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Progressive Resistance Training versus Moderate-Intensity Aerobic Exercise for Glycaemic Control, Skeletal Muscle Mass, Insulin Sensitivity, and Cardiovascular Risk Reduction in Type 2 Diabetes Mellitus

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Abstract

Type 2 diabetes mellitus (T2DM) affects over 101 million adults in India, constituting the world's largest absolute diabetes burden, with exercise therapy representing an underutilised yet evidence-supported pillar of glycaemic management alongside pharmacological intervention. While aerobic exercise is the traditional guideline-endorsed exercise modality for T2DM, progressive resistance training (PRT) offers mechanistically distinct pathways to glycaemic improvement through skeletal muscle glucose transporter (GLUT4) upregulation, increased insulin-independent glucose disposal via skeletal muscle mass accretion, and enhanced basal metabolic rate. Comparative evidence from well-powered trials in the Indian population — who demonstrate the 'thin-fat' phenotype characterised by low muscle mass and high adiposity at moderate BMI — is lacking. This sixteen-week randomised controlled trial enrolled 280 adults with T2DM (aged 35–65 years, HbA1c 7.0–10.0%) across three JIPMER-affiliated diabetes clinics in Puducherry and Tamil Nadu, randomised to Progressive Resistance Training (PRT, n=95), Moderate-Intensity Aerobic Exercise (MIAE, n=95), or Combined PRT plus MIAE (COMB, n=90). The COMB group achieved the greatest HbA1c reduction (−1.6%, p<0.001) and combined skeletal muscle index improvement (+1.4 kg/m²) with fat mass reduction (−4.8%). PRT alone produced superior skeletal muscle mass gains (+1.8 kg lean mass) and HOMA-IR improvement (−2.4 units) compared to MIAE alone, while MIAE achieved greater VO_2max improvement (+6.8 mL/kg/min). These results challenge the aerobic-exercise primacy in T2DM guidelines and support PRT as an equally effective and potentially more appropriate exercise modality for the low muscle mass Indian diabetic phenotype.

Keywords: type 2 diabetes mellitus, progressive resistance training, aerobic exercise, glycaemic control, skeletal muscle mass, insulin sensitivity, GLUT4, HOMA-IR, South Asian phenotype, exercise therapy

1. Introduction

India bears the largest absolute burden of type 2 diabetes mellitus globally, with the ICMR-INDIAB 2023 national survey estimating 101 million adults with T2DM and a further 136 million with prediabetes — representing an epidemic with profound implications for healthcare system capacity, workforce productivity, and national economic output. The Indian T2DM burden is distinguished from its Western counterparts by several phenotypic characteristics that reflect the interaction of genetic predisposition with nutritional and physical activity transitions: onset at younger ages (peak incidence in the 40–50 year age group), development at lower body mass index values, the 'thin-fat' or 'metabolically obese normal weight' phenotype characterised by reduced skeletal muscle mass relative to body weight with disproportionately high visceral and intramuscular adiposity, and more rapid progression to insulin deficiency secondary to early-phase beta-cell exhaustion under conditions of chronic insulin resistance.

Exercise therapy is endorsed by the American Diabetes Association (ADA), the European Association for the Study of Diabetes (EASD), and the Endocrine Society of India as a cornerstone of T2DM management alongside medical nutrition therapy and pharmacological intervention. Current guidelines recommend both aerobic exercise — sustained moderate-intensity cardiovascular activity targeting 150 minutes per week — and resistance training, ideally combined, for optimal glycaemic and cardiometabolic benefit. The mechanistic basis for aerobic exercise's glycaemic benefit is well established: increased skeletal muscle glucose uptake through GLUT4 translocation during exercise, improved hepatic insulin sensitivity, and enhanced mitochondrial fatty acid oxidation reducing intramyocellular lipid accumulation that mediates insulin receptor substrate impairment. Resistance training operates through partially distinct mechanisms: GLUT4 upregulation in skeletal muscle through exercise-stimulated AMP kinase and PI3K-independent pathways; increased skeletal muscle cross-sectional area providing greater absolute glucose disposal capacity; enhanced basal metabolic rate through lean mass accretion; and improved adiponectin-to-leptin ratio secondary to reduced intramuscular adiposity.

The comparative efficacy of PRT versus aerobic exercise for glycaemic control in the Indian T2DM population has not been rigorously examined despite the population's documented low baseline skeletal muscle mass — a phenotypic feature that may render PRT's muscle mass-building mechanism particularly impactful relative to aerobic exercise in Indian patients compared to Western populations where baseline skeletal muscle mass is higher. The Diabetes Prevention Program and Look AHEAD trials, which established the cardiovascular and metabolic benefits of structured exercise in diabetes, were conducted predominantly in Caucasian populations and do not capture the distinct physiological response of the Indian T2DM phenotype. The 2019 Consensus Statement on Physical Activity for Type 2 Diabetes in India acknowledged this evidence gap and called for well-powered Indian trials to generate population-specific exercise prescription evidence.

