

Original Paper

Association between Upper Airway Symptomatology and Metabolic Profile with Risk of Obstructive Sleep Apnea in Women with Polycystic Ovary Syndrome: A Cross-sectional Study

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ABSTRACT

Obstructive sleep apnea (OSA) is more common in women with polycystic ovary syndrome (PCOS), yet screening remains inconsistent; upper-airway symptoms and metabolic abnormalities could help select women for definitive sleep assessment. In this analytical cross-sectional study, 250 women with PCOS aged 18–45 years were consecutively recruited from gynecology, infertility and reproductive-endocrinology clinics in Babylon Province, Iraq, between June 2025 and February 2026. OSA risk was classified with the validated Arabic Berlin questionnaire, and daytime sleepiness and nasal obstruction were measured with the Arabic Epworth Sleepiness Scale (ESS) and Nasal Obstruction Symptom Evaluation (NOSE) instruments. Standardized anthropometry, blood pressure, glycated hemoglobin, insulin, glucose, lipids and upper-airway examination were obtained, and multivariable logistic regression was used to assess associations with high OSA risk with explicit adjustment for adiposity. Eighty-two women (32.8%) were at high risk of OSA. Compared with the low-risk group, they had higher BMI (34.1 ± 5.1 vs. 27.8 ± 4.4 kg/m²), waist circumference (104.8 ± 11.6 vs. 89.5 ± 10.7 cm), neck circumference (37.5 ± 2.8 vs. 34.1 ± 2.4 cm), NOSE score (47.6 ± 20.8 vs. 24.3 ± 18.1), ESS score (11.8 ± 4.7 vs. 6.7 ± 3.8) and HOMA-IR (4.7 [3.5–6.4] vs. 2.8 [2.0–4.0]; all $p < 0.001$). In the fully adjusted model, neck circumference (adjusted odds ratio [aOR] per cm 1.25; 95% confidence interval [CI] 1.08–1.45), NOSE score (aOR per 10 points 1.26; 95% CI 1.09–1.46), ESS score (aOR per point 1.14; 95% CI 1.06–1.23) and HOMA-IR (aOR per unit 1.17; 95% CI 1.04–1.32) remained associated with high risk after adjustment for age, BMI and waist circumference. The bootstrap-corrected AUC of a combined non-Berlin-component model was 0.846. Women with PCOS therefore had a high prevalence of questionnaire-defined high OSA risk, and upper-airway symptoms, central adiposity, sleepiness and insulin resistance were associated with this risk; the association of HOMA-IR persisted after adjustment for adiposity.

KEYWORDS: Polycystic ovary syndrome (PCOS), Upper airway, Nasal obstruction, Obstructive sleep apnea (OSA), Insulin resistance.

1-INTRODUCTION

Polycystic ovary syndrome (PCOS) is a common endocrine-metabolic disorder of women of reproductive age, characterized by ovulatory dysfunction, clinical and/or biochemical hyperandrogenism and polycystic ovarian morphology in the absence of other etiologies. Beyond its reproductive features, PCOS is strongly associated with insulin resistance, dyslipidaemia, obesity, hypertension, impaired glucose regulation and increased long-term cardiometabolic risk [1].

There is growing evidence that sleep health is an undervalued facet of the clinical burden of PCOS [2]. According to a systematic review and meta-analysis, women with PCOS experience significantly more sleep disturbances and poorer sleep quality, and sleep disturbance is associated with higher body mass index (BMI), waist circumference (WC), blood pressure, fasting glucose and low-density lipoprotein cholesterol (LDL-C) [3]. A bidirectional link

has therefore been proposed, in which the metabolic and hormonal abnormalities of PCOS impair sleep, while poor sleep in turn worsens adiposity, insulin resistance and metabolic health [4]. In obstructive sleep apnea (OSA), the upper airway repeatedly collapses or becomes obstructed during sleep, producing recurrent episodes of airflow limitation, intermittent hypoxia, sleep fragmentation and arousals. These events activate the sympathetic nervous system and induce oxidative stress and metabolic changes that may underlie hypertension, insulin resistance, dysglycaemia and cardiovascular risk [5]. Importantly, the clinical presentation of OSA in women may differ from the classic presentation in men: women more often report fatigue, insomnia, non-restorative sleep, morning headache, mood disturbance or poor sleep quality rather than witnessed apnoea or excessive daytime sleepiness, which may contribute to delayed recognition and referral [6,7]. This is particularly relevant in PCOS, where fatigue, obesity, mood symptoms and metabolic abnormalities overlap with those of sleep-disordered breathing. Accordingly, the 2023 International Evidence-based Guideline for PCOS recommends screening for symptoms of OSA (snoring, waking unrefreshed, daytime sleepiness or fatigue) and the use of validated screening tools or referral for formal evaluation as clinically appropriate [1].

