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Disproportionate Improvement in Obstructive Sleep Apnea Relative to Weight Loss Following Tirzepatide Therapy: A Case Report

Authors: Dr. Abdul Wahid[1], Dr. Amna Tabassum[1] *, Dr. Shahid Khan[1], Dr. Ayesha Mehboob[1], Dr. Muhammad Bilawal Abbas Janjua[2] Dr. Tooba Khalil[1]

[1] *Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan*

[2] *Dr. Abdul Qadeer Khan Hospital, Kahuta Research Laboratories, Islamabad, Pakistan*

***Corresponding Author: Dr. Amna Tabassum**

Email: amnatabassum99@gmail.com

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Abstract

Obstructive sleep apnea (OSA) is a highly prevalent disorder with obesity which is its single most important modifiable factor. Tirzepatide, a dual agonist at glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptors. It has shown remarkable metabolic efficacy across many randomized trials. Whether its beneficial effects on sleep-disordered breathing work through mechanisms beyond total body weight reduction remains an active and clinically critical question. An equally important factor that is overlooked at times is considering the need to exclude thyroid dysfunction, particularly hypothyroidism which is an independent and treatable driver of obesity and OSA. It must be ruled out before attributing clinical outcomes to pharmacotherapy.

We present a 46-year-old male journalist carrying a multimorbidity profile that included morbid obesity (initial weight 136 kg, BMI 44.1 kg/m^2), poorly controlled type 2 diabetes mellitus (HbA1c 8.5%), hypertension, post-traumatic stress disorder, lumbar disc degeneration, and newly diagnosed severe OSA (Apnoea-Hypopnoea Index [AHI] 38.3 events/hour; nadir SpO_2 57%). After Ruling out both hypothyroidism and tirzepatide was started at 2.5 mg weekly and titrated to 5.0 mg weekly. It was maintained over approximately 19 weeks and 4 days with full adherence. The patient achieved a 14 kg weight reduction (10.4% total body weight loss) while reporting a clinically disproportionate improvement in OSA symptoms, near-resolution of habitual snoring without continuous positive airway pressure (CPAP) therapy. Adverse effects were self-resolving episodes of nausea and diarrhea.

This case supports the hypothesis that tirzepatide have beneficial effects on upper-airway physiology through multiple mechanisms that extend beyond the simple fat-mass reduction. Possibly including selective reduction of pharyngeal adipose tissue, direct incretin-mediated anti-inflammatory actions, and neurohumoral modulation of airway collapsibility. The confirmed euthyroid state eliminates thyroid disease as a confounding variable and enhance the causal attribution of observed improvements to tirzepatide. Such mechanistic implications have to be validated in prospective studies with objective polysomnographic re-assessments.

Keywords: Tirzepatide, Obstructive sleep apnea, GIP/GLP-1 receptor agonist, Obesity, Weight loss, Case Report

Table 1. List of Abbreviations

Abbreviation	Full Term
AHI	Apnea-Hypo-apnea Index
APAP	Auto-titrating Positive Airway Pressure
AASM	American Academy of Sleep Medicine
BMI	Body Mass Index
CARE	CAse REport Guidelines
CAI	Central Apnea Index
CPAP	Continuous Positive Airway Pressure
CRP	C-Reactive Protein
ECG	Electrocardiogram
ECLIA	Electrochemiluminescence Immunoassay
EF	Ejection Fraction
EPR	Expiratory Pressure Relief
GIP	Glucose-dependent Insulinotropic Polypeptide
GLP-1	Glucagon-Like Peptide-1
HbA1c	Glycosylated Hemoglobin
IgE	Immunoglobulin E
LVH	Left Ventricular Hypertrophy
MCV	Mean Corpuscular Volume
OAI	Obstructive Apnea Index
OSA	Obstructive Sleep Apnea
OSCAR	Open-Source CPAP Analysis Reporter
PTSD	Post-Traumatic Stress Disorder
REI	Respiratory Event Index
SGLT-2	Sodium-Glucose Co-Transporter-2
SpO_2	Peripheral Oxygen Saturation
T3	Triiodothyronine
T4	Thyroxine
TIB	Time In Bed
TSH	Thyroid-Stimulating Hormone

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1. Introduction:

