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A Meta-Analysis – Aerobic and Resistance Exercises Intervention Affect on Blood Glucose Level among Type 2 Diabetes Patients

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Abstract

Context: Exercise is an effective strategy and support to have favorable for glucose control in type 2 diabetes patients. Furthermore, aerobic and resistance exercises examined aerobic, resistance, and combine form exercise blood glucose control among type 2 diabetes patients although, gender of male and female had divergence age range from 20 to 88 years description and cointervention of diet added additional support to result. **Objective:** The meta-analysis examined that above 8 weeks exercises intervention (aerobic, resistance, and combine form exercise) and its impact on hemoglobin A1c (Hba1c) and fasting blood glucose (FBG) control among type 2 diabetes patients. **Data Sources:** In the Web of Science searched full texted journal papers were taken about 179 and Pub Med database provided 58 full text journal papers, and its above 1990 years research papers search term used by phrases, truncation, and Boolean operator. **Study Selection:** The selected studies that evaluated the varied exercise regimen impact >8 weeks duration in type 2 diabetes patients. Twenty-four randomized controlled studies included total participants sample size of 1578 post-intervention exercise and control group. Included studies cointervention of drugs excluded. **Data Extraction:** Two reviewers extract the data baseline and post-intervention, then mean and standard deviation for exercise and control groups. Included study characteristics table, practice of exercise protocols and evaluate the methodological quality and potential bias. **Results:** Overall Hba1c variable data were taken on type 2 diabetes patients totally 1505 participants included in 22 studies post-values on exercises and control groups overall effect size reduced Hba1c favors exercise group would significant difference value $P = 0.00001$ and standardized mean difference SMD= −0.40% (−11.5 mg/dl), 95% Confidence interval (CI) (−0.54, −0.27) random effect model, heterogeneity observed (I^2=23%) no significant value $P = 0.16$. Effect size reduced FBG which would exercise favors significant difference value $P = 0.0001$ and SMD= −0.41% (−11.8 mg/dl), 95% CI (−0.59, −0.24) random effect model, heterogeneity observed (I^2=53%) significant value $P = 0.002$. **Conclusion:** This meta-analysis evidence supported varied exercise regimen and its impact on Hba1c and FBG level concern designed that overall significant impact on intervention such as aerobic, resistance, and combine form exercise (aerobic and resistance exercise) among type 2 diabetes patients. Although, combined exercise had highly better effective strategy results than aerobic or resistance alone, duration >8 weeks, exercise frequency 3 or 5 days/week and combined exercise followed aerobic consecutively and then resistance exercises.

Keywords: Aerobic exercise, Resistance exercise, Type 2 diabetes and meta-analysis

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Introduction

Essential way of life management for type 2 diabetes patients are known as physical exercises. Current exercise guideline suggests, regular aerobic exercise could be either moderate or high intensity on 3–5 days/week and also combined with resistance training on progressive for the glycemic control and insulin sensitivity.[1] Diabetes type 2 patients that chronic affect the blood glucose level cause of pancreas organ as beta cells function does not produce enough insulin and/or insulin resistance, which long-time cause complication on the nerves, eyes, kidney, heart, and blood vessels problems. Type 2 diabetes is caused by lifestyle factors such as obesity and not involved physical activity (sedentary behavior) as obesity and not enough physical activity.[2,3] According to the International diabetes federation (2017), currently 350 million adults are currently at high risk of people affecting type 2 diabetes and may increase 700 million people by 2045.[4] Varies complementary and alternative treatment considered for type 2 diabetes patients, who have been used them to reduce the sugar and those are dietary complement, acupuncture therapy, medicine (drugs, tablets, and pills), massage therapy, hydrotherapy, yoga, and physical exercise.[5,6] Meta-analysis evaluated lifestyle intervention among type 2 diabetes patients, lifestyle intervention consisted such as diet and physical exercise is important factors reveal significant which related to risk factors.[7] Physical exercises intervention has been cornerstone in treating with diabetes type 2 mellitus then improve metabolic parameter and control glucose.[8] Study attempted to evaluate structured physical exercise advised only that either aerobic or resisted exercises, both combine at high intensity level at least 6 weeks training. These could be improving glucose level control and blood pressure on diabetes type 2 patients and reduced the complication of type 2 diabetes patients compare with control group.[9,10] Diabetes has been correlation with cardiovascular morbidity and mortality. The 42 factors that affect blood glucose level which included food, medicine, physical activity, biological, environmental and behavior, and decisions. Food-liquid carbs usually increase blood glucose quickly than solid carbs. Fat food

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accordance with insulin resistant, more insulin requires meal without fat. Raise 20–50 mg/dl blood glucose when eaten a large amount of protein. Caffeine, alcohol, dehydration, and meal time affect blood glucose. Higher dose taken by diabetes patient which mean a largely effect reduced in blood glucose level.[11-13] Hemoglobin A1c (Hba1c) is a standard tool for assessing glycemic control in long term, and it's measured more appropriate depiction of fasting and postprandial glycemic.[1] Meta-analysis of aerobic interval training reported cardiometabolic outcome minimum training duration of 8 weeks and reduced glucose level on Hba1c significantly by 0.26% compare with moderate intensity of continuous training and non-exercise group. The clinical messages in walking training from 30 session on 6 weeks or 20 session on 4 weeks that should be more frequency, average of 3 to 5 time a week and exercise session lasting daily 20–60 min into improve walking speed moment, distance, mobility in the self-care among diabetes type 2 patients associated with cardiac problem.[14,15] Resistance training is exercise help of weighing machine or resistance band or own body weight could be again resist action and its apparatus easily accessible with low price that can reduce blood glucose level as Hba1c and increase muscular strength. Muscle strength quality decrease quickly in adult with diabetes rather than without diabetes patients, specifically in their lower extremities.[16] Meta-analysis term coined in 1976 by gene v. glass, he was the American statistician and researcher. Meta-analysis refer to review analysis, analysis of analysis and also big analysis that analysis statistical approach, amalgamating data syntheses from two or more related the research studies and its lead together results into single value of overall effect size. Meta-analysis that research studies result when disagree that apply to meta-analysis is statistic approach for combined results from two or more numerous research studies with the precision and increase power.[17] According to American Diabetes Association reported that 150 min/week of moderate-intensity exercises corresponding to MET- h/wk latest information's, research qualitative analysis 28 studies among type 2 diabetes patients, highly intensive combine exercises aerobic, and resistance have been strategy effective on Hba1c along with lifestyle change which was supervised that superior continuous supporting counseling. Result found that combine exercise such as aerobic and resistance training greater control on glucose rather than both exercise alone.[18] The World Health Organization (2021), furnished Hba1c test 3 month average value 6.5% and above were diabetes patients and its test mentioned diabetes care since about 1985.[19] This research primary question; what is exercises intervention impact on Hba1c and fasting blood glucose (FBG) level among type 2 diabetes mellitus patients? Does intervention (aerobic, resistance, and combine form exercises) exercise-protocol effect depend on glucose control?

Methods

Literature Search Strategies

Search term - "Diabetes type 2 and Physical activity," "Physical exercise and Diabetes type 2," "Aerobic exercise and DM," "Physical training and Type 2 diabetes mellitus," "Exercise and DM type 2," "Walking training and Diabetes mellitus type 2," "Endurance training and DM* and Hba1c," "Exercise and Diabetes type 2," "Aerobic and FBG*," "Resistance exercise and Hba1c*," "Resistance exercise and DM* type 2," "Resistance exercise and DM*," "Aerobic and Diabetes mellitus type 2," "Resistance exercise and Diabetes mellitus type 2," "Combine exercise and DM* not yoga," "Weight training and Diabetes type 2," "Strength training and Type 2 diabetes," "Exercise and DM," "Fasting blood sugar and DM*," "Fasting glucose and Exercise," "Type 2 diabetes and Training," "Running and Diabetes mellitus type 2," "Physical fitness and Diabetes mellitus type 2," "Physical workout and DM*," "Blood glucose and Exercise training," "Jogging and Walking FBG*" "A1c* and Exercise", "Physical exercise and A1c*," Physical activity and DM* not yoga," "Exercise and FG*," "Exercise and Metabolic disorder," "Glucose and Physical activity," "Physical practices and A1c*," "Phy* and Hba1c and FBG" and theses search term used by phrases, truncation, and Boolean operator.

Data Sources and Study Selection

The literature searched databases of Web of Science and Pub Med and it's used for collection of research paper. Web of Science that provides by the Institute of Scientific Information, various academic research which data support 256 multiple disciplines journal articles records above 90 million and maintained by Clarivate Analytics. Literature could be searched single-word would be taken major articles and user opted research paper subscription basis but it available with free access campus at Bharathidasan University, Tiruchirappalli, India. Pub Med has been largest database among medical and life science, freely access full text journal article and was opened 1996 year. The information provided by national library of medicine at United States which has maintained by national institute of health then Pub Med Central repository given more article along with bio-medical and life science.

In the Web of Science, searched full texted journal papers taken about 179 which were 29 journal papers does not show on baseline or after exercise intervention data (post) values concerned for aim of meta-analysis and given values such as median along with inter-quartile and this types did not include in the research. Seventy-seven journal papers have no correlation due to quasi-experimental group, age blow 20 year, cohort study, case control study, and cross-over study. Thirty-six no relation with Hba1c and fating blood sugar, 11 journal papers other language rather than English, 17 journal papers have been non-randomized controlled trails as intervention allocation method not at random. Nine journal studies finally selected. PubMed database provided 58 full text journal papers which involved eight journal papers no baseline or post data on Hba1c of FBG level, twenty journal papers were no relationship to meta-analysis study, 13 studies did not meet inclusion criteria, two journal papers non-randomized controlled trails then, and 15 journal studies selected to meet inclusion criteria [Figure 1]. For this research, acquired total research journal papers about 24 randomized controlled trails. 24 papers selected out of 237 journal papers reviewed for inclusion by first investigator and finally second investigator selected records. There opted papers on diabetes type 2 patients from which Web of Science and Pub Med databases searched since May 2018 still December 2019 year. Inclusion research studies exercise conducted home based and/or community center and/or clinical setting in countries as Italy, Brazil, England, Belgium, South-Korea, Greece, Denmark, China, Australia, Iran, Netherland, Pakistan, Canada, and Finland, published year range 1992 to 2019. The flow-chart diagram arranged with chain of command, guidance of meta-analysis, Preferred reporting item of systematic review and meta-analysis (PRISMA) and International database of Prospero prospectively registered this meta-analysis

study registered identification number CRD42019155268. This study registered in PROSPERO with ID no.CRD42019155268. Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42019155268.[20]

Eligibility Criteria of Inclusion and Exclusion

The essential criteria of meta-analysis appropriated when research included several studies which analysis similar related aim of research questions which prepared clear idea to find answer. Eligibility criteria of included studies meeting point that address problem solving procedures. Our study track as Participations, Interventions, Comparisons, and Outcomes and would be facilitating pre-specified criteria.

