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### Obstructive Sleep Apnoea and Polycystic Ovary Syndrome; a comprehensive review of clinical interactions and underlying pathophysiology

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**Obstructive Sleep Apnoea and Polycystic Ovary Syndrome; a comprehensive review of clinical interactions and underlying pathophysiology.**

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5 2 **review of clinical interactions and underlying pathophysiology.**  
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34 **Abstract**

35 Polycystic ovary syndrome (PCOS) is the most prevalent endocrine disorder in women of  
36 reproductive age. PCOS is associated with multiple co-morbidities including, obesity, insulin  
37 resistance and type 2 diabetes, as well as mood disorders and impaired quality of life (QoL).  
38 Obstructive sleep apnoea (OSA) is also a common medical condition that is often  
39 undiagnosed, particularly in women. OSA is associated with a similar spectrum of  
40 comorbidities to that observed in PCOS, including manifestations of the metabolic syndrome  
41 and impaired QoL, whilst obesity frequently constitutes a common denominator in the  
42 pathophysiology of both OSA and PCOS. Hence, it is not surprising that OSA and PCOS  
43 may co-exist in women of reproductive age, and the current clinical guidelines on the  
44 management of PCOS recommend screening for OSA symptoms in overweight/obese women  
45 with PCOS. In this review, we examine the relationship between OSA and PCOS and explore  
46 the potential underlying mechanisms that link these two conditions.

47

## 1. Introduction

Polycystic ovary syndrome (PCOS) is the most common **endocrine** disorder in women of reproductive age with a prevalence of 6–15% (3, 4). PCOS is associated with obesity, subfertility, insulin resistance (IR) and type 2 diabetes (T2DM), depression and impaired quality of life (QoL) (1, 5). **However, despite its high prevalence and significant comorbidities, our understanding of its underlying pathophysiology remains poor; with limited treatment options available to manage this lifelong disorder in everyday clinical practice.**

Hence, there is a need to improve the understanding of the pathogenesis of PCOS and the spectrum of factors that might contribute to the clinical manifestations and comorbidities of this very common condition.

Obstructive sleep apnoea (OSA) is also an obesity-related disorder. OSA prevalence in the general population is estimated at 17–26% in men and 9–28% in women, but this difference varies depending on the definition and methods used to diagnose OSA (6). OSA is characterised by recurrent episodes of partial (hypopnoea) or complete (apnoea) upper airway obstructions associated with recurrent oxygen desaturations and cyclical changes in heart rate, blood pressure, intrathoracic pressure and sympathetic activity (7). In addition, OSA results in changes in the sleep architecture, including loss of deep sleep (stages 3 and 4) and/or of REM sleep (7).

Patients with OSA may present with nocturnal symptoms, including snoring, witnessed apnoea episodes, choking or gasping, insomnia, nocturia, enuresis, frequent arousals, diaphoresis, and impotence (8). In addition, common daytime OSA symptoms may include excessive daytime sleepiness, fatigue, memory impairment, morning headaches, and depression (8). Prompt diagnosis and treatment of OSA is highly important in clinical practice, since undiagnosed/untreated OSA is associated with increased risk of hypertension,

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3 72 cardiovascular disease, mortality, IR and T2DM, road traffic accidents, depression and  
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5 73 impaired QoL (8, 9) . Continuous positive airway pressure (CPAP) therapy, combined with  
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7 74 weight loss for overweight/obese patients, is the treatment of choice for symptomatic OSA  
8  
9 75 (10).

