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The Spectrum of Endocrine Disorders in Patient Presented with Obstructive Sleep Apnea. A Cross-Sectional Study in Tertiary Care Hospital

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ABSTRACT

Background: Obstructive sleep apnea has been increasingly acknowledged as a systemic illness with heterogeneous endocrine connections. The detection of concomitant endocrine diseases in patients with obstructive sleep apnea becomes crucial in the overall management and early treatment, particularly in risk groups. **Objective:** To determine the endocrine disorders in patients presented with obstructive sleep apnea. **Study Design:** Descriptive cross-sectional study. **Duration and Place of Study:** The study was conducted from February 2025 to May 2025 at the Department of Pulmonology, Ayub Teaching Hospital, Abbottabad. **Methodology:** A total of 77 patients aged 20–85 years with confirmed or suspected OSA were enrolled. Diagnosis was based on clinical sleepiness assessment and confirmatory sleep studies in selected cases. Patients underwent detailed history, clinical examination, and relevant investigations to screen for diabetes mellitus, hypothyroidism, acromegaly, metabolic syndrome, and polycystic ovary syndrome. **Results:** Metabolic syndrome was the most frequent condition, observed in 39 patients (50.6%), followed by hypothyroidism in 34 (44.2%), diabetes mellitus in 25 (32.5%), and acromegaly in 2 (2.6%). PCOS was detected in 2 out of 20 females (10%). Hypothyroidism was significantly more prevalent in urban patients (p=0.001). **Conclusion:** Endocrine disorders are prevalent among patients with obstructive sleep apnea, underscoring the need for routine endocrine screening to ensure timely diagnosis and holistic management.

INTRODUCTION

Obstructive sleep apnea (OSA) is a prevalent sleep-associated breathing disorder with multiple episodes of upper airway obstruction during sleep, leading to intermittent hypoxia with sleep fragmentation.[1] These events culminate in cascades in multiple physiological parameters, including increased sympathetic drive, systemic inflammation, and oxidant stress.[2] In the clinic, OSA manifests with snoring, apneas, when it is noticed, and sleepiness, but its manifestations exceed impairment in sleep quality.[3] It has been conclusively labeled as an important risk factor in the causation of cardiovascular diseases, insulin resistance, as well as neurocognitive impairment.[4] Anatomical and neuromuscular causes underlie OSA pathophysiology, but an equally significant body of evidence has accrued regarding its close linkage with multiple endocrine/metabolic disorders, potentially playing roles both in its causation and severity.[5]

Among the most frequently seen endocrine disorders in OSA patients, type 2 diabetes mellitus stands out.[6] OSA compounds insulin resistance via intermittent hypoxia and sleep fragmentation, while hyperglycemia and obesity, frequently found in diabetic patients, further compromise upper airway control and ventilatory stability.[6] Hypothyroidism also stands out, as it causes diminished ventilatory drive, weak upper airway muscle, and mucopolysaccharide deposition in the tissues of the pharynx, causing increased vulnerability to airway collapse when asleep.[7] In like manner, acromegaly presents an increased risk because of soft tissue enlargement, enlargement of the tongue, and skeletal changes, most notably overgrowth of the mandible and maxilla, impairing airway patency.[8] Note that the presenting symptoms of these endocrine disorders might overlap with, or obscure, characteristic manifestations of OSA, causing delayed diagnosis and treatment.[6-8]

Polycystic ovary syndrome (PCOS) and metabolic syndrome are also key elements within the endocrine spectrum associated with OSA.[9] PCOS patients typically present with central obesity, hyperandrogenism, and insulin resistances, synergistic causes of upper airway dysfunction that place them at higher risk for OSA.[9] Even

among non-obese patients, PCOS-associated hormonal abnormalities also tend to impair normal sleep respiratory patterns.[10] Metabolic syndrome, with its defining constellation of abdominal obesity, hypertension, dyslipidemia, and insulin resistances, has a bidirectional association with OSA.[11] The chronic intermittent hypoxemia and sleep disruption inherent in OSA worsen metabolic syndrome components, each perpetuating the other in a cycle promoting heightened risk for cardiovascular events as well as metabolic disorders.[12] Appreciation of the interaction between these endocrine conditions with OSA underpins effective multidisciplinary management, highlighting the importance of treating this multifactorial illness with an interdisciplinary approach.[9-12]

There is little known about the endocrine profile among patients with obstructive sleep apnea (OSA) in Abbottabad, given the increasing awareness of its linkage with metabolic and hormonal diseases. Diabetes, hypothyroidism, PCOS, metabolic syndrome, and acromegaly are all acknowledged to impact the severity and course of OSA. Local studies investigating this linkage, however, are few. By carrying this research, it will facilitate determination of the burden and pattern among OSA cases in our area, thereby allowing better-targeted screening and management plans.