Obstructive sleep apnea ranks among the most burdensome chronic respiratory conditions of the modern time, with reliable estimates say that it affects about 936 million people around the world, with varying levels of severity.[1] OSA is defined as a failure of the upper airway to preserve structural patency during sleep. This is due to adipose deposition in pharyngeal and peri-pharyngeal soft tissues, exacerbated by central adiposity-related decreases in functional residual capacity, resulting in recurrent cycles of partial or complete airway collapse. [2] The downstream consequences affect the cardiovascular, metabolic, and neurocognitive systems, and they add up to make life expectancy shorter for people who don't receive treatment. [3]According to the American Academy of Sleep Medicine (AASM), weight-centric management, whether through lifestyle changes, medication, or bariatric surgery, is an important part of treating OSA.[4]

Clinicians must first exclude secondary endocrine causes of obesity before attributing weight-related OSA to primary nutritional excess that independently worsen sleep-disordered breathing. Primary hypothyroidism is the most clinically important of these: it promotes weight gain through a reduction in basal metabolic rate, induces myxoedematous infiltration of pharyngeal soft tissues, impairs hypoglossal nerve function, and blunts the hypercapnic ventilatory drive each mechanism independently capable of precipitating or amplifying OSA. [5] Subclinical hypothyroidism, which may be present in up to one quarter of individuals with obesity, occupies a grey zone in which TSH is elevated but thyroid hormones remain apparently normal, yet metabolic and airway consequences can still accumulate. [6] At the opposite end of the spectrum, hyperthyroidism also carries its own confounding potential through sleep disruption, adrenergic hyperactivation, and weight loss that can artefactually alter metabolic indices. So, systematic thyroid evaluation is not merely a formality but a scientific necessity for achieving mechanistic clarity in any analysis of obesity; OSA cases.

Tirzepatide (Mounjaro®/Zepbound®) is a first-in-class, once-weekly subcutaneous dual agonist at GIP and GLP-1 receptors. Across the SURMOUNT programme, it has delivered weight reductions of up to 22.5% of total body weight at the 15 mg dose a magnitude that is greater than any other anti-obesity drug therapy.[7] The SURMOUNT-OSA trial, published in the New England Journal of Medicine in 2024, took the critical step of directly evaluating tirzepatide's effects on OSA severity as a primary endpoint and demonstrated reductions in AHI of 27–30 events/hour at 52 weeks that exceeded what regression nomograms for weight-dependent AHI improvement would predict. It pointed toward weight-independent incretin-mediated mechanisms. [8]

We report a 46-year-old euthyroid male with objectively severe OSA who showed a clinically striking and apparently disproportionate symptomatic improvement following approximately 19 weeks and 4 days of tirzepatide therapy at a modest dose of 5 mg weekly. His confirmed euthyroid, thyroid profile eliminates the single most important secondary endocrine confounder, allowing the observed outcomes to be attributed to tirzepatide with much greater confidence.

2. Case presentation

A 46-year-old male journalist and father of three children came to outpatient with a week history of progressive exertional dyspnea with productive cough and undocumented mild fever,

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snoring and excessive day time somnolence. The consultation revealed a collection of long-standing comorbidities and sleep-related symptoms that collectively gave the picture of a man whose metabolic health had been silently deteriorating for over a decade.

2.1 Demographic and Anthropometric Profile

Table 2 summarizes the patient's important demographic and anthropometric data that was collected over a series of clinical visits. As shown in Table *2*, his weight at the time of the diagnostic sleep study was 132 kg, with a BMI of 44.1 kg/m² (Class III obesity), and his neck circumference of 19 inches (48.3 cm) placed him well above the 17-inch threshold beyond which OSA risk increases substantially.

Table 2. Demographic and Anthropometric Profile

Parameter	Value
Age	46 years
Sex	Male
Occupation	Journalist
Height	173 cm (5’7”)
Weight at initial presentation	136 kg
Weight at sleep study (18/11/2025)	132 kg
Weight at tirzepatide initiation (27/11/2025)	135 kg
Weight at follow-up (13/04/2026)	121 kg
BMI at sleep study	44.1 kg/m² (Class III Obesity)
Neck circumference	19 inches (48.3 cm)
Waist circumference	64 inches
Waist-Hip ratio	1.02

3. Clinical Findings

3.1 History of Present Illness

The patient’s presentation with worsening exertional breathlessness with productive cough prompted a thorough pulmonological and metabolic workup that unveiled far more than the index respiratory complaint. An examination of his sleep history disclosed a pattern of longstanding loud habitual snoring witnessed every night by his family members, episodes of observed apnea, non-restorative and disrupted sleep, morning headaches, and excessive daytime somnolence. When looked at along with his neck circumference and body shape, this group of symptoms had a high chance of clinically significant OSA before the test. He had been using alprazolam 0.5 mg three times daily (half a tablet in the morning, half in the afternoon, and a

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full tablet at night) to manage sleep initiation difficulties in the setting of his longstanding PTSD a pharmacological choice with the side-effect of reducing upper-airway muscle tone and potentially worsening sleep-disordered breathing [4].

