Effects of Continuous Positive Airway Pressure, Lifestyle Modification, and Pranayama on Sleep Architecture, Insulin Resistance, Adipokines, Inflammatory Markers, and Cardiometabolic Biomarkers in Obese Adults with Type 2 Diabetes Mellitus and Obstructive Sleep Apnea

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Abstract:

Background:

Obstructive sleep apnea (OSA) frequently coexists with obesity and type 2 diabetes mellitus (T2DM), creating a complex cardiometabolic disorder characterized by intermittent hypoxia, insulin resistance, chronic inflammation, and adipokine dysregulation. Although continuous positive airway pressure (CPAP) remains the standard treatment for OSA, the additional benefits of lifestyle modification and pranayama on metabolic and inflammatory outcomes remain inadequately investigated.

Objective:

To evaluate and compare the effects of CPAP alone, CPAP combined with lifestyle modification, and CPAP combined with pranayama on sleep parameters, glycaemic control, insulin resistance, lipid profile, inflammatory markers, and adipokines in obese adults with T2DM and OSA.

Methods:

In this prospective interventional study, obese adults with T2DM and polysomnography-confirmed OSA were allocated to three intervention groups: CPAP alone, CPAP plus lifestyle modification, and CPAP plus pranayama. Participants were followed for six months. Clinical characteristics, anthropometric indices, polysomnographic parameters, fasting plasma glucose, HbA1c, fasting insulin, HOMA-IR, lipid profile, leptin, adiponectin, ghrelin, and interleukin-6 (IL-6) were assessed at baseline and after intervention. Correlation analyses were performed to examine associations between apnea-hypopnea index (AHI) and metabolic, inflammatory, and adipokine biomarkers.

Results:

All three interventions significantly improved sleep quality and cardiometabolic parameters after six months ($p < 0.05$). However, CPAP combined with lifestyle modification and CPAP combined with pranayama produced significantly greater improvements than CPAP alone. The CPAP plus pranayama group demonstrated the greatest reductions in AHI, body mass index, HbA1c, fasting insulin, HOMA-IR, IL-6, and leptin, together with significant increases in adiponectin and favourable modulation of ghrelin. AHI showed significant positive correlations with HbA1c, fasting insulin, HOMA-IR, IL-6, and leptin, while exhibiting a significant inverse correlation with adiponectin (all $p < 0.05$), highlighting the close relationship between OSA severity, metabolic dysfunction, and adipose tissue dysregulation.

Conclusions:

CPAP therapy substantially improves sleep and metabolic health in obese patients with T2DM and OSA, while adjunctive lifestyle modification and particularly pranayama provide additional benefits through enhanced glycaemic control, reduced systemic inflammation, improved adipokine homeostasis, and better insulin sensitivity. The principal novelty of this study lies in the integrated evaluation of polysomnographic, metabolic, inflammatory, and adipokine biomarkers within a single prospective interventional framework, demonstrating that multimodal therapy targeting both airway obstruction and cardiometabolic dysfunction yields superior clinical

outcomes compared with CPAP alone. These findings support the incorporation of structured lifestyle interventions and pranayama into comprehensive OSA management strategies.

Keywords: Obstructive sleep apnea; Type 2 diabetes mellitus; Continuous positive airway pressure; Pranayama; Lifestyle modification; Adipokines; Leptin; Adiponectin; Ghrelin; Interleukin-6; Insulin resistance.

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Introduction:

Obstructive sleep apnea (OSA) is among the most common sleep-related breathing disorders and is defined by recurring episodes of partial or total collapse of the upper airway during sleep leading to intermittent hypoxia, hypercapnia, frequent arousals and sleep fragmentation. Such repetitive respiratory events cause sympathetic nervous system activation, oxidative stress, endothelial dysfunction, and systemic inflammation that ultimately result in the development of hypertension, cardiovascular disease, insulin resistance, type 2 diabetes mellitus (T2DM), stroke, and increased all-cause mortality [1]. Recent epidemiologic data indicate that around 1 billion persons globally have OSA, and a large number of middle-aged and older adults have moderate to severe illness. Despite its high prevalence, OSA remains significantly underdiagnosed as many patients present with nonspecific symptoms such as excessive daytime sleepiness, fatigue, impaired concentration, decreased work performance and poor quality of life instead of classic nocturnal respiratory symptoms [2].

Obesity is the most important modifiable risk factor for OSA and is central in its pathogenesis and progression. Excess adipose tissue in the neck, pharyngeal airway, thorax, and abdomen predisposes to upper-airway collapsibility, reduces lung volume, impairs respiratory mechanics, and increases the frequency of obstructive respiratory events during sleep. On the other hand, untreated OSA leads to weight growth due to persistent sleep deprivation, hormone dysregulation, increased appetite, decreased physical activity, and poor energy expenditure, so establishing a bidirectional link between obesity and sleep-disordered breathing [2]. Obesity is present in approximately 60–70% of patients with moderate-to-severe OSA, and increased body mass index (BMI), waist circumference, neck circumference, and visceral adiposity are all independently linked with increased disease severity and higher apnea-hypopnea index (AHI) values [4].

In addition to recurrent airway blockage, the systemic metabolic dysfunction of OSA is rapidly being recognized. Chronic intermittent hypoxia and repeated sleep fragmentation activate hypoxia-inducible factor-1α (HIF-1α), nuclear factor-kappa B (NF-κB) and reactive oxygen species (ROS) related pathways leading to endothelial dysfunction, chronic low-grade inflammation and vascular damage. These processes induce the production of pro-inflammatory cytokines, such as interleukin-6 (IL-6), tumour necrosis factor-α (TNF-α) and C-reactive protein (CRP), which contribute to dyslipidaemia, insulin resistance, endothelial dysfunction and accelerated atherosclerosis. Therefore, systemic inflammation has been proposed as a key biological link between obesity, OSA, and cardiometabolic disease [2]. There is increasing evidence that insulin resistance is one of the early metabolic effects of OSA, independent of obesity alone. Recurrent nocturnal hypoxia disrupts insulin receptor signaling, decreases glucose uptake in skeletal muscle, increases hepatic gluconeogenesis, modifies pancreatic β-cell function and increases sympathetic nervous system activity, leading to hyperinsulinaemia and poor glucose metabolism. Furthermore, the severity of OSA has been associated with a progressive deterioration in glycaemic control and metabolic dysfunction, underscoring the necessity of early diagnosis and prompt treatment [6].

Adipose tissue is now considered to be an active endocrine organ, secreting a variety of bioactive adipocytokines that control hunger, energy homeostasis, inflammation, insulin sensitivity and vascular function. In obesity-associated OSA, leptin, adiponectin and ghrelin have received particular attention. Obese patients with OSA are usually hyperleptinaemic with leptin resistance, resulting in prolonged sympathetic activation, dysregulation of appetite, and metabolic dysfunction. Adiponectin is an anti-inflammatory and insulin sensitizing adipokine, which is on the contrary frequently diminished in obesity and OSA, causing endothelial dysfunction and insulin

resistance. Ghrelin is an orexigenic hormone that plays an important role in the control of hunger and energy balance and may also be dysregulated by sleep deprivation and fragmented sleep, thus perpetuating obesity and metabolic derangements [7]. Taken together, these changes in adipokines indicate adipose tissue dysfunction and may be useful markers of disease severity and response to therapy.

In addition to metabolic problems, OSA radically changes normal sleep architecture. Repetitive apneic and hypopneic episodes interfere with normal sleep architecture, decreasing sleep efficiency, increasing light sleep (N1) and decreasing restorative slow wave (N3) and rapid eye movement (REM) sleep. Such changes have deleterious effects on neurocognitive performance, mood, memory consolidation, endocrine regulation and daytime functioning. There is emerging evidence that changes in sleep architecture, especially reduced slow-wave and REM sleep, are associated with poor glucose metabolism, autonomic dysfunction, hypertension and increased cardiovascular risk. Therefore, measurement of sleep architecture apart from the apnea–hypopnea index in the setting of complete polysomnography offers significant information on the severity of the disease and responsiveness to therapy [11]. CPAP remains the gold standard treatment for moderate to severe OSA and works by preventing upper airway collapse with pneumatic splinting throughout the breathing cycle. CPAP reliably improves respiratory events, oxygen saturation, daytime drowsiness, and sleep quality, however the impact on metabolic abnormalities, inflammatory pathways, insulin resistance, and adipokine modulation has been inconsistent among studies. This variability implies that the isolated repair of upper-airway obstruction may not completely cure the complex metabolic and inflammatory changes associated with obesity-related OSA [14].

A cornerstone in the management of obesity is lifestyle modification which includes dietary intervention, regular physical activity, behavioural counselling and weight reduction, and has been demonstrated to reduce visceral adiposity, improve upper-airway mechanics, improve insulin sensitivity, reduce systemic inflammation and improve cardiovascular risk factors. Similarly, pranayama, a structured yogic breathing practice, has been found to be a promising complementary intervention due to its beneficial effects on autonomic balance, vagal tone, respiratory muscle function, oxidative stress, psychological stress and inflammatory responses. Both lifestyle modification and pranayama have shown beneficial physiological effects separately, however the combined role as adjuncts to CPAP therapy has not been extensively investigated using integrated polysomnographic, metabolic, inflammatory and adipokine-based outcomes [18].

