REVIEW ARTICLE

Pooled Prevalence of Obstructive Sleep Apnea in Patients with Polycystic Ovary Syndrome: A Systematic Review

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Objective: To estimate the prevalence of obstructive sleep apnea (OSA) in patients with polycystic ovary syndrome (PCOS).

Materials and Methods: The present study is a systematic review. The inclusion criteria were observational or epidemiological studies conducted in patients with PCOS to evaluate the prevalence of OSA. Four electronic databases were used for systematic searching, including PubMed, Science Directe, Scopus, and CINAHL Plus, from inception to September 26, 2022. Meta-analysis using a random-effects model was used to pool the results of the included studies.

Results: Among the 3,940 records retrieved from the four databases, they were screened to identify an included study. Of those, 12 observational studies (82,460 patients) met our inclusion criteria and were included in the meta-analysis. The most common study type was cohort study (5 studies). Six studies were conducted in the US, while other studies were conducted in Brazil, the UK, China, Taiwan, and India. Our findings found that the pooled prevalence of OSA from 10 studies (887 patients) was 40.4% (95% CI 24.3% to 58.9%). A subgroup analysis by age group found that adult patients (9 studies with 859 patients) had a lower prevalence of OSA than adolescents (1 study with 28 patients) (38.7% vs. 57.1%). While the pooled incidence of OSA from 2 studies (81,573 patients) was low at 0.7% (95% CI 0.2% to 2.0%).

Conclusion: The pooled prevalence of OSA in patients with PCOS was higher than previous systematic reviews at 40.4%. Physicians should be aware of OSA in patients with PCOS.

Keywords: Obstructive sleep apnea; Polycystic ovary syndrome; Prevalence; Systematic review; Meta-analysis

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Polycystic ovary syndrome (PCOS) is a complex endocrine disorder in women with a prevalence of 8 to 13%[1]. Patients with PCOS have clinical features of irregular menses, hyperandrogenism, and polycystic ovarian morphology[1,2]. PCOS is related to insulin resistance, obesity, and several other consequences, such as cardiovascular diseases. Obstructive sleep apnea (OSA) is characterized by repetitive hypoxemia while sleeping. OSA is also related to insulin resistance and cardiovascular consequences such as hypertension[3-7]. High body mass index is related to OSA and hypertensive emergency by 1.666 times[3].

Both PCOS and OSA share similar mechanisms and consequences, such as obesity or diabetes. These two diseases may be linked to each other[8]. A meta-analysis from a previous systematic review found that patients with PCOS and OSA had a significantly higher body mass index of 6.01 kg/m^2 (95% confidence intervals, CI of 4.69 to 7.33) than patients with PCOS without OSA[9]. PCOS is an independent risk factor for OSA by 9.74 times (95% CI of 2.76 to 34.41)[10]. A previous systematic review published in 2017 found that the prevalence of OSA in patients with PCOS was 22%[10]. Another recent systematic review reported that the pooled prevalence of OSA in patients with PCOS was increasing to 35% (95% CI of 22.2 to 48.9)[11]. To update the information about the prevalence of the disease from published research articles, the present study aimed to perform a systematic review to estimate the prevalence of OSA in patients with PCOS.

Materials and Methods

The present study design was a systematic review to

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investigate the prevalence of OSA in patients with PCOS from published research articles. The inclusion criteria were as follows: 1) participants was patients with PCOS; 2) primary outcome was the prevalence of OSA in the patients, and the secondary outcome was the incidence of and 3) study design was observational or epidemiological studies.

The authors excluded studies with randomized controlled trials, case reports or case series, and review articles. Those studies without prevalence or incidence of OSA and diagnosis of OSA other than polysomnography were also excluded. Potential included studies were systematic searches from four electronic databases including, PubMed, Science Direct, Scopus, and CINAHL Plus, from inception to September 26, 2022. Search terms included obstructive sleep apnea, prevalence, incidence, epidemiological study, and observational study.

After deduplicating records from the search results, the title and abstract of the records were screened by two independent authors (PH and SK). Potential included studies selected by each reviewer were compared and entered the full-text review process. The full texts were reviewed, and data extraction was performed by two independent authors (PH, SK). A PRIMA flow diagram for selecting included studies is shown in Figure 1[12-14].

