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COMPREHENSIVE DIABETIC CARE PROGRAM TARGETING INSULIN RESISTANCE: DOSE-DEPENDENT GLYCEMIC OUTCOMES, ANTIDIABETIC DRUG REDUCTION, AND GTT-DOCUMENTED REMISSION IN URBAN INDIAN ADULTS WITH TYPE 2 DIABETES — A RETROSPECTIVE COHORT STUDY

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ABSTRACT

Background: Insulin resistance is the foundational metabolic lesion of type 2 diabetes mellitus (T2DM), driving both progressive beta-cell failure and the accumulation of cardiovascular risk factors. Pharmacotherapy addresses symptoms of insulin resistance but does not reverse its root cause — excess adiposity, sedentary muscle metabolism, and chronic low-grade inflammation. Intensive lifestyle interventions combining caloric restriction, exercise, and metabolic therapies have demonstrated T2DM remission, but real-world implementation of multimodal insulin resistance reversal programs remains limited. This study reports outcomes from the Comprehensive Diabetic Care (CDC) program, a structured multimodal intervention combining very-low-calorie dietary modification, structured botanical therapy targeting insulin-signaling pathways, physical conditioning, and antidiabetic medication tapering. **Objectives:** To evaluate the clinical efficacy of the Comprehensive Diabetic Care (CDC) program — comprising caloric restriction, structured herbal per-rectal therapy (Panchakarma) (structured botanical per-rectal therapy with Gymnema sylvestre, Berberis aristata, and Glycyrrhiza glabra), exercise and yoga — on glycemic control, anthropometric parameters, insulin resistance surrogates, and antidiabetic drug reduction; to quantify the dose-dependent relationship between treatment intensity and outcomes; and to report Oral Glucose Tolerance Test (GTT) outcomes as a remission criterion. **Methods:** Retrospective observational study of 79 consecutive T2DM patients enrolled in the CDC (Comprehensive Diabetic Care) program at an integrative metabolic clinic in Mumbai, India. The multimodal intervention included: (1) an 800 kcal/day low-carbohydrate, high-protein dietary program (Prameha diet); (2) Panchakarma comprising herbal oleation, medicated sudation, and per-rectal botanical therapy delivering berberine, gymnemic acids, and glycyrrhizin via direct colonic-portal absorption; and (3) individualized yoga and exercise prescription targeting muscle glucose uptake and insulin sensitization. Antidiabetic medications were systematically tapered based on glycemic response. Outcomes included HbA1c, fasting/random blood glucose, weight, BMI, abdominal girth, blood pressure, and heart rate. Treatment intensity was quantified by Panchakarma sessions completed (range 1–20). Pearson correlations and paired t-tests were used. GTT results were documented for 5 patients as a remission criterion.

Results: All primary metabolic parameters improved significantly. HbA1c declined from 9.38 ± 2.10% to 7.62 ± 1.87% (Δ −1.76 ± 1.64%, p<0.001). Random blood glucose reduced from 208.3 ± 87.5 to 160.8 ± 57.3 mg/dL (Δ −47.5 mg/dL, p<0.001). Weight reduced by −3.79 ± 4.00 kg (p<0.001), BMI by −1.33 ± 1.43 kg/m² (p<0.001), and abdominal girth by −5.12 ± 5.85 cm (p<0.001) — reflecting visceral fat reduction and insulin resistance reversal. Blood pressure normalized significantly (SBP Δ −6.74 mmHg, DBP Δ −4.46 mmHg; both p<0.001). Treatment intensity correlated significantly with both HbA1c reduction (r=−0.533, p<0.001) and weight loss (r=−0.565, p<0.001), confirming a dose-dependent relationship. High-intensity treatment (15+ sessions, n=14) achieved 3-fold greater HbA1c reduction (Δ −2.72%) and 4-fold greater weight loss (Δ −9.34 kg) compared to low-intensity (1–8 sessions, n=36, Δ −0.87% HbA1c, Δ −2.31 kg). Among 78 patients with documented medication data, 51.3% achieved partial-to-complete antidiabetic drug reduction; mean reduction among those who tapered was 69.2%. Post-treatment, 43.9% achieved HbA1c <7.0% and 17.5% achieved the <6.5% remission threshold. Three of five patients with documented GTT achieved GTT Negative (normal glucose tolerance restored), representing the most stringent available evidence of T2DM remission. **Conclusion:** The CDC (Comprehensive Diabetic Care) program targeting insulin resistance through caloric restriction, Panchakarma-delivered botanical therapy, and exercise-based muscle conditioning achieves clinically significant glycemic improvement, dose-dependent weight reduction, antidiabetic drug tapering in over half of patients, and GTT-documented remission in a real-world urban cohort. These findings support the role of comprehensive insulin resistance reversal as a disease-modifying strategy in T2DM and provide a mechanistically coherent framework for integrating botanical therapy with established lifestyle medicine approaches.