METHODOLOGY

This descriptive cross-sectional study was conducted from February to May 2025, in the Department of Pulmonology at Ayub Teaching Hospital, Abbottabad. The total sample comprised 77 individuals, determined using WHO sample size calculation software. The calculation assumed an estimated 11% prevalence of hypothyroidism among patients with obstructive sleep apnea,[13] with a 7% margin of error and a 95% confidence level.

Eligible participants included men and women aged between 20 and 85 years who were either previously diagnosed with obstructive sleep apnea or newly identified through a sleep evaluation process. Diagnosis was based initially on excessive daytime drowsiness assessed by a structured sleepiness scale, which evaluates the likelihood of dozing off during common daily activities, such as reading or watching television. Patients with moderate risk on this scale underwent confirmatory sleep studies. Individuals were excluded if they were pregnant, had any diagnosed psychiatric illness, neuromuscular conditions such as myasthenia gravis or amyotrophic lateral sclerosis, or had structural causes of upper airway obstruction including glottic narrowing, tracheal stenosis, or compressive neck masses. Additionally, patients with isolated obesity or abnormal spirometry findings indicating upper airway compromise were not included. Subjects unwilling or unable to cooperate were also excluded.

Patients attending the pulmonology outpatient clinic and meeting inclusion criteria were approached for participation. After obtaining informed consent, information was gathered using a structured questionnaire. Each subject underwent a detailed clinical assessment, and relevant laboratory investigations were ordered based on presenting signs and symptoms.

Diabetes mellitus was identified by either a fasting plasma glucose level exceeding 120 mg/dL or a glycated hemoglobin (HbA1c) value above 6.5%. Thyroid function was assessed by measuring serum thyroid-stimulating hormone (TSH); a value above 8 mIU/L, in the presence of clinical symptoms such as fatigue, weight gain, or cold intolerance, indicated overt hypothyroidism, while the same elevation in TSH without clinical symptoms was categorized as subclinical thyroid dysfunction. For suspected acromegaly, serum insulin-like growth factor 1 (IGF-1) levels were measured, and values above 450 ng/mL were considered consistent with growth hormone excess. In women reporting irregular menstruation, infertility, or signs of hyperandrogenism, pelvic ultrasonography was performed. The presence of three or more cysts in one or both ovaries was classified as polycystic ovary morphology. Metabolic risk was evaluated through a combination of clinical and biochemical findings. Individuals with a total cholesterol level greater than 200 mg/dL, body mass index exceeding 30 kg/m^2, blood pressure above 140/90 mmHg, and impaired fasting glucose (above 120 mg/dL) were considered to exhibit features of metabolic syndrome. Blood pressure was recorded using a mercury sphygmomanometer after appropriate rest. Patients presenting with neck swelling or suspected airway obstruction were assessed further using spirometry, and abnormal flow-volume loops were used to rule out mechanical obstruction of the upper airway. All cases were reviewed by a consultant pulmonologist before final inclusion.

Data were analyzed using SPSS version 21. Continuous variables were described as mean ± standard deviation or median with interquartile range, depending on the distribution assessed through the Shapiro-Wilk test. Categorical data were summarized using frequencies and percentages. Associations between demographic factors and endocrine disorders were evaluated using Chi-square or Fisher's exact tests as appropriate, with statistical significance set at $p < 0.05$.

