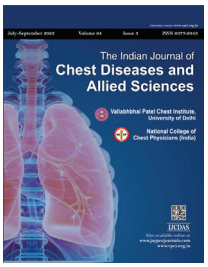
ORIGINAL ARTICLE

Obstructive Sleep Apnea and Sleep Quality in Women with Polycystic Ovary Syndrome: A Cross-sectional Study



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Srishti Saha[1], Sumitabh Singh[2], RM Pandey[3], Neeraj Nischal[4], Atul Malhotra[5], Sanjeev Sinha[6]

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Abstract

Background: Polycystic ovary syndrome (PCOS) is a common disorder in women of reproductive age. Although PCOS patients have a high prevalence of obstructive sleep apnea (OSA), there is limited data on sleep quality and abnormalities in sleep architecture among this patient population. We conducted a study to assess the frequency of OSA and poor sleep quality in women with PCOS and to assess any association between these sleep disorders and metabolic abnormalities.

Materials and methods: An observational study of adults with PCOS (by revised Rotterdam criteria) from May 2015 to June 2017 was conducted. Patients with thyroid disorders, pre-existing depression, current pregnancy, and recent drug use (benzodiazepines, antidiabetics, antiepileptics, steroids, and androgens) were excluded. The evaluations included the following: overnight polysomnography (PSG), lipid profile, testosterone, fasting insulin, fasting glucose levels, free androgen index (FAI), and homeostatic model assessment for insulin resistance (HOMA-IR); sleep quality [Pittsburgh Sleep Quality Index (PSQI), Jenkins Sleep Scale (JSS)], daytime sleepiness and possible depression were assessed by standard questionnaires. Descriptive statistics, *t*-test/Mann–Whitney test, Chi-squared test/Fischer's test were used as appropriate; $p < 0.05$ was considered statistically significant.

Results: A total of 65 patients, mean age 24.3 ± 4.0 years; mean body mass index (BMI) 26.4 ± 5.3 kg/m^2 were included. Frequencies of sleep disorders were evaluated as follows: Obstructive sleep apnea 10.9% (7/64) [95% confidence interval (CI): 5.4–20.9%], poor sleep quality 35.0% (21/60) (95% CI: 24.2–47.6%) by JSS, 54.2% (32/59) (95% CI: 41.6–66.3%) by PSQI. The PSG indicators of sleep quality were abnormal in arousal index, 96.8% (62); %wake time, 62.5% (40); sleep latency, 40.6% (26); and sleep efficiency, 12.5% (8). Anthropometric indicators of obesity were higher in OSA vs non-OSA patients ($p < 0.05$). The OSA patients had lower total sleep time and %N2 stage, and higher desaturation index than non-OSA patients. When patients with good and poor sleep quality were compared, poor sleepers (by JSS and PSQI) had higher depression scores; poor sleepers by JSS had a lower waist–hip ratio ($p < 0.05$). Daytime sleepiness scores were similar in OSA and non-OSA patients, and in good and poor sleepers.

Conclusion: Sleep disorders, particularly poor sleep quality, are frequent in women with PCOS. Patients should be screened for these disorders using specific questionnaires. Further research into the metabolic consequences of these sleep disorders is mandated.

Keywords: Apnea, Metabolic, Polysomnography, Sleep disorder, Sleep quality.

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Abbreviations used in this Article

PCOS = Polycystic ovary syndrome; OSA = Obstructive sleep apnea; PSG = Polysomnography; FAI = Free androgen index; HOMA-IR = Homeostatic model assessment for insulin resistance; PSQI = Pittsburgh Sleep Quality Index; JSS = Jenkins Sleep Scale; BMI = Body mass index; CI = Confidence interval; AIIMS = All India Institute of Medical Sciences; TSH = Thyroid stimulating hormone; SHBG = Sex hormone binding globulin; NC = Neck circumference; PPNC = Percentage predicted neck circumference; ESS = Epworth Sleepiness Scale; CESD-R = Centre for Epidemiologic Studies Depression Scale – Revised; EOG = Electrooculogram EOG; AASM = American Association of Sleep Medicine; AHI = Apnea hypopnea index; PAP = Positive airway pressure; OCPs = Oral contraceptive pills; LDL = Low-density lipoprotein; VLDL = Very low-density lipoprotein; REM = rapid eye movement; WASO = Wake after sleep onset; HDL = High-density cholesterol.