Nevertheless, despite significant advances in understanding the pathophysiology of OSA, there are significant gaps in the current understanding of the comparative effectiveness of CPAP alone vs CPAP in combination with structured lifestyle modification or pranayama on sleep architecture, insulin resistance, adipokine regulation, inflammatory status and cardiometabolic biomarkers in obese adults with type 2 diabetes mellitus and obstructive sleep apnea. Further assessment of these therapies may enhance the understanding of multimodal treatment options that can target both respiratory problems and the underlying metabolic dysfunction in OSA. Therefore, the present study was conducted to assess and compare the effect of continuous positive airway pressure (CPAP) alone, CPAP with lifestyle modification and CPAP with pranayama on sleep architecture, insulin resistance, adipokines (leptin, adiponectin and ghrelin), inflammatory marker interleukin-6 (IL-6) and cardiometabolic biomarkers in obese-diabetic adults with obstructive sleep apnea.

2. MATERIALS AND METHODS

2.1 Study Design and Place of Study: This prospective interventional comparative study was undertaken in the Department of Biochemistry and Respiratory Medicine, MGM Medical College and Hospital, Kamothe, Navi Mumbai, Maharashtra, India. The study was conducted for 18 months from January 2024 to June 2025 to evaluate the effects of continuous positive airway pressure (CPAP) alone, CPAP with lifestyle modification and CPAP with pranayama on sleep architecture, insulin resistance, adipokines, inflammatory markers and cardiometabolic biomarkers in obese adults with type 2 diabetes mellitus and obstructive sleep apnea. The aim of the study was to examine the efficacy of three therapeutic strategies on clinical, polysomnographic, metabolic, inflammatory and biochemical outcomes over a 6-month follow-up period.

2.2 Study Population: Consecutive patients attending the Sleep Medicine and Respiratory Medicine outpatient clinics with symptoms suggestive of OSA were recruited. These symptoms included habitual snoring, witnessed apneic episodes, excessive daytime sleepiness, morning headache, nocturnal choking, and non-restorative sleep. All eligible people had overnight attended polysomnography for confirmation of OSA. Only obese-diabetic adults diagnosed with OSA were

included in this investigation. Fifty-three adults with obesity, type 2 diabetes mellitus, and obstructive sleep apnea were randomly allocated to one of three preset intervention groups in accordance with the study protocol.

Study Group	Intervention	Number of Participants
G1	CPAP therapy alone	16
G2	CPAP therapy + Lifestyle modification	20
G3	CPAP therapy + Pranayama	17
Total		53

All patients were subjected to extensive clinical and anthropometric baseline screening, overnight polysomnography and laboratory tests before the start of therapy. The same evaluations were repeated after the six-month intervention period to assess changes in sleep parameters, insulin resistance, adipokines, inflammatory markers and cardiometabolic biomarkers.

2.3 Inclusion criteria: Participants were included if they met the following criteria: Age group of 30–60 years, BMI ≥30 kg/m² and classified as obese according to criteria set by World Health Organization. New diagnosis of obstructive sleep apnea defined as an AHI of ≥15 events/hour on overnight polysomnography as per AASM criteria. Confirmed diabetic status by clinical history and laboratory investigations. He had never undergone treatment with CPAP, bilevel positive airway pressure, mandibular advancement devices, upper airway surgery, or structured weight-loss programs. Willingness to comply with the intervention procedure and to attend scheduled follow-up appointments, Provision of written informed consent.

2.4 Exclusion Criteria: Participants were excluded if they had any of the following: Type 1 diabetes mellitus, Secondary causes of obesity, Chronic obstructive pulmonary disease, bronchial asthma or other chronic respiratory disorders, Congestive heart failure, significant valvular heart disease, recent myocardial infarction or unstable cardiovascular disease, Chronic kidney disease or chronic liver disease, Thyroid disorders or other endocrine diseases affecting metabolism, Active infection, autoimmune disease, chronic inflammatory disorders or malignancy, Pregnancy or lactation, Current smoking or alcohol dependence. Use of systemic corticosteroids, immunosuppressive agents or pharmaceuticals known to impair insulin sensitivity or inflammatory indicators. Previous CPAP therapy or intolerance to CPAP treatment. Inability to adhere to the study interventions and/or to attend regular follow-up. The exclusion criteria were chosen in order to reduce the possible confounding factors that could affect metabolic, inflammatory and sleep indices individually.

2.5 Sample Size Estimation: It was a prospective interventional comparative study carried out at a single tertiary care center. All consecutive eligible patients meeting the inclusion criteria during the study period (January 2024 to June 2025) were enrolled. Fifty-three obese adults with type 2 diabetes mellitus and obstructive sleep apnea were selected by a sequential sample procedure. Therefore, the sample size was determined by the availability of eligible individuals throughout the study period and not by a formal a priori sample size calculation. According to the study methodology, participants were allocated to one among three pre-determined intervention groups and were prospectively followed up for 6 months.

• Group 1 (G1): CPAP treatment alone (n = 16)
• Group 2 (G2): CPAP therapy plus lifestyle change (n = 20)
• Group 3 (G3): CPAP therapy plus pranayama (n = 17)

2.6 Ethical Considerations: The study methodology was reviewed and approved by Institutional Ethics Committee, MGM Medical College and Hospital, Navi Mumbai before commencing participant recruitment. All participants gave written informed consent after having been informed about the objectives, study procedures, potential benefits and possible risks associated with participation. A unique study identification number was used to keep participants' identities confidential throughout the trial. All data obtained were anonymised prior to statistical analysis.

2.7 Clinical examination: All participants completed a detailed clinical examination at recruitment by a pulmonologist and research investigator using a predesigned case record form. Detailed medical history included demographic parameters, occupational history, smoking and alcohol consumption, sleep-related symptoms, duration of obesity, associated comorbidities, medication history, and family history of sleep disorders or metabolic diseases. Symptoms possibly indicative of obstructive sleep apnea such as chronic snoring, witnessed apnea, nocturnal choking or gasping, excessive daytime sleepiness, morning headache, lethargy, poor focus, irritability, non-restorative sleep were thoroughly documented. The clinical examination involved assessment of pulse rate, blood pressure, breathing rate and general physical examination. Upper airway examination was performed for any anatomical abnormality which could result in upper airway obstruction. Daytime drowsiness was assessed using

the Epworth drowsiness Scale (ESS), a standardized self-administered questionnaire with eight circumstances of daily living, where the likelihood of dozing is graded from 0 to 3. The overall ESS score ranges from 0 to 24, with higher values suggesting increased daily sleepiness. Excessive daytime sleepiness was defined as an ESS score ≥ 10 [23].

2.8 Anthropometric measurements: Anthropometric measurements were taken by trained investigators using established protocols both at baseline and after the 6-month intervention period. Body weight was measured to the nearest 0·1 kg with the subjects dressed in light clothing and without shoes using a calibrated digital weighing scale. Height was measured in standing position to the closest 0.1 cm using a wall-mounted stadiometer. The body mass index (BMI) was computed using the formula: BMI (kg/m²) = Weight (kg) / Height² (m²) Waist circumference was measured with a non-stretchable measuring tape at the midway between the inferior border of the last palpable rib and the iliac crest. The hip circumference was measured at the broadest region of the buttocks with the person standing erect with the feet together. The waist-to-hip ratio (WHR) was computed as waist circumference divided by hip circumference. The neck circumference was measured just behind the laryngeal prominence while the person was standing upright. To reduce variability between observers, all measurements were made in duplicate and the average value was recorded [24].

2.9 Blood Pressure Measurement: Resting blood pressure was measured using a calibrated automated sphygmomanometer during a calm seated rest for at least five minutes. Two measurements were taken five minutes apart and the average was computed for statistical analysis. If the difference between the two measurements was greater than 5 mmHg, a third reading was taken and the average of the two closest readings was recorded. **Overnight polysomnography**: All participants completed attended overnight polysomnography (PSG) in the Sleep Laboratory utilizing a computerized digital polysomnography equipment. **Physiological parameters recorded**: Electroencephalography (EEG), Electro-oculography (EOG), Chin electromyography (EMG), Electrocardiography (ECG), Nasal airflow with pressure transducer, Oral airflow with thermistor, Thoracic respiratory effort, Abdominal respiratory effort, Pulse oximetry, Body position, Snoring microphone Sleep stages and respiratory events were scored manually by an experienced sleep physician based on the AASM Manual for the Scoring of Sleep and Associated Events [25].

2.11 Evaluation of Sleep Parameters:

The following polysomnographic variables were recorded and analysed: Sleep Architecture, Total sleep time (minutes), Sleep efficiency (%), Sleep latency (minutes), REM sleep latency (minutes), Stage N1 sleep (%), Stage N2 sleep (%), Stage N3 sleep (%), REM sleep (%), Arousal index (events/hour).

Respiratory Parameters: Apnea-Hypopnea Index (AHI), Oxygen Desaturation Index (ODI), Mean oxygen saturation (SpO_2), Minimum oxygen saturation, Duration of oxygen saturation below 90%, Snoring index. According to the American Academy of Sleep Medicine (AASM) Manual for the Scoring of Sleep and Associated Events (Version 3.0) and the International Classification of Sleep Disorders, Third Edition, Text Revision (ICSD-3-TR) [26,27], moderate OSA was defined as an apnea-hypopnea index (AHI) of 15.0-29.9 events/hour and severe OSA was defined as an AHI of ≥30 events/hour.