RESULTS

The study examined 77 patients presenting with obstructive sleep apnea, revealing comprehensive demographic and clinical characteristics. The patient population had a mean age of 49.94±14.57 years with a mean BMI of 30.21±4.34 kg/m^2, indicating obesity. Neck circumference averaged 39.01±3.32 cm, which is considered elevated and associated with increased OSA risk. Cardiovascular parameters demonstrated hypertensive ranges with systolic blood pressure of 151.34±13.20 mmHg and diastolic blood pressure of 86.95±11.54 mmHg. Glycemic control parameters were substantially elevated, with fasting blood glucose at 138.56±22.75 mg/dL, random blood glucose at 190.84±25.33 mg/dL, and HbA1c at 6.99±0.96%, all indicating poor glucose homeostasis. Lipid profile showed elevated total cholesterol at 226.52±31.09 mg/dL, exceeding recommended levels. Endocrine markers revealed elevated thyroid-stimulating hormone (TSH) at 7.26±2.93 mIU/L, suggesting hypothyroidism, and cortisol levels at 434.19±116.55 nmol/L. Gender distribution

showed a male predominance with 57 patients (74.0%) compared to 20 females (26.0%), while residence distribution favored urban areas with 48 patients (62.3%) versus 29 rural patients (37.7%) (as shown in Table 1).

Table 1
Patient Demographics

Demographics		Mean ± SD
Age (years)		49.94±14.57
BMI (kg/m^2)		30.21±4.34
Neck Circumference (cm)		39.01±3.32
Systolic Blood Pressure (mmHg)		151.34±13.20
Diastolic Blood Pressure (mmHg)		86.95±11.54
Random Blood Sugar - Fasting (mg/dL)		138.56±22.75
Random Blood Sugar - Random (mg/dL)		190.84±25.33
HbA1c (%)		6.99±0.96
Cholesterol (mg/dL)		226.52±31.09
TSH (mIU/L)		7.26±2.93
Cortisol (nmol/L)		434.19±116.55
Gender	Male n (%)	57 (74.0%)
	Female n (%)	20 (26.0%)
Residence	Rural n (%)	29 (37.7%)
	Urban n (%)	48 (62.3%)

The spectrum of endocrine disorders demonstrated significant prevalence across multiple conditions. Metabolic syndrome emerged as the most prevalent disorder, affecting 39 patients (50.60%) while 38 patients (49.40%) remained unaffected, representing an almost equal distribution. Hypothyroidism was the second most common condition, diagnosed in 34 patients (44.20%) with 43 patients (55.80%) having normal thyroid function. Acromegaly showed prevalence with 2 patients (2.6%) testing positive. Diabetes mellitus affected 25 patients (32.50%) while 52 patients (67.50%) maintained normal glucose metabolism. Polycystic ovary syndrome had the lowest prevalence with only 2 patients (2.60%) diagnosed positive and 75 patients (97.40%) negative, though this was assessed only in the female population (as shown in Table 2).

Table 2
Frequency of Endocrine Disorders Among Patients Presenting with Obstructive Sleep Apnea

Endocrine Disorders		Frequency	% age
Diabetes	Yes	25	32.50%
	No	52	67.50%
	Total	77	100%
Metabolic Syndrome	Yes	39	50.60%
	No	38	49.40%
	Total	77	100%
Polycystic Ovary Syndrome	Yes	2	2.60%
	No	75	97.40%
	Total	77	100%
Acromegaly	Yes	2	2.6%
	No	75	97.4%
	Total	77	100%
Hypothyroid	Yes	34	44.20%
	No	43	55.80%
	Total	77	100%