Evidence that women with PCOS are at increased risk of OSA continues to accumulate. Meta-analytical data have shown a significantly higher risk of OSA in adult women with PCOS than in women without PCOS, and numerous studies and subsequent systematic reviews and meta-analyses have confirmed both the increased risk of OSA and its association with an unfavorable metabolic profile [8–10]. Given the clinical and pathophysiological relationship between the two disorders, obesity, visceral adiposity, hyperandrogenism, insulin resistance and altered upper-airway physiology may interact to increase susceptibility to sleep-disordered breathing in PCOS. Published prevalence estimates nevertheless vary widely according to age, obesity, ethnicity, recruitment site, PCOS phenotype and diagnostic criteria, and particularly according to the method used to identify OSA (polysomnography versus symptom-based screening questionnaires). These methodological differences matter because high OSA risk defined by a questionnaire cannot be equated with OSA defined by polysomnography.

Adiposity is an important potential confounder of the PCOS–OSA relationship. Upper-airway collapsibility and metabolic dysfunction are both strongly related to BMI and central obesity, and failure to adjust for these measures may overestimate any independent association between PCOS and sleep-disordered breathing. Anthropometric measurements, however, may not capture the whole clinical risk profile. Upper-airway symptoms and anatomical characteristics provide additional information that is inexpensive and readily accessible in clinical practice. Nasal obstruction increases nasal airflow resistance, predisposes to oral breathing, raises negative inspiratory pressure in the collapsible pharyngeal airway and contributes to snoring and disturbed sleep, although on its own it cannot explain moderate or severe OSA in most patients [11,12]. During clinical screening, habitual snoring, night-time choking or gasping, dry mouth on waking, morning sore throat and non-restorative sleep may therefore be informative. Upper-airway anatomy (e.g. neck circumference and oropharyngeal examination with the modified Mallampati classification) has also been incorporated into the clinical evaluation of patients with suspected OSA [13].

The Nasal Obstruction Symptom Evaluation (NOSE) scale is a validated patient-reported instrument of perceived nasal obstruction that can complement objective anthropometric and metabolic measurements [14]. Of particular interest is insulin resistance, a central pathophysiological mechanism of PCOS that may be involved in the PCOS–OSA association. Early studies demonstrated a strong relationship between PCOS, sleep-disordered breathing, insulin resistance and daytime sleepiness, indicating that metabolic dysfunction, in addition to reproductive dysfunction, may contribute to susceptibility to OSA in PCOS [15]. Subsequent work showed that women with PCOS and OSA had poorer insulin sensitivity and glucose tolerance, and that the relationship between OSA and insulin resistance remained significant after controlling for age and adiposity [16]. Recent findings have confirmed a bidirectional relationship between disturbed sleep or OSA and insulin resistance and cardiometabolic dysfunction

in PCOS [3,4]. Whether HOMA-IR provides information beyond BMI and WC for predicting high OSA risk nevertheless remains unclear, especially in Iraqi women with PCOS. Combining a validated OSA-risk screening tool with upper-airway symptoms, daytime sleepiness, anthropometric measures and metabolic markers could therefore offer a practical multidimensional approach to identifying women with PCOS who should undergo further sleep assessment, particularly in settings where routine polysomnography is not readily available.

The main purpose of the present study was to determine the prevalence of high OSA risk in women with PCOS and to examine the association of high OSA risk with upper-airway symptoms, anthropometric characteristics and metabolic profile. Secondary aims were to investigate the relationship of NOSE and Epworth Sleepiness Scale (ESS) scores with metabolic parameters, to test whether the association between HOMA-IR and high OSA risk persisted after accounting for BMI and WC, and to assess whether a combined clinical model incorporating questionnaire, upper-airway, anthropometric and metabolic variables improved discriminatory performance. It should be emphasized that the study outcome is screening-defined OSA risk and not a diagnosis of OSA, because polysomnography was not performed.

2-MATERIALS AND METHODS

2.1. Design, setting and reporting

This analytical cross-sectional study was conducted in the gynecology, infertility and reproductive-endocrinology clinics of Babylon Maternity and Children Teaching Hospital and Imam Al-Sadiq Teaching Hospital in Hilla city, Babylon Province, Iraq, from 1 June 2025 to 28 February 2026. Upper-airway examination was performed either by the ENT services of Al-Hilla Surgical Teaching Hospital and Imam Al-Sadiq Teaching Hospital or by study physicians who had been trained and assessed for competency by an ENT specialist. Biochemical tests were carried out in certified specialized private laboratories in Hilla using standardized platforms. Reporting followed the STROBE recommendations [17].

2.2. Study population

Women aged 18–45 years with PCOS were invited consecutively. PCOS was diagnosed according to the current international definition, namely the presence of at least two of the following: ovulatory dysfunction, clinical/biochemical hyperandrogenism, and polycystic ovarian morphology or elevated anti-Müllerian hormone (AMH) levels where applicable, with exclusion of relevant alternative diagnoses.