Importantly, there were no indications or manifestations of thyroid dysfunction observed during the clinical evaluation. The patient denied cold intolerance, constipation, unexplained weight gain, periorbital puffiness, voice hoarseness, hair thinning, or slowness of cognition (features that would prompt suspicion of hypothyroidism). Equally, he did not complain of heat intolerance, palpitations, tremors, ophthalmopathy, or unexplained weight loss (features pointing toward hyperthyroidism).

3.2 Past Medical History

The burden of comorbidity is substantial and clinically interrelated in the patient, that showed years of uncontrolled accumulation of metabolic risk.

- **Type 2 Diabetes Mellitus** (diagnosed in 2011, 15 years ago from the current presentation): Managed on metformin, vildagliptin, and empagliflozin. HbA1c was 8.5% at the index visit and improved to 7.6% by February 2026 following tirzepatide initiation.
- **Hypertension** (10-year duration): Drug regimen comprised of telmisartan and diltiazem
- **Post-Traumatic Stress Disorder, Class 3** (8+ years, following a gunshot wound 10 years ago and subsequent exploratory laparotomy): On sertraline (long-term) and alprazolam 0.5 mg three times daily.
- **Lumbar Disc Degeneration at L4–L5**): On pregabalin 100 mg twice daily.
- **Severe Obstructive Sleep Apnea** (newly diagnosed at this presentation): AHI/REI 38.3 events/hour.
- **Additional history:** Incisional hernia (mesh-repaired, no active complications); two COVID-19 episodes (full recovery); multiple severe herpes zoster re-activation involving genitalia and oral mucosa (resolved after antiviral therapy).

Family history is notable for paternal death from ischemic heart disease and paternal type 2 diabetes mellitus. These together conferred a substantive heritable cardiovascular and metabolic risk burden. There is no known family history of thyroid disease or autoimmune endocrinopathy.

3.3 Presenting Complaints and Physical Examination Context

The presenting triad comprised: (1) exertional dyspnea (2) morbid obesity with severely curtailed exercise tolerance; and (3) a symptom profile highly consistent with moderate-to-severe OSA. There was no abdominal pain, hematuria, dysuria, constipation, diarrhea, or active cutaneous infection. The patient denied chronic corticosteroid use and had no history of substance misuse. His socioeconomic circumstances were stable, with homeownership, adequate residential ventilation, and access to a filtered water supply.

4. Diagnostic Assessment

4.1 Thyroid Function Assessment: Confirmation of Euthyroidism

Due to this patient's Class III obesity, dyslipidemia, diastolic dysfunction, and multisystem metabolic dysregulation, a formal

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assessment of thyroid function was required to rule out endocrine factors influencing his clinical presentation. The thyroid panel was measured by electrochemiluminescence immunoassay (ECLIA) which is the contemporary gold-standard platform for thyroid hormone quantification it showed the following results: Total T3 1.01 ng/mL (reference range 0.94–2.41 ng/mL), Total T4 6.94 µg/dL (reference range 5.10–14.06 µg/dL), and TSH 3.52 uIU/mL (reference range 0.6–8.84 uIU/mL). All three analytes fell within their respective reference intervals, establishing clinical and biochemical euthyroidism.

4.2 Respiratory Investigations

Chest X-ray on demonstrated air-space opacification in the right lower zone with bilateral reticulonodular markings in the lower zones and minimal right hemidiaphragm elevation, interpreted as lower respiratory tract infection. A repeat film showed coarsened broncho-vascular markings without consolidation, collapse, or pneumothorax, consistent with resolving viral pneumonia. The ECG recorded on the same day showed sinus rhythm at 85 bpm with normal intervals and segments and no pathological Q-waves.

4.3 Echocardiography

Echocardiography revealed mild left ventricular hypertrophy, Grade I diastolic dysfunction, and a preserved ejection fraction of 65%. Regional wall motion was normal. Beyond physiological tricuspid regurgitation, no valvular pathology was identified. A small pericardial effusion and epicardial fat of normal thickness were noted. These findings are consistent with the early subclinical myocardial remodeling that accumulates in the setting of sustained hypertension and metabolic syndrome.