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12 76 Despite the high prevalence of OSA in the general population, this condition is generally  
13  
14 77 under-recognised and frequently remains undiagnosed in everyday clinical practice,  
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16  
17 78 particularly in women who may not present with typical OSA symptoms (11). As obesity is a  
18  
19 79 common risk factor, it is not surprising that OSA and PCOS might co-exist. **The association**  
20  
21 80 **between PCOS and OSA has also been recognised in the latest guidelines by the European**  
22  
23 81 **and the US Endocrine Societies (Box 1) (1, 2). However, these guidelines acknowledge the**  
24  
25 82 **limited evidence behind their recommendations that is largely based on limited, ‘weak’, or**  
26  
27 83 **‘low quality’ data. This highlights the need for further research to better understand the**  
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29 84 **relationship between PCOS and OSA. In addition,** the implications of OSA in women with  
30  
31 85 PCOS are not clear, though important as both conditions are associated with overlapping  
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33 86 comorbidities, and OSA is associated with essential factors that may contribute to the burden  
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35 87 of PCOS (*e.g.* to IR, increased inflammation, and oxidative stress) (6, 12). In this article we  
36  
37 88 present a concise review of key studies that examined the relationship between OSA and  
38  
39 89 PCOS, and we explore the potential mechanisms linking both conditions.  
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45 **Box 1. Clinical guidelines/recommendations on screening women with PCOS for OSA.**

46 1. Endocrine Society, 2013 (1):

47 We suggest screening overweight/obese adolescents and women with PCOS for symptoms  
48 suggestive of OSA and, when identified, obtaining a definitive diagnosis using  
49 polysomnography. If OSA is diagnosed, patients should be referred for institution of  
50 appropriate treatment.  
51

52 2. European Society of Endocrinology, 2014 (2):

53 It seems wise at this moment to screen sleep disorders by clinical questionnaires in obese  
54 women with PCOS. In the case of clinical suspicion resulting from these questionnaires,  
55 patients should be referred to a centre of sleep disorders for polysomnography and further  
56 evaluation.  
57

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60

## 91 **2. Methodology**

92 We conducted a narrative review of the relevant literature. In this context, we searched  
93 PubMed using the terms '(PCOS OR polycystic ovary syndrome) AND (OSA OR obstructive  
94 sleep apnoea OR obstructive sleep apnea)'. Clinical studies and review articles examining the  
95 presence of OSA in women with PCOS were obtained, reviewed, and their results were  
96 critically appraised. We also hand-searched references from relevant papers and review  
97 articles.

## 98 **3. Epidemiology**

### 99 **3.1 PCOS prevalence in OSA**

100 PCOS has a prevalence of 6–15% in women of reproductive age (3); however, the reported  
101 prevalence rates vary depending on the populations studied and the applied PCOS diagnostic  
102 criteria. The prevalence of PCOS in women with OSA remains unknown.

103

### 104 **3.2 OSA prevalence in PCOS**

105 The prevalence of OSA in the general population varies considerably between studies, mainly  
106 due to differences in the populations studied, study designs, and the methods and criteria used  
107 to diagnose OSA (8). The prevalence from three well-conducted studies with similar designs  
108 from the USA (Wisconsin and Pennsylvania), and Spain showed an OSA prevalence of 9–  
109 28% in women, with 2–7% for moderate to severe OSA (13).

110 To date, a limited number of studies have examined the prevalence of OSA in women with  
111 PCOS with the majority of these being conducted in the USA. Based on the existing  
112 published studies (14-22) (Table 1), the reported prevalence of OSA in women with PCOS



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3 113 ranges from 0% to 69% (median: 55.8%; mean: 39.8%). This large variability and wide range  
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5 114 in the reported prevalence may be attributed to a combination of reasons, including  
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7 115 application of different cut-off points and methods to diagnose OSA, the small size of the  
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10 116 studied cohorts, and potential selection bias by recruitment of study participants from  
11  
12 117 specialised clinics. As expected, the available data suggest that OSA risk in women with  
13  
14 118 PCOS is increased with age and obesity. While the only published study that examined the  
15  
16 119 presence OSA in lean women with PCOS showed no evidence of the condition (18), the  
17  
18 120 small number of study participants (n=18) precludes generalisability or drawing firm  
19  
20 121 conclusions from these data. The reported prevalence and potential links between PCOS and  
21  
22 122 OSA in adolescents are even more controversial, with one study showing a prevalence of  
23  
24 123 16/28 (57%) (20) and another showing 0/22 (0%) prevalence (19). Based on the available  
25  
26 124 data on the prevalence and natural history of these two conditions, it is probable that PCOS  
27  
28 125 precedes the development of OSA; however, it cannot be excluded that OSA may precede the  
29  
30 126 clinical presentation of PCOS in some women, worsening the PCOS-related  
31  
32 127 symptomatology. Observational long-term studies are needed to accurately assess the  
33  
34 128 incidence of OSA in women with PCOS and *vice versa*.