2.3. Eligibility criteria

Inclusion required informed consent, completion of the Arabic screening instruments, fasting blood sampling and clinical examination. Exclusion criteria were pregnancy, lactation, a previous diagnosis of OSA treated with CPAP or other OSA-specific therapy, acute upper-respiratory infection, recent nasal or pharyngeal surgery, severe cardiopulmonary disease, active malignancy, severe renal or hepatic disease, uncontrolled hypothyroidism, Cushing syndrome, major congenital craniofacial abnormality, and medication-related inability to complete the sleep assessment. Women with diabetes or hypertension were retained because these are clinically relevant phenotypes.

2.4. Sample size and recruitment

A target of 250 women was expected to yield approximately 80 high-risk outcomes at a prevalence of about 30%, which is sufficient to fit a parsimonious multivariable model. Consecutive recruitment was used to limit investigator selection, the number of predictor degrees of freedom was kept small, and a prespecified bootstrap validation was performed.

2.5. OSA-risk assessment

The primary screening tool was the validated Arabic version of the Berlin questionnaire, which comprises three categories addressing snoring/witnessed apnea, daytime fatigue/sleepiness, and hypertension/obesity. Participants with at least two positive categories were classified as high risk for OSA; all others were classified as low risk.

Because the questionnaires used do not diagnose OSA, the term "high OSA risk" is used throughout, and women at high risk were advised to undergo definitive sleep assessment [18].

2.6. Daytime sleepiness and nasal obstruction

Daytime sleepiness was assessed with the Arabic ESS, which scores eight situations from 0 to 3 for a total score of 0 to 24 [19]. Nasal obstruction was assessed with an Arabic-validated NOSE instrument, in which five items are scored and transformed to a 0–100 scale, higher scores indicating greater obstruction. Both scores were analyzed as continuous variables; for descriptive purposes, an ESS score above 10 was considered to indicate excessive daytime sleepiness [20].

2.7. Upper-airway symptoms and examination

Habitual or loud snoring, witnessed breathing pauses, nocturnal choking or gasping, nasal obstruction, daytime mouth breathing, waking with a dry mouth, morning sore throat, morning headache, non-restorative sleep and breathing-related awakenings were recorded on a structured checklist. Neck circumference at a standard level, modified Mallampati class, tonsillar grade, septal deviation, inferior turbinate hypertrophy, visible nasal obstruction and nasal polyps (if present) were examined. Examiners were trained to use uniform categories.

2.8. Anthropometry and blood pressure

Weight and height were measured with calibrated equipment and BMI was calculated (kg/m^2). Waist and hip circumferences were measured at standard sites and the waist-to-hip ratio was calculated. Neck circumference was measured below the laryngeal prominence. After 5 minutes of seated rest, blood pressure was measured twice with an appropriately sized cuff, and the mean of the two readings was analyzed.

2.9. Metabolic assessment

After an overnight fast of 8–12 hours, glucose, insulin, HbA1c, total cholesterol, triglycerides, HDL-C and LDL-C were measured on standardized laboratory platforms. HOMA-IR was calculated as $\text{fasting insulin } (\mu\text{IU/mL}) \times \text{fasting glucose } (\text{mg/dL}) / 405$. The use of metformin, hormonal therapy, antihypertensive agents and lipid-lowering medication was documented.

2.10. Outcomes and analytic considerations

The primary outcome was high OSA risk on the Berlin questionnaire. Secondary outcomes were ESS and NOSE scores, upper-airway symptoms and examination findings, anthropometric measures and metabolic variables. Crude associations with obesity and hypertension are partly definitional, because obesity contributes directly to Berlin category 3 and snoring/apnea contributes directly to Berlin category 1. The principal multivariable model therefore focused on non-Berlin-component measures (neck circumference, NOSE, ESS and HOMA-IR), with age, BMI and waist circumference as adjustment variables; BMI, hypertension and Berlin symptoms were not treated as new independent predictors.

2.11. Statistical analysis

Continuous data are presented as mean $\pm$ SD or median (IQR) and categorical data as n (%). The high-risk and low-risk groups were compared with the independent t test, Mann–Whitney U test, chi-square test or Fisher's exact test as appropriate. Correlations between scores and metabolic measures were quantified with Spearman coefficients. Logistic regression was performed in steps: Model 1 included age, neck circumference, NOSE, ESS and HOMA-IR; Model 2 added BMI and waist circumference; and Model 3 further added PCOS duration, metformin use and hormonal therapy. Collinearity, linearity in the logit and influential observations were checked. Results are reported as adjusted odds ratios (aORs) with 95% confidence intervals (CIs). ROC analysis was performed for each non-component marker and for their combination; apparent discrimination, calibration slope and intercept, the Brier score and bootstrap optimism correction with 1,000 resamples were reported. Secondary p values were corrected for the false-discovery rate by the Benjamini–Hochberg method. Missing predictor values, which accounted for

less than 10% of observations, were handled by multiple imputation; the outcome was not imputed. A two-sided p value < 0.05 was considered significant. Analyses were performed with R 4.4 and SPSS 29.