4.4 Hematological and Biochemical Profile

Serial full blood counts demonstrated a stable pattern of microcytic hypochromic anemia (MCV 76–79fl; reference range: 80-95fl; MCH 25pg; reference range 27-31pg; MCHC 31–33 g/dl; reference range 32-36 g/dL; hemoglobin 14.1–14.9 g/dl; reference range 14-18 g/dL). During an acute febrile illness few months from current presentation, leukocytosis (11,300/mm³); reference range 4000-11,000/mm³) with neutrophilia and lymphopenia was documented. That normalized to 8,690/mm³ consistent with infective resolution.

The lipid profile from six months ago was striking: total cholesterol 299 mg/dL (<200 is desirable, 200-239 is borderline and >240 is high risk), LDL 163 mg/dL (130 is desirable, 130-159 is borderline and >160 is high risk) , VLDL 95 mg/dL (<30 is desirable), triglycerides 535 mg/dL (< 150 is desirable, 150-199 is borderline and 200-499 high risk and >500 very high risk) and a cholesterol/HDL ratio of 7.2 (<4.97 is desirable). CRP at 47 mg/L confirmed the acute inflammatory state. Elevated GGT (115 U/L; reference range ,55U/L) and ALT (54 U/L; reference range 5-55U/L) are consistent with metabolic-associated steatotic liver disease.

4.5 Diagnostic Sleep Study (18/11/2025)

The baseline respiratory sleep study represents the cornerstone diagnostic document of this case. Table 3 summarizes the key polysomnographic parameters. As shown in Table *3*, the AHI/REI of 38.3 events/hour placed the patient firmly in the severe OSA category per AASM criteria (threshold ≥30 events/hour), with a nadir SpO_2 of 57% reflecting clinically dangerous nocturnal hypoxemia. The highly elevated desaturation index of 65.1/hour and the finding that SpO_2 fell below 90% for nearly a quarter of time during sleep are independently associated with adverse cardiovascular outcomes. [9]

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Table 3. Diagnostic Sleep Study Parameters

Parameter	Value	Clinical Interpretation
AHI / REI	38.3 events/hour	Severe OSA (AASM: ≥30 = severe)
Obstructive Apnoea Index	7.4 events/hour	Significant obstructive component
Central Apnoea Index	11.0 events/hour	Elevated central component
Total Apneas + Hypo-apneas	238 events	Over 372.5 minutes monitoring
Hypo-apnea Index	19.2 events/hour	119 total hypo-apneas
Lowest SpO_2 (nadir)	57%	Severe nocturnal hypoxemia
Mean SpO_2 during sleep	90%	Below recommended ≥92%
Time SpO_2 <90%	23.2% of TIB	Clinically significant burden
Time SpO_2 <85%	12.1% of TIB	Moderate-severe burden
Desaturation Index	65.1/hour	Very high desaturation frequency
Total Snoring Episodes	784	25.4% of monitoring time
Supine AHI	45.0 events/hour	Position-dependent worsening
Left-side AHI	40.1 events/hour	Persistent severity off-supine

4.6 CPAP Titration Study (21/11/2025)

Auto-CPAP titration (A-Flex; mean pressure 7.7 cm H_2O; 90th-percentile pressure 9.1 cm H_2O) over 8 hours 59 minutes achieved an AHI of 2.3 events/hour with complete snoring elimination, confirming outstanding CPAP responsiveness.

4.7 OSCAR CPAP Compliance Data (April 2026)

OSCAR data from the (APAP mode, EPR 2 cm H_2O) showed that during use, AHI was well controlled and reaching a nadir of 0.76 events/hour. However, device usage was not regular during the follow-up window, and the patient volunteered that he was increasingly tolerating nights without the device without experiencing the florid symptomatic recurrence he would have expected at baseline. He attributed this tolerability directly to his improvement on tirzepatide.

4.8 Continuous Pulse Oximetry Monitoring

Longitudinal SpO_2 monitoring between February and April 2026 showed a progressive trend toward fewer severe desaturation events. Nadir values of 74–80% were recorded during February-March 2026, whereas later readings from April 2026 demonstrated more sustained saturations in the 90–98% range with fewer excursions below 85%. Even though they were made by recording at different times rather than all the time, these trends are in line with real improvements in how quickly oxygen moves through the body at night during the treatment period.

5. Therapeutic Intervention

5.1 Acute Respiratory Illness

The clinical triad, mild fever, elevated CRP, and radiological findings led to the clinical diagnosis of viral pneumonia in the acute presentation. Appropriate antiviral and supportive treatment were administered; full symptomatic resolution followed.