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#### 40 41 42 130 **4. Proposed mechanisms linking OSA to PCOS and its comorbidities**

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45 131 Depending on ethnicity and geography, 30–88% of women with PCOS are overweight or  
46  
47 132 obese (23). Obesity may contribute to the development of PCOS through increased android  
48  
49 133 (central) type adiposity and IR (24); lipotoxicity (25); and increased 5 $\alpha$ -reductase activity  
50  
51 134 (23). Obesity is also a major risk factor for OSA (8). The mechanisms that link obesity to  
52  
53 135 OSA are multifactorial (8, 26). Weight gain can alter normal upper airway mechanics during  
54  
55 136 sleep by various mechanisms, such as increased parapharyngeal fat deposition resulting in a

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3 137 smaller upper airway; altering the neural compensatory mechanisms that maintain airway  
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5 138 patency; reducing the functional residual capacity with a resultant decrease in the stabilising  
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7 139 caudal traction on the upper airway; reducing lung volume due to increased abdominal fat;  
8  
9  
10 140 increasing breathing workload due to increased chest wall thickness; and affecting the  
11  
12 141 chemosensitivity to O<sub>2</sub> and CO<sub>2</sub> which reduces the ventilatory drive (8, 26). Subsequently,  
13  
14 142 obesity is a key factor that predisposes to both PCOS and OSA. However, other shared  
15  
16 143 features between PCOS and OSA may also play an important mechanistic role in the  
17  
18 144 development/interaction between these two common conditions.

#### 145 **4.1 Sex Hormones**

146 An increase in circulating androgens of ovarian origin is one of the main features of PCOS  
147 and is present in both ovulatory and anovulatory women. Androgens cause many of the  
148 clinical features of PCOS (*e.g.* hirsutism, acne and alopecia); contribute to anovulation by  
149 promoting ovarian early follicular growth and subsequently disrupt follicular development  
150 and dominant follicle selection (27); and exacerbate IR. Anovulation will result in lower  
151 progesterone levels. Hyperandrogenism and low progesterone levels may play a role in the  
152 pathogenesis of OSA by increasing upper airway collapsibility, and/or impairing the  
153 sensitivity and responsiveness of the ventilatory chemoreceptors (28). However, the effect of  
154 hyperandrogenism on OSA risk in women with PCOS is probably small, as androgen levels  
155 are relatively low compared to men. Sleep, on the other hand, appears to have a significant  
156 effect on the female hormone production (29). Indeed, sleep deprivation and/or interruption,  
157 and sleep disordered breathing have been suggested to influence gonadotropin releasing  
158 hormone (GnRH), follicular stimulating hormone (FSH) and luteinising hormone (LH)  
159 pulsatility and may cause menstrual disturbances (30, 31). Subsequently, OSA may alter sex  
160 hormones production and contribute to the development or worsening of the clinical features  
161 of PCOS.

## 162 **4.2 Insulin resistance**

163 IR is seen in more than 50% of women with PCOS, independent of obesity (32). Insulin may  
164 act directly on the ovaries to enhance androgen production (33); reduce SHBG production  
165 from the liver with subsequent increase in bioavailable testosterone; and cause the premature  
166 arrest of follicle growth and anovulation (34). Most studies also suggest an association  
167 between OSA and IR (8); and studies in healthy lean men found OSA to be associated with  
168 IR even in the absence of obesity (35). In addition, in a cohort study, OSA, apnoea/hypopnea  
169 index (AHI), oxygen desaturation index (ODI), and minimal oxygen saturations were  
170 independently associated with IR development over an 11-year follow-up period after  
171 adjustment for age, baseline BMI, BMI change over follow-up, hypertension, and CPAP  
172 treatment (36). Two recent meta-analyses showed that CPAP treatment was associated with a  
173 reduction in the homeostasis model assessment of insulin resistance (HOMA-IR) (37, 38),  
174 although this benefit may occur only in those using CPAP >4 hours per night (39).  
175 Subsequently, it is plausible that OSA, through IR, may contribute to the development of a  
176 more severe PCOS phenotype in women affected by both conditions; or to a *de novo*  
177 presentation of PCOS in genetically/metabolically predisposed women.