Background

Polycystic ovary syndrome is a common endocrine disorder affecting 9–18% of women in the reproductive age-group.[1] Clinical

[1]Division of Gastroenterology and Hepatology, Mayo Clinic, Rochester, Minnesota, United States of America; Department of Medicine, All India Institute of Medical Sciences, New Delhi, India

[2]Division of Endocrinology, Mayo Clinic, Rochester, Minnesota, United States of America

[3]Department of Biostatistics, All India Institute of Medical Sciences, New Delhi, India

[4,6]Department of Medicine, All India Institute of Medical Sciences, New Delhi, India

[5]Division of Pulmonary, Critical Care and Sleep Medicine, University of California – San Diego, California, United States of America

Corresponding Author: Sanjeev Sinha, Department of Medicine, All India Institute of Medical Sciences, New Delhi, India, Phone: +91 11 26593688, email: drsanjeevsinha@gmail.com

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features include menstrual abnormalities (oligomenorrhea/amenorrhea) and manifestations of hyperandrogenism (hirsutism, androgenic alopecia, and acne). A key feature of this disorder is the frequent occurrence of metabolic abnormalities, most notably insulin resistance.[1]

In the last few years, there has been increasing interest in sleep disorders in PCOS. Studies have shown women with PCOS are at higher risk for sleep disorders compared to healthy women.[2,3] Obstructive sleep apnea is caused by recurrent upper airway collapse during sleep leading to transient episodes of airflow cessation and oxygen desaturation. The resultant sleep fragmentation and episodic hypoxemia causes hypothalamic–pituitary axis hyperactivity, sympathetic nervous system stimulation, increased cortisol levels and adipokine release.[4,5] These factors lead to the development and exacerbation of metabolic abnormalities, particularly insulin resistance.[4,5] Since PCOS patients are already predisposed to metabolic abnormalities, OSA adds insult to injury. Sleep disorders other than OSA also adversely affect metabolism, mood and cognition; however, data on non-OSA sleep disorders in PCOS are limited.[6–13]

In this study, we sought to determine the frequency of OSA and poor sleep quality in women with PCOS and to find associations between sleep disorders and metabolic parameters. We conducted this study in a developing country where research on sleep disorders has been sparse.

Materials and Methods

A cross-sectional study of patients attending the outpatient clinics of Departments of Medicine, Obstetrics and Gynecology, and Endocrinology at All India Institute of Medical Sciences (AIIMS), New Delhi, India during a 2-year period from May 2015 to June 2017 was conducted. Consecutive adults with suspected PCOS were screened for eligibility based on presence of definite PCOS [2003 Revised Rotterdam criteria: Above or equal to 2 of chronic oligoovulation, clinical and/or biochemical hyperandrogenism, polycystic ovaries, with exclusion of other etiologies (congenital adrenal hyperplasia, androgen secreting tumors, Cushing's syndrome, hyperprolactinemia)].[14] Patients with thyroid disorders, pre-existing clinical depression, current pregnancy and recent drug use (benzodiazepines, anti-diabetic medications, anti-epileptics, steroids, androgens within 3 months) were excluded. Due to the clinic-based setting of the study, and the labor and economically intensive procedures included, a consecutive sampling technique was utilized. Ethics approval was obtained from the Institutional Ethics Committee for Post Graduate Research, AIIMS, New Delhi, India. Patients who provided written informed consent were included and underwent evaluations discussed in the following.

Laboratory Testing

To confirm eligibility, patients underwent the following laboratory investigations: Total T4, (TSH), cortisol, prolactin, total testosterone (all measured using radio immunoassay, COBAS E 411 analyzer) and 17-hydroxy progesterone [17-OHP; using enzyme-linked immunoassay (ELISA)]. Those who were included were tested for lipid profile (immune–colorimetric assay), fasting blood glucose (thyroid stimulating hormone COBAS Integra 400; glucose oxidase method), fasting insulin (COBAS E 411 analyzer), and sex hormone binding globulin (SHBG; using ELISA). Also, HOMA-IR (normal <3.8),[15] a measure of insulin resistance and FAI (normal <4) were calculated using the following formulas:

$$\text{HOMA-IR} = \text{Fasting insulin (mIU/L)} \times \text{Fasting glucose (mg/dL)}/405$$

$$\text{FAI} = \text{Total testosterone} \times 100/\text{SHBG}$$

Anthropometry

Measurements of height, weight, BMI, neck length, neck circumference (NC), waist and hip circumferences were taken. Percentage predicted neck circumference (PPNC) was calculated using Davies and Stradling formula as follows:

$$\text{PPNC} = 100 \times \text{NC}/0.55 \times 4 + 310$$

Height was measured using a stadiometer and weight measured using Tanita body composition analyzer. Body mass index was interpreted according to Indian reference standards.[16]