Data collection for each included study was retrieved for the following sections: publication characteristics, study characteristics, and outcomes. The publication characteristics comprise the first author, year of publication, country of study origin, study design, setting, age of patients with PCOS, diagnosis of PCOS, and diagnosis of OSA. The outcomes were the prevalence or incidence of OSA in patients with PCOS. The Newcastle-Ottawa Scale, adapted for observational studies, was used to evaluate the quality of the included studies[15,16].

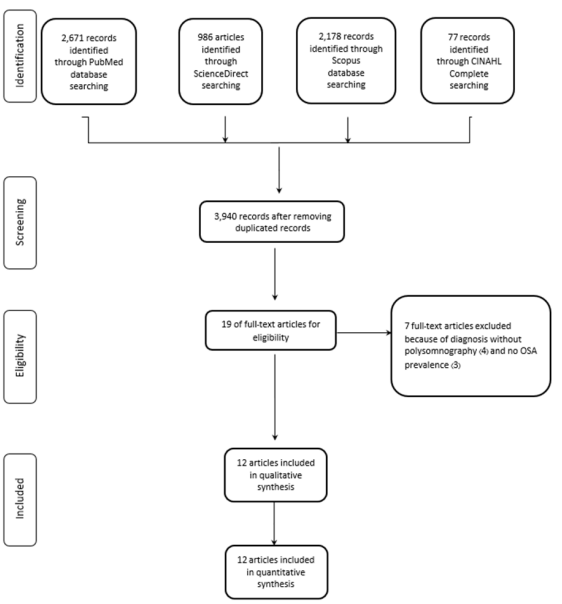

Figure 1. A PRISMA flow diagram.

Statistical analysis

The Cochrane Q test and the I^2 statistic were used to assess the amount of between-study heterogeneity. We conducted a meta-analysis using the random-effects model due to substantial heterogeneity (I^2 >50% and p-value of the Cochrane Q test <0.1). The meta-analysis was used for pooling proportions of OSA in patients with PCOS from the included studies. The results of the meta-analyses were presented by the forest plot. Egger's test was used to evaluate a potential publication bias in the meta-analysis of the prevalence of OSA in patients with PCOS. All statistical analyses were performed using RStudio in the R language with the "meta" package[17-19].

Results

There were 3,940 records after deduplication that were retrieved from four electronic databases and screened for title and abstract (Figure 1). Of those, 19 published articles were eligible for full text review; seven articles were excluded due to diagnosis without polysomnography (4 articles) and no OSA prevalence (3 articles). In total, 12 studies were included for qualitative and quantitative analysis[20-31]. The included studies were published between 2001 and 2022 and conducted mostly in the US (6 studies), as shown in Table 1. The other studies were performed in Brazil (2 studies), the UK (1 study), China (1 study), Taiwan (1 study), and India (1 study). The most common study design was a cohort study (5 studies).

Among the 12 included studies, ten studies evaluated the prevalence of OSA in PCOS (Table 1 and Figure 2), while two studies evaluated the incidence of OSA in patients with PCOS in the general population (Table 1 and Figure 3). The mean age of most studies ranged from 16.8 to 31.1 years. PCOS was mainly diagnosed by the Rotterdam consensus (5 studies), while OSA was diagnosed by polysomnography. The total study population from all included studies was 82,460 patients with PCOS. There was substantial heterogeneity in the meta-analysis of the prevalence of OSA (I^2=93.2%, p-value of Q test <0.001). The pooled prevalence of OSA was 40.4% (10 studies, 887 patients, 95% CI 24.3% to 58.9%) by the random-effects model (Figure 2). A subgroup analysis by age group found that adult patients had a lower prevalence of OSA than adolescents (38.7% vs. 57.1%), as shown in Figure 2. We found that there was no publication bias in the meta-analysis (p-value of Egger's test=0.7945). In addition, the incidence of OSA was low at 0.7% (random-effects model, 95% CI 0.2% to 2.0%) with substantial heterogeneity (I^2 of 98.2%,