Participants: Diabetes type 2 patients, participants were with obesity and/or over-weight, cardiac problem and some had comorbidities. Patients use insulin, non-insulin, pills, tablets, and drugs. Both male and female are study participant from which ranged age 20 and 88 year selected.

Intervention: Physical exercise of varied regimen and its specific training or combined form exercise involved as aerobic, resistance and both combine form exercise, Endurance exercise based interval training or walking exercise, these all form two or more groups in which research co-intervention consisted diet and medication. Duration on exercise included only 8 and above weeks training, exercise sessions were taken minimum 30 min and consisted 3 or 5 days weekly base either morning or evening. No limitation was imposed on quantity of exercise as intensity.

Comparison

Exercise intervention compared from which no treatment group or standard care group or placebo group or conventional group or active control group and sham group. These groups compare the exercise treating groups which were varied regimen exercise, diet and education, example training volume as session, duration, repetition, frequency, intensity, and set.

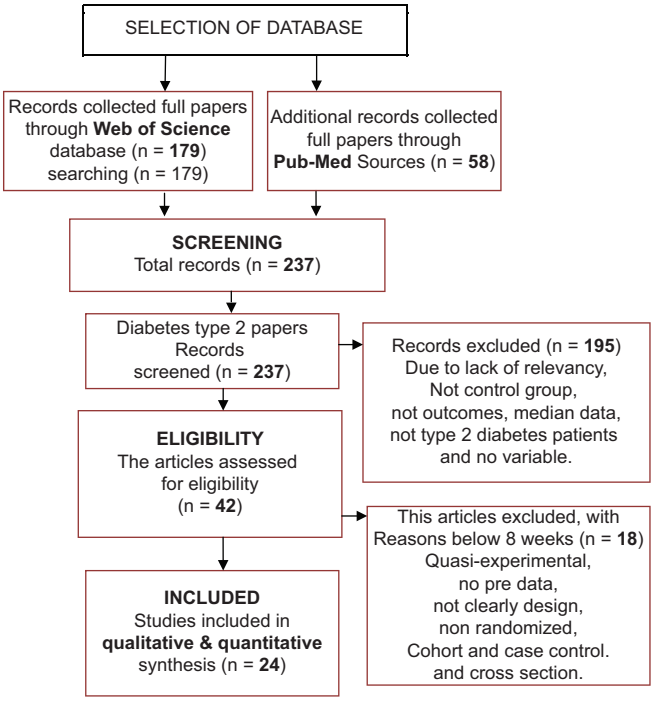

Figure 1: Flow chart of the result of literature search

Outcomes

It randomized controlled studies that dependent variables of outcomes names FBG and Hba1c contain study opted for inclusion.

Physical exercises carry-out community center, home, and clinical setting. Article inclusion published only English language and study taken no restriction on countries then, did not any restriction due to medication the exclusion criteria which were non-randomized controlled study, case series study and case control study. Yogic exercise exclusion and exercise below 8 weeks and its excluded in the research.

Evaluation of Methodological Quality and Potential Bias

Critical evaluation in health-care studies and its qualitative aspects of analysis an inclusion and exclusion criteria. Bias is taken away from using specific tools for quality assessment.[21] Bias is a systematic error in results. Different bias might lead to overestimate or underestimate of the true intervention effect. Cochrane collaboration recommends "specific tool for assessing risk of bias in the included studies" assessment of methodological quality. Studies validity consider two dimensions, first study asked appropriate research hypotheses that describe external validity. Second study answers its research question correctly often described internal validity. Risk of bias in randomized controlled trails of methodological quality assessed by evaluation seven domain bias consisted (1) random sequence generation (selection bias), (2) allocation sequence concealment (selection bias), (3) blinding of participants and personal (performance bias), (4) blinding of outcome assessment (detection bias), (5) incomplete outcome data (attrition bias), (6) selecting outcome reporting (reporting bias), and (7) other potential sources bias. Figures generated by Revman software that first figure represent "Risk of bias graph" such explain, proportion of included studies judgments such as low risk, high risk, and unclear risk presented Figure 2 and second figure showed risk of bias summary represent judgments' of included study in cross-tabulation presented Figure 3. Assess the risk of bias in included randomized controlled studies, for guideline execution Cochrane hand book for systematic review of intervention chapter-8.[22] Funnel plot is a graph and it shows the results from which individual studies, meta-analysis funnel plot refer to measure publication bias but funnel plot does not show the publication bias indication in which study was unpublished presented Figure 4.[10] In this research followed accordance into meta-analysis from the PRISMA and also Cochrane collaboration- *handbook for systematic reviews of interventions. In the health-care intervention evaluate evidence summary to efficacy that accurately and reliably*.[20]

Data Extraction

This research makes ensure all retrieved information relevant to include study. The data drawing-out by first and second authors assessed from randomized controlled included studies, it attempted to address to reduce error, full text information involved results of interpretation used Microsoft office-excel worksheet. The trails enclosure characteristic follows names

author/year, country, study design, age in year (Mean±Sd), sample size/groups male/female, co-intervention, treatment, and control/active control groups presented Table 1. Specific training protocol revealed author/year, exercise, control groups, intensity, duration which included session, repetition, set and interval then follow as outcome time point and outcome measures presented Table 2. Data were presented as mean and standard deviation from included studies and opted values baseline data then post data for Hba1c and FBG the collecting data for meta-analysis,[23,24] in studies have presented male Group 1 and female Group 2 separately and these make combined form using formula given table "7.7.a table of Cochrane handbook" then got the appropriate single sample size, mean and standard deviation value Studies mentioned standard error of mean convert to standard deviation taken from standard error of the mean by multiplying by square root of the sample size.[22] Included studies not existing standard deviation data, for using meta-analysis and three research paper found standard error studies[25-27] that convert to estimated formula using from Ishiguro *et al*. (2016) and using by Revman calculator.[28] Included studies existed standard deviation from standard errors

Figure 2: Risk of bias graph

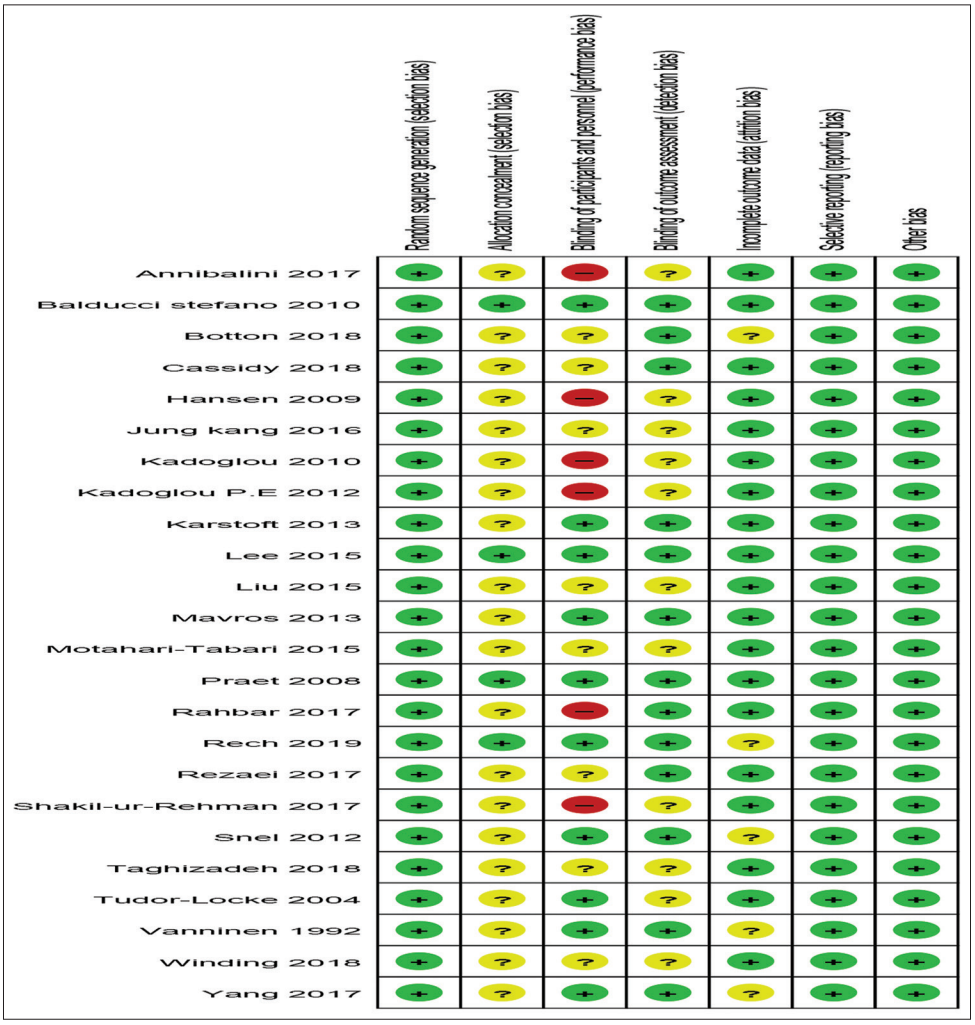

Figure 3: Risk of bias summary

of men which studies Hba1c and FBG level, theses data were converted to desired formed mean and standard deviation of mg/dl from percentage, mmol/mol and mmol/l. these could be opted desired format mg/dl from UK glucose the Global Diabetes