Questionnaires

Standard questionnaires were administered to the patients by the investigator. Epworth Sleepiness Scale (ESS) was used to assess daytime sleepiness; ESS score above 10 indicated excessive daytime sleepiness. To assess sleep quality, the JSS and PSQI were used. The JSS assesses difficulty in initiation and maintenance of sleep, nighttime arousals and daytime functioning; a score above or equal to 12 signifies poor sleep quality.[17] The PSQI uses seven component scores derived from 19 questions; score above 5 suggests poor sleep quality.[18] Both questionnaires assess sleep quality within the previous 1 month, with higher scores indicating poorer sleep quality.

To evaluate for possible depression, Centre for Epidemiologic Studies Depression Scale – Revised (CESD-R) was used.[19] It measures symptoms of depression using 20 questions; score above or equal to 16 indicates possible depression.

Polysomnography

Patients underwent an overnight PSG at Sleep Laboratory, Department of Medicine, AIIMS, New Delhi, India. It was conducted and interpreted by trained personnel using Alice PDx (Respironics Inc., Pennsylvania, USA) and SOMNOscreen™ plus (SOMNOmedics America Inc., Florida, USA). The following channels were used: Central and occipital electroencephalogram (EEG), electrooculogram (EOG), submentalis electromyogram (EMG), nasal and/or oral airflow, nasal pressure sensor, microphone for snore data, thoracic and abdominal wall motion, anterior tibialis EMG, body position and electrocardiogram. Arterial oxygen saturation was monitored with a pulse oximeter. The tracing was scored in 30 second epochs using the American Association of Sleep Medicine (AASM) 2012 guidelines.[20] Apnea was scored when there was a drop in the peak signal excursion by more than or equal to 90% of pre-event baseline for more than or equal to 10 seconds. Hypopnea was scored when the peak signal excursions dropped by more than or equal to 30% of pre-event baseline for more than or equal to 10 seconds in association with either more than or equal to 3% arterial oxygen desaturation or an arousal. Apnea hypopnea index (AHI) was defined

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as the number of apnea and hypopnea events per hour of sleep. Obstructive sleep apnea was diagnosed when AHI was more than or equal to 5 per hour. Obstructive sleep apnea severity was defined as mild (AHI 5–15/hour), moderate (AHI 15–30/hour), and severe (AHI more than or equal to 30/hour). Patients with OSA underwent a split–night study for positive airway pressure (PAP) titration.

Additional PSG indicators for assessing sleep quality and quantity were reported as follows: Arousal index (normal: <5%), wake percent (normal: <10%), sleep latency (normal: <20 minutes), and sleep efficiency (normal: >75%). A cut-off of 75% was used for sleep efficiency to account for first night effect.

The primary outcome was the frequency of OSA and poor sleep quality in the study cohort. Secondary outcomes included exploring associations between sleep disorders and metabolic parameters.

Statistical Analysis

Data were analyzed using statistical software STATA 14.0 and JMP 14.0. Descriptive statistics were used to summarize baseline characteristics. Independent *t*-test and Mann–Whitney (rank–sum) test were used to compare continuous variables as appropriate. Chi-squared and Fischer's exact test were used to find the association between categorical variables as appropriate; $p < 0.05$ was considered statistically significant.

Results

Baseline Characteristics

A total of 65 consecutive patients with definite PCOS and meeting eligibility criteria were included. Mean age was 24.3 ± 4.0 years and mean BMI was 26.4 ± 5.3 kg/m^2 (Table 1). Based on BMI, 1.6% patients were underweight, 16.9% were overweight, and 53.8% were obese and the rest were normal. Level of education among the patients was as follows: Illiterate, 3.3% (2); school education, 33.3% (20); graduate degree, 46.7% (28); and professional/honors degree, 16.7% (10). Overall, 25.4% (15) patients received treatment above 3 months before inclusion in the study, and among these patients, 12.3% (7) received oral contraceptive pills (OCPs), 7.0% (4) underwent prior ovulation induction with clomiphene citrate, 1.7% (1) received aldosterone ,and 3.5% (2) received oral hypoglycemic agents. Of all patients, 64 underwent PSG; one patient with an initial technically inadequate PSG refused a repeat study. Baseline characteristics of patients are shown in Table 1.