## 178 **4.3 Oxidative stress**

179 In a recent systematic review and meta-analysis, PCOS was associated with increased levels  
180 of oxidative stress, independent of age and BMI (40). Oxidative stress may play a role in the  
181 pathogenesis of PCOS by exacerbating IR (41); causing hyperandrogenism (41); and  
182 contributing to infertility (42). Many studies suggest that OSA is a cause of oxidative stress  
183 (8). Recurrent hypoxia and mitochondrial dysfunction in OSA result in the formation of  
184 reactive oxygen species (ROS) which leads to cellular and DNA damage and oxidative stress

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3 185 (43). Subsequently, OSA may complicate the clinical picture in PCOS by promoting  
4  
5 186 oxidative stress.  
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#### 8 187 **4.4 Endothelial dysfunction**

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11 188 Women with PCOS have been found to have lower flow-mediated dilatation (FMD)  
12  
13 189 compared to age- and weight-matched controls (44). Obesity, IR, oxidative stress, advanced  
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15 190 glycation end products (AGE) and inflammation are believed to play a role in the  
16  
17 191 pathogenesis of endothelial dysfunction in PCOS (45). OSA is also associated with  
18  
19 192 endothelial dysfunction and the underlying mechanisms are likely related to ischemia-  
20  
21 193 reperfusion injury (46). Repetitive episodes of re-oxygenation after hypoxemia in patients  
22  
23 194 with OSA result in increased production of AGE and ROS (43); altered protein kinase C  
24  
25 195 signaling; decreased endothelial nitric oxide synthase (47); increased endothelin-1 levels and  
26  
27 196 inflammation (48). Notably, CPAP treatment was found to increase FMD in patients with  
28  
29 197 OSA (49).  
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#### 34 198 **4.5 Sympathetic activity**

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37 199 Sympathetic activity is increased in obesity and is associated with visceral adiposity (50);  
38  
39 200 high leptin levels (51) and IR (52) are thought to play a role in its pathogenesis. However,  
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41 201 increased sympathetic activity may further exacerbate IR and creates a vicious cycle (52).  
42  
43 202 Women with PCOS have evidence of increased sympathetic activity (52), even in the absence  
44  
45 203 of obesity (53). Sympathetic activity may contribute to the pathogenesis of PCOS through  
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47 204 increased IR, altered ovarian function and the development PCO morphology (52). OSA is  
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49 205 also associated with an increase in sympathetic activity independent of body weight (54). It is  
50  
51 206 likely that both the recurrent hypoxia (55) and recurrent arousals (56) contribute to the  
52  
53 207 activation of the sympathetic nervous system (SNS). Moreover, treatment with CPAP is  
54  
55 208 associated with a reduction in sympathetic activity (57).  
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## 209 **4.6 Summary of the proposed mechanisms linking OSA and PCOS**

210 OSA and PCOS are both associated with comorbidities including obesity, IR, oxidative  
211 stress, endothelial dysfunction, sympathetic hyperactivity, and hormonal disturbances that  
212 could potentially contribute to the pathophysiology and development of either condition. It is  
213 thus plausible that the relationship between OSA and PCOS is bidirectional, where PCOS  
214 contributes to the development of OSA, and *vice versa*, OSA contributes to the clinical  
215 presentation of PCOS, worsening its symptomatology and creating a vicious cycle between  
216 the two conditions. An illustration of the possible pathophysiological links between OSA and  
217 PCOS and their clinical consequences is provided in Figure 1.