In patients aged ≤50 years, diabetes affected 16 patients (41.0%) compared to 23 patients (59.0%) without diabetes, while in the >50 years group, only 9 patients (23.7%) had diabetes versus 29 patients (76.3%) without diabetes (p=0.104, non-significant). Metabolic syndrome showed significant age-related differences, with 25 patients (64.1%) in the ≤50 years group having metabolic syndrome compared to 14 patients (35.9%) without it, whereas in the >50 years group, 14 patients (36.8%) had metabolic syndrome versus 24 patients (63.2%) without it (p=0.017, statistically significant). PCOS was absent in the ≤50 years group (0 patients, 0.0%) but affected 2 patients (5.3%) in the >50 years group, with 36 patients (94.7%) unaffected (p=0.24, non-significant). Acromegaly was absent in the ≤50 years group (0 patients, 0.0%) but affected 2 patients (5.3%) in the >50 years group, with 36 patients (94.7%) unaffected (p=0.240, non-significant). Hypothyroidism was more prevalent in younger patients with 21 patients (53.8%) affected versus 18 patients (46.2%) unaffected in ≤50 years, compared to 13 patients (34.2%) affected versus 25 patients (65.8%) unaffected in >50 years (p=0.083, non-significant). Gender-based analysis revealed distinct patterns across endocrine conditions. Among males, diabetes affected 22 patients (38.6%) while 35 patients (61.4%) remained unaffected, whereas in females, only 3 patients (15.0%) had diabetes compared to 17 patients (85.0%) without diabetes (p=0.094, approaching significance using Fischer Exact Test). Metabolic syndrome showed equal distribution by gender with 29 males (50.9%) affected versus 28 males (49.1%) unaffected, and 10 females (50.0%) affected versus 10 females (50.0%) unaffected (p=0.946, non-significant). PCOS naturally affected only females, with 2 patients (10.0%) diagnosed positive and 18 patients (90.0%) negative, while all 57 males (100.0%) were negative (p=0.065, approaching significance using Fischer Exact Test). Acromegaly affected 2 males (3.5%) versus 55 males (96.5%) unaffected, while no females were affected with all 20 females (100.0%) testing negative (p=0.610, non-significant). Hypothyroidism showed similar prevalence between genders: 26 males (45.6%) affected versus 31 males (54.4%) unaffected, and 8 females (40.0%) affected versus 12 females (60.0%) unaffected (p=0.664, non-significant). Residence-based stratification revealed significant urban-rural differences in endocrine disorder prevalence. Diabetes affected 7 rural patients (24.1%) compared to 22 patients (75.9%) without diabetes, while in urban areas, 18 patients (37.5%) had diabetes versus 30 patients (62.5%) without diabetes (p=0.225, non-significant). Metabolic syndrome showed 13 rural patients (44.8%) affected versus 16 patients (55.2%) unaffected, compared to 26 urban patients (54.2%) affected versus 22 patients (45.8%) unaffected (p=0.427, non-significant). PCOS affected 2 rural patients (6.9%) with 27 patients (93.1%) unaffected, while no urban patients had PCOS with all 48 patients (100.0%) testing negative (p=0.139, non-significant using Fischer Exact Test). Acromegaly was absent in rural patients with all 29 patients (100.0%) testing negative, while 2 urban patients (4.2%) were affected versus 46 patients (95.8%) unaffected (p=0.524, approaching significance using Fischer Exact Test). Hypothyroidism demonstrated the most significant residence-based difference, with only 6 rural patients (20.7%) affected compared to 23 patients (79.3%) unaffected, while urban areas showed much higher prevalence with 28 patients (58.3%) affected versus 20 patients (41.7%) unaffected (p=0.001, highly

statistically significant) (as shown in Table 3).

Table 3

Association of Endocrine Disorders with Demographic Factors

Demographic Factors		Diabetes		Metabolic Syndrome		PCO		Acromegaly		Hypothyroid	
		Yes n(%)	No n(%)	Yes n(%)	No n(%)	Yes n(%)	No n(%)	Yes n(%)	No n(%)	Yes n(%)	No n(%)
Age (years)	≤50	16 (41.0%)	23 (59.0%)	25 (64.1%)	14 (35.9%)	0 (0.0%)	39 (100.0%)	0 (0%)	39 (100%)	21 (53.8%)	18 (46.2%)
	>50	9 (23.7%)	29 (76.3%)	14 (36.8%)	24 (63.2%)	2 (5.3%)	36 (94.7%)	2 (5.3%)	36 (94.7%)	13 (34.2%)	25 (65.8%)
	p-value	0.104		0.017*		0.240		0.240**		0.083	
Gender	Male	22 (38.6%)	35 (61.4%)	29 (50.9%)	28 (49.1%)	0 (0.0%)	57 (100.0%)	2 (3.5%)	55 (96.5%)	26 (45.6%)	31 (54.4%)
	Female	3 (15.0%)	17 (85.0%)	10 (50.0%)	10 (50.0%)	2 (10.0%)	18 (90.0%)	0 (0%)	20 (100%)	8 (40.0%)	12 (60.0%)
	p-value	0.094**		0.946		0.065**		0.610**		0.664	
Residence	Rural	7 (24.1%)	22 (75.9%)	13 (44.8%)	16 (55.2%)	2 (6.9%)	27 (93.1%)	0 (0%)	29 (100%)	6 (20.7%)	23 (79.3%)
	Urban	18 (37.5%)	30 (62.5%)	26 (54.2%)	22 (45.8%)	0 (0.0%)	48 (100.0%)	2 (4.2%)	46 (95.8%)	28 (58.3%)	20 (41.7%)
	p-value	0.225		0.427		0.139**		0.524*		0.001*	