Table 1: Characteristics of included study

S. no	*Author/year*	*Country*	*Study design*	*Age in year (Mean±SD)*	*Sample size/ groups (M/F)*	*Co-intervention*	*Treatment*	*Control/Active Con*
1	Annibalini *et al*., 2017	Italy	Parallel group randomized control design	55–70 year Ex-57±9.1 Co-60±6.8	16/Ex-8, C0-8(M16)	None	Aerobic and strength exercise; 16 weeks, 2–3 times a week	Usual care
2	Botton *et al*., 2018	Brazil	Parallel group randomized control design	60–88 year Ex-70.6±6.7 Co-68.6±7.06	26/Ex-13, Co-13	Diet	Resistance training; 12 weeks and 3 days/week	Stretching low intensity once per week
3	Cassidy *et al*., 2018	England	Parallel group randomized control design	60±2 year Ex-60±3 Co-59±3	22/Ex-11, Co-12 (M17, F6)	None	High intensity interval training; pedal cadence and band resisted exercise 12 weeks, 3 days a week	Standard care
4	Hansen *et al*., 2009	Belgium	Parallel group randomized control design	59±8 year Hi-59±2 Li-58±1	37/ExHi-19, Li-18(M37)	None	Endurance type exercise program; high intensity, 6 months, 3 session per week	Low intensity exercise
5	Kadoglou *et al*., 2010	Greece	Parallel group randomized control design	50–65 year Ex-56.83±6.76 Co-60.32±9.28	47/Ex-23, Co-24(M15, F32)	None	Brisk walking; 16 weeks, 4 days/ week	No exercise, maintain with usual activities
6	Kadoglou *et al*., 2012	Greece	Parallel group randomized control design	50–70 year Ex-58.4±5.7 Co-62.9±4.2	53/Ex-26, Co-27(M19, F34)	Diet	Aerobic exercise; treadmill 12 weeks and 4 times per week	Low intensity PA
7	Kang Jung *et al*., 2016	South Korea	Parallel group randomized control design	Ex-56.0±7.4 Co-57.5±4.6	16/Ex-8, C0-8(F16)	None	Aerobic exercise; walking and resistance exercise, 12 weeks, 3 times per week	Standard care
8	Karstoft *et al*., 2013	Denmark	Three group randomized control design	Iwt-57.5±2.4 Cwt-60.8±2.2 Co-57±3.0	32/Iwt-12, Cit-12Co-8 (M20, F12)	Diet –CMG	IWT; Walking, Target energy expenditure, 4 months, 5 session per week CWT; Slow walking Target energy expenditure, 4 months, 5 session per week	Habitual routine lifestyle
9	Lee *et al*., 2015	China	Three group randomized control design	20–65 year 55.5±9.09	120/Age-40, Amsg-40, Cg40(M 58, F62)	None	AEG; Jagging, walking, Ridding and bike exercise AMSG; target 10,000 steps each days- pedometer, 12 month 5 days a week	No form of exercise with usual nursing care
10	Liu *et al*., 2015	China	Parallel group randomized control design	Ex-52.59±11.43 Co-51.20±11.34	42/Ex-22, Co20 (M19, F23)	None	Aerobic and resistance training; 12 weeks, 2–3 session per week	Conventional and drug therapy and psychological counseling

(Contd...)

Table 1: *(Continued)*

S. no	Author/year	Country	Study design	Age in year (Mean±SD)	Sample size/ groups (M/F)	Co-intervention	Treatment	Control/Active Con
11	Mavros *et al*., 2013	Australia	Parallel group randomized control design	Older than 60 year	84/Ex-36, Sham-48	None	PRT; high intensity exercise, 12 months, 3 days/ week	Sham exercise; low intensity usual care
12	Motahari-Tabari, *et al*., 2015	Iran	Parallel group randomized control design	30–65 year Ex-49.29 (1.12) Co-49.0 (1.60)	53/Ex-27, C0-26(F53)	Diet	Aerobic exercise; stretching and Flexibility 8 weeks and 3 days/week	Normal routine activity
13	Praet *et al*., 2008	Netherlands	Parallel group randomized control design	60±9 year Bric-61±9 Madi-59±9	37/Bric-18, Medi-19	Diet	Brisk walking; 12 months, 3 days/ week	Medical fitness programme; 12 months, 3 session/week
14	Rahbar *et al*., 2017	Iran	Parallel group randomized control design	40–60 year Ex-48.31 (5.02) Co-$8.60 (4.80)	28/Ex-13, Co-15	None	Aerobic exercise; treadmill 8 weeks and 3 days/week	Normal routine activity
15	Rech *et al*., 2019	Brazil	Parallel group randomized control design	≥60 year Ex-70.5±7.4 Sham-68±6.5	38/Ex-18, Co-21 (m20, F18)	None	Resistance training; 12 weeks and 3 days/week	Active con; stretching workout once per week
16	Rezaei *et al*., 2017	Iran	Parallel group randomized control design	30–45 year Ex-42±3.6 Co-43.5±2.8	20/Ex-10 Co-10 (M0, F20)	None	Progressive endurance training 10 weeks and 3 session/week	Patients, participate did not any exercise program
17	Shakil-ur-Rehman *et al*., 2017	Pakistan	Parallel group randomized control design	30–70 year Ex-(M)59.12±05.78 (F)51.31±5.78 Co-(m)55.00±8.03 (F)57.93±06.83	102/Ex-51, Co-51(M55, F47)	Routine medicine and diet plan	Aerobic exercise; SSAET program 25 weeks, 3 days/ week	Routine medicine and diet plan
18	Snel *et al*., 2012	Netherlands	Parallel group randomized control design	Vex-53.0±2.5 Vlcd-56.1±2.4	27/VlcdEx-13, Vlcd-14(M14, F13)	Diet	Aerobic exercise; cycloergometer, 16 weeks, 4 session/week	Very low calorie diet
19	Stefano Balducci *et al*., 2010	Italy	Parallel group randomized control design	(<60 vs. ≥60) year Ex-58.8 (8.5) Co-58.8 (8.6)	563/Ex-288, Co-275(M329, F234)	diet±oral agent, life style change	Intensive exercise; 12 months and 3 days/week	Standard care alone Counselling
20	Taghizadeh *et al*., 2018	Iran	Parallel group randomized control design	62.25±3.81 Yr	20/Ex-10, Co-10(F20)	None	Endurance training; treadmill, 8 weeks, 3 session/ week	Not involve any kinds of exercise training
21	Tudor-Locke *et al*., 2004	Canada	Parallel group randomized control design	40–60 year Ex-52.8±5.7 Co-52.5±4.8	47/Ex-24, C0-23(M26, F21)	PA behavior change, Education	First step Program; walking, 16 weeks, 3–4 days/week	Standard care
22	Vanninen, *et al*., 1992	Finland	Parallel group randomized control design	40–60 year male-53±7 Female-54±6	78/Ex-38, Co-40(M45, F33)	Diet	Aerobic exercise; walking, jogging, 12 months, 3–4 times week	Conventional treatment
23	Winding *et al*., 2018	Denmark	Three group randomized control design	Hiit-54±6 Yr End-58±8Yr Co-57±7	32/Hiit-13, End-12, Co7 (M19, F13)	Diet	HIIT; cycling, 11 weeks, 3 session/ week Endurance training; cycling, do same week and session	Energy intake low compare with 2 groups

(Contd...)

Table 1: *(Continued)*

S. no	Author/year	Country	Study design	Age in year (Mean±SD)	Sample size/ groups (M/F)	Co-intervention	Treatment	Control/Active Con
24	Yang *et al*., 2017	Canada	Three group randomized control design	52±1.2 year RT1-52.2±1.2 RT2-49.8±1.4 RT3-54.6±1.2	51/RT1-16, RT2-17, RT3-18(M30.F21)	Diet	Resis and Aerobic training; RT2-High intensity, 6 months, 5 days a week RT3-Endurance, low intensity, do same above	RT1-usual care

Ex: Exercise group, Co: Control group, SD: Standard deviation, M/F: Male/Female, SSAET: Supervised structured aerobic exercise training, CGM: Continuous glucose monitor, IWT: Interval walking training, CWT: Continuous walking training, PRT: Progressive resistance training, PA: Physical activity, HIIT: High-intensity interval training, AEG: Aerobic group, AMSG: Accumulated million steps group, PRT: Progressive resistance training, AC: Active control, VLCD: Very low calorie diet, M: male, F: Female, Yr: year.

Community (2021) that convert blood sugar, and then according to International Federation of Clinical Chemistry working on Hba1c standardization analysis help from NGFP – National Glycohemoglobin Standardization Program (2021) that has been supported on national institutes of diabetes.[29,30]

Statistical Analysis

Quantitative analysis used review manager (Revman 5.3 the Cochrane collaboration), usually meta-analysis principle two stages process as summary statistics refer observed intervention effect then, estimate pooled intervention effect as weight average. Overall effect sizes calculated to using mean and standard deviation. In this research, study could be analyses continuous data as standard mean difference (summary statistics) use when outcomes were measured several ways, FBG and Hba1c, to which measures of intervention frequently enzymatic colorimetric methods assessed, glucose oxides methods, glucometer and chromatography and other measures used less study in medical laboratory. Random effect model, in which research included studies were not same estimate all intervention effect that a distribution follow across individual studies. Outcomes (Hba1c and FBG) of mean of difference that average was received weighted given to each included study due to inverse of its variance. Larger sample size require for weight given more to meta-analysis effect on combined result where as small sample study on meta-analysis given less weight on cumulative effect and its reduce precision on pooled estimate effect. This meta-analysis documented varied exercises intervention and its tested in practice, studies difference in either samples or each study differ, if heterogeneity has present, might be attempt to explain with subgroup and sensitivity analysis. I^2 statistics measured included studies heterogeneity used in meta-analysis. Heterogeneity is expressed as I squared statistics and has been estimated with Chi-square test.[31] The corresponding I^2 statistics percentage's value indicates included studies variability due to sampling error, 30% are mild heterogeneity and more than 50% are notably substantial heterogeneity that depends on size and direction of treatment effect.[32] Further discussion I^2 statistic regarded to estimation of confidence interval (CI) in the order of overall effect size. Between studies variance of the estimate was calculated in the tau^2 statistic. One study to another study variance has been familiar into calculations in the CI around treatment effect. In this research, summary effect size in the 95% CI opted sources had been variance, within study as well as between study sampling variation.[33] Forest plot is a graph and it was showed the results from which individual studies, the estimate overall treatment effect and linked CI, then value ($P < 0.05$) for statistical significance.

Results

Description of study

Total sample size of 1578 participants were post exercise and control group. Hba1c outcome 1505 participants opted and FBG outcome 1472 participants were taken then included in meta-analysis. 24 studies included in meta-analysis that outcomes have 22 studies Hba1c and 22 studies FBG level into meta-analysis conducted post data of control and exercise groups.