2.12 Baseline evaluation: Prior to the intervention, all participants had a detailed baseline evaluation, which included: Clinical parameters: age, sex, medical history, blood pressure, Epworth Sleepiness Scale. Anthropometric parameters: weight, height, BMI, waist circumference, hip circumference, waist-to-hip ratio, neck circumference. Polysomnography Parameters Total sleep time Sleep efficiency Sleep latency REM sleep NREM sleep phases AHI ODI Mean SpO 2 Minimum SpO2 Laboratory Parameters Fasting blood glucose Fasting insulin HOMA-IR Lipid profile Leptin Adiponectin Ghrelin Interleukin 6 (IL-6) After 6 months of intervention, the same clinical, anthropometric, polysomnographic and laboratory evaluations were performed again to identify treatment-related changes.

2.13 Intervention Protocol: Eligible individuals were randomly allocated to one of the three predetermined intervention groups following baseline assessment. All interventions were sustained for 6 months and individuals were periodically assessed for adherence, treatment compliance and adverse events. At the end of the intervention period, clinical, anthropometric, polysomnographic, biochemical, inflammatory and metabolic parameters were re-evaluated.

2.13.1 Group 1: Treatment with Continuous Positive Airway Pressure (CPAP) Group 1 participants were treated with conventional CPAP therapy alone. CPAP pressure was individually titrated by an overnight manual titration

during an attended polysomnography. The best therapeutic pressure was defined as the lowest pressure that eliminated obstructive apneas, hypopneas, respiratory effort-related arousals, snoring and oxygen desaturation.
The participants were asked to wear the CPAP equipment every night during sleep for 6-8 hours. Proper mask fitting, equipment maintenance, humidifier use and troubleshooting were explained before commencement of therapy. Compliance was evaluated by review of CPAP device usage records at the monthly follow-up visits. Participants were deemed to be complying with therapy according on accepted clinical standards [26] if they achieved an average nightly usage of ≥4 hours on ≥70% of nights.

2.13.2 Group 2: CPAP + Lifestyle modification:

Group 2 participants were treatment with CPAP and a systematic lifestyle change plan overseen by a dietician, physiotherapist and research investigator.

Dietary Intervention: Each subject was prescribed an individualized calorie-restricted diet, depending on age, sex, body weight, body mass index, and daily energy requirements. **Nutritional counselling focused on:** Reducing total calorie intake, Reducing saturated fat, trans fat, refined carbohydrates and sugar-sweetened beverages, increasing intake of vegetables, fruits, whole grains, legumes and dietary fibre, Adequate intake of lean protein sources and healthy unsaturated fats, Avoiding late-night meals and excessive alcohol consumption.
The primary outcome was a 10% minimum reduction in baseline body weight with an expected average weight loss of approximately 7% over 6 months.

Physical activity: Participants were asked to practice aerobic exercise of moderate intensity for at least 175 min/week, in line with the current recommendations for the management of obesity. The majority of exercise was brisk walking, cycling or similar aerobic exercise.
Daily physical activity was incrementally increased to about 250 more steps per week until 10,000 steps/day was achieved. The participants kept activity logs and compliance was assessed during the monthly follow-up visits.

Behavioural Counselling: Monthly counselling sessions addressing behaviour change, food adherence, sleep hygiene, motivation, stress management and long-term maintenance of good lifestyle patterns. When appropriate, family members were encouraged to attend counselling sessions to increase adherence and long-term sustainability.

2.13.3 Group 3: CPAP + Pranayama

Participants in Group 3 were treated with standard CPAP therapy and a structured pranayama training program supervised by a trained yoga instructor. The breathing programme was specifically designed to improve the coordination of respiratory muscles, autonomic balance, pulmonary function and sleep quality. The regimen consisted of the following breathing exercises: Anulom-Vilom (Alternate Nostril Breathing), Bhramari Pranayama, Ujjayi Pranayama, Deep Diaphragmatic Breathing

Each supervised session lasted 30–40 minutes, five days a week, over 6 consecutive months. Participants were urged to continue home practice on non-supervised days and to keep a daily practice diary. The intensity and duration of the breathing exercises were incrementally increased according to participant tolerance. Attendance was measured throughout the study and adherence was tested at the monthly follow-up visits.

Lifestyle Modification Programme

Component	Intervention
Diet	Individualized calorie-restricted balanced diet
Weight reduction goal	≥10% reduction in baseline body weight
Expected average weight loss	Approximately 7%
Exercise	Moderate-intensity aerobic activity
Duration	≥175 min/week
Walking goal	Progressive increase to 10,000 steps/day
Counselling	Monthly behavioural and dietary counselling
Follow-up	Monthly assessment of compliance

Pranayama Protocol

Exercise	Duration
Deep diaphragmatic breathing	5 minutes
Anulom–Vilom	10 minutes
Bhramari	10 minutes
Ujjayi	10 minutes
Relaxation	5 minutes
Total session	**40 minutes**

2.14 Compliance with Treatment: Compliance with CPAP therapy was assessed by objective device-recorded utilization statistics. Recipients of lifestyle modification also underwent dietary record, exercise log, and monthly counselling report evaluations. Compliance with pranayama was recorded in attendance registrations for supervised

sessions and participant-kept home-practice diaries. Poor adherence participants received personalized reinforcement counselling to increase long-term compliance with the prescribed intervention.

2.15 Statistical Analysis:

SPSS Statistics for Windows, Version 25.0 was used for statistical analysis. Data were presented as mean ± standard deviation (SD) or frequency and percentage, as appropriate. The Shapiro–Wilk test was used to test the normality of the data distribution. Comparison of baseline and post-intervention values within each group was carried out by paired Student's t-test and between the three intervention groups by one-way analysis of variance (ANOVA) with the Tukey's post hoc test. Statistical significance was defined as a two-tailed P value <0.05. Pearson's correlation analysis was used to assess the relationship between the selected continuous variables. P <0.05 was considered statistically significant.

RESULTS:

Table 1: Gender wise distribution of Diabetic Obese with OSA in G1, G2 and G3 groups

Group	Male N (%)	Female N (%)	Total
CPAP	12 (27%)	4 (44%)	16 (30%)
CPAP with Lifestyle Modification	19 (43%)	2 (22%)	21 (40%)
CPAP with Pranayama	13 (30%)	3 (33%)	16 (30%)
Total	44 (81%)	9 (19%)	53 (100%)

Table 2: Comparison of Polysomnography (PSG) and ESS Score in Diabetic Obese with OSA in G1, G2 and G3 Groups

Variable	**CPAP (G1) Baseline**	**Only CPAP (G1) After 6 Months**	**CPAP with Lifestyle Modification (G2) Baseline**	**CPAP with Lifestyle Modification (G2) After 6 Months**	**CPAP with Pranayama (G3) Baseline**	**CPAP with Pranayama (G3) After 6 Months**
AHI	38.49 ± 18.47	14.66± 7.19**	38.22 ± 9.78	13.47±6.81***	38.60 ± 14.87	11.93 ± 3.52***
Sleep Efficiency %	78.80 ± 5.59	84.01 ± 3.69**	77.33 ± 8.47	85.28±3.89***	78.27 ± 5.81	87.20 ±3.26***
Stage I %	29.79 ± 10.76	14.59±8.30***	30.53 ± 19.43	13.65±5.62***	29.13 ± 9.00	9.45 ± 4.90***
Stage II %	50.61 ± 6.97	53.70 ± 5.20	46.85 ± 16.20	52.10 ± 6.99	45.91 ± 8.53	48.42 ± 6.35
Stage III %	9.17 ± 6.10	16.77 ± 7.56*	11.86 ± 11.06	17.27 ± 3.37*	14.07 ± 10.46	20.33 ± 5.63*
REM %	8.97 ± 5.63	14.94 ± 3.31**	11.57 ± 5.60	17.31 ± 4.35**	10.86 ± 5.23	22.37 ± 3.07***
Mean SpO_2 %	91.60 ± 2.99	93.93 ± 1.84**	90.91 ± 2.06	94.68± 1.55**	90.88 ± 2.01	96.03 ± 0.96***
ESS	16.00 ± 2.58	5.71 ± 3.15***	16.50 ± 4.79	5.00±3.33***	16.30 ± 3.13	4.60 ± 3.10***

Values are presented as mean ± standard deviation (SD). p<0.001 (Very highly significant), **p<0.01 (Highly significant), *p<0.05 (Significant) AHI: Apnea–Hypopnea Index; REM: Rapid Eye Movement; SpO_2: Mean Oxygen Saturation; ESS: Epworth Sleepiness Scale

Table 3: Comparison of Anthropometric evaluation in Diabetic Obese with OSA in G1, G2 and G3 groups.