## 220 **5. The impact of OSA in women with PCOS**

### 221 **5.1 Review of published studies**

222 A limited number of studies have examined the effect(s) of OSA in women with PCOS and  
223 their findings are summarised in Table 1.

224 In the study by Vgontzas *et al.* (15), women with PCOS and sleep disordered breathing (SDB  
225 was defined as either OSA or upper airway resistance syndrome; n=9) were heavier (BMI  
226  $45.7 \pm 2.6$  vs.  $37.2 \pm 1.1$  kg/m<sup>2</sup>, P<0.003), and had higher fasting insulin ( $306.5 \pm 52.4$  vs.  
227  $176.1 \pm 18.5$  pmol/L, P<0.01) and lower glucose-to-insulin ratio ( $0.02 \pm 0.006$  vs.  $0.04 \pm 0.003$ ,  
228 P<0.05) compared to women with PCOS without SDB (n=44). Logistic regression analysis of  
229 the study data showed that insulin levels and glucose-to-insulin ratio had a stronger  
230 association with SDB than age, BMI, or testosterone levels. **However, the difference in BMI**  
231 **between the two groups in this study was rather high (8.5 kg/m<sup>2</sup>), and despite statistical**

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3 232 adjustment, it is difficult to completely rule out an effect of obesity on the metabolic  
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5 233 differences between the two groups.  
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8 234 Similarly, in the study by Tasali *et al.* (17), women with PCOS and OSA (n=29) were older  
9  
10 235 (age 31.6±1.0 vs. 27.3±0.7 years; P=0.002), had a higher BMI (42.2±1.1 vs. 35.3±1.4 kg/m<sup>2</sup> ;  
11  
12 236 P<0.001), and were more insulin resistant (HOMA-IR 5.7±0.4 vs. 3.5±0.4, P=0.006) than  
13  
14 237 women with PCOS without OSA (n=23). After controlling for age, BMI, and ethnicity, AHI  
15  
16 238 was a highly significant predictor of the fasting concentrations of glucose and insulin, as well  
17  
18 239 as of the 2-h glucose concentration (after an oral glucose tolerance test) and HOMA-IR. The  
19  
20 240 data of this study also suggest that the degree of sleep fragmentation, rather than the severity  
21  
22 241 of hypoxia, may be related to the severity of IR and glucose intolerance in women with  
23  
24 242 PCOS. As such, the authors further concluded that women with PCOS and OSA represent a  
25  
26 243 metabolically different, ‘higher risk’ population compared to women with PCOS without  
27  
28 244 OSA. However, this conclusion should be taken with caution considering the small study  
29  
30 245 sample size, and the relatively large difference in BMI (7.1 kg/m<sup>2</sup>) between women with and  
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32 246 without OSA in this study.  
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38 247 Notably, Tasali *et al.* have also conducted a relevant short-term interventional study (58) in  
39  
40 248 19 obese women with PCOS and OSA (age ± SEM: 31.2±1.2 years; BMI: 46.4±2.4 kg/m<sup>2</sup>).  
41  
42 249 These women were treated with CPAP for 8 weeks, exhibiting subsequent improvement in  
43  
44 250 insulin sensitivity (relative increase of nearly 7%), and reduction in diastolic blood pressure  
45  
46 251 (DBP; approximately 2.3 mmHg). In addition, day-time and night-time norepinephrine levels  
47  
48 252 also reduced after CPAP therapy. However, this study lacked a control group, and only a ‘per  
49  
50 253 protocol’ analysis was performed including just 9 study participants, with the data from  
51  
52 254 another 10 study patients being excluded from the analysis due to lack of adequate CPAP  
53  
54 255 treatment compliance (average use of CPAP <4 hours per night). Of note, whether the  
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3 256 reported post-treatment changes in IR and blood pressure observed in this study may  
4  
5 257 translate/result into meaningful clinical outcomes remains to be studied.  
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7