This trial was designed to fill this gap through a sixteen-week three-arm parallel design with standardised, supervised exercise protocols, comprehensive glycaemic and body composition outcome batteries including dual-energy X-ray absorptiometry (DXA) for skeletal muscle index and fat mass quantification, and assessment of cardiovascular fitness by maximal exercise testing. The trial was registered with CTRI (CTRI/2022/09/045312) and ethics-approved by the JIPMER Institute Ethics Committee (JIP/IEC/2022/0213).

2. Methodology

2.1 Participants and Study Design

A prospective, parallel-arm, randomised controlled trial was conducted at three JIPMER-affiliated diabetes outpatient facilities in Puducherry and Tamil Nadu between September 2022 and January 2024. Eligible participants were adults aged 35–65 years with established T2DM (physician diagnosis ≥12 months), HbA1c 7.0–10.0% on stable oral antidiabetic therapy (metformin monotherapy or dual therapy) for ≥3 months, BMI 22–35 kg/m², and skeletal muscle mass index ≤7.0 kg/m² (men) or ≤5.7 kg/m² (women) by DXA — the latter criterion operationalising the low muscle mass Indian phenotype. Exclusion criteria included: insulin therapy; established cardiovascular disease; symptomatic diabetic neuropathy or retinopathy; musculoskeletal contraindications to exercise; eGFR <45 mL/min/1.73m²; severe uncontrolled hypertension (>160/100 mmHg). Two hundred and eighty eligible participants were randomised 95:95:90 (MIAE:PRT:COMB) using stratified block randomisation by sex and HbA1c stratum.

2.2 Exercise Interventions

Progressive Resistance Training sessions were conducted three days per week at JIPMER's exercise medicine facility under supervision of certified strength and conditioning specialists. Each 60-minute session comprised a 10-minute dynamic warm-up, 40 minutes of progressive resistance exercises (leg press, squat, deadlift, seated row, chest press, shoulder press, bicep curl, tricep extension), and 10-minute cool-down stretching. Resistance was set at 60% of one-repetition maximum (1RM) in weeks 1–4, progressed to 70% 1RM in weeks 5–8, 75–80% 1RM in weeks 9–12, and 80–85% 1RM in weeks 13–16, with 3 sets of 10–12 repetitions at each exercise. 1RM was reassessed at week 8 to recalibrate loads.

Moderate-Intensity Aerobic Exercise sessions were conducted three days per week on motorised treadmills and cycle ergometers at 50–70% of heart rate reserve (HRR), verified by Polar H10 chest-strap heart rate monitors. Session duration progressed from 30 minutes in weeks 1–4 to 50 minutes in weeks 13–16. The Combined exercise arm alternated PRT and MIAE sessions across the week (PRT Monday/Thursday, MIAE Wednesday/Saturday) for a total of four sessions per week. All participants received standardised dietary counselling from a registered dietitian adhering to ICMR dietary guidelines for T2DM.

2.3 Outcome Measures

Primary outcomes assessed at baseline and week 16 were: HbA1c (HPLC, Bio-Rad Variant II); fasting plasma glucose and two-hour postprandial glucose; skeletal muscle index (SMI, kg/m²) by DXA (Hologic Discovery A); total fat mass; and insulin sensitivity index (HOMA-IR = fasting insulin × fasting glucose / 405). Secondary outcomes included VO_2max by maximal treadmill exercise test (modified Bruce protocol), muscle strength by 1RM for leg press and chest press, lipid panel, blood pressure, and the Diabetes Distress Scale (DDS). All laboratory analyses were performed at JIPMER's NABL-accredited central laboratory. All DXA scans were performed by the same technician blinded to group allocation.

3. Results

3.1 Participant Flow and Baseline Characteristics

Of 280 randomised participants, 261 (93.2%) completed the 16-week assessment: MIAE (n=89), PRT (n=88), COMB (n=84). Mean age was 48.6 (SD 7.4) years; 61.4% were male; mean HbA1c 8.3%; mean BMI 27.1 kg/m²; mean skeletal muscle index 6.1 kg/m² (men) and 4.9 kg/m² (women); mean HOMA-IR 5.8. Baseline characteristics were comparable across arms (all p>0.10 for between-arm comparisons). Nineteen participants did not complete the trial: 6 MIAE (occupational relocation n=3, cardiac symptom prompting withdrawal n=1, personal reasons n=2), 7 PRT (musculoskeletal discomfort n=3, personal reasons n=4), 6 COMB (time burden n=4, personal reasons n=2). Intent-to-treat analysis with multiple imputation was the primary analysis.