Identification and Methodics of Selection of Studies

Hba1c variables would not be in Motahari-Tabari *et al*., Rezaei *et al.*,[25,26] included studies and FBG would not be in Cassidy *et al*., Mavros *et al.*,[34,35] included studies. Aerobic exercises studies Kadoglou *et al*., Kadoglou *et al*., Shakil-ur-Rehman *et al*., Vanninen *et al*., Motahari-Tabari *et al*., Rezaei *et al*., Hansen *et al*., Karstoft *et al*., Lee *et al*., Praet *et al*., Rahbar *et al*., Snel *et al*., Taghizadeh *et al*., Tudor-Locke *et al*., Winding *et al.*[12,13,23-26,36-44] and Resistance exercises studies Yang *et al*., Cassidy *et al*., Mavros *et al.,* Botton *et al*., Rech *et al.*[27,34,35,45,46] then combine form of aerobic with resistance exercises.[2,3,47,48] Table shows included studies and exercise protocol presented Table 2. This research study involved Yang *et al.,* Karstoft *et al*., Lee *et al.,* Winding *et al.*[27,37,38,44] more than two groups and those studies group favors to research analysis taken only two groups but only favors of two groups as control and relevant intervention group considered. Reliability measure, in this research conducted the meta-analysis on baseline data-test of control and exercise groups among Hba1c and FBG.[49] According to American Diabetes Association, diagnosis of diabetes mellitus type 2 patients included studies.[2,12,23-25,38,40,42,45,46,48] Supervision of exercise sessions included studies such as Vanninen *et al.*, Motahari-Tabari *et al*., Rezaei *et al*., Yang *et al*., Cassidy *et al*., Mavros *et al*., Hansen *et al*., Karstoft *et al*., Lee *et al*., Rahbar *et al*., Snel *et al*., Rech *et al*., Stefano *et al.*[2,12,13,24-27,34-38,40,41,46,48] Exercises regimen in which diet was addition intervention, included trails Sub-group of Hba1c outcome on 12–16 weeks exercises had aerobic exercises[12,13,41] and resistance exercises[34,45,46] then combine exercises.[2,3,47]

Sub-group of FBG outcome on 12–16 weeks exercise had aerobic exercise[12,13,37,41] and resistance exercise[45,46] the combine form exercise.[2,3,25] Sensitivity analysis conducted only 12 weeks exercise outcomes[3,13,34,45-47] and then Cassidy *et al*. (2018)[34] study only did not have FBG values.

Table 2: Training protocol of included study

S. no	*Author/ Year*	*Exercise*	*Control*	*Supervision*	*Intensity*	*Duration/Session/ repetitions/sets/ Intervals*	*Outcome time point*	*Outcome measures*
1	Annibalini *et al*., 2017	Aerobic ex; treadmill (walking) and strength ex-horizontal, leg puss and pull down, lat machine, chest press	Usual diabetics care	Yes	Aerobic 85% vo2 max Resista-45–65% Hr	16 weeks, A 5–10 min, Resis 30–60 min, 2–3 times a week, R 15–20, S 2–4	0 and 16 weeks	Hba1c, FG, BMI, hc, 1-RM, Bp, cholesterol
2	Botton *et al*., 2018	RT program; strength ex on Tradition machine, free weight and F.Ex squat and steps up and down	Joint mobilization and static stretching for large muscle groups, perform low intensity	NR	F.c- Omni Scale (0–10)	12 weeks, 3 days a week, (R) F.Ex 10–15 T.Ex 10–12, (s) F.Ex and T.Ex 2–3, (I) 1–1.30 min	0 and 12 weeks	Hba1c, FG, Cholesterol, muscle strength, sit-to-stand, timed up and go, RTD 50 and 200
3	Cassidy *et al*., 2018	High intensity interval training; the rating exertion (RPE) increased form 9 to 13 comfortable Cadence. And resistance band upper body exercise was light	Standard care and routine normal, not change their medicine, PA, diet	Yes	Borg Scale (9–17) RPE	12 weeks, 3 days a week, (I)3 min	0 and 12 weeks	Hba1c, weight, BMI, BP, Sv, Co, Heart rate variability
4	Hansen *et al*., 2009	Endurance type exercise; walking, cycling, cross-country and sky type exercise. High intensity exercise 40 min, 118±3 beat/min	Low intensity 55 min, 105±3 heart beat	Yes	HI-75% vo2 Peak moderate to high LI-50% vo2 Peak low to moderate	6 months, 40–55 min session, 3 session/week	0, 2 and 6 months	Hba1c, FG, Blood lipid, body com, vo2 max
5	Kado-Glou *et al*., 2010	Brick walking; goal 150 min/ week of self-controlled moderate intensity	No exercise instruction maintain usual habitual activities	Yes	50–70%	16 weeks, 30–60 min per session, 4 days a week	0 and 16 weeks	Hba1c, FG, Bp, W/H ratio, insulin, cholesterol, vo2 peak
6	Kadoglou *et al*., 2012	Aerobic exercise; walking or running on treadmill, cycling, calisthenics of upper and lower limps	Walking 3–5 times/week with low intensity	Yes	60–75% max heart rate	12 weeks, 45–50 min per session, 4 times a week	0 and 12 weeks	Hba1c, FG, Bp, cholesterol, BMI, Waist cm
7	Kang Jung *et al*., 2016	Aerobic = resistance ex; treadmill 30 min, and resistance use weight machine (upper and lower body)	Standard care	NR	Aerobic 60% HRR Resista-60–80%	12 weeks, 60 min per session, 3 times a week, (R)7–12)(S)2	0 and 12 weeks	Hba1c, FG, Wc, insulin cholesterol, Bp, c-reactive protein, HOMA_IR, C peptide

(Contd...)

Table 2: *(Continued)*

S. no	*Author/ Year*	*Exercise*	*Control*	*Supervision*	*Intensity*	*Duration/Session/ repetitions/sets/ Intervals*	*Outcome time point*	*Outcome measures*
8	Karstoft *et al*., 2013	Interval walking training; JD Mate, used as a pedometer, group had the target energy expenditure rate set for 70% with speed walking. Continuous walking training; target energy expenditure rate set at 55% with slow walking	Habitual life style and JD mate pedometer data uploaded monthly	Yes	IWT:Peak energy ex 70% low to high CWT; 55% peak energy ex moderate intensity	4 months, 60 min per session, 5 days a week	0 and 4 months	Hba1c, FG, vo2max, Body com, lipids, Bp, Cgm glucose
9	Lee *et al*., 2015	Aerobic exercise Groups portable oximeter approached (13–15 Borg scale) Jagging, walking, Ridding and bike exercise (moderate exercises) Aerobic million steps group; target 10,000 steps each days- pedometer	No form of Exercise with usual nursing care	Yes	60–80% (HR Max)	12 month, 30 min Per session, 5 days a week	0 and 3 and 12 months	Hba1c, FG, 2 h-ogtt, Fsting c-peptide, Bigtt-si Bigtt-air
10	Liu *et al*., 2015	Aerobic ex; home based ex start with slow and low intensity, Resis ex elastic band (borg scale 11-14)	Convention and drug therapy, psychological counseling	Yes	A 40–60% R 50–60%	12 weeks, 3 session/week, R-2-5 times a week, Re8-10, S-2	0 and 12 weeks	Hba1c, FG, cholesterol, HOMA-IR, Pin, Pbg
11	Mavros *et al*., 2013	Progressive resistance training; High intensity, pneumatic resis Equipment power training was concentric and eccentric for 4 s	Low intensity with usual care	Yes	80% Bore scale rate (15–18)	12 months, 3 days a week, R-8, S-3	0 and 12 months	Hba1c, HOMA2-IR, body com, skeletal muscle mass, Vat, mid-thigh muscle attenuation
12	Motahari-Tabari *et al*., 2015	Aerobic ex; stretching and flexibility ex 50 min daily exercise (Brick walking 30 min)	Standard care (normal routine activity)	Yes	60% max heart rat	8 weeks, 50 min per session, 3 times a week	0 and 8 weeks	FG, Plasma insulin, hip.c, wait.c, BMI, wt,
13	Praet *et al*., 2008	Brick walking; the endurance type ex consisted of 5–6 Km/h and resistance ex, floor ex own body weight or elastic bands	Medical fitness ex; endurance type ex consisted of interval ex on home trainer and 8 difference ex target upper and lower body	NR	brick- 75±5% MF-73±2% max heart rate	12 months, 60 min per session, 3 days a weekly	0 and 12 months	Hba1c, FG, BMI, HOMA, resting heart rate, Bp

(Contd...)

Table 2: *(Continued)*

S. no	Author/ Year	Exercise	Control	Supervision	Intensity	Duration/Session/ repetitions/sets/ Intervals	Outcome time point	Outcome measures
14	Rahbar *et al*., 2017	Aerobic ex; treadmill with no slope. Bruce protocol and its increased gradually	Normal routine activity	Yes	50–70% max heart rate	8 weeks, 30 min session, 3 days per week	0 and 8 weeks	Hba1c, FG, ht, wt, BMI, Ef%, cholesterol, BP, micro albumin
15	Rech *et al*., 2019	RT program included Function ex and tradition ex squat and bench stepping, knee flex and 7 extension and abdominal crunches,	Stretching workout with low intensity-static move for large muscle groups	Yes	F.c- Omni Scale R.E-15 repetition maximum	12 weeks, 3 days a week, (R) F.Ex 10–15 T.Ex 10–12, (s) F.Ex and T.Ex 2–3, (I) 1to 1.30 min	0 and 12 weeks	Hba1c, FG, Cholesterol
16	Rezaei *et al*., 2017	Progressive endurance exercise training on treadmill such as aerobic walking/running	Patients, participate did not any exercise program	Yes	50–70% (HRR)	10 weeks, 3 session/week and 33-50 min/ day	0 and 10 weeks	FG, Insulin (iu/i) Homar-ir, TG, TC, LDL, HDL, Vo2 Max
17	Shakil-ur-Rehman *et al*., 2017	Aerobic ex; supervised structured aerobic ex treadmill training inclination (0–3)divided 5 phases with 5 week duration	Keep routine medication and diet plan	NR	Borg Scale, vo2 maxby the resting heart rate	25 weeks, 20–50 min per session, 3 days a week	0 and 25 weeks	Hba1c, FG, plasma insulin level, Insulin resistance, HDL, LDL, Interleukin-6, nitric oxide, cyclooxygenase, RPE, dyspnea, BMI, Vo2max
18	Snel *et al*., 2012	Adding ex; training at home for 30 min and a 1 h hospital training aerobic exercise +low calorie diet	Very low calorie diet approximately 450 Kcal/day	Yes	70% max capacity cycloergometer	16 weeks, 30 min session, 4 days a week	0 and 16 weeks	Hba1c, FG, Bp, cholesterol, average insulin, BMI, Waist cm
19	Stefano Balducci *et al*., 2010	Intensive ex; 150 min/weeks 2 supervised Session of progressive mixed (aerobic and resistance) training-treadmill, cycle ergometer	Standard care alone counseling	Yes	11.25 MET-h/wk (vo2max)	12 months, weekly twice, (5–8)	0 and 12 months	Hba1c, FG, Upper and lower body Strength, homa-IR, Bp, cholesterol, wc, BMI, OHAS, insulin, Antihypertensive agents, lipid
20	Taghizadeh *et al*., 2018	Endurance type exercise; moderate intensity treadmill walking or running	Not involve any kinds of training	NR	60–75%	8 weeks, 35–50 min/session, 3 session a week	0 and 8 weeks	Hba1c, FG, HOMA-IR, vo2 max, body fat, BMI
21	Tudor-Locke *et al*., 2004	First step programs; pedometer use walking h while energy used activities goal setting self-monitoring	Group received post card for their participation	NR	PA by approximately 3000–12000 step/day	16 weeks, 30 min session, 3–4 days a week	0 and 16 weeks	Hba1c, FG, cholesterol, 2-h glucose, w.c, h.c, Heart rate, Bp

(Contd...)