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5.2 Tirzepatide Initiation and Titration

After clinical stabilization and in the context of a structured plan to address his multimorbidity, particularly obesity and its downstream metabolic and respiratory consequences; tirzepatide was started at 2.5 mg weekly subcutaneous injection on 27/11/2025. The dose was escalated to 5.0 mg weekly after four weeks and maintained at that level for the remainder of the 19-week 4-day observational window. Table *4* details the complete dosing chronology. As shown in Table 4, the patient completed 20 documented doses with 100% adherence. The only adverse effects were single, self-limiting episodes of nausea and diarrhea, each graded 3/5 in severity and managed conservatively.

Table 4. Tirzepatide Dosing Chronology

Dose Period	Formulation	Dose	Duration
27/11/2025 – 25/12/2025	Tirzepatide	2.5 mg weekly	28 days
25/12/2025 – 01/01/2026	Tirzepatide	5.0 mg weekly	7 days
01/01/2026 – 09/04/2026	Mounjaro® / Zepbound®	5.0 mg weekly	~14 weeks
09/04/2026 – 13/04/2026	Zepbound®	5.0 mg weekly	4 days

6. Follow-Up and Outcomes

6.1 Weight and Metabolic Outcomes

Table 5 presents the patient's metabolic course from baseline to the April 2026 follow-up. As shown in Table 5, a 14 kg reduction in body weight (10.4% total body weight loss) was gained at an average rate of 0.7 kg/week, accompanied by a 0.9 percentage-point improvement in HbA1c. Physical activity remained minimal throughout (four sessions totaling 150 minutes over 19 weeks).

Table 5. Metabolic Outcomes at Follow-Up

Parameter	Baseline	Follow-Up	Net Change
Body weight	135.0 kg	121.0 kg	−14.0 kg (−10.4%)
Weekly weight loss	—	—	−0.7 kg/week
HbA1c	8.5%	7.6% (20/02/2026)	−0.9 percentage points
BMI	44.1 kg/m²	Clinically improved	—
Thyroid status	Euthyroid (confirmed)	Stable	No change anticipated
Adverse effects	—	Nausea ×1; Diarrhea ×1	Mild, self-limiting
Medication adherence	—	100% (20 doses)	Exemplary

6.2 OSA-Related Symptomatic Outcomes

The patient himself described a qualitative transformation in his sleep: he was waking more refreshed; his daytime somnolence had lifted substantially. As well as, he no longer felt compelled to use CPAP on every night. The

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independent verification of these changes by his family holds considerable clinical significance, as it mitigates the risk of self-reporting bias.

OSCAR data confirmed that on nights of device use, AHI was effectively suppressed. Yet the patient's increasing tolerance of device-free nights without the expected florid symptomatic recurrence from a baseline AHI of 38.3 events/hour is, in itself. It is a clinically meaningful observation consistent with biological disease amelioration, though it cannot substitute for formal polysomnographic re-evaluation. No repeat off-CPAP sleep study was performed during this window, which constitutes the principal objective limitation of this case report.

7. Discussion

This case is of clinical and scientific interest as it represents a combination of disproportionate symptomatic OSA improvement despite only 10.4% total body weight loss, and clear evidence that thyroid dysfunction was not a contributor to obesity or sleep-disordered breathing, providing a relatively clean model to study tirzepatide's biological effects.

Defining the euthyroid state of the patient has many considerable implications. Overt hypothyroidism affects approximately 1–2% of the adult population but may be substantially overrepresented among individuals with obesity, particularly those carrying autoimmune risk. [10] In hypothyroid states, weight gain is driven by reduced basal metabolic rate, impaired lipolysis, and sodium and water retention; pharyngeal soft tissues may accumulate myxoedematous deposits that narrow the upper-airway lumen independently of general adiposity; and both hypercapnic and hypoxic ventilatory responses are blunted, further predisposing to sleep-disordered breathing [5,11]. If this patient had subclinical hypothyroidism, which is defined as a TSH level above 4.5–5.0 mIU/L with normal thyroid hormone levels, part of his obesity and OSA severity would have needed to be linked to the thyroid axis instead of primary adiposity. The TSH level of 3.52 uIU/mL is not just "normal at the boundary"; it is clearly in the middle of the normal range, which rules out this possibility. [6,12]