Variable	CPAP (G1)		CPAP with Lifestyle Modification (G2)		CPAP with Pranayama (G3)	
	Baseline	After 6 Months	Baseline	After 6 Months	Baseline	After 6 Months
BMI	30.76±4.19	28.19±3.80***	30.40 ± 3.65	27.64±2.62***	30.12 ± 5.02	26.99±3.34***
Waist Circumference (cm)	107.86±16.51	102.43±15.34***	106.10 ± 5.69	99.20±5.61***	108.20±7.97	100.70 ±6.11***
Hip Circumference	110.00 ±14.09	106.71±13.14***	110.80±5.12	105.70 ±4.92***	111.90±6.05	105.90 ±5.59***

(cm)						
W/H Ratio	0.98 ± 0.03	0.96±0.03***	0.96± 0.02	0.94 ± 0.04*	0.97 ± 0.02	0.95 ± 0.01**
Neck Circumference (cm)	39.71 ± 1.35	38.43± 0.73***	40.90 ±1.15	38.60± 0.94**	40.55 ±1.50	37.95± 1.23**

Values are presented as mean ± standard deviation (SD).

***p<0.001 (Very highly significant), **p<0.01 (Highly Significant), *p<0.05 (Significant).

Table 4: Comparison of HbA1c %, Fasting blood sugar, Insulin & HOMA-IR in Diabetic Obese with OSA in G1, G2 and G3 groups.

Variable	CPAP (G1)		CPAP with Lifestyle Modification (G2)		CPAP with Pranayama (G3)	
	Baseline	After 6 Months	Baseline	After 6 Months	Baseline	After 6 Months
HbA1c %	8.19 ±1.55	7.41 ±0.98**	7.28 ±1.43	6.41 ±0.64**	7.32 ±1.68	5.97±0.66***
FBS (mg/dl)	152.87 ± 14.40	142.27 ± 5.19*	133.92 ± 29.04	122.77 ± 16.53*	121.78 ± 19.68	114.10 ± 10.73*
Insulin (mIU/l)	13.23 ± 7.00	10.44 ± 3.96*	12.38 ± 8.47	9.98 ± 5.45*	12.30 ± 5.81	9.16 ± 4.20**
HOMA-IR	1.91 ±1.01	1.47 ±0.56*	1.76 ±1.25	1.38 ±0.75*	1.68 ±0.74	1.24 ±0.56**

HbA1c: Glycosylated Hemoglobin; FBS: Fasting blood sugar; HOMA-IR: Homeostasis Model of Assessment for insulin resistance; Values are presented as mean ± standard deviation (SD).

***p<0.001 (Very highly significant), **p<0.01 (Highly Significant), *p<0.05 (Significant).

Table 5: Comparison of Lipid Profile in Diabetic Obese with OSA in G1, G2 and G3 groups.

Variable	CPAP (G1) Baseline	Only CPAP (G1) After 6 Months	CPAP + Lifestyle Modification (G2)		CPAP + Pranayama (G3)	
			Baseline	After 6 Months	Baseline	After 6 Months
TC (mg/dl)	158.30 ±38.21	164.46 ±27.82	208.13 ± 89.75	175.91± 80.72*	151.54 ±41.05	169.17± 23.94*
TG (mg/dl)	211.94± 134.85	179.17 ±103.87*	143.42 ± 73.54	120.60 ±45.67*	156.79 ±50.67	123.53± 34.40**
HDL (mg/dl)	37.17 ±10.98	41.29± 13.34*	34.89 ± 13.44	39.30 ± 9.82**	39.37 ±17.30	48.50±16.75**
LDL (mg/dl)	91.53 ± 39.66	84.21 ± 32.68*	143.48 ± 81.03	124.70 ±60.10**	78.57 ± 36.52	64.50 ± 25.94*
VLDL (mg/dl)	42.36 ± 26.92	29.76± 15.38*	28.66 ± 14.73	23.88 ± 9.31*	31.36 ±10.13	23.69 ±8.52**

Abbreviations: TC: Total cholesterol; TG: Triglyceride; HDL: High-density lipoprotein cholesterol; LDL: Low-density lipoprotein; VLDL: Very low-density lipoprotein. Values are presented as mean ± standard deviation (SD).

***p<0.001 (Very highly significant), **p<0.01 (Highly significant), *p<0.05 (Significant).

Table 6: Comparison of Serum Adiponectin, Ghrelin, Leptin & IL-6 in Diabetic Obese with OSA in G1, G2 and G3 groups.

Variable	CPAP	CPAP + Lifestyle Modification	CPAP + Pranayama

	Baseline (Mean ± SD)	After 6 Months (Mean ± SD)	Baseline (Mean ± SD)	After 6 Months (Mean ± SD)	Baseline (Mean ± SD)	After 6 Months (Mean ± SD)
Leptin (ng/mL)	12.82 ± 5.48	10.30 ± 4.24**	11.28 ± 4.72	8.08 ± 2.91**	12.70 ± 7.22	7.73 ± 4.28***
Adiponectin (mg/L)	5.49 ± 3.34	7.60 ±3.51***	4.33 ± 3.05	7.12 ±2.39***	4.64 ± 2.59	7.49 ±2.42***
Ghrelin (pg/mL)	30.19 ± 11.27	24.51 ± 7.48*	30.36 ± 9.32	21.29 ±5.98**	30.27 ± 9.72	18.15±3.50***
IL-6 (pg/mL)	7.93 ± 3.57	5.76 ± 1.73**	8.60 ± 4.61	5.46 ± 2.29**	8.33 ± 4.20	4.07 ±2.06***

IL-6: Interleukin-6, Values are presented as mean ± standard deviation (SD).

***p<0.001 (Very highly significant), **p<0.01 (Highly significant), *p<0.05 (Significant)

Discussion:

Table 1 shows there was a significant male predominance in the present investigation, with 44 (81%) males and 9 (19%) females among the 53 obese individuals with type 2 diabetes mellitus (T2DM) and obstructive sleep apnea (OSA). The same distribution of sex across the three intervention groups suggests proper baseline matching and reduces the likelihood of sex-related confounding influencing treatment outcomes. Our findings are comparable with those of Benjafield et al. [3], who found consistently a much greater frequency of OSA among males compared to women in diverse groups. This male preponderance has been related to sex-specific changes in the structure of the upper airway, body fat distribution, ventilatory control, and hormonal modulation. Increased central and upper-body adiposity, notably fat deposition around the neck, tongue base and parapharyngeal tissues, which promotes upper airway collapsibility during sleep, partly explains the greater susceptibility of men to OSA. Moreover, men generally have more visceral fat and lower neuromuscular responsiveness of the upper airway, which increases the likelihood of intermittent hypoxia from repeated pharyngeal blockage. These findings correspond with the extensive reviews of Messineo et al. [2], and Jordan et al. [4] who demonstrated that central obesity is one of the strongest anatomical determinants of OSA severity by reductions in lung volume, reduced caudal traction on the pharynx and increased airway collapsibility. On the other hand, the decreased prevalence of OSA in premenopausal women has been ascribed to the protective effects of female sex hormones, in particular progesterone, which boosts ventilatory drive, upper airway dilator muscle activity and respiratory stability during sleep. However, this protective effect wanes after menopause, with a progressive increase in the prevalence of OSA in older women. These results are in agreement with those of Yeghiazarians et al. [6], who documented significant sex-related differences in the clinical presentation 2 and identification of 2 OSA. Correlation analysis also showed significant positive correlations between the apnea-hypopnea index (AHI) and all anthropometric parameters, such as body mass index (BMI; r = 0.66–0.73), waist circumference (r = 0.58–0.67), hip circumference (r = 0.54–0.72), waist-to-hip ratio (r = 0.53–0.64) and neck circumference (r = 0.60–0.74). Of these, neck circumference in the CPAP + pranayama group (r = 0.74) and hip circumference in the CPAP + lifestyle modification group (r = 0.72) had the strongest positive correlation with AHI. This is a reflection of the preponderant role of central and upper body adiposity in determining OSA severity. Our results are consistent with those of Peppard et al. [27], who showed a significant association between increasing body weight and increasing severity of sleep disordered breathing, Tuomilehto et al. [28] who showed that reductions in central obesity have a significant effect on the severity of OSA, and Tai et al. [29] who argued that neck circumference and visceral adiposity are better predictors of upper airway obstruction than BMI. Excess cervical and visceral adipose tissue mechanistically narrows the pharyngeal lumen, raises extraluminal tissue pressure, decreases functional residual capacity, and hinders upper airway neuromuscular compensation, consequently promoting repeated airway collapse during sleep and raising AHI. Collectively, these results underscore the relevance of central obesity, particularly neck circumference, as a clinically important anthropometric marker for the identification of patients at higher risk of severe OSA and support targeted weight reduction strategies as a key component of OSA management