2.12. Ethical considerations

Scientific and ethical approval was obtained from the appropriate institutional research ethics committee, and administrative authorization was obtained from each participating site before recruitment. All participants gave written informed consent, and data were coded and kept confidential. Women classified as high risk on the questionnaire received written counselling explaining that screening does not diagnose OSA and were referred for appropriate sleep-medicine evaluation; urgent cardiopulmonary findings were referred immediately.

2.13. Questionnaire standardization and reliability

Trained female research personnel conducted the interviews in a quiet setting using the validated Arabic versions of the Berlin questionnaire, ESS and NOSE with standardized instructions. Staff could clarify the meaning of words but did not suggest answers. Twenty eligible women took part in a pilot study to assess comprehension, completion time, workflow and internal consistency; pilot participants were not included in the analytic cohort unless no changes were made to the instruments or procedures. A 10% sample of questionnaires was independently rescored, and Cronbach's alpha and item-level missingness were reported for the study sample. Permission and licensing requirements for each instrument were observed.

2.14. Airway examination and anthropometric quality assurance

All ENT examiners completed a common training module for modified Mallampati class, tonsil grade, septal deviation, turbinate hypertrophy and visible obstruction. Neck, waist and hip circumferences were measured twice with a non-stretch tape; a third measurement was taken if the first two readings differed by more than the prespecified tolerance, and the mean of the two closest readings was analyzed. Scales and sphygmomanometers were calibrated regularly. Weighted kappa or intraclass correlation coefficients were computed after random re-grading of airway findings by a blinded second examiner in 10% of cases.

2.15. Laboratory quality assurance and control of interfering factors

Fasting status and time of collection were confirmed. Samples were processed within the laboratory-defined stability interval on a single analytic platform, and calibrators and internal quality controls had to be acceptable before results were released. Insulin and glucose units were checked automatically before HOMA-IR was calculated. Metformin, hormonal therapy, lipid-lowering and antihypertensive medication, physical activity, smoking, sleep duration, history of shift work, allergic rhinitis, asthma, history of depression or anxiety, and sedating medications were documented as potential confounders. Women using exogenous insulin were excluded from HOMA-IR analyses but were included in descriptive reporting if otherwise eligible.

2.16. Outcome validity, sensitivity analyses and referral pathway

The Berlin questionnaire result was explicitly defined as a screening risk. Variables that contribute directly to the score, namely snoring/apnea, obesity and hypertension, were not claimed as new predictors. Sensitivity analyses used a symptom-defined endpoint (Berlin categories 1 and 2), excluded women with known diabetes or current respiratory allergies, and excluded users of sedating medications. A stratified validation subset of high-risk and low-risk participants was referred, where feasible, for home sleep apnea testing or polysomnography, and objective results (without imputation) were analyzed separately. ROC results against Berlin risk are described as classification agreement rather than diagnostic accuracy for OSA.

2.17. Data management and reproducibility

Units, scoring algorithms, ranges, timing windows and derived variables were prespecified in a case-report form and a data dictionary. Data were entered twice, with automated range and logic checks and a documented query-resolution process, before the database was locked. Outcome scoring was verified independently of the metabolic analyses. Missing predictors were multiply imputed when necessary, and complete-case analyses were performed

to check robustness. The statistical analysis plan, scoring syntax, de-identified data template and final code were version-controlled for audit and replication.

3-RESULTS

Of the 276 women evaluated, 18 were ineligible and eight declined, leaving 250 participants. Mean age was 29.8 ± 6.1 years and mean BMI 29.9 ± 5.3 kg/m² (Table 1). High OSA risk was identified in 82 women (32.8%; 95% CI 27.0–38.9%).

Table (1) Demographic and clinical characteristics of the study population (N = 250)

Characteristic	Value
Age, years	29.8 ± 6.1
PCOS duration, years	5.2 (2.8–8.1)
Married	176 (70.4)
Infertility history	112 (44.8)
Current smoker	13 (5.2)
Metformin use	147 (58.8)
Hormonal therapy	91 (36.4)
Diabetes mellitus	24 (9.6)
Hypertension	31 (12.4)
BMI, kg/m ²	29.9 ± 5.3
Waist circumference, cm	94.5 ± 12.9
Neck circumference, cm	35.2 ± 3.0

Data are presented as mean $\pm$ SD, median (interquartile range) or n (%). BMI: body mass index; PCOS: polycystic ovary syndrome.

Berlin category 1 was positive in 42.0% of women, category 2 in 35.6% and category 3 in 38.4%, and 29.6% had excessive daytime sleepiness (Table 2). Non-restorative sleep, dry mouth on waking and morning headache were common complaints among high-risk women.

Table (2) OSA-risk classification and sleep-related symptoms (N = 250)

Measure	n (%)
High Berlin OSA risk	82 (32.8)
Berlin category 1 positive	105 (42.0)
Berlin category 2 positive	89 (35.6)
Berlin category 3 positive	96 (38.4)
ESS > 10	74 (29.6)
Habitual snoring	101 (40.4)
Witnessed breathing pauses	47 (18.8)
Nocturnal choking/gasping	58 (23.2)
Non-restorative sleep	117 (46.8)
Morning headache	83 (33.2)

ESS: Epworth Sleepiness Scale; OSA: obstructive sleep apnea. The Berlin result indicates screening risk, not a diagnosis of OSA.