8 258 In another study by Tock *et al.* (21), women with PCOS and OSA (n=12) had higher BMI  
9  
10 259 (37.8±4.8 vs. 30.67±7.7 kg/m<sup>2</sup>, P=0.006); waist circumference (114.4±12.0 vs. 98.1±19.9 cm,  
11  
12 260 P=0.013); waist-to-hip ratio (1.0±0.1 vs. 0.9±0.1, P=0.029); free testosterone (1.9±1.3 vs.  
13  
14 261 1.1±0.8 ng/dL, P=0.014); HOMA-IR (4.4±3.2 vs. 2.3±1.4, P=0.009); total cholesterol  
15  
16 262 (205.0±28.7 vs. 172.3±35.8 mg/dL, P=0.009); low density lipoprotein-cholesterol (LDL,  
17  
18 263 128.6±21.6 vs. 98.9±29.6, P=0.004); and higher prevalence of non-alcoholic fatty liver  
19  
20 264 disease (NAFLD, 83.3% vs. 26.9%, P<0.001) compared to those without OSA (n=26). After  
21  
22 265 adjusting for obesity in multivariate logistic regression analysis, raised serum free  
23  
24 266 testosterone levels ≥1.07 ng/dL increased the risk of OSA in women with PCOS by 8.2 fold.  
25  
26 267 Accordingly, the authors concluded that hyperandrogenism may be a predisposing factor for  
27  
28 268 OSA in PCOS. However, a limitation of this study is the fact that testosterone was measured  
29  
30 269 by immunoassay rather than by tandem mass spectrometry. In a subsequent multiple logistic  
31  
32 270 regression analysis, with OSA (AHI ≥5), IR (HOMA-IR ≥2.7), and obesity (BMI ≥30 kg/m<sup>2</sup>)  
33  
34 271 considered as independent variables and NAFLD as the dependent variable, only OSA was an  
35  
36 272 independent predictor of the presence of NAFLD. The presence of OSA increased the chance  
37  
38 273 of NAFLD 7.6 fold in woman with PCOS. As such, the authors concluded that OSA is a  
39  
40 274 predictor of NAFLD along with, but independent of, obesity and IR.  
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46 275 In a recent study by Chatterjee *et al.* (22), women with PCOS and SDB (n=33) had higher  
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48 276 BMI (29.8±3.4 vs. 24.36±2.29 kg/m<sup>2</sup>, P<0.001), waist circumference (95.58±6.47 vs.  
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50 277 85.12±4.34, P<0.001), systolic BP (SBP, 129.27±10.93 vs. 119.18±8.03 mmHg, P=0.002),  
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52 278 diastolic BP (78.61±9.07 vs. 73.53±6.22 mmHg, P=0.044), and hirsutism (Ferriman–Gallwey  
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54 279 score 9.82±2.78 vs. 8.00±2.5, P=0.028) compared to women with PCOS without SDB  
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3 280 (n=17). Interestingly, in a logistic regression analysis which adjusted for BMI, only the  
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5 281 associations between fasting plasma glucose and diastolic BP with SDB remained significant.  
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8 282 Finally, in the study by Nandalike *et al.* (20), adolescent girls with PCOS and OSA (n=16)  
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10 283 had higher prevalence of the metabolic syndrome (56.3% vs. 8.3%, P=0.03); higher HOMA-  
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12 284 IR >4 (81.3% vs. 41.6%, P=0.03), systolic BP (128.4±12.8 vs. 115.6±11.4 mmHg, P=0.009),  
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14 285 triglycerides (149.7±87.7 vs. 93.3±25.8 mg/dl, P=0.03), and lower high density lipoprotein  
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16 286 (HDL, 38.6±8.7 vs. 49±10.9 mg/dl, P=0.01) compared to girls with PCOS without OSA  
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18 287 (n=12).  
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## 25 289 **5.2 Summary of the literature**

