript critically for important intellectual content.
TA: Substantial contribution in revising the manuscript critically for important intellectual content.
SIF: Substantial contribution to the final approval of the version to be published and agreement to be accountable for all aspects of work ensuring that questions related to accuracy.
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