Every upper-airway symptom assessed was more prevalent among high-risk than low-risk participants (Table 3). The Berlin category components are listed descriptively and are not interpreted as independent findings.

Table (3) Upper-airway symptoms according to OSA-risk status

Symptom	High risk (n = 82)	Low risk (n = 168)	p value
Habitual snoring	70 (85.4)	31 (18.5)	< 0.001
Witnessed apnea	35 (42.7)	12 (7.1)	< 0.001
Nocturnal choking/gasping	38 (46.3)	20 (11.9)	< 0.001
Nasal obstruction	52 (63.4)	55 (32.7)	< 0.001
Mouth breathing during sleep	49 (59.8)	53 (31.5)	< 0.001
Awakening with dry mouth	58 (70.7)	66 (39.3)	< 0.001
Morning sore throat	31 (37.8)	30 (17.9)	0.001
Breathing-related awakenings	34 (41.5)	25 (14.9)	< 0.001

Values are n (%). OSA: obstructive sleep apnea.

Mean NOSE and ESS scores were significantly higher in the high-risk group than in the low-risk group (Table 4). This difference persisted when women with acute allergy symptoms were excluded and when women receiving current hormonal therapy were excluded.

Table (4) Nasal obstruction and sleepiness scores according to OSA-risk status

Measure	High risk (n = 82)	Low risk (n = 168)	Mean difference (95% CI)	p value
NOSE score	47.6 ± 20.8	24.3 ± 18.1	23.3 (18.3–28.3)	< 0.001
ESS score	11.8 ± 4.7	6.7 ± 3.8	5.1 (4.0–6.2)	< 0.001
NOSE ≥ 50, n (%)	42 (51.2)	29 (17.3)	—	< 0.001
ESS > 10, n (%)	50 (61.0)	24 (14.3)	—	< 0.001

Data are mean ± SD or n (%). CI: confidence interval; ESS: Epworth Sleepiness Scale; NOSE: Nasal Obstruction Symptom Evaluation.

High-risk women had greater general, central and cervical adiposity and higher blood pressure, and were more likely to have Mallampati class III–IV and inferior turbinate hypertrophy (Table 5). Tonsil grade ≥ 3 was rare but was more frequent in the high-risk group.

Table (5) Anthropometric measurements and upper-airway examination findings according to OSA-risk status

Measure	High risk (n = 82)	Low risk (n = 168)	p value
BMI, kg/m ²	34.1 ± 5.1	27.8 ± 4.4	< 0.001
Waist circumference, cm	104.8 ± 11.6	89.5 ± 10.7	< 0.001
Waist-to-hip ratio	0.91 ± 0.07	0.84 ± 0.06	< 0.001
Neck circumference, cm	37.5 ± 2.8	34.1 ± 2.4	< 0.001
Systolic BP, mmHg	126.7 ± 12.8	116.3 ± 11.4	< 0.001
Diastolic BP, mmHg	81.4 ± 8.7	75.2 ± 8.1	< 0.001
Mallampati class III–IV	43 (52.4)	38 (22.6)	< 0.001
Tonsil grade ≥ 3	13 (15.9)	9 (5.4)	0.005
Septal deviation	25 (30.5)	35 (20.8)	0.091
Inferior turbinate hypertrophy	37 (45.1)	42 (25.0)	0.001

Data are mean ± SD or n (%). BMI: body mass index; BP: blood pressure; OSA: obstructive sleep apnea.

Fasting insulin, HOMA-IR, HbA1c, triglycerides and LDL-C were higher and HDL-C was lower in high-risk women, whereas the difference in fasting glucose was smaller (Table 6). After FDR correction, all primary metabolic differences remained significant, with the exception of total cholesterol.

Table (6) Metabolic and biochemical profile according to OSA-risk status

Parameter	High risk (n = 82)	Low risk (n = 168)	p value	FDR q
Fasting glucose, mg/dL	101 (94–111)	94 (88–102)	< 0.001	< 0.001
Fasting insulin, μ IU/mL	18.9 (14.6–24.8)	12.1 (8.9–16.4)	< 0.001	< 0.001
HOMA-IR	4.7 (3.5–6.4)	2.8 (2.0–4.0)	< 0.001	< 0.001
HbA1c, %	5.8 ± 0.7	5.4 ± 0.5	< 0.001	< 0.001
Triglycerides, mg/dL	164 (127–212)	121 (91–161)	< 0.001	< 0.001
HDL-C, mg/dL	41.2 ± 9.1	48.7 ± 10.2	< 0.001	< 0.001
LDL-C, mg/dL	119.5 ± 31.8	107.0 ± 29.4	0.003	0.004
Total cholesterol, mg/dL	196.8 ± 39.7	185.6 ± 37.5	0.031	0.035

Data are mean ± SD or median (IQR). FDR: false-discovery rate; HbA1c: glycated hemoglobin; HDL-C: high-density lipoprotein cholesterol; HOMA-IR: homeostatic model assessment of insulin resistance; LDL-C: low-density lipoprotein cholesterol.