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28 290 It seems plausible that OSA is associated with the severity of the PCOS phenotype,  
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30 291 particularly in overweight/obese and insulin resistant women with PCOS. However, it is  
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32 292 difficult to draw firm conclusions from the studies conducted so far since significant  
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34 293 variables (*e.g.* abdominal adiposity and ethnicity) have often not been accounted for in the  
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36 294 presented analyses. In addition, while the association between OSA and increased insulin  
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38 295 resistance in women with PCOS seems to be a common theme, the relationship between OSA  
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40 296 and hyperandrogenism is more controversial and require further evaluation. While the US  
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42 297 and European Endocrine societies' guidelines consider the presence of OSA as a  
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44 298 cardiovascular risk factor in women with PCOS (1, 2), there is lack of data on the exact  
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46 299 relationship between OSA and important clinical outcomes in women with PCOS (*e.g.* on  
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48 300 T2DM risk, cardiovascular risk, subfertility, depression, and impaired QoL). Subsequently,  
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50 301 well conducted observational studies are needed to examine the effects of OSA in women  
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52 302 with PCOS. Interventional studies are also required in women with PCOS and OSA. The  
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54 303 existing short-term, pilot, interventional study in such patients suggests that CPAP therapy  
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3 304 may significantly improve insulin sensitivity and reduce blood pressure. However, it remains  
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5 305 unclear whether this can translate into long-term meaningful clinical outcomes.  
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## 10 11 307 **6. Conclusions** 12