Table 2: *(Continued)*

S. no	Author/ Year	Exercise	Control	Supervision	Intensity	Duration/Session/ repetitions/sets/ Intervals	Outcome time point	Outcome measures
22	Vanninen *et al*., 1992	Aerobic ex; walking, jogging, cycling, cross-country, occupation and recreational activity	Standard care	Yes	30–60%	12 months, 3–4 times a week, 30-60 min per session	3, 0, 12 months	Hba1c, FG, FP insulin, cholesterol, max oxygen uptake, serum triglycerides
23	Winding *et al*., 2018	High intensity Interval training; 11 week bicycle intervention consisting of 20 min/session and 95% of W peak Endurance training; 11 week bicycle intervention consisting of 40 min/session and 50% of W peak	Energy intake low compare to both groups	NR	HIIT- cycling of 1 min at 95% W peak ENDU-cycling at 50% W peak	11 weeks, 3 session/week, In-1 min	0 and 11 weeks	Hba1c, FG, vo2max, Body com, lipids, CGM
24	Yang *et al*., 2017	RT2; High intensity RT low repetition 75% of 1 RM RT3; Endurance RT low intensity High repetition 50 % of 1 RM	RT1; low intensity, high repetition lowest ex volume 50% of 1 RM	Yes	R2-High intensity (7-RM) R3-Low Intensity (15-RM)	6 months, 5 days a week, R2-(Re) 7, R3-(Re)15, S 2–3	0 and 6 months	Hba1c, FG, cholesterol, vo2 max, BMI, hc, body fat, lean mass

RT: Resistance training, F.Ex: Functional exercise, T.Ex: traditional exercise, Hba1c: Glycosylated hemoglobin, FG: Fasting blood glucose, RPE: Rating of perceived exertion, NR: Not report, Sv: Stroke volume, Co: Cardiac output, Bp: Blood pressure, PR: peripheral resistance, Ex: Exercise, PA: Physical activity, HOMA-IR: Homeostasis model assessment, OHAS: Oral hypoglycemic agents, BMI: Body mass index, HT: Height, WT-Weight, EF: Max, ejection fraction, Hip.C: Hip circumference, Wait.C: waist circumference, HDL: high density lipoprotein, LDL: Low density lipoprotein, CGM: Continuous glucose monitor, HRR: Heart rate reserve, 1RM: Maximum repetition, FIN: Fasting insulin, RTD: The rate of torque development, Min: Minutes, Max: Maximum, HI: High-intensity, LI: Low-intensity, Cm: Circumference, Bd.C: body Composition, C-Peptide: Substance mingle with insulin, IR: Insulin resistance, IWT: Interval walking training, CWT: Continuous walking training, HR Max: Heart rate maximum, S: Sets, Re: Repetition, I-Interval, OGGT: Oral glucose tolerance test, $BIGTT_{-SI}$: Insulinogenic index insulin sensitivity, $BIGTT_{-AR}$: Insulinogenic index acute response, W peak: Workload peak, PIN: Postprandial Insulin, PBG: Postprandial blood glucose, VAT: Visceral adipose tissue

Baseline Data Effect on Hba1c and FBG

A total of 1505 type 2 diabetes participants involved in 22 studies baseline data on Hba1c and included exercises (aerobic, resistance, and combine form exercise) compared to control groups. Between exercise and control groups were Hba1c no significant difference at baseline value $P = 0.25$ and standardized mean difference (SMD)= −0.06% (−1.7 mg/dl), 95% CI (−0.16, 0.04). FBG participants involved 1472, baseline was not significant difference value $P = 0.36$ and SMD= −0.05% (−1.4 mg/dl), 95% CI)−0.15, 0.05) this recorded concerning to reliability.

Analysis of Overall Effect on Hba1c

Hba1c variables data taken on type 2 diabetes patients totally 1505 participants included in 22 studies post-values on exercises and control groups there have overall effect size reduced Hba1c favors exercise significant difference value $P = 0.00001$ and SMD= −0.40% (−11.5 mg/dl), 95% CI (−0.54, −0.27) and heterogeneity observed (I^2=23%) no significance value $P = 0.16$ [Figure 5].

Analysis of Overall Effect on FBG

FBG on type 2 diabetes patients totally 1472 participants included in 22 studies post-values on exercises and control groups, there has overall effect size reduced FBG and favors significant difference value $P = 0.0001$ and SMD= −0.41% (−11.8 mg/dl), 95% CI (−0.59, −0.24) and heterogeneity observed (I^2=53%) significant value $P = 0.002$ [Figure 6].

Sub-groups Analysis

Varied exercises regimen groups divided into three sub-groups such as aerobic, resistance, and combined form exercises on 12 to 16 weeks exercise conducted about nine randomized controlled studies and effect results Hba1c overall effect size reduced favors exercise have been significant difference value $P = 0.00001$

and SMD= −0.65% (−18.7 mg/dl), 95% CI (−0.88, −0.42) and heterogeneity observed (I^2=0%) no significant value *P* = 0.96. FBG analysis reduced favors exercise have overall effect size significant difference value *P* = 0.00001 and SMD= −0.53% (−15.2 mg/dl), 95% CI (−0.76, −0.29) and heterogeneity observed (I^2=1%) no significant value *P* = 0.43.

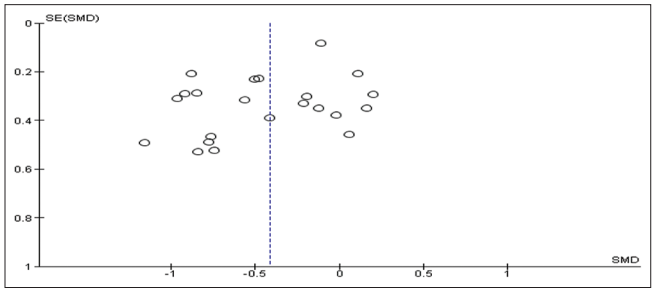

Figure 4: Funnel plot. SE: Standard error, SMD: Standardized mean difference. Funnel plot for publication bias

Sensitivity Analysis

Sensitivity analysis conducted randomized controlled studies in which selected protocol outcome point only 12 weeks exercises (aerobic, resistance and combine exercises) 3 days/week scheduled six studies of analysis Hba1c reduced favors exercise have overall effect size significant difference value *P* = 0.00001 and SMD= −0.70% (−20.1 mg/dl), 95% CI (−0.98, −0.42) and heterogeneity observed (I^2=0%) no significant difference value *P* = 0.98. FBG involved five studies and

Study or Subgroup	EXERCISES GROUP Mean	SD	Total	CONTROL GROUP Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
Annibalini 2017 (3)	146	20.1	8	151	23	8	1.7%	-0.22 [-1.20, 0.76]
Botton 2018 (7)	150	18.9	22	164	30.1	22	4.1%	-0.55 [-1.15, 0.06]
Cassidy 2018 (9)	150	27.52	11	165	19.89	11	2.2%	-0.60 [-1.46, 0.26]
Hansen 2009 (17)	143	21.2	17	160	38.5	20	3.5%	-0.52 [-1.18, 0.14]
Kadoglou 2010 (23)	161	17.8	23	175	17.2	24	4.2%	-0.79 [-1.38, -0.19]
Kadoglou P.E 2012 (24)	157	28.7	26	180	31.6	27	4.6%	-0.75 [-1.31, -0.19]
Kang J 2016 (25)	123	14.4	8	137	17.2	8	1.6%	-0.83 [-1.87, 0.20]
Karstoft 2013 (26)	148	29.6	12	148	24.1	8	2.1%	0.00 [-0.89, 0.89]
Lee 2015 (28)	150	33	40	188	54.2	40	6.3%	-0.84 [-1.30, -0.38]
Liu 2015 (30)	122	17.5	22	138	18.7	20	3.8%	-0.87 [-1.50, -0.23]
Mavros 2013 (32)	147	25.5	36	161	30.1	48	6.7%	-0.49 [-0.93, -0.05]
Praet 2008 (42)	156	39.3	49	151	32.4	43	7.3%	0.14 [-0.27, 0.55]
Rahbar 2017 (44)	143	43.6	13	155	47.1	15	2.9%	-0.26 [-1.00, 0.49]
Rech 2019 (45)	147	14.9	14	162	28.1	20	3.2%	-0.62 [-1.32, 0.08]
Shakil-ur-Rehman 2017 (48)	163	41.3	51	189	40.5	51	7.6%	-0.63 [-1.03, -0.23]
Snel 2012 (49)	134	41.3	13	146	32.1	14	2.8%	-0.32 [-1.08, 0.44]
Stefano Balducci 2010 (50)	146	31.6	288	155	34.4	275	17.0%	-0.27 [-0.44, -0.11]
Taghizadeh 2018 (51)	154	25.5	10	161	43.1	10	2.1%	-0.19 [-1.07, 0.69]
Tudor-Locke 2004 (53)	160	54.5	24	160	48.8	23	4.5%	0.00 [-0.57, 0.57]
Vanninen1992 (54)	144	45.9	38	163	45.9	40	6.5%	-0.41 [-0.86, 0.04]
Winding 2018 (57)	146	23	13	151	28.7	7	2.0%	-0.19 [-1.11, 0.73]
Yang 2017 (59)	146	23.5	17	140	22.8	16	3.3%	0.25 [-0.43, 0.94]
Total (95% CI)			**755**			**750**	**100.0%**	**-0.40 [-0.54, -0.27]**