Table 1. Characteristics of included studies

Study	Year	Country	Study Design	Setting	Age, years*	BMI, kg/m²	PCOS Diagnosis	OSA Diagnosis	Prevalence
Adult									
Vgontzas	2001	USA	Prospective cross-sectional	Premenopausal	30.4±0.9	38.7±1.1	Chronic anovulation, hyperandrogenemia, PCO	AHI ≥10 along with symptoms	6/53
Fogel	2001	USA	Case-control	Overweight	31.1±1.3	36.9±1.3	Chronic oligomenorrhea, hyperandrogenemia	AHI >5	13/18
Gopal	2002	USA	Cohort	Premenopausal	NA	42.7±8.5	documented PCOS	RDI >5	16/23
Tasali	2008	USA	Prospective cross-sectional	Endocrinology	29.7±0.7	39.2±1.0	Oligo/amenorrhea, hyperandrogenemia, hyperandrogenism	AHI ≥5	29/52
Chatterjee	2014	India	Prospective cross-sectional	Adults, gynecology outpatient	NA	29.8±3.4	Rotterdam criteria	RDI ≥5 along with symptoms or RDI >15	33/50
Tock	2014	Brazil	Retrospective cohort	Endocrinology	28.3±6.8	37.8±4.8	2003 Rotterdam consensus	AHI ≥5	12/38
Hachul	2019	Brazil	Cross-sectional	Endocrinology	29.7±1.2	34.3±1.1	2003 Rotterdam consensus	AHI ≥5 or 15**	9/30
Eisenberg	2021	USA	Cohort	Infertility	28.9±4.2	35.2±9.3	modified Rotterdam criteria	PSG	19/267
Yang	2022	China	Cross-sectional	Infertility	29.2±3.9 (mild), 30.0±4.0 (moderate), 33.5±3.6 (severe)	28.4±3.7 (mild), 31.7±4.9 (moderate), 32.1±3.3 (severe)	oligoovulation or anovulation, clinical manifestations of hyperandrogen and hyperandrogenemia, polycystic change in ovaries (2/3)	AHI ≥5	131/328 (mild 92, moderate 33, severe 6)
Adolescent									
Nandalike	2012	USA	Retrospective cohort	Obese adolescent girl	16.8±1.9	44.8±8.8	modified Rotterdam criteria	AHI >5	16/28
Lin	2017	Taiwan	Retrospective cohort	National Health Research Institute database	28.00±6.79	NA	ICD-9-CM code: 256.4 by gynecological ultrasonography	PSG: ICD-9-CM codes: 327.23, 780.51, 780.53, 780.57	54/4,595
Kumarendran	2019	UK	Retrospective cohort	Population-based	30.2±7.4	28.6±7.6	NA	PSG	298/76,978

NA=not applicable; PSG=polysomnography; RDI=respiratory disturbance index; AHI=apnea-hypopnea index

* Indicated mean±SD unless indicated otherwise; ** AHI ≥5 (with sleep complaints) or >15 (regardless of sleep complaints).

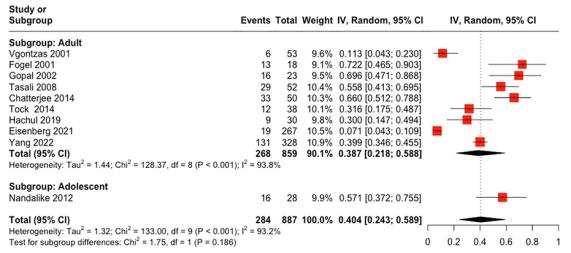

Figure 2. Prevalence of OSA with PCOS.

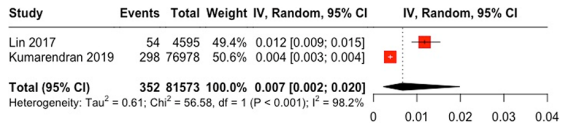

Figure 3. Incidence of OSA with PCOS.

p-value of Q test <0.001) (Figure 3). Regarding study quality, 11 out of 12 studies had good study quality (Table 2). Another study had fair quality[22].