Metabolic and Hormonal Profile

Among the metabolic and hormonal parameters, abnormal lipid profile was seen in the following manner: Low-density lipoprotein (LDL), 12.9% (7); very low-density lipoprotein (VLDL), 18.9% (10); triglycerides, 18.5% (10). Parameters of glucose metabolism were abnormal in the following: Fasting glucose (impaired), 8.9% (5); fasting insulin, 17.6% (9); and insulin resistance (HOMA-IR), 18.8% (12).

Biochemical hyperandrogenism was present in 37.0% (20) by total testosterone and 39.5% (15) by FAI.

Clinical and PSG Assessment of Sleep Disorders

Obstructive Sleep Apnea

Among the 64 patients with a technically adequate PSG, mean AHI was 2.36 ± 4.15 per hour. Overall, 7 patients had OSA; frequency, 10.9% (95% CI: 5.4–20.9%). Six patients had mild OSA, while one had moderate OSA. All OSA patients were obese. Clinically, 13.8% experienced excessive daytime sleepiness by ESS; only 1 patient with OSA had excessive daytime sleepiness.

When patients with and without OSA were compared, there were statistically significant differences in anthropometric parameters of obesity (Table 1). Daytime sleepiness and sleep quality were similar in both groups. The OSA patients had lesser total sleep time and %N2 stage, and higher desaturation index than non-OSA patients. They also tended to be older, had lower sleep efficiency and higher %N3 stage, though the difference was not statistically significant. Fasting blood glucose and FAI were higher in the OSA group, though the difference was not statistically significant (Table 1).

Sleep Quality

A significant proportion of patients had poor sleep quality: 54.2% (32/59 patients; 95% CI: 41.6–66.3%) by PSQI and 35.0% (21/60 patients; 95% CI: 24.2–47.6%) by JSS.

When patients with good and poor sleep quality were compared, those with poor sleep quality (by JSS and PSQI) had higher depression scores and poor sleepers by JSS had lower waist–hip ratio (Tables 2 and 3). Poor sleepers also spent more time in rapid eye movement (REM) stage (by JSS and PSQI) and had lower fasting insulin, though the differences were not statistically significant (Tables 2 and 3).

A significant proportion of patients had one or more of the several PSG indicators of poor sleep quality (Table 4). We used the 75% cut-off for sleep efficiency to account for first night effect. The PSG indicators of sleep quality were not different in patients with and without OSA or poor sleep quality (Tables 1 to 3).

Discussion

Polycystic ovary syndrome is a common disorder in young women, with a high risk of sleep disorders and metabolic abnormalities.[2,3,7] In this clinic-based study of PCOS patients, 10.9% patients had OSA. Over half of the patients reported poor sleep quality when assessed by PSQI and 35% when assessed by JSS. Patients with and without OSA had statistically significant differences in obesity parameters and PSG variables such as total sleep time, %N2 stage and desaturation index. Patients with poor sleep quality, had higher depression scores than those with good sleep quality.

The frequency of OSA in PCOS patients ranges from 11% to 72%; in a recent meta-analysis, pooled OSA prevalence in adults with PCOS was 32%.[2,3,21–25] Heterogeneous study design, varying patient populations, inconsistent testing methods and variable diagnostic criteria (for both OSA and PCOS) may account for the range in estimates. In our study, the frequency of OSA was lower than most previous studies. There could be several reasons for this: first, our patients were younger and leaner than those included in most studies. Second, to provide a robust estimate of OSA frequency across the spectrum of PCOS patients, we did not screen patients using sleep questionnaires or by OSA-specific risk factors. Third, contraceptive pills and metformin (used for treating PCOS) can reduce the risk of OSA and could have influenced our results, though the proportion of patients receiving treatment were similar in OSA and non-OSA groups.[26–28]

In our study, several indicators of obesity were higher in the OSA group, which is known to predict OSA.[29] Daytime sleepiness was similar in patients with and without OSA; this is consistent with a previous report which suggests that ESS may not be a reliable