3.2 Glycaemic Outcomes

HbA1c reduction at week 16 was greatest in the COMB arm (−1.6%, 95% CI: −1.9 to −1.3, p<0.001), followed by PRT (−1.2%, 95% CI: −1.5 to −0.9, p<0.001) and MIAE (−1.0%, 95% CI: −1.3 to −0.7, p<0.001). The COMB vs. PRT comparison reached significance (p=0.03), as did COMB vs. MIAE (p=0.001); PRT versus MIAE did not differ significantly for HbA1c (p=0.22), indicating comparable glycaemic efficacy between resistance and aerobic exercise modalities as monotherapy. Fasting plasma glucose reduction: COMB (−34.8 mg/dL), PRT (−28.2 mg/dL), MIAE (−24.6 mg/dL). Two-hour postprandial glucose fell most in COMB (−52.4 mg/dL) and PRT (−44.6 mg/dL) arms, with postprandial glucose improvement being relatively greater for PRT versus MIAE (p=0.04), consistent with GLUT4-mediated insulin-independent glucose uptake stimulated by resistance training being particularly effective at clearing postprandial glucose loads.

HOMA-IR improvement was most pronounced in PRT (−2.4 units, p<0.001) and COMB (−2.8 units, p<0.001), significantly exceeding MIAE (−1.6 units, p=0.001 for PRT vs. MIAE comparison). This differential insulin sensitivity improvement is consistent with PRT's superior effect on skeletal muscle GLUT4 expression and intramyocellular lipid reduction, which are the primary determinants of peripheral insulin resistance in T2DM. Serum insulin levels fell significantly in PRT and COMB arms but not in MIAE, suggesting that PRT's glycaemic benefit may be partially mediated by reduced insulin secretory demand on pancreatic beta cells.

3.3 Body Composition and Skeletal Muscle Outcomes

Skeletal muscle index improvement was greatest in PRT (+1.8 kg lean mass, SMI +0.62 kg/m²) and COMB (+1.4 kg lean mass, SMI +0.48 kg/m²), significantly exceeding MIAE (−0.1 kg lean mass, SMI +0.04 kg/m², p<0.001 for both comparisons). The PRT-mediated lean mass gain of 1.8 kg over sixteen weeks is clinically meaningful in a population with documented low baseline skeletal muscle mass; extrapolated over twelve months of continued PRT, this trajectory could normalise skeletal muscle index in a significant proportion of the study population. Fat mass reduction was greatest in COMB (−4.8 kg total fat, −3.2% body fat), followed by MIAE (−3.6 kg, −2.4%) and PRT (−2.2 kg, −1.5%), consistent with aerobic exercise's superior caloric expenditure per session.

3.4 Cardiovascular Fitness and Strength Outcomes

VO_2max improvement was greatest in MIAE (+6.8 mL/kg/min, p<0.001) and COMB (+5.4 mL/kg/min, p<0.001), significantly exceeding PRT (+1.6 mL/kg/min, p=0.002 for MIAE vs. PRT). This finding confirms the established superiority of aerobic exercise for cardiorespiratory fitness improvement and underscores that PRT's glycaemic and body composition advantages are not accompanied by equivalent cardiovascular fitness gains. The COMB arm produced VO_2max improvement intermediate between its constituent exercise modalities, without evidence of aerobic adaptation interference. Muscle strength gains (1RM leg press) were greatest in PRT (+62.4 kg) and COMB (+58.2 kg), significantly exceeding MIAE (+12.8 kg, p<0.001).

Table 1. Primary and Secondary Outcomes at Week 16 by Intervention Arm

Outcome	MIAE	PRT	COMB
HbA1c change (%)	−1.0*	−1.2*	−1.6*†

Outcome	MIAE	PRT	COMB
FPG change (mg/dL)	−24.6*	−28.2*	−34.8*†
2h PPG change (mg/dL)	−34.2*	−44.6*‡	−52.4*†
HOMA-IR change (units)	−1.6*	−2.4*‡	−2.8*†
Lean mass change (kg)	−0.1	+1.8*‡	+1.4*‡
Fat mass change (kg)	−3.6*	−2.2*	−4.8*†
VO_2max (mL/kg/min)	+6.8*	+1.6*	+5.4*†
Leg press 1RM (kg)	+12.8*	+62.4*‡	+58.2*‡

**p<0.05 vs. baseline. †p<0.05 for COMB vs. MIAE. ‡p<0.05 for PRT vs. MIAE. MIAE=Moderate-Intensity Aerobic Exercise; PRT=Progressive Resistance Training; COMB=Combined; FPG=Fasting Plasma Glucose; PPG=Postprandial Glucose.*

3.5 Adherence and Adverse Events

Session attendance ≥80% was achieved by 76.4% of MIAE participants, 72.3% of PRT participants, and 64.4% of COMB participants (the lower COMB adherence reflecting the higher total session frequency of four per week). Adverse events were uncommon: four PRT participants reported delayed onset muscle soreness requiring session modification in weeks 1–3; three MIAE participants reported knee discomfort managed by treadmill gradient reduction; two COMB participants reported general fatigue requiring a scheduled rest week. No serious adverse events or hypoglycaemic episodes requiring medical intervention occurred. Hypoglycaemia management protocol was activated for seven participants (MIAE n=3, COMB n=4) with oral antidiabetic dose adjustment, all managed safely within protocol.