Table 2 shows significant reductions in polysomnographic parameters and daytime sleepiness in obese patients with type 2 diabetes mellitus (T2DM) and obstructive sleep apnea (OSA) after six months of treatment. The three intervention groups had significant reduction of apnea-hypopnea index (AHI) with significant improvement in sleep efficiency, restoration of normal sleep architecture, increased mean oxygen saturation (SpO2) and significant reduction of Epworth Sleepiness Scale (ESS) scores. CPAP alone showed significant

therapeutic benefits but the addition of lifestyle modification and especially pranayama resulted in greater improvement in several sleep parameters. This indicates that multimodal therapies offer therapeutic benefits beyond positive airway pressure therapy in isolation. These findings are in agreement with the studies of Patil et al. [14] and Wilckens et al. [17], who proposed that CPAP is the mainstay of therapy for OSA as it prevents recurrent collapse of the upper airway, improves oxygenation, normalises sleep continuity and decreases excessive daytime sleepiness. The most significant change was found in apnea-hypopnea index (AHI). In CPAP group it reduced from 38.49 ± 18.47 to 14.66 ± 7.19, in CPAP and lifestyle modification group from 38.22 ± 9.78 to 13.47 ± 6.81, and in CPAP and pranayama group from 38.60 ± 14.87 to 11.93 ± 3.52 (all $p<0.001$). Continuous positive airway pressure splints the upper airway mechanically throughout the entire breathing cycle, thereby preventing pharyngeal collapse and abolishing recurrent episodes of apnea and hypopnea. Lifestyle modification also improves upper-airway obstruction by reducing body weight, visceral adiposity, neck size, and upper-airway fat deposition, decreasing pharyngeal critical closing pressure and improving airway patency. Pranayama may also help improve respiratory muscle strength and diaphragmatic excursion, increase parasympathetic tone, reduce sympathetic over-activity and stabilize ventilatory control during sleep. Our findings are consistent with the randomized INTERAPNEA trial by Carneiro-Barrera et al. [26], showing the significant reduction in OSA severity and AHI with structured lifestyle intervention; the landmark trial by Chirinos et al. [15] showing the additive benefit of weight reduction and CPAP, and the obesity review by Tai et al. [29] demonstrating the significant improvement in upper-airway patency and OSA severity that reduction in central obesity and neck circumference can confer.

The current correlation analysis also revealed significant positive correlations of AHI with BMI, waist circumference, neck circumference, waist-to-hip ratio, fasting blood glucose, HbA1c, fasting insulin, HOMA-IR, leptin, inflammatory markers, and ESS and significant negative correlations with adiponectin and mean SpO2 indicating that an increase in the severity of OSA is positively correlated with the deterioration of obesity, insulin resistance, inflammation, and metabolic dysfunction. These findings are in line with the results of Muscogiuri et al. [9], Ryan and McNicholas [5] who demonstrated that obesity, inflammation, metabolic dysregulation and sleep-disordered breathing have a strong interaction. The improvement in sleep architecture is the other proof of the therapeutic effectiveness of therapies. All groups had significantly less Stage I sleep (light and fragmented), but significantly more of the restorative Stage III (slow-wave sleep) and REM sleep after therapy. These changes are suggestive with stabilization of sleep architecture with elimination of repeated respiratory arousals.

Recurrent apneic episodes lead to repeated cortical arousals that fragment sleep and thus prevent deep nonrapid eye movement (NREM) and rapid eye movement (REM) sleep from occurring. Successful CPAP treatment reduces respiratory arousals and allows uninterrupted transit through physiological stages of sleep. Pranayama and weight loss also aid in sleep stability via optimization of respiratory mechanics, autonomic regulation and ventilatory efficiency. Our findings are in accordance with the results reported by Wilckens et al. [17] who showed a significant recovery of slow-wave and REM sleep following CPAP therapy, and by Pépin et al. [30] who demonstrated an improvement in sleep continuity and architecture after successful OSA treatment, and by Cui et al. [31] whose systematic review indicated that yoga-based breathing exercises improve autonomic function and sleep quality.

The greater increase in REM sleep observed in the CPAP plus pranayama group could therefore be related to improved autonomic modulation, increased vagal activity and decreased nocturnal sympathetic activation, all of which are beneficial for the restoration of physiological REM sleep. Similar benefits were noted for sleep efficiency, mean oxygen saturation, and daytime somnolence. Sleep efficiency increased significantly in all intervention groups. Mean SpO2 was ~91% at baseline and increased to 94–96% after treatment, correcting intermittent nocturnal hypoxemia. Restoration of oxygen saturation improves sleep quality and cardiovascular physiology by reducing oxidative stress, sympathetic activation, endothelial dysfunction and systemic inflammation. These findings are in accordance with the American Heart Association Scientific Statement by Yeghiazarians et al [6], which showed that adequate treatment of OSA reverses intermittent hypoxia, improves endothelial function, reduces sympathetic activity and decreases cardiovascular risk. Moreover, ESS scores were significantly reduced from ~16 at baseline to <6 post-intervention, indicating significant improvement in excessive daytime sleepiness and functional alertness. These data are consistent with observations reported by Patil et al. [14], Wilckens et al. [17] and Pépin et al. [30], who all demonstrated clinically significant reductions in daytime sleepiness following CPAP therapy. This study found a strong positive relationship between AHI and ESS which further supports the fact that the reduction in respiratory events led to significant improvement in daytime symptoms and quality of

life. In summary, the present data suggest that CPAP can effectively reverse the major pathophysiological consequences of OSA by eliminating the upper-airway obstruction, normalizing sleep architecture, improving nocturnal oxygenation, and decreasing excessive daytime sleepiness. Our results are consistent with previous evidence reported by Chirinos et al. [15], Carneiro-Barrera et al. [26], and Tai et al. [29], showing that adjunctive lifestyle modification and pranayama further enhance the therapeutic effects of CPAP through improvements in obesity-related mechanical factors, autonomic balance, metabolic regulation, inflammatory status, and overall sleep quality.

All three intervention groups showed significant improvements in all anthropometric measures (including BMI, waist circumference, hip circumference, W/H ratio and neck circumference) after six months of intervention (Table 3). CPAP alone produced significant reductions in anthropometric indices. However, the larger improvement was seen in CPAP and lifestyle modification and CPAP and pranayama showing added benefits of adjunctive non-pharmacological interventions in reducing obesity related risk factors. These findings are in agreement with Chirinos et al. [15], Carneiro-Barrera et al. [26], Tai et al. [29] and Messineo et al. [2] who showed that the combination of structured weight loss interventions with CPAP results in a greater reduction of body weight, central obesity and OSA severity compared with CPAP alone. Obesity is the single most important modifiable risk factor for obstructive sleep apnea (OSA). Increased adiposity around the upper airway, thorax and abdominal compartments leads to increased pharyngeal collapsibility, decreased lung volumes, impaired respiratory mechanics and a propensity for recurrent airway obstruction during sleep. Lifestyle management enhances weight reduction by calorie restriction and increased physical activity. On the other hand, pranayama may further improve respiratory muscle performance, autonomic balance, and energy metabolism, thus enhancing reductions in body weight and central adiposity. These data are consistent with the systematic review of Cui et al. [31] that showed that yoga-based breathing therapies improve body composition, respiratory efficiency and autonomic regulation.

Significant improvement in polysomnographic parameters was associated with significant BMI reduction after intervention, confirming the strong link between obesity and severity of OSA. Correlation analysis confirmed the association, there were significant positive correlations between AHI and BMI in all the three intervention groups (G1: r = 0.66; G2: r = 0.73; G3: r = 0.69), showing that increasing of body mass was associated with greater severity of sleep-disordered breathing. Similarly, waist circumference showed a strong positive relationship with AHI (G1: r = 0.67; G2: r = 0.62; G3: r = 0.58) confirming the significant role of visceral fat to upper-airway obstruction and respiratory dysfunction. Our findings are consistent with the landmark longitudinal study of Peppard et al. [27] that demonstrated that increases in BMI significantly increase the risk and severity of OSA and the review of Tai et al. [29] that identified visceral adiposity as one of the strongest predictors of sleep-disordered breathing. Excess abdominal fat worsens OSA severity by increasing intra-abdominal pressure, limiting diaphragmatic mobility, decreasing functional residual capacity and increasing upper-airway collapsibility during sleep. In a similar way, Jordan et al. [4] and Lévy et al. [1] showed that the reduction in lung capacity and the impairment of respiratory mechanics caused by obesity are essential in the development of OSA.

A reduced hip circumference and waist to hip ratio is also a marker of better distribution of total body fat post-intervention. Hip circumference was moderately to strongly and positively correlated to AHI (G1: r= 0.71; G2: r= 0.72; G3: r= 0.54) and waist-hip ratio was positively correlated with the severity of disease (G1: r= 0.53; G2: r= 0.60; G3: r= 0.64). This study suggests that central obesity rather than diffuse obesity plays an important role in the pathophysiology of OSA. Our results are in line with those of Tai et al. [29] who demonstrated that waist circumference and visceral adiposity are better predictors of OSA severity than BMI alone and with Blüher [32] who stated that visceral adipose tissue is metabolically active and involved in insulin resistance, chronic low-grade inflammation, oxidative stress and dysregulated adipokine secretion. These metabolic dysregulations further compromise the neuromuscular control of the upper airway and respiratory stability, worsening sleep-disordered breathing.