Table 1: Comparison of variables between patients with and without OSA

Variable (unit) (normal range)	*All patients (n = 65)*	*Without OSA (n = 57)*	*With OSA (n = 7)*	*p-value*[#]
Baseline and anthropometric variables				
Age (years)	24.3 ± 4.0	24.1 ± 3.9	27.3 ± 5.0	0.056*
BMI (kg/m^2)	26.4 ± 5.3	25.7 ± 5.0	32.5 ± 3.7	0.001
Waist circumference (cm)	89.8 ± 11.2	88.1 ± 10.3	103.3 ± 9.3	<0.001
Hip circumference (cm)	98.6 ± 9.9	97.4 ± 9.1	108.3 ± 12.2	0.005
Waist–hip ratio (<0.8)	0.91 (0.74–1.11)	0.9 (0.7–0.8)	0.96 (0.9–1.1)	0.15
NC (cm) (<32)	32 (25–43)	31.6 ± 2.8	35 ± 2.9	0.004
PPNC (<100)	80.9 ± 7.4	79.9 ± 6.8	88.8 ± 7.2	0.002
Treatment history				
Received any treatment, % (*n*)	25.4 (15)	25.5 (13)	28.6 (2)	0.86
OCPs, % (*n*)	12.3 (7)	14.3 (7)	0 (0)	0.28
Clinical evaluation: Excessive daytime sleepiness, sleep quality, depression				
ESS (≤10)	7 (0–14)	7 (0–13)	5 (1–14)	0.67
PSQI (≤5)	6 (1–17)	6 (1–17)	5.5 (1–15)	0.91
JSS (<12)	9.5 (4–23)	10 (4–23)	12 (4–22)	0.69
CESD-R (<16)	17.5 (1–46)	17 (1–40)	21.5 (12–46)	0.26
PSG variables				
Total sleep time (min)	440.3 ± 71.8	450.0 ± 58.8	361.4 ± 117.0	0.016
Sleep efficiency (%) (>75)	84.9 ± 8.8	85.5 ± 7.5	78.6 ± 17.4	0.07*
Sleep latency (min) (<20)	16 (2.5–73.5)	16.0 (2.5–60.5)	12.5 (6.0–73.5)	0.33
N1 stage %	15.2 (4.1–42.4)	14.3 (4.1–42.4)	18.2 (5.2–36)	0.57
N2 stage %	33.8 ± 11.2	40.3 ± 7.5	33.8 ± 11.2	0.046
N3 stage %	34.8 ± 6.4	28.2 ± 9.1	34.8 ± 6.4	0.07*
REM stage %	13.6 (0–27.4)	13.6 (0–27.4)	14.2 (3.9–21.6)	0.81
WASO (min)	41.8 (0–223.5)	42 (0–193.5)	37 (12–223.5)	0.59
%WASO (<10)	12.4 (1.5–53.9)	12 (1.5–37.3)	13.4 (5.6–53.9)	0.44
Arousal index (/hr) (<5)	15.3 (3.6–96.9)	15.2 (3.6–96.9)	15.4 (10.3–35.2)	0.96
Desaturation index (/hr)	0.5 (0–22.4)	0.3 (0–2.6)	4.8 (0.5–22.4)	<0.001
Metabolic and hormonal studies				
Fasting blood glucose (mg/dL) (<126)	87.7 ± 10.4	86.6 ± 10.4	95.3 ± 7.7	0.053*
Fasting insulin (mIU/L) (<25)	10.9 (0.4–132.9)	10.6 (0.4–132.9)	15.3 (6.0–23.2)	0.39
HOMA-IR (<3.8)	2.1 (0–28.8)	1.9 (0–28.8)	2.6 (0–5.04)	0.87
Testosterone (ng/mL) (<0.481)	0.415 ± 27.140	0.419 ± 0.205	0.420 ± 0.195	0.98
SHBG (nmoL/L) (<120)	46.7 (0.4–108.7)	48.9 (0.4–107.6)	29.1 (13.6–69.3)	0.12
FAI (<4)	3.5 (0.7–10.9)	3.4 (0.8–7.5)	6.2 (1.7–10.9)	0.06*
Total cholesterol (mg/dL) (<200)	160.9 ± 31.0	162.7 ± 32.1	150 ± 19.2	0.34
LDL (mg/dL) (<130)	96.5 ± 25.6	98.2 ± 26.5	87.5 ± 14.4	0.34
HDL (mg/dL) (≥50)	41.8 ± 9.2	42.1 ± 9.6	39.2 ± 6.9	0.47
VLDL (mg/dL) (<30)	23.3 ± 13.4	23.2 ± 14.0	23.3 ± 8.9	0.97
Triglycerides (mg/dL) (<150)	104 (47–439)	103 (47–439)	109 (63–184)	0.68