Discussion

This systematic review found that the pooled prevalence of OSA in patients with OSA was 40.4% using polysomnography to diagnose OSA. OSA was more prevalent in adolescent patients with PCOS than in adult patients with PCOS, at as high as 57.1%.

The present study has different results from the previous systematic review on the pooled prevalence of OSA in patients with PCOS[11] because the present study included more studies than the previous one (12 vs. 9 articles). Additionally, we included only published articles. The previous study included both published articles and conference abstracts. This study found a higher rate of OSA in patients with PCOS than the previous study (40.4% vs. 35.0%)[11]. These differences may be explained by the inclusion criteria. The present study enrolled only studies with a reported rate of OSA in patients with PCOS, while the previous study included two studies that did not report on prevalence of OSA[32,33]. We also found two additional studies reporting the incidence of OSA in patients with PCOS[23,30]. These two studies were conducted in Taiwan and the UK. Not surprisingly, the incidence rate of OSA in patients with PCOS was low at 0.7% as polysomnography was not performed in all patients. Only those with reported polysomnography were used for the incidence calculation.

The present study found that the prevalence of OSA in patients with PCOS may be different by age group. In adults, the prevalence of OSA in patients with PCOS was 38.7%, while the prevalence of OSA was slightly higher in adolescents with PCOS (57.1%). These results were different from the previous study published in 2017[10]. Helvaci et al.

Table 2. Risk of bias assessment using the Newcastle-Ottawa Scale of included studies.

Study	Year	Study design	Selection process (4)	Comparability (2)	Outcome measures (3)	Total (9)	Interpretation
Gopal	2002	Cohort	3	1	3	7	Good
Tock	2014	Retrospective cohort	4	1	3	8	Good
Nandalike	2012	Retrospective cohort	3	1	3	7	Good
Lin	2017	Retrospective cohort	4	1	3	8	Good
Kumarendran	2019	Retrospective cohort	4	1	3	8	Good
Eisenberg	2021	Cohort	3	1	3	7	Good
Study	**Year**	**Study design**	**Selection process (5)**	**Comparability (2)**	**Outcome measures (3)**	**Total (10)**	**Interpretation**
Vgontzas	2001	Prospective cross-sectional	3	0	3	6	Good
Tasali	2008	Prospective cross-sectional	3	0	3	6	Good
Chatterjee	2014	Prospective cross-sectional	3	0	3	6	Good
Hachul	2019	Cross-sectional	3	0	2	5	Fair
Yang	2022	Cross-sectional	3	1	2	6	Good
Study	**Year**	**Study design**	**Selection process (4)**	**Comparability (2)**	**Exposure (3)**	**Total (9)**	**Interpretation**
Fogel	2001	Case-control	2	2	3	7	Good

(2017) reported that the prevalence of OSA in adult patients with PCOS was quite higher than that in adolescents with PCOS (32% vs. 8%). These different results may be due to different study criteria. The previous study included four studies from Germany which did not report on criteria for OSA, that this study enrolled only studies with a definition of OSA. Note that there was only one study in the adolescent group in the present study[24].

As OSA is related to cardiovascular diseases, a concomitant of OSA in patients with PCOS may increase the risk of cardiovascular consequences[34]. Physicians should be aware of OSA in patients with PCOS because of its high prevalence and increasing risk for future cardiovascular diseases. There are some limitations to this study. First, there is no evaluation of risk factors for having OSA in patients with PCOS or treatment intervention for OSA[35-40]. Second, most studies were conducted in Western countries (9/12; 75%) with quite a high I^2 in the calculations. Finally, there are various study populations, including but not limited to infertility, premenopausal, endocrinology clinics, the general population, and obese adolescent girls.

Conclusion

The pooled prevalence of OSA in patients with PCOS was higher than previous systematic reviews at 40.4%. Physicians should be aware of OSA in patients with PCOS.

What is already known on this topic?

Previous systematic reviews that showed the prevalence of OSA in patients with PCOS were published a few years ago.

What this study adds?

This systematic review showed that the pooled prevalence of OSA in patients with PCOS in the meta-analysis was 40.4%.

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Conflicts of interest

The authors declare no conflict of interest.

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