NOSE and ESS scores were moderately correlated, and NOSE showed weak-to-moderate correlations with anthropometric measures and HOMA-IR (Table 7). ESS was positively correlated with waist circumference and HOMA-IR. These correlations do not indicate directionality.

Table (7) Spearman correlations between airway, sleep and metabolic measures

Variables	r_s	p value
NOSE score vs. ESS score	0.46	< 0.001
NOSE score vs. BMI	0.31	< 0.001
NOSE score vs. neck circumference	0.38	< 0.001
NOSE score vs. HOMA-IR	0.29	< 0.001
ESS score vs. waist circumference	0.35	< 0.001
ESS score vs. HOMA-IR	0.33	< 0.001
HOMA-IR vs. waist circumference	0.58	< 0.001
HOMA-IR vs. neck circumference	0.42	< 0.001

r_s : Spearman correlation coefficient. BMI: body mass index; ESS: Epworth Sleepiness Scale; HOMA-IR: homeostatic model assessment of insulin resistance; NOSE: Nasal Obstruction Symptom Evaluation.

Neck circumference, NOSE, ESS and HOMA-IR remained associated with high OSA risk in the fully adjusted model (Table 8). The HOMA-IR estimate was attenuated, but not abolished, by adjustment for BMI and waist circumference. Because obesity and hypertension are components of Berlin category 3, these coefficients represent associations with the screening classification rather than causal effects or independent diagnostic predictors.

Table (8) Logistic regression models for high Berlin questionnaire OSA risk

Predictor	Model 1 aOR (95% CI)	Model 2 aOR (95% CI)	Model 3 aOR (95% CI)	Model 3 p
Age, per year	1.04 (0.99–1.09)	1.03 (0.98–1.08)	1.03 (0.98–1.09)	0.229
Neck circumference, per cm	1.34 (1.18–1.52)	1.27 (1.10–1.47)	1.25 (1.08–1.45)	0.003
NOSE, per 10 points	1.29 (1.13–1.47)	1.27 (1.10–1.46)	1.26 (1.09–1.46)	0.002
ESS, per point	1.16 (1.09–1.25)	1.15 (1.07–1.24)	1.14 (1.06–1.23)	< 0.001
HOMA-IR, per unit	1.24 (1.12–1.38)	1.18 (1.05–1.32)	1.17 (1.04–1.32)	0.009
BMI, per kg/m ²	—	1.08 (0.99–1.18)	1.07 (0.98–1.17)	0.134
Waist circumference, per cm	—	1.03 (0.99–1.07)	1.03 (0.99–1.07)	0.107

aOR: adjusted odds ratio; BMI: body mass index; CI: confidence interval; ESS: Epworth Sleepiness Scale; HOMA-IR: homeostatic model assessment of insulin resistance; NOSE: Nasal Obstruction Symptom Evaluation. Model 1: non-component markers (neck circumference, NOSE, ESS, HOMA-IR) and age. Model 2: Model 1 + BMI and waist circumference. Model 3: Model 2 + PCOS duration, metformin use and hormonal therapy.

Neck circumference, NOSE, ESS and HOMA-IR each showed moderate discrimination (Table 9). The apparent AUC of the combined non-Berlin-component model was 0.862, with a bootstrap-corrected AUC of 0.846, and the model was well calibrated. The cutoffs shown are exploratory and not diagnostic.

Table (9) ROC analysis of non-Berlin-component markers and the combined model

Marker/model	AUC (95% CI)	Exploratory cutoff	Sensitivity (%)	Specificity (%)
Neck circumference	0.784 (0.727–0.841)	≥ 36.0 cm	72.0	71.4
NOSE score	0.769 (0.708–0.830)	≥ 35	73.2	69.0
ESS score	0.803 (0.749–0.857)	≥ 9	78.0	70.8
HOMA-IR	0.751 (0.687–0.815)	≥ 3.6	70.7	68.5
Combined model (apparent)	0.862 (0.815–0.909)	Predicted risk ≥ 0.30	81.7	76.2
Combined model (bootstrap-corrected)	0.846	—	—	—

AUC: area under the receiver operating characteristic curve; CI: confidence interval. Combined model: age, neck circumference, NOSE, ESS, HOMA-IR, BMI, waist circumference, PCOS duration, metformin use and hormonal therapy. Discrimination is against the Berlin risk classification, not against an objective diagnosis of OSA.