Values are given as mean ± SD for and median (minimum–maximum) for normal and skewed distribution, respectively;[#]*p* values compare OSA and non-OSA patients; **p* values approaching significance; PPNC, percentage predicted neck circumference; CESD-R, Centre for Epidemiologic Studies Depression Scale – Revised; REM, rapid eye movement; WASO, wake after sleep onset; HOMA-IR, homeostatic model assessment-insulin resistance; SHBG, sex hormone binding globulin; FAI, free androgen index; LDL, low-density cholesterol; HDL, high-density cholesterol; VLDL, very low-density cholesterol

Table 2: Comparison of variables between good and poor sleepers by JSS

Variable (unit) (normal range)	*Without poor sleep quality (n = 39)*	*With poor sleep quality (n = 21)*	*p-value*
Age (years)	24 ± 4.2	24.8 ± 3.6	0.46
BMI (kg/m^2)	26.5 ± 5.0	26.8 ± 6.0	0.87
Waist circumference (cm)	91.3 ± 9.9	88.2 ± 12.9	0.30
Hip circumference (cm)	98.7 ± 9.8	99.3 ± 11.1	0.82
Waist–hip ratio	0.93 (0.78–1.11)	0.89 (0.74–1.02)	0.03
NC (cm)	32.2 ± 2.8	32.1 ± 3.3	0.89
PPNC (%)	81.4 ± 7.1	81.1 ± 8.1	0.88
Treatment history			
Received any treatment, % (*n*)	21.1 (8)	28.6 (6)	0.51
OCPs, % (*n*)	8.1 (3)	20.0 (4)	0.19
Clinical evaluation: Daytime sleepiness, depression			
ESS	6 (0–13)	8 (0–14)	0.66
CESD-R	15 (1–38)	24 (8–46)	0.001
PSG parameters			
Total sleep time (min)	440.6 ± 75.2	447.9 ± 61.9	0.71
Sleep efficiency (%)	84.2 ± 9.7	85.0 ± 7.7	0.75
Sleep latency (min)	18.5 (2.5–73.5)	12.5 (2.5–56)	0.18
N1 stage %	16.1 (4.1–38.5)	14.3 (5.2–42.4)	0.72
N2 stage %	39.8 ± 8.9	40.2 ± 7.1	0.85
N3 stage %	29.2 ± 9.6	28.1 ± 8.9	0.66
REM stage %	12.6 (0–24.5)	16.8 (1.5–27.4)	0.09*
WASO (min)	41.8 (9–223.5)	56.5 (0–193.5)	0.29
%WASO	12.7 (1.9–53.9)	13.4 (4.3–37.3)	0.77
Arousal index	15.1 (5.5–52.7)	14.8 (3.6–78.4)	0.87
AHI (events/hr)	1.1 (0–26)	1 (0.1–9)	0.98
Metabolic parameters			
Fasting blood glucose (mg/dL) (<126)	89.2 ± 11.5	84.7 ± 8.32	0.15
Fasting insulin (mIU/L) (<25)	11.1 (0.4–132.9)	8.8 (3.6–29.5)	0.08*
HOMA-IR (<3.8)	2.2 (0–28.8)	1.8 (0–6.1)	0.43
Testosterone (ng/mL) (<0.481)	0.346 (0.114–0.984)	0.471 (0.128–0.696)	0.71
SHBG (nmoL/L) (<120)	49.9 (16.3–108.7)	39.4 (0.4–107.6)	0.46
FAI (<4)	3.6 (0.7–7.5)	3.4 (0.9–460.5)	0.69
Total cholesterol (mg/dL) (<200)	162.6 ± 37.7	157.4 ± 19.3	0.58
LDL (mg/dL) (<130)	98.2 ± 30.1	92.4 ± 17.4	0.43
HDL (mg/dL) (≥50)	40.9 ± 10.7	43.5 ± 6.8	0.35
VLDL (mg/dL) (<30)	20.5 (7–88)	19.5 (10–59)	0.52
Triglycerides (mg/dL) (<150)	109 (47–439)	99.5 (49–294)	0.43

