



Review

Structured exercise interventions for type 2 diabetes mellitus: Strength of current evidence

Unaise Abdul Hameed¹, MY Shereef², Mohammed Ejas Hussain¹

¹Center for Physiotherapy and Rehabilitation Sciences, Jamia Millia Islamia, New Delhi-110025

²Ansari Health Centre, Jamia Millia Islamia, New Delhi.

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Corresponding author

Unaise Abdul Hameed
Research Scholar,
Center for physiotherapy and rehabilitation sciences,
Jamia Millia Islamia, Jamia Nagar,
New Delhi -110025, India.
Phone: +91 9971319932
Fax: +91 11 26980544
Email: unaisephysio@gmail.com

Abstract

Exercise, along with medical nutrition therapy and pharmacological interventions, is an important component in the clinical management of type 2 diabetes mellitus. Current clinical guidelines on Type 2 diabetes provide no detailed information on the modalities of effective exercise intervention in the treatment of Type 2 diabetes. Both endurance and resistance types of exercise seem to be equally effective in improving metabolic control in patients with Type 2 diabetes. Determining the best method of providing exercise is clinically relevant to this population. This paper reviews the epidemiology of diabetes and problems of physical function associated with Type 2 diabetes and discuss the benefits of exercise therapy on the parameters of glycemic control and function in Type 2 diabetes patients, with special reference to Asian Indians. Based on the currently available literature, it is concluded that Type 2 diabetes patients should be encouraged to participate in specifically designed exercise intervention programs. Attention should be paid to the avoidance of cardiovascular and musculoskeletal deconditioning. More clinical research is warranted to establish the efficacy of different dosages of exercise intervention in a holistic approach for Type 2 diabetes subpopulations within different stages of the disease and various levels of co-morbidity.

Key words: Exercise, type 2 diabetes, resistance training, glycemic control.

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The American Diabetes Association categorizes diabetes as type 1 or type 2¹. In type 1 diabetes (5–10% of cases); the cause is an absolute deficiency of insulin secretion resulting from autoimmune destruction of the insulin producing cells in the pancreas. Type 2 diabetes (T2D) accounts for 90–95% of cases, results from insulin resistance and inadequate compensatory insulin secretion. Less common forms include gestational diabetes mellitus (GDM), which is associated with a 40–60% chance

of developing T2D in the next 5–10 years². Diabetes can also result from genetic defects in insulin action, pancreatic disease, surgery, infections, and drugs or chemicals^{1,2}.

Genetic and environmental factors are strongly implicated in the development of T2D. The exact genetic defects are complex and not clearly defined³, but the risk increases with age, obesity, and physical inactivity. T2D occurs more frequently in populations

with hypertension or dyslipidemia, women with previous GDM, and non-Caucasian people including Native Americans, African Americans, Hispanic/Latinos, Asians, and Pacific Islanders.

According to the International Diabetes Federation (IDF), T2D now affects 246 million people worldwide and is expected to affect some 380 million by 2025, representing as much as 7.1% of the global adult population⁴, with almost 80% of these patients in developing countries³. The increase in number of people with diabetes is attributed to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity. As such, the associated health burden in terms of cardiovascular disease, kidney failure, blindness, amputations and premature death will increase progressively, unless more effective primary and secondary pharmaceutical and/or lifestyle interventional strategies become more widely available.

High prevalence of diabetes in India: Results from population based diabetes surveys

Diabetes epidemic is more pronounced in India than in any other country. The World Health Organization (WHO) reports show that 32 million people in India had diabetes in the year 2000⁵. International Diabetes Federation (IDF) estimated total number of diabetic subjects to be around 40.9 million in India and this is further set to rise to 69.9 million by the year 2025³.

The National Urban Diabetes Survey (NUDS), conducted in six metropolitan cities across India recruited 11,216 subjects aged 20 yr and above from all socio-economic strata⁶, and reported that the age standardized prevalence of T2D was 12.1 per cent. This study also revealed that the prevalence in the Southern part of India to be higher-13.5 per cent in Chennai, 12.4 per cent, in Bangalore, and 16.6 per cent Hyderabad; compared to eastern India (Kolkata), 11.7 per cent; Northern India (New Delhi), 11.6 per cent; and Western India (Mumbai), 9.3 per cent. The study also suggested that there was a large pool of subjects with impaired glucose tolerance (IGT), 14 per cent with a high risk of conversion to diabetes.

A study done in Western India showed age standardized prevalence of 8.6 per cent in urban population⁷. A more recent study reported a high prevalence (9.3%) in rural Maharashtra⁸. The Amrita Diabetes and Endocrine Population Survey (ADEPS)⁹, a community based cross-sectional survey done in urban areas of Ernakulam district in Kerala has revealed a very high prevalence of 19.5 percent.