Hyperthyroidism, while less commonly associated with obesity, carries its own confounding role in OSA-metabolic analyses. Thyrotoxicosis can produce sleep disruption, tachyarrhythmias, and adrenergic hyperactivation that distort both sleep pattern and metabolic parameters; If hyperthyroidism goes undetected, it could make the apparent pharmacological effect of an anti-obesity drug on weight change seem bigger than it really is. [12,13] The entirely normal Total T4 and TSH values in this patient exclude both overt and subclinical hyperthyroidism. A note on methodology: the panel measured Total rather than Free T3 and T4, which include both protein-bound and biologically active fractions. In clinical practice, the AASM-endorsed and American Thyroid Association–endorsed position holds that a normal TSH the most sensitive index of hypothalamo-pituitary-thyroid axis function in combination with normal total thyroid hormone levels constitutes complete exclusion of thyroid dysfunction in a symptomatic evaluation. [12,13]

The euthyroid baseline further ensures that none of these improvements can be attributed to resolution of hypothyroid-driven pharyngeal mucosal congestion or blunted ventilatory drive. This consolidated tirzepatide as the primary operative agent. [10,13] Thus this endocrine clarity is not incidental; it is foundational to the mechanistic argument presented in this report.

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There are three lines of evidence that all point to the same conclusion: that tirzepatide works on the upper airway without affecting weight. First, incretin-based therapies do not reduce fat diffusely in the same pattern as caloric restriction alone. Imaging studies of GLP-1 receptor agonist-treated individuals have consistently demonstrated preferential reduction in visceral and ectopic adipose depots including tongue base, retropalatal space, and peri collarbone fat that are anatomically disproportionate to overall body weight metrics and directly relevant to upper-airway collapsibility. [14] A 10.4% total weight reduction may therefore represent a substantially greater fractional reduction in the pharyngeal fat compartments that most directly govern airway patency.

Second, GLP-1 receptor agonism carries direct anti-inflammatory properties that operate independently of weight. GLP-1 receptors are expressed in airway smooth muscle, pulmonary vasculature, and brainstem respiratory control centers. [15] Tirzepatide's dual incretin engagement may reduce mucosal oedema, attenuate the pro-inflammatory microenvironment of the upper airway, and modulate hypoglossal motor neuron activity in ways that improve airway tone during sleep. The partial normalization of the patient's IgE (from 1,094 to 769 IU/mL) over the treatment period raises the additional possibility that tirzepatide's anti-inflammatory reach may extend into the atopic immune axis, though this remains speculative. [16]

Third, the metabolic improvements themselves are not immunologically or mechanistically inert with respect to OSA. Glycemic improvement, HbA1c declining from 8.5% to 7.6%, reduces advanced glycation end-product accumulation in connective tissue, improving structural compliance and neuromuscular function of pharyngeal dilator muscles. [17] The concurrent empagliflozin therapy offers additive benefit through its natriuretic, cardioprotective, and anti-inflammatory mechanisms. It potentially contributed to the favorable cardiac and respiratory phenotype documented at follow-up. [18]

The SURMOUNT-OSA trial remains the definitive randomized evidence base for tirzepatide in OSA. [8] At doses of 10–15 mg over 52 weeks, AHI reductions of 27–30 events/hour were observed, exceeding weight-prediction nomograms and supporting weight-independent mechanisms. Our patient, at a lower 5 mg dose over only 19 weeks, demonstrated symptomatic rather than polysomnography confirmed improvement. This spectrum of effect was consistent with an earlier-phase, dose-limited pharmacological response.[19] The absence of repeat objective polysomnography without CPAP remains the central limitation of this report and must be addressed before any conclusion regarding true AHI modification can be drawn.

The significance of this case report persists alongside the SURMOUNT-OSA trial for several complementary reasons. First, the SURMOUNT-OSA trial enrolled patients receiving tirzepatide at 10–15 mg for 52 weeks; our patient received only 5 mg over 19 weeks, establishing that clinically meaningful symptomatic benefit may be demonstrable at substantially lower doses and shorter treatment durations than those studied in the landmark trial. Second, randomized controlled trials inherently exclude patients with complex multimorbidity profiles—this patient's concurrent PTSD, chronic benzodiazepine use, empagliflozin co-administration, prior COVID-19 illness, and metabolic-associated steatotic liver disease are precisely the co-morbid phenotypes that generalize drug effects to real clinical populations. Third, the SURMOUNT-OSA trial did not systematically mandate thyroid function screening before enrolment; our case provides a framework for how confirmatory thyroid assessment strengthens mechanistic attribution by eliminating the single most

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clinically relevant endocrine confounder. Fourth, case reports documenting treatment effects at submaximal doses in patients with pharmacologically unfavorable backgrounds—such as concomitant benzodiazepine use that predictably worsens OSA—add ecological validity that complements trial-derived estimates and expands the evidence base across the full spectrum of clinical practice.