KEYWORDS: *Type 2 diabetes remission, insulin resistance, lifestyle intervention, botanical therapy, Panchakarma, berberine, Gymnema sylvestre, HbA1c, GTT, antidiabetic drug reduction, very-low-calorie diet, dose-response, Madhavbaug, Andheri East.*

1. INTRODUCTION

Insulin resistance — defined as the impaired ability of peripheral tissues to respond to insulin-mediated glucose uptake — is the fundamental metabolic lesion from which type 2 diabetes mellitus (T2DM) emerges. It precedes clinical hyperglycemia by a decade or more, drives progressive pancreatic beta-cell exhaustion, and underlies the cardiometabolic cluster of hypertension, dyslipidemia, and central adiposity that makes T2DM the most consequential metabolic disease of our era.[1]

Conventional pharmacotherapy for T2DM — metformin, sulfonylureas, DPP-4 inhibitors, SGLT-2 inhibitors, GLP-1 receptor agonists — addresses the downstream consequences of insulin resistance without resolving its primary drivers: excess visceral adiposity, skeletal muscle dysfunction, and hepatic lipid accumulation.[2] This explains why conventional therapy requires lifelong dose escalation: as insulin resistance deepens with weight gain and physical deconditioning, pharmacological compensation must increase proportionally. The treatment becomes management of a progressive disease rather than reversal of its cause.

The evidence that insulin resistance is reversible through intensive lifestyle intervention is now well-established. The DiRECT trial demonstrated T2DM remission in 46% of participants through an 825 kcal/day meal replacement formula diet at one year.[3] The ACCORD and Look AHEAD trials established the cardiometabolic benefits of sustained weight loss.[4] The common thread is caloric deficit sufficient to reduce hepatic and visceral fat — the primary anatomical drivers of insulin resistance — combined with improved skeletal muscle insulin sensitivity through physical activity. When adipose-mediated insulin resistance is reversed, beta-cell insulin secretion may recover sufficiently to maintain normoglycemia without pharmacological support.

The CDC program described in this study operationalizes this insulin resistance reversal framework through three coordinated mechanisms. First, a very-low-calorie (800 kcal/day) low-carbohydrate, high-protein dietary prescription creates a sustained caloric deficit targeting visceral fat mobilization. Second, structured Panchakarma — a classical Indian botanical therapy system delivering herbal preparations via the per-rectal route — provides pharmacobotanical insulin sensitization through berberine (*Berberis aristata*), which activates hepatic AMP-activated protein kinase (AMPK) mimicking the mechanism of metformin[5]; gymnemic acids (*Gymnema sylvestre*), which regenerate pancreatic beta-cells and reduce intestinal glucose absorption[6]; and glycyrrhizin (*Glycyrrhiza glabra*), which modulates insulin signaling and reduces hepatic gluconeogenesis.[7] Third, individualized yoga and exercise prescription improves skeletal muscle insulin sensitivity through GLUT-4 transporter upregulation and mitochondrial biogenesis in muscle tissue[8] — the largest peripheral site of insulin-mediated glucose disposal.

Together, these three mechanisms address insulin resistance at its three primary anatomical sites — liver (berberine/AMPK), adipose tissue (caloric restriction/weight loss), and skeletal muscle (exercise/yoga) — in a coordinated, simultaneous intervention. Antidiabetic medications are then systematically tapered based on glycemic response, with the goal of reducing polypharmacy burden as metabolic normalization is achieved.

This retrospective cohort study from a dedicated integrative metabolic clinic in Mumbai reports: (1) overall clinical outcomes across 79 consecutively enrolled T2DM patients; (2) a dose-dependent relationship between treatment intensity and glycemic and anthropometric outcomes; (3) antidiabetic drug tapering rates and outcomes; and (4) Oral Glucose Tolerance Test (GTT) documentation of metabolic remission — the most rigorous available criterion for T2DM reversal — in a subset of patients.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

Retrospective observational cohort study at a dedicated integrative metabolic clinic (Madhavbaug Clinics, Andheri East, Mumbai, India). Mumbai is India's financial capital — a high-density urban environment characterized by sedentary professional occupations, calorie-dense food environment, significant psychosocial stress burden, and high background prevalence of T2DM and metabolic syndrome. The clinic implements the Comprehensive Diabetic Care (CDC) program — a structured, reproducible multimodal protocol. Patient records were extracted for all consecutively enrolled T2DM patients with documented pre- and post-intervention parameters. The study was conducted in accordance with the principles of the Declaration of Helsinki.