Heterogeneity: Tau² = 0.02; Chi² = 27.22, df = 21 (P = 0.16); I² = 23%

Test for overall effect: Z = 5.87 (P < 0.00001)

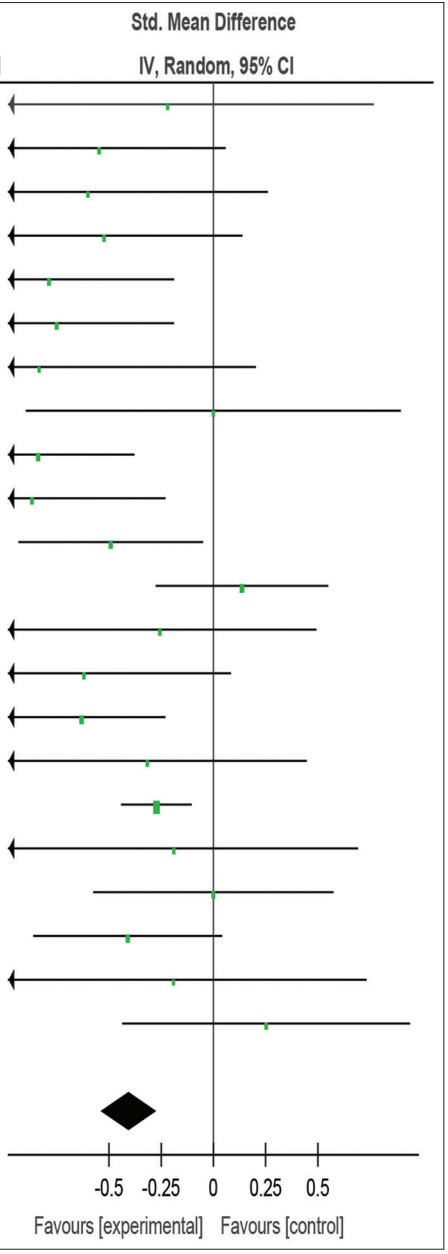

Figure 5: Forest plot of overall effect on hemoglobin A1c

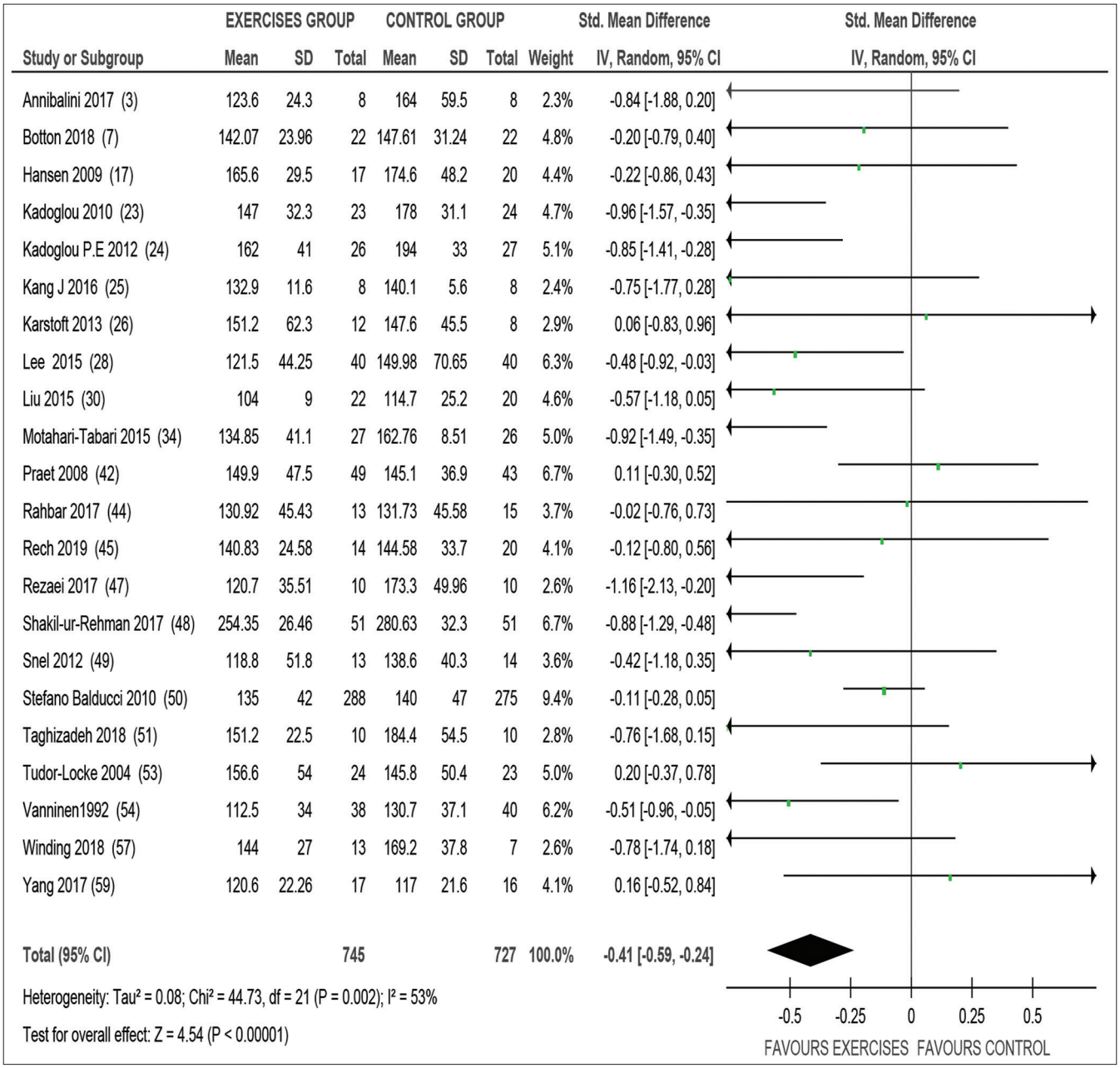

Figure 6: Forest plot of overall effect on fasting blood glucose

overall effect size favors exercise group was significant difference value $P = 0.001$ and SMD= −0.49% (−14.1 mg/dl), 95% CI (−0.78, −0.19) and heterogeneity observed (I^2=0%) no significant value $P = 0.42$.

Discussion

Meta-analysis examined exercises intervention affect on Hba1c and FBG control among type 2 diabetes mellitus patients. As per reported American College of Sports Medicine and American Diabetes Association and Joint Position Statement that in physical exercise have been conducted weekly 150 min exercise, 3 days training program per week but not consecutive 2 days and combined each session follow approximately 30–60 min.[50] The pervious meta-analysis of aerobic interval training reported cardio-metabolic outcome minimum training duration of 8 weeks and reduced glucose level on Hba1c significantly by 0.26% compared with moderate intensity of continuous training and non-exercise group. Aquatic exercise reduced Hba1c 0.96%.[15,51] Walking exercise patients had persistent motive to goal follow supervised session and strictly diet control, is increase insulin-sensitivity to glucose uptake and showed individually increased glucose delivery and transport to myocytes, and oxidative enzyme activities. Furthermore, the capacity for glycogen synthesis increases with physical training from 30 sessions on 6 weeks or 20 sessions on 4 weeks that should be more frequency, average of 3–5 time a week and exercise session lasting daily 20–60 min into improve walking speed moment, distance, mobility in the

self-care among diabetes type 2 patients associated with cardiac problem.[14,52]

In the meta-analysis result overall treatment effect exercise compare to control group on Hba1c decreased SMD= −0.40% (−11.5 mg/dl), although this research varied exercise regimen. Controlled clinical trials of meta-analysis stated that exercise training reduces Hba1c but was not significantly in spite of would be reduce the complication of type 2 diabetes patients compare with control group.

Rees *et al*. (2017) that meta-analysis small study analysis, FBG of aquatic exercise compare to land exercise 8–12 weeks post-exercise result did not significant difference in aquatic exercise weighted mean difference mg/dl −5.06 (−12.32, −2.21) among type 2 diabetes.[51] In this research analysis, FBG overall impact of varied exercise regimen had significantly reduced FBG favors exercise group significant difference $P = 0.0001$ and SMD= −0.41% (−11.8 mg/dl), but heterogeneity observed (I^2=53%) significant value $P = 0.002$ for this reason subgroup analysis conducted on the three groups as aerobic, resistance, and combine form exercises. Larger effect size depend with exercise prescription, fitness testing, supervised exercise, group session and frequency, longer duration exercise session when comparisons type 2 diabetes patients' on standard group.[31]

The present research of meta-analysis was documented FBG from varied exercises regimen interventions in which studies difference in either samples or each study differ thus, heterogeneity is expressed as I^2 statistics has been estimated with chi-square test.[31] Variability among included studies might be termed heterogeneity, the variability in participant, intervention, outcome are described as clinical heterogeneity, variability in risk of bias and study design as methodological heterogeneity, variability in intervention effects being more different from each other expect due to random error. Variance included studies that due to between patients variation (within study) and between study variation (heterogeneity). I^2 statistic corresponds to measures of quantifying heterogeneity in the meta-analysis that describes percentage of variability in estimate value that due to heterogeneity rather than sampling error. The corresponding I^2 statistics values that percentages indicate included trail variability due to sampling error, 30% are mild heterogeneity and more than 50 percentages are notably substantial heterogeneity that depends on size and direction of treatment effect.[32] One study context reflected conflicting results diabetes type 2 patients would have small sample size of exercise intervention 8 and above week's effect promote to glycemic control and weight loss.[10] Variations in trails quality design and carry out, into imprecision or bias individual estimate of treatment effect. Imprecision is a random error that same study replication effect estimate might differ, its reason of sampling variation. The grater sampling variation on few studies can lead to less precise. High precise result depends on more weight given by precisions are within study variance of effect. An intervention has effective on error that positive conclusion is false and would direct overestimating in intervention's effect. Negative conclusion is false on no-effect can lead to underestimating in intervention's effect, if small number of studies on bias.[33,53,54] Short-time period of exercise measured continuous glucose monitor on daily spent significant reduced hyperglycemia 10.0 Mmol/L, whereas FBG level change not significantly.[55]

An ideal exercised protocol for resistance training and prescribed tailor-made exercise program for patients' type 2 diabetes. Authors specify that the Hba1c reduction differed according to the resistance training program such as frequency, intensity or number of sets.[28] According to Mcginley (2014) analysis study resistance not assessed precisely, band group lesser effect 12–16 weeks on type 2 diabetes mellitus Hba1c −0.18% had been no significantly reduction compare with other resistance exercise (weight machine/free weight) but, 3 and 6 months have showed that reduction significant.[6,16] Author conducted rigorous aerobic verses resistance exercise that conclude may be general concept on physical activity or physical exercise much essentials than more specific mixture exercise that diverse form of exercise intervention.[27]

According to American Diabetes Association suggested that 150 min/week of moderate-intensity exercises corresponding to MET- h/week latest information, research qualitative analysis 28 studies among type 2 diabetes patients, highly intensive combine exercises aerobic and resistance have been strategy effective on Hba1c along with lifestyle change which was supervised that superior continuous supporting counseling. Results found that combine exercise form such as aerobic and resistance training greater control on glucose rather than both exercise alone further, meta-analysis did not conduct exercise alone.[18] That study recommendation, in this current research sub-group analysis could be made alone aerobic, resistance and combine exercises.