The patient's psychosocial complexity warrants recognition as both a confounding factor and a dysfunctional internal control. Chronic benzodiazepine use (alprazolam) is recognized by the AASM as a class of medication that predictably worsens OSA by reducing upper-airway dilator muscle tone. [4] That OSA symptoms improved meaningfully despite ongoing alprazolam use not only argues against pharmacological confounding by medication changes but actually represents a pharmacologically unfavorable background against which tirzepatide's could provide benefit, lending the observation additional biological credibility. [20]

Going back to the thyroid dimension, the mechanistic importance of ruling out hypothyroidism goes beyond just making sure the diagnosis is complete. In hypothyroid-associated OSA, the primary treatment is thyroid hormone replacement, which can substantially improve AHI independent of weight change. [5] If subclinical hypothyroidism had existed and remained untreated, any observed improvement in OSA would necessitate attribution to the thyroid axis rather than to tirzepatide. The mid-normal TSH of 3.52 uIU/mL, combined with normal total T3 and T4, excludes this alternative explanation entirely. [12,13]

8. Conclusion

We describe a 46-year-old euthyroid male with severe, objectively confirmed obstructive sleep apnea (AHI/REI 38.3 events/hour; nadir SpO_2 57%), morbid obesity, type 2 diabetes mellitus, hypertension, PTSD, and lumbar disc degeneration, who experienced near-resolution of OSA-related snoring and marked improvement in sleep quality following 19 weeks and 4 days of tirzepatide at 5 mg weekly with only a 10.4% total body weight reduction. Formal ECLIA-based thyroid assessment confirmed complete euthyroidism, excluding both hypothyroidism and hyperthyroidism as contributors to the patient's clinical phenotype and as alternative explanations for the observed improvements. The symptomatic improvement was disproportionate to the observed weight loss, consistent with the hypothesis that tirzepatide's dual incretin pharmacology involves upper-airway physiology through pathways that act alongside, and beyond, systemic fat reduction.

Patient Perspective

The patient has been fully informed of this case report and has provided written informed consent for its preparation and submission. He describes a genuine and meaningful improvement in quality of life since beginning tirzepatide, particularly in the texture of his sleep, his energy on waking, and the near-disappearance of snoring that had previously disrupted his household for years. He is honest that the weight he has lost, while satisfying, does not in his own mind explain all of the changes in his symptoms. He remains committed both to continuing therapy and to undergoing the planned repeat sleep evaluation.

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Informed Consent

Written informed consent was obtained from the patient for the preparation, publication, and dissemination of this case report, inclusive of all de-identified clinical data and investigation results. A copy of the signed consent form is available to journal editors upon request.

Conflicts of Interest

The authors declare no conflicts of interest. Tirzepatide (Mounjaro®/Zepbound®) was prescribed as part of routine clinical care. No pharmaceutical industry funding, sponsorship, or material support of any kind was received in relation with this report.

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Ethics Statement

This report was prepared in accordance with the ethical principles of the Declaration of Helsinki (2013 revision). Single de-identified clinical case reports do not require formal institutional ethics committee approval at the authors' institution; however, written patient consent was obtained as detailed above.

References

1. Benjafield AV, Ayas NT, Eastwood PR, Heinzer R, Ip MSM, Morrell MJ, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med. 2019 Aug;7(8):687–98. doi:10.1016/S2213-2600(19)30198-5

2. Messineo L, Bakker JP, Cronin J, Yee J, White DP. Obstructive sleep apnea and obesity: A review of epidemiology, pathophysiology and the effect of weight-loss treatments. Sleep Med Rev. 2024 Dec;78:101996. doi:10.1016/j.smrv.2024.101996

3. McNicholas WT, Korkalainen H. Translation of obstructive sleep apnea pathophysiology and phenotypes to personalized treatment: a narrative review. Front Neurol. 2023 Aug 24;14:1239016. doi:10.3389/fneur.2023.1239016

4. Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K, et al. Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med. 2017 Mar 15;13(3):479–504. doi:10.5664/jcsm.6506

5. Green ME, Bernet V, Cheung J. Thyroid Dysfunction and Sleep Disorders. Front Endocrinol. 2021 Aug 24;12:725829. doi:10.3389/fendo.2021.725829

6. Lu N, Chen B, Liu P, Wang C, Lu Z, Li S. Causal association between hypothyroidism and obstructive sleep apnea: A bidirectional 2-sample Mendelian Randomization study. Medicine. 2024 Oct 18;103(42):e40114. doi:10.1097/MD.0000000000040114