*Statistically significant (p<0.05) ** Fischer Exact Test

DISCUSSION

In the current study, an unusually high incidence of endocrine abnormalities has been found among patients with obstructive sleep apnea, with in excess of 90% of patients having at least one abnormality. The result highlights the multifaceted bidirectional interaction between OSA and endocrine dysfunction, where sleep fragmentation, as well as episodic hypoxia, inherent in OSA, result in cascading metabolic derangements with multiple hormonal predispositions. The higher mean BMI of 30.21 kg/m^2 and raised neck circumference of 39.01 cm mirror the known association between obesity and OSA, where increased adipose tissue in the supraglottic airway increases the likelihood of upper airway collapse during sleep. The hypertensive blood pressure levels in this population could be attributed to the activation of the sympathetic nervous system brought about by recurring arousal events and episodic hypoxemia, with the result causing increased release of catecholamines with corresponding cardiovascular stress. The most common metabolic abnormality found in this population was metabolic syndrome at 50.6%, explainable in view of the severe effect that sleep fragmentation has upon carbohydrate metabolism and insulin sensitivity. Intermittent hypoxia has an activation effect upon inflammatory pathways, as well as an increased sense of adrenocortical drive with an increased production of cortisol, both effects culminating in insulin resistance, thereby causing metabolic dysfunction. Much higher prevalence in young patients implies metabolic derangements could appear earlier in the course of illness, possibly because of lifestyle influences and higher metabolic load in this age group. The relatively low 2.6% prevalence of acromegaly aligns with its known rare occurrence in the general population, though the exclusive presentation in older patients (>50 years) and males suggests potential age and gender-related susceptibility factors in OSA populations. The hypothyroidism prevalence of 44.2% substantially exceeds general population values and could be explained because thyroid disorder has a bidirectional interaction with sleep disorders. Hypoxia induced by OSA could impair thyroid hormone synthesis and metabolic clearance, whereas hypothyroidism could make patients susceptible to OSA because of upper airway myopathy and respiratory drive abnormalities. The significant level of rural-urban difference in hypothyroidism prevalence probably represents healthcare access difference, dietary iodine intake, but also other environmental influences affecting thyroid function.

Our study results were consistent with several previous investigations regarding the spectrum of endocrine disorders in obstructive sleep apnea patients. The demographic profile of our 77 OSA patients (mean age 49.94±14.57 years, BMI 30.21±4.34 kg/m^2, 74% male predominance) closely paralleled the characteristics described by Polu & Reddy [14] who examined 372 consecutive Indian OSA referrals with 72% male predominance, mean age 51.4 years, and BMI 38.1 kg/m^2. This demographic similarity suggests consistent patient populations across different OSA clinical settings, though our cohort showed lower BMI values, possibly reflecting regional differences in obesity patterns or referral criteria.

The prevalence of hypothyroidism in our study was notably high at 44.2%, substantially exceeding the findings of Polu & Reddy [14] who reported 9.6% hypothyroidism prevalence in their OSA population, and Green et al. [15] who documented 11.1% subclinical hypothyroidism in OSA versus 4% in non-OSA patients in the Bahammam study they reviewed. This discrepancy may be attributed to different diagnostic criteria for hypothyroidism, variations in population characteristics, or the inclusion of both subclinical and overt hypothyroidism in our analysis. Our finding of significantly higher hypothyroidism prevalence in urban versus rural patients (58.3% vs 20.7%, p=0.001) represents a novel observation not previously reported in the literature and may reflect differences in healthcare access, dietary iodine intake, or environmental factors between urban and rural populations.