Among all anthropometric factors, neck circumference carried the greatest clinical importance as increasing cervical adiposity immediately narrows the upper airway and increases pharyngeal collapsibility. In the current study, neck circumference was significantly and positively correlated with AHI in all intervention groups (G1: r=0.60; G2: r=0.64; G3: r=0.74) and was strongest in the CPAP + pranayama group. These results are consistent with those of Jordan et al. [4], Messineo et al. [2] and Tai et al. [29] who reported that neck circumference is one of the strongest anthropometric predictors of upper-airway narrowing and OSA severity. The reduction in neck circumference after intervention probably contributed to the marked reduction in AHI and improvement in sleep architecture, observed in the present study, by reducing peripharyngeal fat deposition and improving upper-airway patency. These findings,

together, suggest that the changes in anthropometric measurements were significantly correlated with decreases in OSA severity, supporting the concept that successful obesity management via lifestyle modification and pranayama supplements CPAP treatment by addressing the mechanical (reduced upper airway collapsibility and improved respiratory mechanics) and metabolic (enhanced insulin sensitivity, reduced inflammation, and favourable adipokine profile) mechanisms that underlie OSA. Overall, our results are consistent with the findings of Chirinos et al. [15], Carneiro-Barrera et al. [26], Tai et al. [29], Messineo et al. [2] and Blüher [32], who all consistently found that reduction of central obesity is important for sustained improvement in OSA severity and cardiometabolic health.

After 6 months of intervention, there were significant improvements in glycaemic control and insulin resistance in all three groups (Table 4). HbA1c decreased from 8.19 ± 1.55% to 7.41 ± 0.98% in the CPAP group, from 7.28 ± 1.43% to 6.41 ± 0.64% in the CPAP + lifestyle modification group and from 7.32 ± 1.68% to 5.97 ± 0.66% in the CPAP + Pranayama group. The CPAP plus pranayama group showed the greatest reduction, followed by the CPAP plus lifestyle modification and CPAP-alone groups, suggesting that whilst CPAP effectively improves metabolic regulation, adjunctive lifestyle modification and pranayama provide additional glycaemic benefits. Our study results are consistent with the results of Shang et al. [33] who conducted a meta-analysis of randomized controlled trials and showed that CPAP treatment significantly reduced HbA1c, fasting plasma glucose, fasting insulin and HOMA-IR in patients with T2DM and OSA. Similarly, the combination of CPAP and structured weight-loss interventions improved glycaemic control, insulin sensitivity and overall cardiometabolic health more than CPAP alone (Chirinos et al. [15]; Carneiro-Barrera et al. [26]).

The correlation analysis also supports the relationship between OSA severity and chronic glycaemic exposure. AHI was significantly positively correlated with HbA1c in G1 ($r = 0.57$, $p < 0.05$), G2 ($r = 0.64$, $p < 0.05$) and G3 ($r = 0.71$, $p < 0.05$), indicating that the increasing severity of sleep-disordered breathing was associated with poorer long-term glycemic control. Recurrent upper-airway obstruction causing intermittent hypoxaemia, sleep fragmentation, sympathetic nervous system activation, oxidative stress and chronic inflammatory signalling all impair insulin-mediated glucose uptake, increase hepatic glucose output, alter cortisol and catecholamine secretion, and contribute to persistent hyperglycaemia and elevated HbA1c levels. CPAP improves glucose homeostasis by reversing some of the pathophysiological disturbances through the prevention of recurrent airway collapse and reduction in nocturnal hypoxaemia. These results are consistent with those of Ryan and McNicholas [5] and Yeghiazarians et al. [6], who showed that intermittent hypoxia and sleep fragmentation are important factors in the development of insulin resistance, impaired glucose metabolism and chronic hyperglycemia in OSA patients. Moreover, the progressively strong association between AHI and HbA1c across the intervention groups indicates that chronic glycaemic burden is a good mirror of OSA severity and supports the idea that effective treatment of sleep-disordered breathing may have a role to play in improved long-term metabolic control.

Fasting blood glucose also showed significant decrease in all three groups from 152.87 ± 14.40 to 142.27 ± 5.19 mg/dL in G1, 133.92 ± 29.04 to 122.77 ± 16.53 mg/dL in G2, and 121.78 ± 19.68 to 114.10 ± 10.73 mg/dL in G3. The correlations between AHI and fasting blood glucose were weak and statistically insignificant in G1 ($r=0.19$), G2 ($r=0.21$), and G3 ($r=0.26$). This difference between HbA1c and fasting glucose is clinically plausible because a single fasting glucose value is affected by recent food intake, medication timing, hepatic glucose output, stress, sleep the night before, and day-to-day biological variation. HbA1c, meanwhile, reflects average glycaemic exposure over the last few weeks and may therefore show a more consistent association with chronic OSA severity.

The reduction in fasting insulin was also significant, 13.23 ± 7.00 to 10.44 ± 3.96 mIU/L in G1, 12.38 ± 8.47 to 9.98 ± 5.45 mIU/L in G2 and 12.30 ± 5.81 to 9.16 ± 4.20 mIU/L in G3. These findings suggest that lower circulating insulin concentrations could sustain improved glucose levels after the intervention, indicating improved insulin sensitivity, rather than merely an increase in insulin secretion. AHI was positively correlated with fasting insulin in all three groups (G1: $r = 0.56$; G2: $r = 0.62$; G3: $r = 0.71$; all $p < 0.05$) supporting a dose-dependent relationship between OSA severity and compensatory hyperinsulinaemia. Chronic intermittent hypoxia and sleep fragmentation increase sympathetic nervous system activity, oxidative stress and pro-inflammatory cytokine release, which impair insulin receptor signalling in skeletal muscle, liver and adipose tissue. Thus, greater OSA severity requires higher circulating insulin concentrations to maintain glucose homeostasis. Our results are consistent with the findings of Ryan and McNicholas [5], and Muscogiuri et al. [9], who have demonstrated that intermittent hypoxia causes insulin resistance via sympathetic activation, chronic inflammation,

oxidative stress and dysregulation of insulin signalling pathways.

Similarly, HOMA-IR was decreased from 1.91 ± 1.01 to 1.47 ± 0.56 in G1, from 1.76 ± 1.25 to 1.38 ± 0.75 in G2 and from 1.68 ± 0.74 to 1.24 ± 0.56 in G3. The corresponding correlations between AHI and HOMA-IR were higher than those for fasting glucose (G1: $r = 0.62$; G2: $r = 0.67$; G3: $r = 0.79$; all $p < 0.05$), indicating a close association between OSA severity and insulin resistance. HOMA-IR takes into account fasting glucose and fasting insulin, and therefore better represents whole-body insulin resistance than fasting glucose alone. Thus, the simultaneous reductions in fasting insulin and HOMA-IR strongly support the interventions to improve insulin sensitivity. These results are consistent with the systematic review and meta-analysis by Shang et al. [33] who reported significant improvements in HOMA-IR after CPAP therapy, and with the work of Ryan and McNicholas [5] who reported that insulin resistance is one of the main metabolic consequences of untreated OSA. CPAP can improve insulin sensitivity by reversing the effects of intermittent hypoxaemia, reducing nocturnal sympathetic surges, restoring normal sleep continuity and dampening inflammatory and oxidative stress pathways. However, CPAP alone does not directly cause significant weight loss, which could explain why the metabolic improvement seen in G1 was smaller than that achieved with the combined interventions. Our findings are consistent with those of Banghøj et al. [36], who showed by continuous glucose monitoring that the metabolic response to CPAP is affected by treatment adherence, nightly duration of CPAP use, baseline obesity, OSA severity, antidiabetic therapy, and follow-up duration. At the same time, Gottlieb and Punjabi [35] pointed out the critical role of adequate CPAP adherence to obtain clinically relevant metabolic benefits in OSA patients.

This additional improvement in the CPAP plus lifestyle modification group can be explained by reductions in body weight and visceral adiposity combined with increased skeletal muscle glucose uptake and hepatic insulin sensitivity. Dietary modification is effective in reducing excess caloric and refined carbohydrate intake, and regular physical activity promotes GLUT-4 translocation and glucose utilization through insulin-dependent and insulin-independent pathways. Further reduction of visceral adiposity decreases free fatty acid release and pro-inflammatory adipokine secretion that impair insulin signalling. Our findings are consistent with the INTERAPNEA randomized clinical trial by Carneiro-Barrera et al. [26], in which an interdisciplinary weight loss program plus CPAP resulted in clinically relevant improvements in OSA severity, insulin sensitivity, body weight and cardiometabolic risk. Chirinos et al. [15] reported similar findings, demonstrating that combined weight reduction and CPAP therapy resulted in greater improvements in metabolic health compared to CPAP therapy alone.

The greatest improvements in HbA1c, fasting glucose, fasting insulin and HOMA-IR were seen in the CPAP + pranayama group. Pranayama may be an adjunct to CPAP, by encouraging slow, controlled breathing, improving autonomic balance, decreasing sympathetic overactivity, increasing parasympathetic activity and attenuating psychological stress. These physiological adaptations decrease catecholamine- and cortisol-mediated hepatic glucose production and improve peripheral insulin sensitivity. However, as pranayama was administered with CPAP and no pranayama-only group was included, these metabolic improvements should be interpreted as the effects of the combined intervention rather than pranayama alone. Our findings are in line with the systematic reviews by Cui et al. [31] which showed that yoga-based breathing interventions ameliorate glycaemic control, autonomic function, stress regulation and insulin sensitivity in patients with type 2 diabetes mellitus.