Values are given as mean ± SD for and median (minimum–maximum) for normal and skewed distribution, respectively;**p* values approaching significance; PPNC, percentage predicted neck circumference; CESD-R, Centre for Epidemiologic Studies Depression Scale – Revised; REM, rapid eye movement; WASO, wake after sleep onset; HOMA-IR, homeostatic model assessment-insulin resistance; SHBG, sex hormone binding globulin; FAI, free androgen index; LDL, low-density cholesterol; HDL, high-density cholesterol; VLDL, very low-density cholesterol

indicator of sleepiness in women.[30] The OSA patients had less total sleep time, more %N2 stage and higher oxygen desaturation index compared to non-OSA, findings which are consistent with previous reports.[31,32] There was a difference in fasting blood glucose and FAI between the non-OSA and OSA patients which did not reach statistical significance, probably due to limited sample size. Previous studies have found OSA to be associated with insulin resistance and some have found insulin resistance to predict OSA in PCOS. Evidence regarding androgen levels in OSA is conflicting.[3,21,22,29,33–35]

Table 3: Comparison of variables between good and poor sleepers by PSQI

Variable	*Without poor sleep quality (n = 27)*	*With poor sleep quality (n = 32)*	*p-value*
Age (years)	24.2 ± 4.6	24.4 ± 3.6	0.88
BMI (kg/m^2)	26.3 ± 4.7	26.8 ± 5.9	0.69
Waist circumference (cm)	91.4 ± 10.4	89.0 ± 11.7	0.41
Hip circumference (cm)	98.0 ± 9.2	99.3 ± 10.9	0.64
Waist–hip ratio	0.92 (0.8–1.11)	0.90 (0.74–1.02)	0.09*
NC (cm)	31.8 ± 2.4	32.2 ± 3.4	0.60
PPNC (%)	80.6 ± 5.9	81.5 ± 8.5	0.64
Treatment history			
Received any treatment, % (*n*)	19.2 (5)	28.1 (9)	0.43
OCPs, % (*n*)	7.7 (2)	16.7 (5)	0.31
Clinical evaluation: Daytime sleepiness, depression			
ESS	5 (0–13)	8 (0–14)	0.11
CESD-R	14 (1–34)	22 (7–46)	<0.001
PSG parameters			
Total sleep time (min)	432.6 ± 84.2	448.5 ± 54.8	0.41
Sleep efficiency (%)	83.4 ± 10.8	85.5 ± 7.2	0.39
Sleep latency (min)	18.5 (2.5–73.5)	13.8 (2.5–56)	0.25
N1 stage %	16.1 (4.1–38.5)	14.3 (5.2–42.4)	1.0
N2 stage %	40.2 ± 9.3	39.9 ± 7.2	0.91
N3 stage %	29.2 ± 9.7	28.3 ± 9.1	0.74
REM stage %	10.1 (0–24.5)	15.1 (1.5–27.4)	0.07*
WASO (min)	41.8 (9–223.5)	45 (0–193.5)	0.42
%WASO	13.4 (1.9–53.9)	13.1 (4.3–37.3)	0.75
Arousal index	13.9 (5.5–52.7)	15.4 (3.6–78.4)	0.65
AHI (events/hr)	0.8 (0–26)	1.0 (0.1–9)	0.44
Metabolic parameters			
Fasting blood glucose (mg/dL) (<126)	89.7 ± 12.3	85.9 ± 8.9	0.21
Fasting insulin (mIU/L) (<25)	10.8 (0.39–117.7)	9.53 (3.64–132.9)	0.40
HOMA-IR (<3.8)	2.1 (0–22.4)	2.0 (0–28.8)	0.77
Testosterone (ng/mL) (<0.481)	0.345 (0.114–0.984)	0.382 (0.128–0.696)	0.72
SHBG (nmoL/L) (<120)	57.3 (16.3–108.7)	42.7 (0.4–107.6)	0.26
FAI (<4)	2.2 (0.7–7.5)	3.6 (0.9–460.5)	0.34
Total cholesterol (mg/dL) (<200)	164.3 ± 38.4	158.0 ± 27.3	0.52
LDL (mg/dL) (<130)	98.2 ± 27.9	94.6 ± 25.3	0.64
HDL (mg/dL) (≥50)	41.7 ± 12.2	41.9 ± 7.0	0.93
VLDL (mg/dL) (<30)	20.5 (7–88)	20 (9–59)	0.35
Triglycerides (mg/dL) (<150)	110 (63–439)	102 (47–294)	0.26

Values are given as mean ± SD for and median (minimum–maximum) for normal and skewed distribution, respectively;*p values approaching significance; PPNC, percentage predicted neck circumference; CESD-R, Centre for Epidemiologic Studies Depression Scale – Revised; REM, rapid eye movement; WASO, wake after sleep onset; HOMA-IR, homeostatic model assessment-insulin resistance; SHBG, sex hormone binding globulin; FAI, free androgen index; LDL, low-density cholesterol; HDL, high-density cholesterol; VLDL, very low-density cholesterol