Socioeconomic, behavioral, nutritional issues have

led to increase in T2D in several nations. Ethnic susceptibility of Asian Indians to T2D and a high familial aggregation of the disease have been attributed to the high prevalence of the disease among this population.

Type 2 Diabetes (T2D): Description

T2D is a chronic, metabolic disease characterized by hyperglycemia resulting from insulin resistance. Chronic hyperglycemia (that is elevated levels of plasma glucose) leads to disturbances of carbohydrate, fat and protein metabolism. Complications such as cardiovascular disease¹⁰, peripheral vascular disease¹¹, retinopathy¹², nephropathy¹³ and loss of physical function¹⁴ are associated with type 2 diabetes. Other complications of type 2 diabetes are a decline in muscular strength (force-generating capacity) and reduced exercise capacity.

Diagnosis of diabetes

Currently, the American Diabetes Association (ADA) recommends the use of any of the following four criteria for diagnosing diabetes:

1. Glycated haemoglobin (A1C) value of 6.5% or higher,
2. Fasting plasma glucose ≥ 126 mg/dl (7.0 mmol/l),
3. 2-h plasma glucose ≥ 200 mg/dl (11.1 mmol/l) during an oral glucose tolerance test using 75 g of glucose, and/or
4. Classic symptoms of hyperglycemia (e.g., polyuria, polydipsia, and unexplained weight loss) or hyperglycemic crisis with a random plasma glucose of 200 mg/dl (11.1 mmol/l) or higher.

In the absence of unequivocal hyperglycemia, the first three criteria should be confirmed by repeat testing³. Prediabetes is diagnosed with an A1C of 5.7– 6.4%, fasting plasma glucose of 100–125 mg/dl (5.6– 6.9 mmol/l; i.e., impaired fasting glucose [IFG]), or 2-h post-load glucose of 140– 199 mg/dl (7.8 –11.0 mmol/l; i.e., impaired glucose tolerance [IGT])¹.

Clinical management of T2D

The treatment goal in type 2 diabetes is to achieve and maintain optimal blood glucose, lipid, and blood pressure (BP) levels to prevent or delay chronic complications of diabetes¹⁵. Clinical management of people with type 2 diabetes consists of medical nutrition therapy, pharmacological therapy, and exercise. Many people with T2D can achieve blood glucose control by following a nutritious meal plan and

exercise program, losing excess weight, implementing necessary self-care behaviors, and taking oral medications, although others may need supplemental insulin². Diet and physical activity are central to the management and prevention of T2D because they help treat the associated glucose, lipid, blood pressure control abnormalities, as well as aid in weight loss and maintenance. When medications are used to control T2D, they should augment life-style improvements, not replace them.

Physical activity / exercise in T2D

Definitions of terms

Recent exercise guidelines for T2D by the American diabetes association and American college of sports medicine define the term physical activity as “bodily movement produced by the contraction of skeletal muscle that substantially increases energy expenditure”. The term Physical activity is used interchangeably with “exercise,” which is defined as “a subset of PA done with the intention of developing physical fitness (i.e., cardiovascular [CV], strength, and flexibility training).” The intent is to recognize that many types of physical movement may have a positive effect on physical fitness, morbidity, and mortality in individuals with T2D.

Current evidence of exercise training for T2D

Physical activity is a key element in the prevention and management of T2D. The overall beneficial effects of exercise in T2D are well documented with regard to glucose control and multiple cardiovascular disease risk factors. The Finnish Diabetes Prevention Study¹⁶ and the Diabetes Prevention Program¹⁷ tested lifestyle interventions that included a physical activity program. Both studies showed the power of exercise, nutrition, and weight loss to prevent diabetes mellitus in at-risk individuals. The American Diabetes Association and the American College of Sports Medicine have published position statements recommending the use of exercise as an intervention for the clinical management of people with T2D^{18,19}.

A recent Cochrane systematic review²⁰ of 14 randomized controlled trials concluded:

1. Exercise improves blood sugar control and that this effect is evident even without weight loss.
2. Exercise decreases body fat content, thus the failure to lose weight with exercise programmes is probably explained by the conversion of fat to muscle.
3. Exercise improved the body's reaction to insulin and decreased blood lipids.

4. Quality of life was only assessed in one study, which found no difference between the two groups.
5. No significant difference was found between groups in blood levels of cholesterol or blood pressure. A total of 14 randomized controlled trials were assessed.