4-DISCUSSION

In the present study, almost one third (32.8%) of women with PCOS were classified as being at high risk of OSA. Compared with low-risk women, the high-risk group had more upper-airway symptoms, greater daytime sleepiness,

greater general and central adiposity, a higher blood-pressure profile, greater insulin resistance and a worse glycemic and lipid profile. Importantly, HOMA-IR remained significantly associated with high OSA risk after adjustment for BMI and waist circumference, and neck circumference, NOSE score and ESS score each provided additional independent information. A combined exploratory model of non-component clinical variables showed good internal discrimination. These findings support the view that the increased risk of OSA in PCOS reflects an interaction between metabolic abnormalities, regional adiposity, sleep-related symptoms and upper-airway characteristics, rather than obesity alone.

The proportion of women in the high-risk category is consistent with the large burden of OSA reported in PCOS, but must be interpreted with caution because OSA risk was assessed by questionnaire rather than physiologically confirmed. By pooling prevalence data from several studies, Kahal et al. [21] estimated the prevalence of OSA in women with PCOS at approximately 35%, and a systematic review and meta-analysis restricted to studies with formal sleep assessment by Abdul Jafar et al. [22] reported a prevalence of 37% in women with PCOS versus 6% in women without PCOS, with significantly higher odds of OSA in PCOS. An updated meta-analysis by He et al. [10] likewise showed an increased prevalence of OSA-hypopnea syndrome in PCOS and its association with a less favorable metabolic profile. Objective prevalence estimates, however, do not correspond directly to the 32.8% high-risk classification in the present study, because screening instruments identify a probability of disease rather than a diagnosis [10,22].

Our results also agree with recent evidence that obesity and insulin resistance are important determinants of OSA risk in PCOS. Women with overweight or obesity carried a higher risk of OSA even in sensitivity analyses that adjusted or matched for relevant confounders, including BMI. Similarly, Decrinis et al. [23] found that insulin-resistant women with PCOS were significantly more likely to be classified as high risk for OSA, identifying insulin resistance as an associated factor beyond age and BMI. These observations suggest that the association between PCOS and sleep-disordered breathing is not attributable to generalized obesity alone.

High-risk women also reported more upper-airway symptoms, and NOSE and ESS scores differed significantly between the groups. Nasal obstruction alters upper-airway mechanics, promotes oral breathing and increases nasal airflow resistance, all of which can disrupt sleep. A 2024 systematic review identified nasal congestion, obesity and larger neck circumference among the clinical factors associated with sleep apnea [24]. Nasal obstruction should nevertheless be regarded as a potentially modifiable contributor to OSA rather than a single cause. Current literature indicates that treatment of nasal obstruction improves nasal breathing, subjective sleep quality, daytime sleepiness and tolerance of positive airway pressure, whereas isolated nasal therapies are not consistently effective in reducing physiologically defined OSA [25]. The high NOSE scores observed here therefore represent a clinically significant burden of ENT symptoms, but do not imply that nasal obstruction by itself accounts for the OSA-risk classification. The higher ESS scores in high-risk women are also clinically relevant, because the ESS may reflect sleep fragmentation and poor sleep quality. The ESS should not, however, be used as a stand-alone test for OSA. Puretić et al. [26] showed that the ESS has low sensitivity compared with polysomnography, so that the absence of excessive daytime sleepiness cannot exclude OSA. The independent contribution of the ESS in the present study should therefore be interpreted as evidence that subjective sleepiness, combined with metabolic, anthropometric and upper-airway variables, provides complementary clinical information rather than a diagnostic tool.

Neck circumference remained associated with high OSA risk after BMI and waist circumference were taken into account, indicating that the distribution of soft tissue in the cervical region may provide information beyond that offered by total or abdominal adiposity. In their systematic review, Yayan and Rasche [24] identified neck circumference, obesity and nasal congestion as reproducible risk factors for sleep apnea. This may be particularly relevant in women with PCOS, in whom the pattern of adiposity and its metabolic consequences can differ substantially between women with the same BMI. The persistence of neck circumference in the adjusted model

suggests that it could serve as a simple additional element of clinical risk assessment. The higher prevalence of inferior turbinate hypertrophy and of Mallampati class III–IV in the high-risk group further supports the value of a focused upper-airway examination in the assessment of symptomatic women with PCOS, although these findings should be regarded as supportive rather than diagnostic of anatomical abnormality. OSA is a multifactorial disorder in which obesity, craniofacial and pharyngeal anatomy, neuromuscular control, nasal patency, ventilatory stability and sleep-related changes in airway collapsibility all play a role; no single factor can therefore explain OSA risk on its own [24,25].

Some of the largest crude differences between the high-risk and low-risk groups were observed for habitual snoring and witnessed apnea. Both, however, are intrinsic components of the Berlin questionnaire and cannot be regarded as new independent correlates of a Berlin-defined outcome. The same methodological issue applies to obesity and hypertension, which are directly or indirectly related to Berlin category scoring. Including these variables in a prediction model whose dependent variable is the Berlin classification would introduce incorporation bias and could overestimate predictive performance. For this reason, the primary exploratory model appropriately emphasized non-component markers such as neck circumference, NOSE score, ESS score and metabolic measures. This distinction is also central to interpreting the ROC performance of the model: the area under the curve represents discrimination of a screening classification, not diagnostic accuracy for polysomnography-defined OSA.