A major proportion of patients in our study reported poor sleep quality, similar to previous studies.[6,35] A population based study using diagnostic codes found much lower prevalence of non-OSA sleep disorders compared to our findings.[7] Being a clinic-based study, our patients likely had more severe disease than the prior reports from community samples. Also, we evaluated global sleep quality without limiting our definition to specific sleep disorders. These issues could explain the high frequency of sleep disturbance seen in our study. In the absence of a control group matched for age, socioeconomic status and comorbid conditions, the frequent

Table 4: Polysomnographic indicators of poor sleep quality ($n = 64$)

Polysomnographic variable	*Patients with abnormality % (n)*
High arousal index	96.8 (62)
High wake percent	62.5 (40)
Prolonged sleep latency	40.6 (26)
Poor sleep efficiency	12.5 (8)

occurrence of poor sleep in PCOS is hypothesis-generating but needs to be validated in future studies.

The underlying cause for the frequent occurrence of poor sleep is of particular interest. Sleep quality assessed by PSQI and JSS is composite of the perception of sleep by patients. It may or may not be entirely related to underlying sleep disorders. Several factors such as depression, hormonal variations, heightened hypothalamic–pituitary–adrenal axis reactivity, altered cytokine profile can contribute to poor sleep quality.[6] These should be further explored in future studies.

When comparing poor and good sleepers, depression scores were higher in poor sleepers; this finding is consistent with a previous study in which depression partly accounted for poor sleep.[6]. Previous studies have also found sleep disturbances to be associated with metabolic abnormalities, though they have focused mostly on sleep duration rather than quality.[10,11,13] Surprisingly, we found fasting insulin, a surrogate marker of insulin resistance, to be lower in poor sleepers, though this finding was not statistically significant. Waist–hip ratio, but not other indicators of obesity, was lower in poor sleepers. Future studies on determinants of sleep quality and its metabolic consequences are needed.

Our study is one of the few assessing sleep disorders, especially sleep quality in PCOS patients. To our knowledge, this is the first study reporting associations between metabolic parameters and sleep quality in PCOS. Strengths of our study include use of PSG for diagnosis of OSA, evaluation of sleep quality using sleep scales as well as PSG. Our study adds to the limited body of evidence from developing countries. However, our study had several limitations. Sample size was modest and was based on outpatient clinic attendees. Patients attending hospital clinics are likely to have more severe disease than non-clinic patients, and may not adequately reflect the characteristics of a population-based cohort of patients. Women are less likely to report to hospitals for sleep related complaints, and under-report snoring and daytime symptoms.[36] Thus, the actual frequency of sleep disorders could be higher outside the hospital setting. Due to the labor and economically extensive procedures included, and the clinic-based setting of the study, a consecutive sampling method was used, which can lead to bias in estimates. Being a tertiary care referral center, we elected to include patients who received treatment for PCOS in the past. Considering the similar distribution of such patients in those with and without sleep disorders, any resulting bias is likely to be minimal. While the Epworth sleepiness questionnaire has been validated in Hindi,[37] which was the primary language of the study population, the other questionnaires used in the study have not been previously validated. Finally, absence of a control group and the low event rates make it difficult to control for confounders.

Conclusion

Poor sleep quality is frequent in patients with PCOS. Physicians must have a low threshold for screening for sleep disorders in this patient population. Larger studies in the future are needed to evaluate the determinants and metabolic consequences of sleep quality in PCOS.

Ethics Approval

Ethics approval was obtained from the Institutional Ethics Committee for Post Graduate Research, AIIMS, New Delhi, India (No. IESC/T-251/05.05.2015). Written informed consent was obtained from patients as stated above.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' Contributions

SS (Srishti Saha): Study design, data acquisition, data analysis and interpretation, manuscript writing and revision; SS (Sumitabh Singh): Intellectual inputs, data interpretation, manuscript writing and revision; RMP: Intellectual inputs, data analysis and interpretation; NN: Intellectual inputs, data interpretation, manuscript writing and revision; AM: Intellectual inputs, data interpretation, manuscript writing and revision; SS (Sanjeev Sinha): Study design, data interpretation, manuscript writing and revision, corresponding author who had full access to the all data in the study, and had final responsibility for the decision to submit for publication. All authors have read and approved the manuscript.

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