2.2 Study Participants

Patients with confirmed T2DM enrolled in the integrative program with documented baseline and follow-up clinical measurements were included. The cohort comprised 79 patients (50 male, 29 female; mean age 50.1 ± 11.5 years; range 27–77). Comorbidities included hypertension (n=27, 34.2%), obesity (n=21, 26.6%), dyslipidemia (n=14, 17.7%), and hypothyroidism (n=5, 6.3%). BMI ranged from 17.0 to 51.0 kg/m², with 5 patients meeting criteria for morbid obesity (BMI ≥40 kg/m²). Baseline HbA1c ranged from 5.8% to 15.9%, with 91.9% of patients above the 7.0% glycemic control target.

2.3 Intervention Components

2.3.1 Dietary Modification: Caloric Restriction Targeting Visceral Fat

All patients received a standardized very-low-calorie diet (VLCD) of approximately 800 kcal/day, delivered as a ready-to-use meal formulation. The macronutrient composition was low carbohydrate (<30% of energy), high protein (>40%), and moderate fat — designed to maximize hepatic fat clearance through caloric deficit while preserving lean muscle mass through adequate protein provision. This dietary approach is consistent with the formula used in the DiRECT trial[3] and with Ayurvedic dietary principles for metabolic disease management, which prescribe light, easily digestible, protein-rich foods for *Prameha* (the classical correlate of T2DM).

2.3.2 Panchakarma: Pharmacobotanical Insulin Sensitization

Panchakarma therapy comprised three sequential components delivered at each session:

Oleation (Snehan): Full-body therapeutic massage with Neem-processed medicated oil (*Neem Siddha Taila*). The cutaneous application of warm medicated lipids facilitates transdermal absorption of anti-inflammatory phytoconstituents from *Azadirachta indica* and promotes parasympathomimetic activation through stimulation of cutaneous Ruffini mechanoreceptors — initiating the autonomic recalibration component of the protocol.

Sudation (Swedan): Medicated steam therapy using a decoction of Dashmula (ten classical roots). Diaphoretic sudation promotes metabolic clearance of inflammatory lipid intermediates from peripheral tissues and enhances peripheral blood flow — improving delivery of insulin and glucose to skeletal muscle.

Per-Rectal Botanical Therapy (Basti): The pharmacologically active core of the protocol. A Kwath (aqueous decoction)-based preparation of three herbs is administered per-rectally, delivering active compounds via direct colonic mucosal absorption into the portal venous circulation:

Gudmar (Gymnema sylvestre): Gymnemic acids reduce intestinal glucose absorption and promote pancreatic beta-cell regeneration through direct insulinotropic action on islet cells. Meta-analyses confirm significant HbA1c reduction with Gymnema supplementation in T2DM.

Daru Haridra (Berberis aristata): Berberine activates hepatic AMP-activated protein kinase (AMPK), the same pathway targeted by metformin, reducing hepatic glucose output and improving peripheral insulin sensitivity. Clinical trials demonstrate HbA1c reductions of 1.0–2.0% with berberine monotherapy.

Yashti Madhu (Glycyrrhiza glabra): Glycyrrhizin modulates the cortisol-insulin axis, reduces hepatic gluconeogenesis, and has anti-inflammatory effects on visceral adipose tissue reducing adipokine-mediated insulin resistance.

The per-rectal route provides a pharmacokinetic advantage: colonic mucosal absorption allows direct portal venous delivery of active compounds to the liver, bypassing intestinal and pulmonary first-pass metabolism. This maximizes hepatic AMPK activation (the primary site of berberine action) at lower systemic doses compared to oral administration.

2.3.3 Yoga and Exercise: Skeletal Muscle Insulin Sensitization

Individualized yoga and exercise prescriptions were provided to each patient by the treating physician, targeting skeletal muscle insulin sensitivity — the largest site of insulin-mediated glucose disposal in the human

body. The exercise protocol emphasized resistance training components (to increase GLUT-4 transporter density in muscle membranes[8]) and specific yogasanas known to improve insulin signaling in peripheral tissues. Yoga additionally addresses the psychoneuroendocrine component of insulin resistance: chronic cortisol elevation from psychosocial stress is a primary driver of visceral adiposity and hepatic insulin resistance, and yoga-mediated HPA axis normalization contributes to metabolic improvement.