7. Jastreboff AM, Aronne LJ, Ahmad NN, Wharton S, Connery L, Alves B, et al. Tirzepatide Once Weekly for the Treatment of Obesity. N Engl J Med. 2022 Jul 21;387(3):205–16. doi:10.1056/NEJMoa2206038

8. Malhotra A, Bednarik J, Chakladar S, Dunn JP, Weaver T, Grunstein R, et al. Tirzepatide for the Treatment of Obstructive Sleep Apnea: Rationale, Design, and Sample Baseline Characteristics of the SURMOUNT -OSA Phase 3 Trial [Internet]. SSRN; 2024 [cited 2026 Apr 16]. Available from: https://www.ssrn.com/abstract=4710000 doi:10.2139/ssrn.4710000

9. Gottlieb DJ, Punjabi NM. Diagnosis and Management of Obstructive Sleep Apnea: A Review. JAMA. 2020 Apr 14;323(14):1389. doi:10.1001/jama.2020.3514

10. Zhao M, Huang X, Zheng H, Cai Y, Han W, Wang Y, et al. Association between hypothyroidism and obstructive sleep apnea: a bidirectional Mendelian randomization study combined with the geo database. Front Neurol. 2024 Dec 10;15:1420391. doi:10.3389/fneur.2024.1420391

11. Dragonieri S, Portacci A, Quaranta VN, Carratu P, Lazar Z, Carpagnano GE, et al. Therapeutic Potential of Glucagon-like Peptide-1 Receptor Agonists in Obstructive Sleep Apnea Syndrome Management: Diseases. 2024 Sep 23;12(9):224. doi:10.3390/diseases12090224

12. Jonklaas J, Bianco AC, Bauer AJ, Burman KD, Cappola AR, Celi FS, et al. Guidelines for the Treatment of Hypothyroidism: Prepared by the American Thyroid Association Task Force on Thyroid Hormone Replacement. Thyroid®. 2014 Dec;24(12):1670–751. doi:10.1089/thy.2014.0028

13. Ross DS, Burch HB, Cooper DS, Greenlee MC, Laurberg P, Maia AL, et al. 2016 American Thyroid Association Guidelines for Diagnosis and Management of Hyperthyroidism and Other Causes of Thyrotoxicosis. Thyroid®. 2016 Oct;26(10):1343–421. doi:10.1089/thy.2016.0229

14. Rubino DM, Greenway FL, Khalid U, O'Neil PM, Rosenstock J, Sørrig R, et al. Effect of Weekly Subcutaneous Semaglutide vs Daily Liraglutide on Body Weight in Adults With Overweight or Obesity Without Diabetes: The STEP 8 Randomized Clinical Trial. JAMA. 2022 Jan 11;327(2):138–50. doi:10.1001/jama.2021.23619 PubMed PMID: 35015037; PubMed Central PMCID: PMC8753508.

15. Qian B, Huang Y, Yan C, Feng S, She D. Effect of Glucagon-Like Peptide 1 Receptor Agonists on Obstructive Sleep Apnea. Obes Sci Pract. 2025 Aug;11(4):e70090. doi:10.1002/osp4.70090

16. Li M, Lin H, Yang Q, Zhang X, Zhou Q, Shi J, et al. Glucagon-like peptide-1 receptor agonists for the treatment of obstructive sleep apnea: a meta-analysis. SLEEP. 2025 Apr 11;48(4):zsae280. doi:10.1093/sleep/zsae280

17. Reutrakul S, Mokhlesi B. Obstructive Sleep Apnea and Diabetes. Chest. 2017 Nov;152(5):1070–86. doi:10.1016/j.chest.2017.05.009

18. Zinman B, Wanner C, Lachin JM, Fitchett D, Bluhmki E, Hantel S, et al. Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes. N Engl J Med. 2015 Nov 26;373(22):2117–28. doi:10.1056/NEJMoa1504720

19. Frías JP, Davies MJ, Rosenstock J, Pérez Manghi FC, Fernández Landó L, Bergman BK, et al. Tirzepatide versus Semaglutide Once Weekly in Patients with Type 2 Diabetes. N Engl J Med. 2021 Aug 5;385(6):503–15. doi:10.1056/NEJMoa2107519

20. Trzepizur W, Blanchard M, Ganem T, Balusson F, Feuilloy M, Girault JM, et al. Sleep Apnea–Specific Hypoxic Burden, Symptom Subtypes, and Risk of Cardiovascular Events and All-Cause Mortality. Am J Respir Crit Care Med 2022 Jan 1;205(1):108–17. doi:10.1164/rccm.202105-1274OC