`Table 5 shows the variable changes in the lipid profile of obese adults with T2DM and OSA after 6 months of intervention. The most consistent favorable changes were significant reductions in triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) and very low-density lipoprotein cholesterol (VLDL-C), coupled with increases in high-density lipoprotein cholesterol (HDL-C), in all three intervention groups. However, total cholesterol (TC) did not uniformly improve, with a non-significant increase following CPAP alone, significant decrease with CPAP plus lifestyle modification, and significant increase in the CPAP plus pranayama group. Thus, the lipid findings should be interpreted on an individual basis rather than taking the entire lipid profile as uniformly improved. Our findings are consistent with those reported by Ryan and McNicholas [5], and Yeghiazarians et al. [6], who showed that successful treatment of OSA improves nocturnal oxygenation, reduces intermittent hypoxia and sympathetic activation, and may beneficially affect lipid metabolism. However, these authors also highlighted that CPAP alone generally produces modest improvements in dyslipidaemia unless combined with weight reduction and comprehensive lifestyle modification. In the CPAP-only group (G1), TG was significantly decreased from 211.94 ± 134.85 to 179.17 ± 103.87 mg/dL, HDL-C was increased from 37.17 ± 10.98 to 41.29 ± 13.34 mg/dL, LDL-C was decreased from 91.53 ± 39.66 to 84.21 ± 32.68 mg/dL, and VLDL-C was decreased from 42.36 ± 26.92 to 29.76 ± 15.38 mg/dL. These

changes suggest a partial improvement of the atherogenic lipid profile after correction of the nocturnal airway obstruction. Repeated intermittent hypoxia in OSA activates sympathetic pathways, oxidative stress, inflammatory signalling, adipose-tissue lipolysis and hepatic lipid synthesis while impairing lipoprotein lipase activity, thus promoting dyslipidaemia. CPAP may improve triglyceride-rich lipoprotein metabolism and attenuate these metabolic disturbances by preventing recurrent hypoxaemia and sleep fragmentation. These results are consistent with the meta-analyses from Xu H et al. [36] and Liu L et al. [37], which showed CPAP therapy modestly reduces triglycerides and total cholesterol, but has inconsistent effects on LDL-C and HDL-C, suggesting CPAP alone has limited lipid-lowering efficacy. Correlation analysis further supported an association between OSA severity and dyslipidaemia. In G1, AHI showed a positive correlation with TC ($r = 0.42$, $p < 0.05$) and TG ($r = 0.34$, $p < 0.05$), and a negative correlation with HDL-C ($r = -0.54$, $p < 0.05$). Thus, worse sleep-disordered breathing was associated with increased atherogenic lipids and decreased cardioprotective HDL-C. However, correlations between AHI and LDL-C ($r = 0.36$) and VLDL-C ($r = 0.23$) were weak and statistically not significant. These results are consistent with the findings reported by Muscogiuri et al. [9], who showed that increasing OSA severity is more consistently associated with elevated triglycerides and reduced HDL-C than with LDL-C, reflecting the close relationship between intermittent hypoxia, insulin resistance, adipose tissue dysfunction, and altered lipid metabolism.

The most profound improvement in lipid metabolism was in the CPAP plus lifestyle modification group (G2). TC was significantly decreased from 208.13 ± 89.75 to 175.91 ± 80.72 mg/dL, TG from 143.42 ± 73.54 to 120.60 ± 45.67 mg/dL, LDL-C from 143.48 ± 81.03 to 124.70 ± 60.10 mg/dL and VLDL-C from 28.66 ± 14.73 to 23.88 ± 9.31 mg/dL, whereas HDL-C was increased from 34.89 ± 13.44 to 39.30 ± 9.82 mg/dL. Lifestyle modification has additional metabolic benefits to CPAP by reducing visceral adiposity, improving insulin sensitivity, increasing skeletal muscle lipid oxidation, enhancing lipoprotein lipase activity, and promoting reverse cholesterol transport. Diet modification further reduces intake of saturated fat and refined carbohydrates, while regular physical activity increases lipid utilization and reduces hepatic triglyceride synthesis. Our results agree with the INTERAPNEA randomized clinical trial by Carneiro-Barrera et al. [26] and the study by Chirinos et al. [15], which showed that the association of CPAP with structured weight-loss interventions had significantly greater improvements in body weight, lipid profile, insulin sensitivity, and overall cardiometabolic risk compared to CPAP alone. These results were also confirmed by significant positive correlations between AHI in G2 and TC ($r = 0.61$, $p < 0.05$) and TG ($r = 0.39$, $p < 0.05$) and a significant negative correlation between AHI in G2 and HDL-C ($r = -0.67$, $p < 0.05$). However, correlations with LDL-C ($r=0.16$) and VLDL-C ($r=0.17$) remained weak and statistically non-significant. These findings are consistent with those of Tai et al. [29], who highlighted that visceral adiposity and metabolic dysfunction associated with obesity have a stronger impact on dyslipidaemia than the severity of OSA alone, which may account for the weaker correlation between AHI and LDL-C. In the CPAP plus pranayama group (G3), there were significant reductions in TG (156.79 ± 50.67 to 123.53 ± 34.40 mg/dL), LDL-C (78.57 ± 36.52 to 64.50 ± 25.94 mg/dL), and VLDL-C (31.36 ± 10.13 to 23.69 ± 8.52 mg/dL), along with a significant increase in HDL-C (39.37 ± 17.30 to 48.50 ± 16.75 mg/dL). By slowing and controlling the breathing during pranayama, autonomic balance may improve, sympathetic overactivity may reduce, neuroendocrine stress responses may attenuate, and insulin sensitivity may improve, which in turn may favorably influence lipid metabolism. Our results are consistent with the systematic reviews of Cui et al. [31], which showed that yoga-based interventions significantly lower triglyceride concentrations, increase HDL-C, improve autonomic function and cardiometabolic health, although changes in total cholesterol are inconsistent between studies.

In G3, correlation analysis showed significant positive associations between AHI and TC ($r = 0.60$, $p < 0.05$) and TG ($r = 0.46$, $p < 0.05$) and the strongest inverse correlation between AHI and HDL-C among the three intervention groups ($r = -0.73$, $p < 0.05$). There were weak, statistically non-significant correlations between AHI and LDL-C ($r = 0.28$) and VLDL-C ($r = 0.32$). These data are consistent with the findings published by Ryan and McNicholas [5] and Yeghiazarians et al. [6] who demonstrated that intermittent hypoxia impairs HDL maturation and function via oxidative stress and chronic inflammation, while successful treatment of OSA improves HDL metabolism by restoring normal oxygenation and reducing systemic inflammation. An important discordant observation was the behavior of total cholesterol in G3, which increased from 151.54 ± 41.05 to 169.17 ± 23.94 mg/dL, despite favorable reductions in TG, LDL-C, and VLDL-C along with a substantial increase in HDL-C. Since total cholesterol is the sum of cholesterol carried by both atherogenic and anti-atherogenic lipoproteins, part of this increase may reflect the marked rise in HDL-C. However, total cholesterol must not be interpreted in isolation, and more importance must be given to the individual

lipid fractions. Medication use, dietary habits, baseline variability and sample size may also have contributed to this observation. The findings are in accordance with Nadeem et al. [40], who observed significant heterogeneity in the effects of CPAP on serum lipid parameters between studies and suggested that changes in individual lipoprotein fractions instead of total cholesterol alone provide a more meaningful assessment of the metabolic response to CPAP therapy.

In summary, the current results reveal that with increased OSA severity, there is a concomitant increase in triglycerides and a decrease in HDL-C levels. However, the associations between OSA severity and LDL-C or VLDL-C were weaker and not statistically significant. Intervention led to improvements in the atherogenic lipid profile, as evidenced by significant reductions in TG, LDL-C, and VLDL-C levels and increases in HDL-C levels especially when CPAP was combined with lifestyle modification or pranayama. In summary, our findings are in agreement with those reported by Ryan and McNicholas [5], Muscogiuri et al. [9] and Chirinos et al. [15], who all demonstrated only modest improvements in lipid metabolism with CPAP alone, but significant cardiometabolic benefit when CPAP was combined with weight loss, dietary intervention, physical activity, and lifestyle modification. These results are in accordance with the importance of a multidisciplinary treatment strategy to improve dyslipidaemia and reduce CV risk in patients with obesity, T2DM and OSA.

Table 6 shows that 6 months of intervention dramatically improved adipokine balance and systemic inflammatory status in obese adults with type 2 diabetes mellitus (T2DM) and obstructive sleep apnea (OSA). Serum leptin, ghrelin and interleukin-6 (IL-6) levels were significantly reduced and adiponectin levels were significantly increased after CPAP alone, CPAP with lifestyle change and CPAP with pranayama. The most significant changes were always observed in the group that received CPAP plus pranayama, indicating that correction of upper-airway blockage with concurrent improvement in body composition and autonomic regulation provides synergistic metabolic and anti-inflammatory benefits. Our results are consistent with those reported by Lévy et al. [1] and Yeghiazarians et al. [6], who showed that successful treatment of OSA reduces intermittent hypoxia, sympathetic overactivity, oxidative stress and systemic inflammation, and improves adipokine regulation and overall cardiometabolic health.