2.3.4 Antidiabetic Medication Tapering

Antidiabetic medications were not discontinued abruptly but tapered systematically based on documented glycemic response. The treating physician reviewed blood glucose and HbA1c at each follow-up visit and reduced medication doses or discontinued agents when fasting glucose and HbA1c reached pre-defined reduction thresholds. This structured tapering — rather than abrupt discontinuation — ensures patient safety while progressively reducing pharmacological dependence as insulin resistance reversal is achieved.

2.4 Outcome Measures

Primary outcomes: HbA1c (%), random blood glucose (RBS, mg/dL), and antidiabetic medication reduction status. Secondary outcomes: body weight (kg), BMI (kg/m²), abdominal girth (cm — as surrogate of visceral adiposity and insulin resistance), SBP and DBP (mmHg), and heart rate (bpm). Treatment intensity was quantified as Panchakarma sessions completed (range 1–20). Patients were stratified into Low (1–8 sessions), Mid (9–14), and High (15+) intensity tiers. GTT results were documented for 5 patients and interpreted per WHO criteria: GTT Negative (<140 mg/dL 2-hour glucose) or GTT Impaired (140–199 mg/dL).

2.5 Statistical Analysis

Data analyzed using Python (pandas, scipy.stats). Descriptive statistics as mean ± SD. Pre-post comparisons by paired Student's t-test (two-tailed; $p<0.05$). Dose-response assessed by Pearson correlation between sessions completed and change in each outcome. Tier analysis used independent t-tests for between-group comparisons. GTT outcomes are reported descriptively (n=5).

3. RESULTS

3.1 Baseline Characteristics

Seventy-nine patients were enrolled (50 male, 29 female; mean age 50.1 ± 11.5 years). Baseline HbA1c distribution: 8.1% of patients were controlled (<7.0%); 41.9% at moderate dyscontrol (7–9%); 38.7% at poor control (9–12%); and 11.3% at severe dyscontrol (≥12%). Mean baseline HbA1c was 9.41 ± 2.05%, indicating a predominantly uncontrolled cohort with substantial room for glycemic improvement. Mean BMI was 28.73 ± 5.93 kg/m² with a bimodal distribution: 11 lean patients (BMI <23 kg/m², enrolled in the protein-supplemented nourishing protocol variant) and 13 obese patients (BMI ≥32.5 kg/m²). Panchakarma sessions completed: mean 9.1 ± 5.3 (range 1–20), with 44.6% completing Low intensity (1–8 sessions), 31.6% Mid (9–14), and 17.7% High (15+). Mean follow-up duration was 66 ± 63 days (median 47 days).

Table 1: Baseline Characteristics by Treatment Intensity Tier.

Parameter	Overall (n=79)	Low Intensity 1–8 sessions (n=36)	Mid Intensity 9–14 sessions (n=25)	High Intensity 15+ sessions (n=14)
Age (years)	50.1 ± 11.5	50.2 ± 11.5	48.6 ± 11.5	52.5 ± 12.0
Sex (M/F)	50/29	22/13	17/8	9/5
Baseline HbA1c (%)	9.38 ± 2.10	9.41 ± 2.36	9.38 ± 1.70	9.57 ± 2.17
Baseline Weight (kg)	79.2 ± 18.5	78.4 ± 13.7	73.7 ± 19.7	93.0 ± 21.4
Baseline BMI (kg/m²)	28.73 ± 5.93	28.75 ± 4.41	27.66 ± 7.83	31.12 ± 5.35
Baseline SBP (mmHg)	131.5 ± 18.5	132.2 ± 20.9	129.0 ± 16.0	134.4 ± 17.3
Hypertension (%)	34.2%	—	—	—
Obesity (%)	26.6%	—	—	—
Mean sessions completed	9.1 ± 5.3	4.2 ± 2.0	11.8 ± 1.7	16.7 ± 1.3
Median follow-up (days)	47	41	50	71

3.2 Overall Clinical Outcomes

Seven of eight measured parameters showed statistically significant improvement (Table 2). HbA1c declined from 9.38 ± 2.10% to 7.62 ± 1.87% (Δ −1.76 ± 1.64%, p<0.001). Abdominal girth — the most direct surrogate of visceral adiposity and insulin resistance — reduced by −5.12 ± 5.85 cm (p<0.001). Weight and BMI both improved significantly (p<0.001). Blood pressure showed significant improvement in both SBP and DBP (p<0.001 each). Heart rate did not reach statistical significance (Δ −2.45 bpm, p=0.080), consistent with the cohort's near-normal baseline autonomic status. Stage 3 systolic hypertension (SBP ≥160 mmHg) was completely eliminated: 7 patients at baseline, 0 at follow-up. SBP <130 mmHg rose from 36 (48.6%) to 46 (62.2%) patients.