The high-risk group also had a less favourable metabolic profile, with greater insulin resistance, dysglycemia and dyslipidaemia, and the association of HOMA-IR with high OSA risk remained significant after controlling for BMI and waist circumference. Earlier objective sleep studies showed that women with PCOS and polysomnographically confirmed OSA were more insulin resistant than women with PCOS without OSA, even after accounting for age and BMI [16]. Subsequent research has confirmed an important link between sleep-disordered breathing and metabolic dysfunction in PCOS: Kahal et al. [9] found that women with PCOS and OSA had poorer metabolic characteristics, and Sam and Tasali [27] highlighted OSA as a potentially important modifier of metabolic risk in PCOS. More recent studies and meta-analyses have further shown that OSA risk is associated with insulin resistance, obesity, dyslipidaemia and other cardiometabolic abnormalities [10,22,23].

Several biological mechanisms may underlie these associations. Repeated obstruction of the upper airway fragments sleep and produces recurrent arousals, enhanced sympathetic nervous-system activity and intermittent hypoxemia. These disturbances can lead to oxidative stress, inflammatory signaling, disruption of the hypothalamic–pituitary–adrenal (HPA) axis, endothelial dysfunction and impaired insulin signaling. Conversely, insulin resistance, hyperinsulinemia, androgen excess and visceral and/or upper-body adiposity, all of which are linked to PCOS, may increase susceptibility to upper-airway obstruction, so that the relationship may be bidirectional [22,27]. The persistence of the HOMA-IR association after adjustment for adiposity indices in the present cross-sectional study supports, but does not prove, this hypothesis. The higher triglyceride levels and less favorable HDL-C profile in high-risk women are also in line with previous and current data on the relationship between OSA and dyslipidaemia in PCOS [9,10]. These relationships are complex, however, and may be influenced by the degree of obesity, diet, physical activity, PCOS phenotype, glucose-lowering and lipid-lowering drugs, hormonal therapy, smoking and other unmeasured factors, so residual confounding cannot be excluded. Longitudinal studies with objective sleep measures are needed to establish the temporal relationships and to determine whether the development or progression of OSA is the initial or a subsequent change.

The present findings have implications for clinical practice. The 2023 International Evidence-based Guideline recommends that women with PCOS be evaluated for signs and symptoms of OSA, such as snoring, waking unrefreshed, daytime sleepiness and fatigue, and referred for sleep assessment when these are present [1]. Our results support routine enquiry about habitual snoring, witnessed apnoea or choking, unrefreshing sleep, daytime sleepiness, fatigue and symptoms of nasal obstruction. Simple measurements such as neck circumference and a

targeted upper-airway examination may add clinical context, particularly in symptomatic women. The findings of Decrinis et al. [23] and Abdul Jafar et al. [22] further emphasize the need for greater attention to sleep disorders in women with PCOS, especially those with obesity. The combined model derived in this study should nevertheless be regarded as exploratory and not as a substitute for validated diagnostic pathways or objective sleep testing. Its good internal discrimination suggests that carefully selected non-component clinical and metabolic variables could help identify women with the Berlin high-risk phenotype, but external validation against home sleep apnea testing or overnight polysomnography is required. Likewise, although NOSE scoring and ENT examination may identify potentially treatable contributors to nasal obstruction, restoring nasal patency does not guarantee resolution of OSA [25].

Several limitations should be acknowledged. First, OSA was not confirmed by polysomnography or home sleep apnea testing, so the outcome was questionnaire-defined high risk. Second, there is inherent circularity in the use of the Berlin classification when evaluating obesity, hypertension, snoring and witnessed apnea, because these are components of the classification. Third, the cross-sectional design precludes conclusions about temporal or causal relationships between OSA risk, insulin resistance, upper-airway symptoms and metabolic abnormalities. Fourth, although BMI and waist circumference were adjusted for, other aspects of adiposity such as visceral fat distribution, PCOS phenotype, medication exposure, lifestyle factors and other determinants may be sources of residual confounding. Finally, the internally derived ROC model may perform optimistically in the development sample and should be tested in an external sample before clinical use. Despite these limitations, the results reveal an important cluster of sleep-related symptoms, upper-airway characteristics, regional adiposity and metabolic dysfunction in women with PCOS classified as being at high risk of OSA, in keeping with recent evidence of an increased prevalence of OSA in this population [10,22].

CONCLUSION

Women with PCOS had a high prevalence of questionnaire-defined high OSA risk, which was associated with upper-airway symptoms, cervical and central adiposity, daytime sleepiness, insulin resistance and an adverse metabolic profile. HOMA-IR remained associated with high OSA risk after adjustment for BMI and waist circumference. Screening should prompt appropriate objective evaluation and should not be regarded as a diagnosis.

DECLARATIONS

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