In this research, 11 studies have diet as co-intervention, diet, and exercise do combine to control glucose modulating response as time of exercise have been completed training before meals that lead hypoglycemic incident are low, exercise completed after meals consumed that would correlation night-time hypoglycemia.[52] The trails might differ in the way as inclusion and exclusion criteria difference, patient's selection criteria, broader variation in patient management such as difference setting patients care, intermediate outcome and co-intervention. Outcome measure in follow-up time, control group or treatment groups difference in dose, time, and brand. Systematic review research, reflected the combined diet and physical exercises, was controlled bio-chemical parameter and the fundamental treatment diabetes type 2 patients to Hba1c and blood glucose level then impact of exercises consisted as aerobic, resistance, flexibility and combine form and healthy nutrition, carbohydrate, much consumption polyunsaturated fatty acid and almond are essential for good glucose level maintain suitable information scientifically discovered strategy in treatment.[56] Random effect model is to need regarding heterogeneity and further discussion I^2 statistic into regard to estimation of CI in the order of overall effect size. The tau^2 statistic is the variance of the effect size parameters (Hba1c and FBG) across the population (type 2 diabetes) of studies and it reflects the variance of the true effect sizes. Between studies variance of the estimate is calculated in the tau^2 statistic. One study to another study variance has been familiar into calculations in the CI around treatment effect. In this research, summary effect size in the 95% CI opted sources had been variance, within study as well as between study sampling variation.[33]

Oxman (1992) conclusion "the subgroups have the criteria in deciding when analysis that differential response to the treatment in a definable form of participant and dose. Inference based on between study comparison and its look preliminary within-study comparison that lead comparison has been doing with different groups or different intervention. When assessing the consistency of result that is important to consider, on power of comparison

and other difference between studies might influence the result.[57] Our sub-group analysis 12–16 weeks exercise regimen compare to control groups have −0.65% (18.7 mg/dl) Hba1c reduced (aerobic −19.2 mg/dl, resistance exercise −16.6 mg/dl and combine exercise mg/dl 20.4 mg/dl) and no heterogeneity found. Hba1c compare with control group that Hba1c showed average long time glycemic control level among diabetes patients last 2–3 months. Subgroups analysis of exercise was each physical activity frequency per week conducted analysis but heterogeneity reduced based on frequency per week all study physical activity, although when frequency high result most effective decrease glucose level. Heterogeneity decreased in sub-group analyses 8–12 weeks exercise based 3 or 4 days/week exercise frequency on regimen.[14] FBG sub-group analysis has overall effect size exercise regimen compare to control groups have −0.53% (15.2 mg/dl) Hba1c reduced (aerobic −18.4mg/dl, resistance exercise −4.6 mg/dl and combine exercise mg/dl 18.9 mg/dl) and no found heterogeneity when strictly exercise set regimen. Both Hba1c and FBG favors to combined form of exercise reduced rather than aerobic or resistance exercise. Evidence based medicine is research evidence solving the problem by conducting systematic approach. It were five step to deduct answer consist on (1) research question, (2) evidence search into concerning valid, (3) validity, applicability and important to the patients, (4) Evidence to apply the patients, and (5) strategy for evaluating performance. These steps could be critical appraisal and principles of randomized controlled trails, systematic review, and meta-analysis help to clinical life scenario.[58] In this study sensitivity analysis schedule only 12 weeks exercise regimen, in which exercise frequency 3 or 4 day/week criteria effect on Hba1c −0.70% (−20.1 mg/dl) and FBG −0.49% (−14.1 mg/dl) decreased significantly exercise group compare to control group, this analysis familiar to varied exercise regimen impact on blood glucose level among type 2 diabetes patients.

Study Strength and Limitation

Increase quality and reliability for values of Hba1c and FBG baseline exercise compare to control group test. The study strengths the indication randomized controlled studies that period of physical exercise 8–12 weeks and frequency follow 3 or 5 days/week in which impacts reduced glucose level favor to exercise group compare to control group. FBG post-intervention has substantial heterogeneity due to sampling variation and somewhere methodology bias as blinding of participants and performance bias. PubMed and Web of Science were used to take research journal paper only, and not use other databases. There were included both gender and their medication no restriction. Three randomized controlled studies papers data converted to desire formed have been average values and could reduce power of statistical analysis.

Implication

The study of Oliveira (2012), systematic review recommendation on combined exercise such as aerobic and resistance exercise grader control glucose than the exercise alone and not conducted meta-analysis, hence our subgroup divided into three groups aerobic, resistance, and combine form exercise could be analyses results favors specifically to combine group exercise. Further study may conduct particular gender with specific age range. Then, combined exercise may compare meticulous exercise as alone.

Conclusion

The meta-analysis varied exercise regimen and its impact on blood glucose as Hba1c and FBG level and evidence support close up randomized controlled studies designed that overall significant impact on intervention such as aerobic, resistance, and combine form exercise (aerobic and resistance exercise) among type 2 diabetes patients. Although, combined exercise highly better effective strategy results than aerobic or resistance alone, duration eight and above weeks, exercise frequency 3 or 5 days/week and combined exercise followed aerobic consecutively and then resistance.

References

1. Way K, Hackett D, Baker M, Johnson N. The effect of regular exercise on insulin sensitivity in Type 2 diabetes mellitus: A systematic review and meta-analysis. Diabetes Metab J 2016;40:253.
2. Annibalini G, Lucertini F, Agostini D, Vallorani L, Gioacchini A, Barbieri E, *et al*. Concurrent aerobic and resistance training has anti-inflammatory effects and increases both plasma and leukocyte levels of IGF-1 in late middle-aged Type 2 diabetic patients. Oxid Med Cell Longev 2017;2017:1-10.
3. Kang S, Ko K, Baek U. Effects of 12 weeks combined aerobic and resistance exercise on heart rate variability in Type 2 diabetes mellitus patients. J Phys Ther Sci 2016;28:2088-93.
4. International Diabetes Federation. IDF Atlas. 8th ed. Brussels, Belgium: International Diabetes Federation; 2017. Available from: https://www.idf.org/search.html?searchword=diabetes%20type%20%202 and searchphrase=all.
5. Kumar V, Jagannathan A, Philip M, Thulasi A, Angadi P, Raghuram N. Role of yoga for patients with Type II diabetes mellitus: A systematic review and meta-analysis. Complement Ther Med 2016;25:104-12.
6. Nery C, Moraes S, Novaes K, Bezerra M, Silveira P, Lemos A. Effectiveness of resistance exercise compared to aerobic exercise without insulin therapy in patients with Type 2 diabetes mellitus: A meta-analysis. Braz J Phys Ther 2017;21:400-15.
7. Chen L, Pei J, Kuang J, Chen H, Chen Z, Li Z, *et al*. Effect of lifestyle intervention in patients with Type 2 diabetes: A meta-analysis. Metabolism 2015;64:338-47.
8. Verboven M, Van Ryckeghem L, Belkhouribchia J, Dendale P, Eijnde B, Hansen D, *et al*. Effect of exercise intervention on cardiac function in Type 2 diabetes mellitus: A systematic review. Sports Med 2018;49:255-68.
9. Figueira F, Umpierre D, Cureau F, Zucatti A, Dalzochio M, Leitão C, *et al*. Association between physical activity advice only or structured exercise training with blood pressure levels in patients with Type 2 diabetes: A systematic review and meta-analysis. Sports Med 2014;44:1557-72.
10. Boule N, Haddad E, Kenny G, Wells G, Sigal R. Effects of exercise on glycemic control and body mass in Type 2 diabetes mellitus: A meta-analysis of controlled clinical trials. Scand J Med Sci Sports 2002;12:60-1.
11. Brown A. 42 Factors That Affect Blood Glucose? A Surprising Update. San Francisco: DiaTribe Foundation; 2019. Available from: https://www.diatribe.org/42factors.
12. Kadoglou NP, Vrabas IS, Sailer N, Kapelouzou A, Fotiadis G, Noussios G, *et al*. Exercise ameliorates serum MMP 9 and TIMP 2 levels in patients with Type 2 diabetes. Diabetes Metab 2010;36:144-51.
13. Kadoglou NP, Vrabas IS, Kapelouzou A, Lampropoulos S, Sailer N, Kostakis A, *et al*. The impact of aerobic exercise training on novel adipokines, apelin and ghrelin, in patients with Type 2 diabetes. Med Sci Monit 2012;18:CR290-5.
14. Peurala S, Karttunen A, Sjogren T, Paltamaa J, Heinonen A. Evidence for the effectiveness of walking training on walking and self-care after stroke: A systematic review and meta-analysis of randomized