Table 2: Clinical Outcomes — Pre- vs. Post-Intervention (n=79)

Parameter	n	Pre (Mean ± SD)	Post (Mean ± SD)	Δ (Mean ± SD)	% Change	p-value
HbA1c (%)	56	9.38 ± 2.10	7.62 ± 1.87	−1.76 ± 1.64	−17.5%	<0.001
Random Blood Glucose (mg/dL)	66	208.3 ± 87.5	160.8 ± 57.3	−47.5 ± 76.0	−14.3%	<0.001
Weight (kg)	76	79.21 ± 18.45	75.42 ± 16.56	−3.79 ± 4.00	−4.4%	<0.001
BMI (kg/m²)	76	28.73 ± 5.93	27.39 ± 5.43	−1.33 ± 1.43	−4.3%	<0.001
Abdominal Girth (cm)	42	98.57 ± 14.72	93.45 ± 12.20	−5.12 ± 5.85	−4.8%	<0.001
SBP (mmHg)	74	131.45 ± 18.45	124.70 ± 11.98	−6.74 ± 16.14	−3.9%	<0.001
DBP (mmHg)	74	85.91 ± 12.76	81.45 ± 7.70	−4.46 ± 10.81	−3.8%	<0.001
Heart Rate (bpm)	74	83.46 ± 12.65	81.01 ± 11.46	−2.45 ± 11.85	−1.8%	0.080 (ns)

3.3 Dose-Response: Treatment Intensity and Outcomes

Pearson correlations confirmed significant dose-dependent relationships between Panchakarma sessions completed and the primary anthropometric and glycemic outcomes (Table 3). Treatment intensity correlated significantly with HbA1c reduction (r=−0.533, p<0.001), weight loss (r=−0.565, p<0.001), and BMI reduction (r=−0.508, p<0.001). These correlations indicate that each additional treatment session is independently associated with greater insulin resistance reversal, as reflected by both glycemic and adiposity markers.

Table 3: Dose-Response Correlations: Treatment Intensity vs. Clinical Outcomes.

Outcome Variable	Pearson r	p-value	n	Interpretation
HbA1c reduction (%)	−0.533	<0.001	55	Significant: more sessions → greater glycemic improvement
Weight reduction (kg)	−0.565	<0.001	74	Significant: more sessions → greater weight loss
BMI reduction (kg/m²)	−0.508	<0.001	74	Significant: more sessions → greater adiposity reduction
Blood glucose reduction	−0.093	0.463	65	Non-significant — primarily driven by baseline severity

3.4 Treatment Intensity Tier Analysis

Stratification into three intensity tiers demonstrates a clear stepwise dose-response (Table 4). The High-intensity group (15+ sessions, mean 16.7) achieved 3-fold greater HbA1c reduction than the Low group (1–8 sessions, mean 4.2) — Δ −2.72% vs. Δ −0.87% — with a 4-fold difference in weight reduction (Δ −9.34 kg vs. Δ −2.31 kg) and a 3-fold difference in abdominal girth

reduction (Δ −14.00 cm vs. Δ −4.42 cm), despite comparable baseline HbA1c across groups. The abdominal girth reduction of 14.0 cm in the High-intensity group represents a substantial reduction in visceral adiposity — the primary anatomical driver of insulin resistance — and is consistent with the magnitude of visceral fat loss seen in intensive lifestyle intervention trials.

Table 4: Clinical Outcomes by Treatment Intensity Tier.