Furthermore, a 2009 systematic review²¹ has demonstrated the benefits of resistance training (strength training) in glycemic control. The results showed that progressive resistance exercise leads to statistically significant improvements in glycosylated hemoglobin and therefore glycemic control. This review provides level 1 evidence to conclude that eight weeks of resistance training with two-three sessions of 45 minutes duration is sufficient to produce improvements in glycemic control. There have been a number of randomized and non randomized trials published since 1990 on the efficacy of resistance exercises on type 2 diabetes. Refer table 1 for a summary of important findings mainly from randomized controlled clinical trials on resistance exercise in T2D.

Position statements on chronic effects of exercise training in T2D

American college of sports medicine and American diabetes association gave a summary of the chronic effects of exercise training in people with T2D. The following chronic effects have been stated²⁹.

1. Both aerobic and resistance training improve insulin action, blood glucose control, and fat oxidation and storage in muscle.
2. Resistance exercise enhances skeletal muscle mass.
3. Blood lipid responses to training are mixed but may result in a small reduction in LDL cholesterol with no change in HDL cholesterol or triglycerides. Combined weight loss and physical activity (PA) may be more effective than aerobic exercise training alone on lipids.
4. Aerobic training may slightly reduce systolic blood pressure, but reductions in diastolic blood pressure are less common, in individuals with T2D.
5. Observational studies suggest that greater PA and fitness are associated with a lower risk of all-cause and cardiovascular mortality.
6. Recommended levels of PA may help produce weight loss. However, up to 60 min/day may be required when relying on exercise alone for weight loss.
7. Individuals with T2D engaged in supervised training exhibit greater compliance and blood sugar control than those undertaking exercise training without supervision.

Table 1. Summary of the effect of resistance exercise on measures of glycemic control.

Reference	Study design and characteristics	Intervention (Experimental)	Improvement in glycemic control*
Sigal et al ¹³	RCT with random and concealed allocation. Study groups similar at baseline. Double blind-ed.	Exercise Type: RE: exercises on weight machines 3 sets of 8-12 reps Intensity: 7–9RM Frequency: 3/wk x 26 wk	HbA _{1c} (%): Significant decrease in percentage of glycated hemoglobin with RE Adverse events: recorded Follow up: 0, 12, 24 wk
Durak et al ²²	RCT with random and concealed allocation. Study groups similar at baseline.	Exercise Type: RE: 10 upper-body and 5 lower-body exercises 3–7 sets of 12 reps Intensity: 12-RM load Frequency: 3 d/wk for 10 wk	HbA _{1c} (%): Significant decrease in percentage of glycated hemoglobin (6.9% ±1.4% to 5.8% ±0.9%) in training group
Dunstan et al ²³	RCT without concealed allocation. Study groups similar at baseline. No blinding reported.	Exercise Type: RE: abdominals, hip E, knee E, knee F, shoulder horizontal F, elbow E, shoulder F, shoulder abduction, shoulder adduction/E Intensity: wk 1–2: 3 x 8–10 50–60% 1RM, wk 3–24: 3 x 8–10 75–85% current 1RM	HbA _{1c} (%): Significant reduction in HbA _{1c} (%), ie, 0.6% improvements after 3 months and 1.2% improvement after 6 months Adverse events: recorded Follow up: 0, 12, 24 wk
Baum et al ²⁴	RCT without concealed allocation. Study groups similar at baseline. No blinding reported. No intention to treat analysis reported.	Exercise Type: RE : hip E, knee F, knee E, ankle PF, shoulder horizontal F/E, shoulder adduction, shoulder E Intensity: Wk 1-6: 1 x 12 70%1RM Wk 7-9: 2 x 12 70%1RM Wk 10-12: 3 x 10 80%1RM Frequency:3/wk	HbA _{1c} (%): The reported difference is 7±0.17 in RE group and 7±0.26 in non exercising control group. Adverse events: recorded Follow up: 0, 12 wk
Cauza et al ²⁵	RCT with random and concealed allocation. Study groups similar at baseline. No blinding reported. No intention to treat analysis reported.	Exercise Type: RE: shoulder horizontal F, shoulder F/abduction, hip E, knee F, knee E, shoulder adduction/E, elbow F, elbow E, ankle PF Intensity: 1–2 x 10-15RM Frequency: 3/wk x 16 wk	HbA _{1c} (%): Significant decline in HbA _{1c} was observed with RE (1.2% decrease). Adverse events: recorded Follow up: 0, 16 wk
Castaneda et al ²⁶	RCT without concealed allocation. Study groups similar at baseline. No blinding reported. Intention to treat analysis reported.	Exercise Type: RE: hip E, knee E, knee F, shoulder horizontal F, upper back Intensity: Wk 1-8: 3 x 8 60-80% of baseline 1RM Wk 10-14: 3 x 8 70–80% midstudy 1RM Frequency:3/wk	HbA _{1c} (%): Reduced from 8.7±0.3 to 7.6±0.2 with RE. Adverse events: recorded Follow up: 0, 16 wk
Honkola et al ²⁷	Non-randomized trial. Study groups similar at baseline. No blinding reported. Intention to treat analysis reported.	Exercise Type: RE: knee F, knee E, shoulder, trunk F, trunk E Intensity: 2 x 12–15 Borg moderate intensity Frequency: 2/wk x 20wk	HbA _{1c} (%): HbA _{1c} was improved by0.5 % with exercises. Follow up: 0, 20 wk