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14 308 OSA appears to be common in obese women with PCOS. There is a lack of high-quality  
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16 309 evidence regarding the clinical benefit or the cost-effectiveness of the current Endocrine  
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18 310 Society clinical practice guidelines which suggest screening all overweight/obese adolescents  
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20 311 and women with PCOS for symptoms suggestive of OSA. While it is probable that PCOS  
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22 312 precedes and contributes to the development of OSA, it is also plausible that OSA may  
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24 313 contribute to the presentation and worsen the clinical manifestations of PCOS. Both  
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26 314 conditions are associated with significant comorbidities in women (*e.g.* depression,  
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28 315 unexplained fatigue, hypertension, dyslipidaemia, IR and impaired glucose tolerance), and  
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30 316 may progress undiagnosed for prolonged periods. In order to inform clinical practice and  
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32 317 support evidence-based guidelines, further clinical research is needed, including prospective  
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34 318 cohort studies in obese and non-obese women with PCOS, to study in detail the relationship  
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36 319 between these two important and prevalent conditions.  
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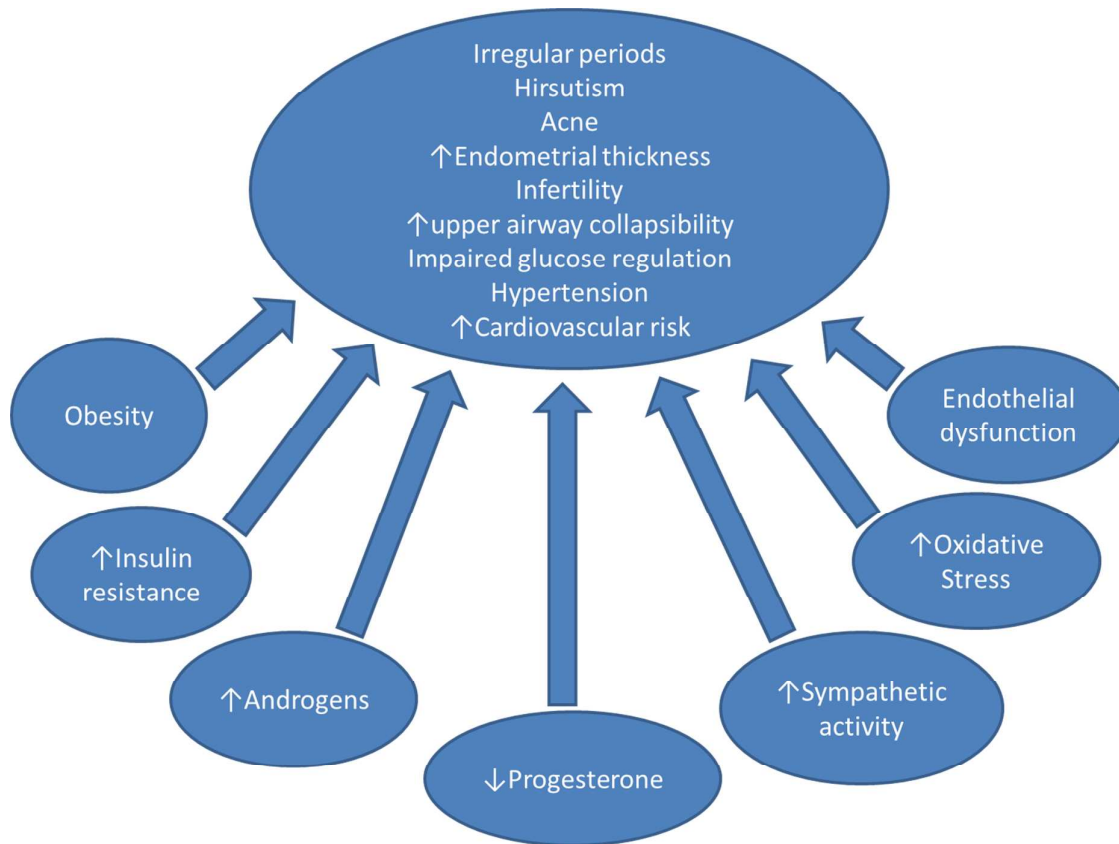
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Study	Notes	n	OSA		Women with PCOS and OSA compared to women with PCOS without OSA							
			Diagnosis	%	Weight or BMI	WC or WHR	IR	Hyperandrogenism	BP	FPG	IGT	MS
Vgontzas et al. 2001; (15)	USA	53	AHI ≥10 + symptoms	11–17%	↑	NA	Insulin ↑*	FT and TT ↔	NA	↔	NA	NA
Fogel et al. 2001; (14)	USA	18	AHI >10	66.8%	NA	↑	NA	NA	NA	NA	NA	NA
Gopal et al. 2002; (16)	USA	23	RDI ≥5 + symptoms	69.6%	↔	NA	NA	NA	NA	NA	NA	NA
Tasali et al. 2008; (17)	USA	52	AHI ≥5	55.8%	↑	NA	HOMA-IR ↑*	FT and TT ↔	NA	↔	↑	NA
Yang et al. 2009; (18)	Taiwan, lean women	18	AHI ≥ 5	0%								
De Sousa et al. 2010; (19)	Germany, adolescents	22	Not stated	0%								
Nandalike et al. 2012; (20)	USA, adolescents, retrospective	28	AHI >5 or apnoea index >1	57.2%	↔	NA	HOMA-IR ↑	FT and TT ↔	↑	↔	NA	↑
Tock et al. 2014; (21)	Brazil	38	AHI ≥5	31.6%	↑	↑	HOMA-IR ↑	FT ↑*	NA	↔	↑	NA
Chatterjee et al. 2014; (22)	India	50	RDI ≥5 + symptoms or RDI >15	66%	↑	↑	HOMA-IR ↔	FT ↔	↑	↑*	NA	↑

**Table 1 Differences between women with PCOS and OSA compared to women with PCOS only.** n, number of participants; OSA, obstructive sleep apnoea; PCOS, polycystic ovary syndrome; AHI, apnoea/hypopnea index; RDI, respiratory distress index; BMI, body mass index; WC, waist circumference; WHR, waist-to-hip-ratio; IR, insulin resistance; HOMA-IR, homeostatic model assessment of insulin resistance; FT, Free testosterone; TT, total testosterone; BP, blood pressure; FPG, fasting plasma glucose; IGT, impaired glucose tolerance; MS, metabolic syndrome; ↑ statistically significant increase; NA, not available; ↔ equal; \*adjusted for weight.



**Figure 1. Possible mechanisms linking common shared features between Obstructive Sleep Apnoea (OSA) and Polycystic Ovary Syndrome (PCOS) with their clinical consequences.**