Outcome	Low Intensity (n=36) 1–8 sessions, mean 4.2	p	Mid Intensity (n=25) 9–14 sessions, mean 11.8	p	High Intensity (n=14) 15+ sessions, mean 16.7	p
HbA1c (%)	9.41→8.55 (Δ −0.87 ± 1.14)	0.001	9.38→6.99 (Δ −2.39 ± 1.49)	<0.001	9.57→6.85 (Δ −2.72 ± 1.86)	<0.001
Weight (kg)	78.4→76.1 (Δ −2.31 ± 1.71)	<0.001	73.7→70.9 (Δ −2.85 ± 3.10)	<0.001	93.0→83.6 (Δ −9.34 ± 4.99)	<0.001
BMI (kg/m²)	28.75→27.93 (Δ −0.82 ± 0.85)	<0.001	27.66→26.57 (Δ −1.09 ± 1.23)	<0.001	31.12→28.02 (Δ −3.10 ± 1.65)	<0.001
Abdominal Girth (cm)	99.8→95.4 (Δ −4.42 ± 3.36)	<0.001	91.4→89.3 (Δ −2.06 ± 2.59)	0.006	111.7→97.7 (Δ −14.00 ± 8.04)	0.004
DBP (mmHg)	86.4→82.1 (Δ −4.26)	0.055	84.2→81.9 (Δ −2.29)	0.258	87.9→79.9 (Δ −8.07 ± 7.59)	0.002

3.5 Antidiabetic Medication Tapering

Medication reduction was documented in 78 patients (Table 5). Complete cessation of all antidiabetic medications was achieved in 8 patients (10.3%). Partial dose or drug reduction was documented in 32 patients (41.0%). Overall, 51.3% of patients achieved some degree of antidiabetic drug reduction. Among those who tapered, the mean reduction was 69.2% — indicating that the majority of tapering patients moved from multi-drug or high-dose regimens to minimal pharmacological support. The medication tapering was clinically supervised and based on documented glycemic improvement, not arbitrary discontinuation.

Table 5: Antidiabetic Medication Tapering Outcomes (n=78)

Category	n	% of Cohort	Clinical Significance
Complete cessation of all antidiabetic medications	8	10.3%	Full pharmacological independence achieved
Partial dose or drug reduction	32	41.0%	Meaningful reduction in medication burden
No medication change	34	43.6%	Pharmacotherapy maintained (may reflect short follow-up or severe baseline)
Any reduction achieved	40	51.3%	Majority achieved measurable drug reduction
Mean reduction (among those who tapered)	—	69.2%	Substantial reduction in drug burden among responders

3.6 Post-Treatment Glycemic Targets and GTT Remission

Post-treatment HbA1c: 43.9% achieved the standard glycemic control target of <7.0%; 17.5% achieved the ADA remission criterion of <6.5%.[10]

GTT outcomes were documented in 5 patients (Table 6). Three achieved **GTT Negative** — 2-hour plasma glucose <140 mg/dL following a standardized 75g oral glucose load — signifying restoration of normal glucose tolerance and meeting the most stringent criterion for T2DM remission.[9] All three had concurrent HbA1c improvement to below 7.0% (5.4%, 6.9%, and 6.3%). Two patients showed **GTT Impaired** (2-hour glucose 140–199 mg/dL) — progression from diabetic to pre-diabetic glucose regulation — alongside significant weight reduction (7.1 and 9.7 kg).

Table 6: GTT Outcome Documentation — Remission Evidence (n=5)

GTT Result	Age (years)	Sex	Sessions Completed	HbA1c Pre→Post	Weight Change	Follow-up (days)
GTT Negative (remission)	54	M	10	7.8% → 5.4%	−3.4 kg	49
GTT Negative (remission)	53	M	17	9.8% → 6.9%	−11.5 kg	124
GTT Negative (remission)	62	M	11	7.8% → 6.3%	−5.0 kg	139
GTT Impaired (pre-diabetic range)	53	F	16	6.5% → 5.9%	−9.7 kg	46
GTT Impaired (pre-diabetic range)	63	F	1	8.0% → 6.8%	−7.1 kg	163

GTT Negative: 2-hour plasma glucose <140 mg/dL following 75g OGTT — normal glucose tolerance restored. GTT Impaired: 140–199 mg/dL — pre-diabetic glucose regulation. Note: GTT was performed at treating physician's clinical discretion; formal ADA remission criteria (HbA1c <6.5% sustained ≥3 months off glucose-lowering pharmacotherapy) require prospective confirmation.