controlled trials. J Rehabil Med 2014;46:387-99.
15. Qiu S, Cai X, Sun Z, Zügel M, Steinacker JM, Schumann U. Aerobic interval training and cardiometabolic health in patients with Type 2 diabetes: A meta-analysis. Front Physiol 2017;8:957.
16. McGinley SK, Armstrong MJ, Boulé NG, Sigal RJ. Effects of exercise training using resistance bands on glycaemic control and strength in Type 2 diabetes mellitus: A meta-analysis of randomised controlled trials. Acta Diabetol 2014;52:221-30.
17. Borenstein M, Hedges LV, Higgins, JP, Rothstein HR. Introduction to Meta-analysis. Hoboken, NJ: John Wiley and Sons; 2011.
18. Oliveira C, Simoes M, Carvalho J, Ribeiro J. Combined exercise for people with Type 2 diabetes mellitus: A systematic review. Diabetes Res Clin Pract 2012;98:187-98.
19. World Health Organization. Use of Glycated Haemoglobin (HBA1C) in the Diagnosis of Diabetes Mellitus. Geneva, Switzerland: World Health Organization; 2021. Available from: https://www.who.int/diabetes/publications/report-hba1c_2011.pdf. [Last accessed on 2021 Jan 01].
20. Liberati A, Altman D, Tetzlaff J, Mulrow C, Gøtzsche P, Ioannidis J, *et al*. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. PLoS Med 2009;6:e1000100.
21. Egger M, Davey-Smith G, Altman D. Systematic Reviews in Health Care: Meta-analysis in Context. 2nd ed. London: BMJ Books; 2001.
22. Higgins JP, Green S. Selecting studies and collecting data and assessing risk of bias in included studies. In: Cochrane Handbook for Systematic Reviews of Interventions. Ch. 7, 8. United Kingdom: Cochrane Collaboration; 2011.
23. Shakil-ur-Rehman S, Karimi H, Gillani SA, Amjad I, Ahmad S, Yaseen A. Response to a supervised structured aerobic exercise training program in patients with Type 2 diabetes mellitus does gender make a difference? A randomized controlled clinical trial. J Natl Med Assoc 2018;110:431-9.
24. Vanninen E, Uusitupa M, Siitonen O, Laitinen J, Länsimies E. Habitual physical activity, aerobic capacity and metabolic control in patients with newly-diagnosed Type 2 (non-insulin-dependent) diabetes mellitus: Effect of 1-year diet and exercise intervention. Diabetologia 1992;35:340-6.
25. Motahari-Tabari N, Shirvani MA, Shirzad-e-Ahoodashty M, Yousefi- Abdolmaleki E, Teimourzadeh M. The effect of 8 weeks aerobic exercise on insulin resistance in Type 2 diabetes: A randomized clinical trial. Glob J Health Sci 2014;7:115-21.
26. Rezaei S, Shamsi M, Mahdavi M, Jamali A, Prestes J, Tibana R, *et al*. Endurance exercise training decreased serum levels of surfactant protein D and improved aerobic fitness of obese women with Type-2 diabetes. Diabetol Metab Syndr 2017;9:74.
27. Yang P, Swardfager W, Fernandes D, Laredo S, Tomlinson G, Oh PI, *et al*. Finding the optimal volume and intensity of resistance training exercise for Type 2 diabetes: The forte study, a randomized trial. Diabetes Res Clin Pract 2017;130:98-107.
28. Ishiguro H, Kodama S, Horikawa C, Fujihara K, Hirose AS, Hirasawa R, *et al*. In search of the ideal resistance training program to improve glycemic control and its indication for patients with Type 2 diabetes mellitus: A systematic review and meta-analysis. Sports Med 2016;46:67-77.
29. The Global Diabetes Community. Convert Blood Sugar/Glucose from mmol/L (UK Standard) to mg/dl (US standard) and Vice Versa Using Our Blood Sugar Converter. United Kingdom: Diabetes; 2021. Available from: https://www.diabetes.co.uk/blood-sugar-converter.html. [Last accessed on 2021 Jan 20].
30. National Glycohemoglobin Standardization Program NGSP: Convert between NGSP, IFCC and eAG; 2021. Available from: http://www.ngsp.org/convert1.asp. [Last accessed on 2021 Jan 01].
31. Nielsen PJ, Hafdahl AR, Conn VS, LeMaster JW, Brown SA. Meta-analysis of the effect of exercise interventions on fitness outcomes among adults with Type 1 and Type 2 diabetes. Diabetes Res Clin Pract 2006;74:111120.
32. Higgins J, Thompson S. Quantifying heterogeneity in a meta-analysis. Statist Med 2002;21:1539-58.
33. Bartolucci A, Hillegass W. Overview, Strengths, and Limitations of Systematic Reviews and Meta-Analyses. In: Evidence-Based Practice: Toward Optimizing Clinical Outcomes. Berlin, Germany: Springer; 2010. p. 17-33.
34. Cassidy S, Vaidya V, Houghton D, Zalewski P, Seferovic JP, Hallsworth K, *et al*. Unsupervised high-intensity interval training improves glycaemic control but not cardiovascular autonomic function in Type 2 diabetes patients: A randomised controlled trial. Diabetes Vasc Res 2019;16:69-76.
35. Mavros Y, Kay S, Anderberg KA, Baker MK, Wang Y, Zhao R, *et al*. Changes in insulin resistance and HbA1c are related to exercise-mediated changes in body composition in older adults with Type 2 diabetes: Interim outcomes from the GREAT2DO trial. Diabetes Care 2013;36:2372-9.
36. Hansen D, Dendale P, Jonkers RA, Beelen M, Manders RJ, Corluy L, *et al*. Continuous low to moderate-intensity exercise training is as effective as moderate-to high-intensity exercise training at lowering blood HbA1c in obese Type 2 diabetes patients. Diabetologia 2009;52:1789-97.
37. Karstoft K, Winding K, Knudsen SH, Nielsen JS, Thomsen C, Pedersen BK, *et al*. The effects of free-living interval-walking training on glycemic control, body composition, and physical fitness in Type 2 diabetic patients: A randomized, controlled trial. Diabetes Care 2013;36:228-36.
38. Lee S, Pei D, Chi M, Jeng C. An investigation and comparison of the effectiveness of different exercise programmes in improving glucose metabolism and pancreatic β cell function of Type 2 diabetes patients. Int J Clin Pract 2015;69:1159-70.
39. Praet SF, Van Rooij ES, Wijtvliet A, Boonman-De Winter LJ, Enneking T, Kuipers H, *et al*. Brisk walking compared with an individualised medical fitness programme for patients with Type 2 diabetes: A randomised controlled trial. Diabetologia 2008;51:736-46.
40. Rahbar S, Naimi SS, Soltani AR, Rahimi A, Baghban AA, Rashedi V, *et al*. Improvement in biochemical parameters in patients with Type 2 diabetes after twenty-four sessions of aerobic exercise: A randomized controlled trial. Iran Red Crescent Med J 2017;19:e13931.
41. Snel M, Gastaldelli A, Ouwens DM, Hesselink MK, Schaart G, Buzzigoli E, *et al*. Effects of adding exercise to a 16-week very low-calorie diet in obese, insulin-dependent Type 2 diabetes mellitus patients. J Clin Endocrinol Metab 2012;97:2512-20.
42. Taghizadeh M, Ahmadizad S, Naderi M. Effects of endurance training on hsa-miR-223, P2RY nd platelet function in Type 2 diabetic patients. Clin Hemorheol Microcirc 2018;68:383-9.
43. Tudor-Locke C, Bell RC, Myers AM, Harris SB, Ecclestone NA, Lauzon N, *et al*. Controlled outcome evaluation of the first step program: A daily physical activity intervention for individuals with Type II diabetes. Int J Obes 2004;28:113-9.
44. Winding KM, Munch GW, Iepsen UW, Van Hall G, Pedersen BK, Mortensen SP. The effect on glycaemic control of low-volume high-intensity interval training versus endurance training in individuals with Type 2 diabetes. Diabetes Obesity Metab 2018;20:1131-9.
45. Botton CE, Umpierre D, Rech A, Pfeifer LO, Machado CL, Teodoro JL, *et al*. Effects of resistance training on neuromuscular parameters in elderly with Type 2 diabetes mellitus: A randomized clinical trial. Exp Gerontol 2018;113:141-9.
46. Rech A, Botton CE, Lopez P, Quincozes-Santos A, Umpierre D, Pinto RS. Effects of short-term resistance training on endothelial function and inflammation markers in elderly patients with Type 2 diabetes: A randomized controlled trial. Exp Gerontol 2019;118:19-25.
47. Liu Y, Liu S, Cai Y, Xie K, Zhang W, Zheng F. Effects of combined aerobic and resistance training on the glycolipid metabolism and inflammation levels in Type 2 diabetes mellitus. J Phys Ther Sci 2015;27:2365-71.
48. Stefano B, Silvano Z, Antonio N, Pierpaolo DF, Stefano C, Patrizia C,

et al. Effect of an intensive exercise intervention strategy on modifiable cardiovascular risk factors in subjects with Type 2 diabetes mellitus: A randomized controlled trial: The Italian diabetes and exercise study (IDES). Arch Intern Med 2010;170:1794-803.
49. Pai L, Li T, Hwu Y, Chang S, Chen L, Chang P. The effectiveness of regular leisure-time physical activities on long-term glycemic control in people with Type 2 diabetes: A systematic review and meta-analysis. Diabetes Res Clin Pract 2016;113:77-85.
50. Colberg SR, Albright AL, Blissmer BJ, Braun B, Chasan-Taber L, Fernhall B, *et al*. Exercise and Type 2 diabetes: American college of sports medicine and the American diabetes association, joint position statement. Med Sci Sports Exerc 2010;42:2282-303.
51. Rees J, Johnson S, Boulé N. Aquatic exercise for adults with Type 2 diabetes: A meta-analysis. Acta Diabetol 2017;54:895-904.
52. Goedecke J, Ojuka E. Diabetes and Physical Activity. Vol. 60. Sydney: Karger Medical and Scientific Publishers; 2014.
53. Detsky A, Naylor C, O'Rourke K, McGeer A, L'Abbé K. Incorporating variations in the quality of individual randomized trials into meta-analysis. J Clin Epidemiol 1992;45:255-65.
54. Higgins J. Measuring inconsistency in meta-analyses. Br Med J 2003;327:557-60.
55. MacLeod S, Terada T, Chahal B, Boulé N. Exercise lowers postprandial glucose but not fasting glucose in Type 2 diabetes: A meta-analysis of studies using continuous glucose monitoring. Diabetes Metab Res Rev 2013;29:593-603.
56. Barreira E, Novo A, Vaz JA, Pereira AM. Dietary program and physical activity impact on biochemical markers in patients with Type 2 diabetes: A systematic review. Atencion Prim 2018;50:590-610.
57. Oxman A. A consumer's guide to subgroup analyses. Ann Intern Med 1992;116:78.
58. Akobeng A. Principles of evidence based medicine. Arch Dis Childhood 2005;90:837-40.