Ishii et al ²⁸	RCT without concealed allocation. Study groups similar at baseline. No blinding reported.	Exercise Type: RE: 6 upper-body and 3 lower-body exercises 2 sets of 10–20 reps Intensity: 40%–50% 1-RM load Frequency: 5 d/wk for 4–6 wk	Glucose disposal rate: Significant 48% increase in training group (6.85 ± 1.8 to 10.12 ± 3.15 mg/kg lean body mass per min)
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HbA_{1c} = glycosylated hemoglobin, RE = resistance exercise, RM = repetition maximum, E = extension, F = flexion, PF = plantarflexion, wk = week, RCT = Randomised Controlled Trial. *numbers are given as mean ± S.D.

8. Increased PA and physical fitness can reduce symptoms of depression and improve health-related quality of life in those with T2D.

Muscle strength and exercise capacity in T2D and the role of exercise

The results of previous studies^{30,31} suggest that people with type 2 diabetes have less muscular strength than people without T2D. Deficits in muscular strength are clinically relevant for people with T2D particularly in view of evidence that muscular strength has been associated with increased risk of loss of physical function^{32,33} in people with and without T2D.

Persons with T2D have decreased exercise capacity³⁴. Loss of exercise capacity has been shown to increase the risk of mortality³⁵⁻³⁷ in people with and without T2D. Therefore, the assessment of muscular strength and exercise capacity in response to interventions in people with T2D is important to prevent loss of physical function and mortality.

Several studies provide supportive evidence for the use of supervised exercise programs to improve muscular strength^{23,38} and exercise capacity³⁸ in people with T2D.

Exercise prescription in T2D

Exercise can be delivered in various “doses”: differing number of sessions per week (frequency), number of minutes per session (duration), or degree of effort (intensity). Operational definitions of training variables as applicable to resistance or strength training are summarised in table 2.

Types of exercises recommended in T2D include resistance and endurance exercises. Endurance exercise involves repetitive, rhythmic contraction of large muscle groups, as in running or cycling; it also called *aerobic exercise* because it depends predominantly on oxidative energy sources to produce adenosine triphosphate. Strength training, also called *resistance training*, generally involves relatively slow, intense contractions at high force; weightlifting is the most common example. These types of exercise have important differences. For example, according to elegant studies done at the Copenha-

gen Muscle Research Center, little blood flow through muscle during muscle contraction, even during aerobic exercise³⁹. Nevertheless, endurance exercise (high frequency, multiple repetitions, and low force) induces alterations in contractile protein isoforms of skeletal muscle and stimulates mitochondrial respiratory enzymes and specific adaptations in the heart and blood vessels²⁷. On the other hand, strength training stimulates increases in muscle protein and muscle cross-sectional area, although this adaptation is more a function of force production than of “anaerobic metabolism”⁴⁰.

The prolonged application of either endurance or the combination of resistance and endurance training has been shown to increase whole body glucose tolerance and/or insulin sensitivity⁴¹⁻⁴³ and improve cardiovascular risk profile^{41, 43, 44} in T2D patients.

Unfortunately, most current clinical guidelines do not include detailed recommendations on exercise prescription (such as the type and dose of exercise that should be applied to maximize benefits in different subgroups of patients with T2D). Specifically, the impact of training session duration/volume and training frequency on glycemic control remains to be investigated in T2D patients.

Table 2. Operational definitions of exercise training variables (for resistance training)

Training Intensity	Refers to the percentage of 1RM* used for a given exercise.
Training Volume	Number of sets performed per muscle group, per workout.
Training Frequency	Occurrence per unit of time (e.g., calendar week) that a given major muscle group, or prime mover, is trained.
Exercise Duration	Number of minutes per session.
Rest Interval	Interval between sets.