Serum leptin concentrations were considerably lowered from 12.82 ± 5.48 to 10.30 ± 4.24 ng/mL in G1, 11.28 ± 4.72 to 8.08 ± 2.91 ng/mL in G2 and 12.70 ± 7.22 to 7.73 ± 4.28 ng/mL in G3 (Table 6). Leptin is an adipocyte hormone that acts via hypothalamic signaling to regulate appetite and energy expenditure. However, obesity and OSA are associated with chronic hyperleptinaemia and leptin resistance, leading to reduced satiety, persistent sympathetic activation, endothelial dysfunction and chronic low-grade inflammation. Recurrent intermittent hypoxia activates hypoxia-inducible factor-1α (HIF-1α), nuclear factor-kappa B (NF-κB) and oxidative stress pathways, which induce leptin synthesis and contribute to cardiometabolic dysfunction. The improvement in nocturnal oxygenation after CPAP and reduction in adiposity and improved autonomic balance after lifestyle change and pranayama certainly contributed to the fall in circulating leptin concentrations. Our findings are consistent with those of Ryan and McNicholas [5], Muscogiuri et al. [9] and Lévy et al. [1] showing that obesity and OSA are associated with hyperleptinaemia and leptin resistance, whereas successful treatment of OSA and reduction in body weight significantly decrease circulating leptin levels and improve metabolic homeostasis.

The correlation study further indicated a strong link between AHI and leptin in G2 ($r = 0.57$, $p < 0.05$) and G3 ($r=0.64$, $p < 0.05$) although the correlation was modest in G1 ($r=0.27$) indicating that a higher OSA severity is associated with a higher leptin dysregulation. Among the biomarkers measured, adiponectin showed the greatest change after the intervention. Serum adiponectin was considerably elevated from 5.49±3.34 to 7.60±3.51 mg/L in G1, 4.33±3.05 to 7.12±2.39 mg/L in G2 and 4.64±2.59 to 7.49±2.42 mg/L in G3 (Table 6). Adiponectin is a powerful anti-inflammatory and insulin-sensitizing adipokine that activates AMP-activated protein kinase (AMPK) and peroxisome proliferator-activated receptor-α (PPAR-α), and promotes glucose uptake, fatty acid oxidation, endothelial nitric oxide synthesis, and mitochondrial function.

Obesity-associated visceral adiposity, intermittent hypoxia and oxidative stress inhibit adiponectin secretion and consequently promote insulin resistance, endothelial dysfunction and accelerated atherosclerosis. Our results are in agreement with Muscogiuri et al. [9] and Chen et al [23] who demonstrated that low adiponectin levels are strongly associated with obesity, insulin resistance, endothelial dysfunction and severity of OSA. A reduction of adiponectin levels has been related with improvements in insulin sensitivity, endothelial function and a reduction in cardiovascular risk after therapeutic intervention. In the present investigation, adiponectin was most associated with OSA severity, with significant negative associations with AHI in G1 ($r = -0.73$, $p < 0.01$), G2 ($r = -0.79$, $p < 0.05$) and G3 ($r = -0.82$, $p < 0.05$). The data are compatible with a progressive deterioration of

adipocyte endocrine function with worsening sleep-disordered breathing and support an important role for adiponectin as a mediator of the association between obesity, insulin resistance, and OSA. Serum ghrelin levels were also significantly reduced after intervention (30.19 ± 11.27 to 24.51 ± 7.48 pg/mL in G1, 30.36 ± 9.32 to 21.29 ± 5.98 pg/mL in G2, and 30.27 ± 9.72 to 18.15 ± 3.50 pg/mL in G3). Ghrelin is an orexigenic peptide hormone released predominantly by stomach endocrine cells that increases hunger by activating neuropeptide Y (NPY) and agouti-related peptide (AgRP) neurons in the hypothalamus.

Sleep deprivation and fragmented sleep associated with OSA increases release of ghrelin promoting excessive caloric intake and weight gain and metabolic dysfunction. With CPAP, normal sleep architecture was restored, as well as weight reduction and improved autonomic regulation after lifestyle modification and pranayama. This probably normalized appetite-regulating pathways and decreased circulating levels of ghrelin. Spiegel et al. [39] have shown similar results that sleep deprivation and fragmentation change the hormone that regulates hunger by increasing the release of ghrelin, decreasing leptin activity, and causing obesity and insulin resistance. However, AHI correlated weakly and non-significantly with ghrelin in G1 ($r = 0.31$), G2 ($r = 0.12$) and G3 ($r = 0.19$) . This suggests that ghrelin is influenced by various physiological factors such as nutritional status, circadian rhythm, gastric function, and energy balance, besides OSA severity. Serum IL-6 concentrations were significantly reduced from 7.93 ± 3.57 to 5.76 ± 1.73 pg/mL in G1, 8.60 ± 4.61 to 5.46 ± 2.29 pg/mL in G2, and 8.33 ± 4.20 to 4.07 ± 2.06 pg/mL in G3.IL-6 is an important pro-inflammatory cytokine secreted from adipocytes, macrophages, endothelial cells and activated immune cells.

Repeated episodes of intermittent hypoxia lead to activation of HIF-1α, NF-κB, reactive oxygen species (ROS), and NLRP3 inflammasome, leading in increased production of IL-6 and persistence of systemic inflammation, endothelial dysfunction, insulin resistance, and cardiovascular damage. CPAP reduces hypoxia caused inflammatory signaling, lifestyle adjustment reduces inflammatory adipose tissue load and pranayama controls sympathetic overactivity and oxidative stress, therefore creating additive anti-inflammatory benefits. Our results are in agreement with Yeghiazarians et al. [6] and Ryan and McNicholas [5] who showed that intermittent hypoxia is a major promoter of systemic inflammation by activating oxidative stress and inflammatory signaling pathways resulting in increased production of IL-6 and cardiometabolic dysfunction. These processes are in accordance with the finding that IL-6 was significantly positively correlated with AHI in G1 ($r = 0.59$, $p < 0.05$), G2 ($r = 0.65$, $p < 0.05$) and G3 ($r = 0.71$, $p < 0.05$), demonstrating that deteriorating systemic inflammation is closely associated with increased OSA severity.

Overall, as seen in Table 6, adipose tissue dysfunction and chronic inflammation are central to the etiology of OSA in obese patients with T2DM. Among the biomarkers tested, adiponectin was most strongly inversely associated with AHI ($r = -0.73$ to -0.82), and IL-6 was most positively associated with OSA severity ($r = 0.59$–0.71). Leptin was moderately positively correlated with illness severity, but ghrelin was relatively weakly associated. In general, our results are consistent with the findings reported by Lévy et al. [1], Ryan and McNicholas [5], Muscogiuri et al. [9] and Yeghiazarians et al. [6] who concluded that intermittent hypoxia-induced dysregulation of adipokines and chronic inflammation are key mechanisms linking obesity, insulin resistance, T2DM and OSA. Our results also suggest that CPAP, especially when combined with lifestyle modification or pranayama, not only resolves upper-airway obstruction but also restores adipokine homeostasis, reduces systemic inflammation, improves insulin sensitivity and may eventually decrease long-term cardiometabolic risk.

Conclusion: The present study demonstrated that 6 months of continuous positive airway pressure (CPAP) therapy significantly improved sleep architecture, anthropometric indices, glycaemic control, insulin resistance, lipid metabolism, adipokine homeostasis and systemic inflammation in obese adults with type 2 diabetes mellitus (T2DM) and obstructive sleep apnoea (OSA). Interestingly, CPAP combined with structured lifestyle modification or pranayama led to substantially greater cardiometabolic benefits than CPAP alone, with the CPAP plus pranayama group showing consistently the most favourable improvements across polysomnographic, metabolic, inflammatory, and adipokine parameters. These data support the concept that successful management of OSA requires interventions that simultaneously address upper-airway obstruction, obesity-related mechanical loading, autonomic imbalance, metabolic derangement and chronic low-grade inflammation.

A major strength and novel contribution of the present study is the comprehensive integration of polysomnographic, anthropometric, metabolic, inflammatory and adipokine biomarkers in a single prospective interventional setting. Unlike previous studies that primarily assessed CPAP-related alterations in isolated clinical or biochemical parameters, this study examined the correlations

between the apnea-hypopnea index (AHI), insulin resistance, lipid abnormalities, leptin, adiponectin, ghrelin and interleukin-6 concurrently. The significant positive correlations of AHI with leptin, IL-6, HbA1c, fasting insulin and HOMA-IR and the significant inverse correlation of AHI with adiponectin support the idea that adipose tissue dysfunction and chronic inflammation induced by intermittent hypoxia are central mechanisms linking obesity, T2DM and OSA.

Another important finding is the demonstration of additive improvements with adjunctive pranayama beyond conventional CPAP therapy especially in adipokine regulation, inflammatory status, insulin sensitivity and sleep quality. These observations suggest that autonomic modulation through controlled breathing exercises may be a practical and inexpensive complementary strategy that can enhance the metabolic and anti-inflammatory effects of CPAP. Thus, this multidisciplinary therapeutic approach may improve long-term treatment outcomes and potentially reduce future cardiovascular and metabolic complications in patients with obesity-associated OSA.

Taken together, the current evidence supports a paradigm shift from symptom-based management of OSA to a holistic cardiometabolic approach that combines CPAP with specific lifestyle modifications and structured breathing exercises to optimize the amelioration of sleep physiology, metabolic health, systemic inflammation and cardiovascular risk.

Limitations: The study was single-centre, with a relatively small sample size and 6-month follow-up, which may limit the generalizability of the findings. Separate groups for lifestyle modification and pranayama were not available to evaluate their individual effects. The findings require validation in larger multicentre studies with longer follow-up.

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