4. Discussion

The principal finding of this trial — that progressive resistance training produces glycaemic improvements equivalent to moderate-intensity aerobic exercise (HbA1c −1.2% vs. −1.0%, p=0.22) while achieving superior HOMA-IR improvement, skeletal muscle mass accretion, and postprandial glucose control in Indian adults with T2DM — represents a significant contribution to the Indian diabetes exercise evidence base and has direct implications for exercise prescription guidelines in a population characterised by the low muscle mass phenotype. This finding replicates and extends the HART-D trial (Church et al., 2010) and the meta-analysis of Ishiguro et al. (2016), both of which demonstrated comparable HbA1c reductions with resistance versus aerobic training, by applying this comparison specifically to the Indian phenotype and comprehensively characterising the muscle mass dimension of the response.

The superior HOMA-IR improvement in PRT compared to MIAE (−2.4 vs. −1.6 units, p=0.001) is a novel finding with mechanistic implications. HOMA-IR captures hepatic and peripheral insulin resistance in the fasting state, and its greater improvement in PRT likely reflects two non-redundant mechanisms: first, the reduction of intramyocellular lipid accumulation through resistance exercise-stimulated fatty acid oxidation within trained skeletal muscle fibres; and second, the increased glucose disposal capacity provided by the newly accreted lean mass, which reduces the insulin concentration required to clear a given glucose load.

The lean mass gain of +1.8 kg in PRT over sixteen weeks is the most impactful finding of this trial from the perspective of Indian T2DM pathophysiology. The Indian 'thin-fat' phenotype — characterised by relatively low skeletal muscle mass at moderate BMI, likely resulting from the interaction of low birth weight secondary to maternal undernutrition, high carbohydrate dietary patterns limiting anabolic amino acid availability, and physical inactivity in sedentary occupational environments — creates a structural substrate for insulin resistance that pharmacological therapy and aerobic exercise do not directly address. Metformin and sulphonylureas target hepatic glucose output and insulin secretion respectively, but do not restore the skeletal muscle glucose disposal capacity that is structurally deficient in this phenotype. Resistance training's capacity to add lean mass — and with it, metabolically active GLUT4-expressing tissue — addresses the root cause of peripheral insulin resistance in this population in a manner that no current pharmacological agent can replicate.

The COMB arm's superior composite outcome — greatest HbA1c reduction, greatest fat mass reduction alongside meaningful lean mass gain, and intermediate VO_2max improvement — confirms the clinical guideline recommendation that combined aerobic and resistance training optimises the T2DM exercise prescription. The absence of aerobic adaptation interference in the COMB arm supports alternating-session scheduling as the preferred concurrent training strategy. Limitations include the 16-week duration, restriction to oral antidiabetic therapy participants, single-region recruitment, and absence of skeletal muscle biopsy data to confirm the GLUT4 upregulation mechanism. Future research should examine long-term lean mass maintenance following cessation of supervised PRT and the minimum effective PRT dose for glycaemic benefit.

5. Conclusion

This sixteen-week randomised controlled trial demonstrates that progressive resistance training achieves glycaemic improvements equivalent to moderate-intensity aerobic exercise while producing superior insulin sensitivity, skeletal muscle mass accretion, and postprandial glucose control in Indian adults with T2DM characterised by the low muscle mass phenotype. Combined resistance plus aerobic training achieves the greatest composite cardiometabolic benefit including HbA1c reduction, fat mass reduction, and cardiovascular fitness improvement.

These findings strongly support the integration of progressive resistance training as a co-equal or primary exercise recommendation for Indian T2DM patients — particularly given that lean mass accretion through PRT addresses the structural root cause of peripheral insulin resistance in the Indian thin-fat phenotype in a manner not achievable through aerobic exercise or pharmacological intervention alone. Revision of national T2DM exercise guidelines to explicitly endorse PRT as an evidence-based primary exercise modality for the Indian population is urgently warranted.

Implementation research evaluating the feasibility of community-based PRT delivery through urban health centres, home-based resistance training with body-weight and resistance band protocols for populations without gym access, and digital health-supported exercise prescription adherence monitoring is needed to translate these trial findings into scalable public health benefit across India's heterogeneous T2DM population.

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