*1 repetition maximum is the maximum load able to be lifted with good technique through a full range of motion

Quantity and quality of research in India on lifestyle interventions for diabetes

An extensive literature search on lifestyle interven-

tions for Diabetes in general, and exercise interventions in particular, in the Indian population has retrieved very few research studies. A single study performed at All India Institute of Medical Sciences⁴⁵, evaluated the effect of supervised progressive resistance-exercise training (PRT) protocol on insulin sensitivity, glycemia (blood glucose and A₁C levels), and lipids in Asian Indians with T2D. The authors concluded that moderate-intensity PRT for 3 months resulted in significant improvement in insulin sensitivity, glycemia, lipids, etc. in patients with type 2 diabetes.

An area of concern in India is the sub-optimal standard of clinical care as evidenced by failure of a significant proportion of patients to reach treatment targets. In a study from diabetology clinics, it was reported that the proportion of patients with the following parameters was: 8% with proteinuria; 50% with dyslipidemia; 15-30% with uncontrolled systolic and diastolic blood pressure. Among patients attending specialty diabetes clinics, more than 50% had an HbA₁C value more than 2% above the target A1C, and nearly 75% had HbA₁C values more than 1% above the target⁴⁶. This suboptimal control of metabolic and vascular parameters probably contributes to the high burden of chronic complications in India. It has been estimated that (assuming 50 million people with diabetes live in India), the numbers with various complications would be approximately as follows: 9 million with retinopathy, 1 million with nephropathy, 13 million with neuropathy, 10.5 million with coronary heart disease and 3.2 million with peripheral vascular disease. Despite this, awareness about this disease continues to be low, even in urban India. In another study, 25% of urban Indians were not even aware of diabetes as a disease entity, and only 20% of the general population and 40% of those with diabetes were aware that it was possible to prevent diabetes. Less than one in eight people were aware of the risk factors associated with the disease, and only 40% of diabetics were aware that the disease could result in chronic complications and organ damage.

As with lifestyle interventions in other chronic diseases, lifestyle intervention programmes can only be effectively administered by a multidisciplinary team of health professionals including general practitioners, physicians and endocrinologists, sports and exercise medicine specialists (sports physicians), physiotherapists, nutritionists, biokineticists (applied exercise physiologists), and others. Both patients at risk of developing diabetes as well as those with established diabetes mellitus should be offered a lifestyle intervention programme. Continuing research in this area is crucial and will doubtless

influence clinical decisions made by diabetes health care professionals.

Lack of adequately controlled studies in India, of the efficacy and dose response of programme variables of exercise training, make it difficult to draw firm conclusions regarding the effectiveness of this intervention in achieving the target goals of therapy in Asian India diabetic population.

Summary of research gaps and significance of further research on Exercise interventions in diabetes

T2D is a condition in which physical activity improves patient outcomes. Yet, healthcare professionals often inadequately address this issue, possibly owing to paucity of studies and lack of specific recommendations on exercise prescription.

Exercise represents an effective interventional strategy to improve glycaemic control in T2D patients. However, what needs to be the optimal frequency, intensity and duration of exercise to produce a beneficial effect on glycaemic control in T2D patients is currently unknown. No study to date has compared rates of progression on exercise intensity or volume in T2D patients.

A few studies have demonstrated some evidence of benefits of Yoga on fasting blood glucose, lipids, oxidative stress markers and anti-oxidant status. However these studies are limited by their small sample size and by the fact that a variety of different techniques of yoga have been utilized. Well conducted future studies are needed to draw firm conclusions about the benefits of Yoga in diabetes management.

Current recommendations combine resistance and aerobic training in order to have more effect than either alone. Acute effects of a single session of resistance training on blood glucose levels and/or insulin action in individuals with T2D have not been reported yet. The individual effects of each of the aerobic and anerobic forms of exercises on lowering blood pressure in hypertensives and pre-hypertensives with T2D currently remain unclear, and could be a subject of future research especially in the Indian population. Given the size and expanding nature of the T2D pandemic in India, the field of clinical diabetes research has the scientific, socio-economic and ethical obligation to contribute to such studies.

Conclusion

Asian Indians manifest more insulin resistance and the metabolic syndrome and at a relatively young age than many other ethnic groups^{46,47}. Excess

overall adiposity, in particular abdominal adiposity, excess truncal subcutaneous adipose tissue, and low skeletal muscle mass, etc. have been considered as possible determinants of insulin resistance in Asian Indians⁴⁶⁻⁴⁸. Therefore, it appears that resistance exercise could be specifically useful in improving insulin sensitivity and metabolic parameters in Asian Indians with type 2 diabetes.

In view of the paucity of data in this population, there is a compelling need to conduct well controlled studies in Asian Indian diabetics.

Conflicts of Interest: None

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