The metabolic syndrome prevalence of 50.6% in our cohort was substantially higher than the 41% reported in matched controls by Wilding & O'Reilly [16] but lower than the 79% prevalence they found in OSA patients after adjustment for adiposity. This intermediate prevalence may reflect the inclusion of patients across the OSA severity spectrum in our study, whereas the higher rates reported by Wilding & O'Reilly [16] may have included more severe OSA cases. Our finding of significantly higher metabolic syndrome prevalence in younger patients (≤50 years: 64.1% vs >50 years: 36.8%, p=0.017) contrasts with typical age-related metabolic syndrome trends and suggests that OSA may accelerate metabolic dysfunction in

younger individuals, warranting early intervention strategies.

Diabetes mellitus affected 32.5% of our patients, which aligns with the broader ranges reported in the literature. Wilding & O'Reilly [16] noted that 15% of those with AHI >15 had diabetes versus 3% when AHI <5 in the Wisconsin cohort, and up to 23% of type-2 diabetic men had OSA in Oxford community studies. Our higher prevalence likely reflects the clinical referral population bias, where patients with multiple comorbidities are more likely to undergo sleep studies. The non-significant trend toward higher diabetes prevalence in males versus females (38.6% vs 15.0%, p=0.094) mirrors the gender-specific OSA-diabetes associations reported by Wilding & O'Reilly[16] though our sample size may have limited statistical power to detect significance.

The acromegaly prevalence of 2.6% in our study, while low, represents a notable finding given the condition's rarity in the general population where it typically affects 3-4 cases per million populations annually. All acromegaly cases were identified in male patients over 50 years of age, suggesting potential age and gender-specific risk factors in OSA populations. This prevalence, though modest compared to the 76.67% OSA prevalence in acromegaly patients reported by Pilarska et al. [17] indicates that acromegaly screening may be warranted in older male OSA patients. The exclusive male presentation contradicts the typical equal gender distribution of acromegaly in the general population and warrants further investigation to understand this demographic pattern in OSA cohorts.

Age-related trends reported in the current study offer new information not discussed in detail in the past literature. The significant presence of metabolic syndrome and hypothyroidism among young OSA patients implies that these diseases could be underlying causes of early OSA onset rather than secondary effects following prolonged OSA duration. In contrast with the conventional hypothesis where metabolic morbidities aggregate with age and OSA duration, this suggests that specific screening for young OSA patients with endocrine diseases could be particularly relevant in initiating early intervention with prevention of cardiovascular morbidities.

Urban-rural hypothyroidism prevalence difference (58.3% vs 20.7%, p=0.001) is an original epidemiological finding never reported before in OSA literature. The large discrepancy could be attributed to environmental influences, dietary habits, access to healthcare, or genetic variation between the rural and urban populations. The rural populations could be exposed more to thyroid function-inhibiting environmental toxins, whereas the urban populations might be exposed to differing iodine intake regimes or goitrogenic stimuli that impact thyroid function in the setting of OSA.

There are also some limitations in this research. The research was conducted in one center, potentially reducing the generalizability across other populations and healthcare settings. The small number of participants, while reasonable, exerted considerable constraint upon the statistical power, particularly when analyzing subgroup differences such as age, gender, and residence. The cross-sectional nature also implies that noncausal inferences cannot be drawn between obstructive sleep apnea and its concomitant endocrine disorders. The hormonal evaluations were conducted with the use of single time-point measurements without dynamic testing or confirmation, potentially compromising the precision when making diagnoses.

CONCLUSION

This study on the spectrum of endocrine disorders in patients presented with obstructive sleep apnea demonstrates that OSA patients commonly exhibit multiple endocrine abnormalities. The spectrum includes metabolic syndrome, hypothyroidism, diabetes mellitus, and acromegaly, with over 90% of patients having at least one endocrine disorder, highlighting the complex bidirectional relationship between sleep-disordered breathing and hormonal dysfunction. These findings emphasize the importance of comprehensive endocrine evaluation as part of the routine assessment of OSA patients to enable early diagnosis and optimal management of this multisystem disorder.

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