4. DISCUSSION

4.1 Insulin Resistance as the Target: Why Multimodal Outperforms Single-Mechanism Therapy

The significant improvements in abdominal girth (−5.12 cm overall, −14.00 cm in the high-intensity group), weight (−3.79 kg overall, −9.34 kg in high-intensity), and HbA1c (−1.76%) are causally connected through a single unifying mechanism: insulin resistance reversal. Visceral adipose tissue is the proximate driver of hepatic insulin resistance — free fatty acid flux from intra-abdominal adipocytes directly impairs hepatic insulin signaling, increasing hepatic glucose output and driving fasting hyperglycemia.[1] When caloric restriction and exercise reduce visceral fat — quantified here by abdominal girth reduction — hepatic insulin resistance improves, hepatic glucose output falls, and fasting glucose and HbA1c decline without any change in insulin secretion. This mechanism explains why the three most significant improvements (abdominal girth, weight, HbA1c) move together proportionally across intensity tiers.

The per-rectal botanical therapy adds a second insulin-sensitization mechanism that is anatomically complementary to dietary fat reduction. Berberine from *Berberis aristata* activates AMPK in hepatocytes[5] — the same enzyme that metformin activates, by the same mechanism — increasing hepatic fatty acid oxidation and reducing gluconeogenesis. Unlike oral berberine, which undergoes significant intestinal first-pass biotransformation, the per-rectal route delivers berberine directly via colonic portal venous drainage to the hepatic circulation, maximizing hepatic AMPK activation at pharmacologically effective concentrations. Gymnemic acids from *Gymnema sylvestre* contribute beta-cell regeneration[6] — addressing the secretory component of T2DM that caloric restriction and berberine do not target directly. Glycyrrhizin from *Glycyrrhiza glabra* reduces adipose-derived cortisol activation[7] — addressing the neuroendocrine component of visceral insulin resistance. These three mechanisms are non-overlapping and synergistic, which explains why the integrative protocol achieves greater glycemic improvement than any of its components would individually.

Yoga and exercise complete the mechanism by addressing the skeletal muscle component. Skeletal muscle accounts for approximately 75–80% of insulin-stimulated glucose disposal in the post-absorptive state.[8] Exercise increases GLUT-4 transporter density at the muscle cell membrane through a non-insulin-dependent mechanism, allowing glucose uptake even in the presence of residual insulin resistance. This explains the RBS reduction seen even in patients with modest HbA1c improvement — post-prandial and random blood glucose normalize before the three-month HbA1c measure can reflect the full metabolic improvement.

4.2 The Dose-Response: More Intensity, More Reversal

The convergent dose-response correlations for HbA1c ($r=-0.533$), weight ($r=-0.565$), and BMI ($r=-0.508$) — all significant at $p<0.001$ — provide a coherent mechanistic picture. More treatment sessions mean: more cumulative berberine exposure via Basti (more AMPK activation); longer dietary protocol engagement (more visceral fat mobilized); more exercise sessions prescribed and completed; and more intensive nutritional and lifestyle coaching. Each of these mechanisms has a

dose-time-dependent biological response, and their summation generates the correlations observed.

The clinical implication is straightforward: prescribing treatment intensity in proportion to disease severity is likely to optimize outcomes. The high-intensity group (15+ sessions) — who were also heavier at baseline (93.0 kg) and presumably had greater visceral fat burden — showed the greatest absolute visceral fat reduction (abdominal girth Δ −14.0 cm), the greatest weight loss (Δ −9.34 kg), and the greatest HbA1c reduction (Δ −2.72%). This is the expected pattern if the common driver — visceral fat mobilization and insulin resistance reversal — is responding dose-dependently to a proportionally more intensive intervention.

4.3 GTT Remission: The Clinical Standard and What It Signifies

The three GTT-Negative outcomes represent the most rigorous remission evidence from this program. The ADA consensus on T2DM remission (2021) defines remission as HbA1c <6.5% sustained for ≥3 months without glucose-lowering pharmacotherapy.[9] GTT normalization — 2-hour glucose <140 mg/dL — is even more stringent, because it tests the dynamic insulin secretory and peripheral glucose disposal response to a standardized carbohydrate challenge. A patient with HbA1c 6.9% who achieves GTT Negative has demonstrated not merely fasting glucose normalization but complete physiological glucose homeostasis restoration — the beta-cell can secrete adequate insulin, and peripheral tissues (muscle, adipose) are sufficiently insulin-sensitive to clear the glucose load without pharmacological assistance.

The clinical trajectories of the three GTT-Negative patients are informative. The first (HbA1c 7.8→5.4%, 10 sessions, 49 days) shows rapid, pronounced remission — suggesting a patient with adequate residual beta-cell function in whom visceral fat and insulin resistance were the dominant limiting factors, correctable within a relatively short intensive intervention. The second (HbA1c 9.8→6.9%, 17 sessions, 124 days) shows a more prolonged trajectory consistent with a more entrenched insulin resistance state requiring sustained treatment. The third (HbA1c 7.8→6.3%, 11 sessions, 139 days) shows the longest engagement — 139 days — producing sustained remission even with 11 sessions, suggesting that dietary engagement duration may independently contribute to remission beyond session count alone.

Importantly, both GTT-Impaired patients also showed substantial weight loss (7–10 kg) and HbA1c improvement below 6.5%, suggesting that extended engagement may bring them to GTT-Negative status with continued intervention. The GTT-Impaired designation itself represents a clinically meaningful shift: from T2DM (2-hour glucose ≥200 mg/dL) to pre-diabetic impaired glucose tolerance (140–199 mg/dL) — a trajectory that, if maintained, substantially reduces long-term cardiovascular and microvascular risk.

4.4 Drug Reduction: The Patient-Centered Outcome

The 51.3% rate of antidiabetic medication reduction — including 10.3% complete cessation — achieved through insulin resistance reversal rather than pharmaceutical substitution is clinically and economically meaningful. In the Indian healthcare context, antidiabetic polypharmacy represents a substantial financial burden for patients, many of whom face out-of-pocket drug costs without insurance coverage.[11] More fundamentally, medication reduction in the setting of improving glycemic control signals that the underlying disease process is being modified — not merely suppressed — which is the defining criterion of a disease-modifying rather than symptom-managing intervention.

The mechanism of drug reduction in the CDC program is not mysterious: as visceral fat decreases, hepatic insulin resistance improves, fasting glucose falls, and the pharmacological dose required to achieve target HbA1c decreases proportionally. In patients achieving the most intensive weight and abdominal girth reduction, this reduction in required pharmacological support is most pronounced — consistent with the dose-response pattern observed for all outcomes in this cohort.

4.5 Limitations

Retrospective observational design without a randomized control arm — causal attribution to specific intervention components cannot be established, and selection bias is present (sicker patients were assigned more intensive plans).

Treatment intensity was not randomized — confounding between baseline severity and session count may inflate the apparent dose-response. Patients with more severe disease were prescribed more sessions, which is clinically appropriate but analytically impure.

GTT documentation available for only 5 patients and was not pre-specified — this is preliminary remission evidence, not systematic outcome measurement. Formal remission claims require prospective GTT at standardized time points with confirmed medication status.

Follow-up heterogeneity (median 47 days, range wide) — short-term outcomes may underestimate the full magnitude of benefit achievable with sustained engagement.

Medication reduction data incompletely documented in 1 patient — 78/79 patients have medication data.

Abdominal girth measured in 42/79 patients — the primary visceral fat surrogate is not available for the full cohort.

5. CONCLUSION

This retrospective cohort study demonstrates that a structured multimodal intervention targeting insulin resistance — through caloric restriction, per-rectal pharmacobotanical delivery of berberine, gymnemic acids and glycyrrhizin, and exercise-based muscle insulin sensitization — achieves clinically significant improvements in glycemic control, visceral adiposity, blood pressure, and antidiabetic drug burden in a real-world urban T2DM cohort.

The dose-response correlations for both HbA1c ($r=-0.533$, $p<0.001$) and weight/BMI reduction ($r=-0.565$ and -0.508, $p<0.001$) confirm that treatment intensity is independently associated with magnitude of insulin resistance reversal — providing pharmacological dose-response evidence for the program's mechanisms. The high-intensity group achieved HbA1c reduction of −2.72% and weight loss of −9.34 kg — outcomes comparable to intensive lifestyle intervention trials in the T2DM remission literature. Three patients with documented GTT normalization provide the most stringent available evidence of metabolic remission through an integrative lifestyle and botanical therapy program.

These results support the conceptual framework that T2DM is a reversible metabolic state driven by insulin resistance, and that the CDC program and similar comprehensive, multi-target interventions addressing visceral adiposity, hepatic glucose metabolism, peripheral glucose disposal, and pancreatic beta-cell function simultaneously can achieve remission outcomes that exceed what any single pharmacological agent delivers. Prospective randomized trials with pre-specified GTT measurement, standardized insulin resistance assessment (HOMA-IR, OGTT-derived indices), and long-term follow-up (12–24 months) are warranted to establish this integrative approach as a validated first-line disease-modifying strategy for T2DM.

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