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Sleep and Cardiometabolic Function in Obese Adolescent Girls with Polycystic Ovary Syndrome

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Abstract

Objective—To compare the polysomnography findings and cardiometabolic function among adolescent girls with PCOS and matched female and male controls.

Method—Retrospective chart review of electronic medical records of 28 girls with PCOS (age: 16.8±1.9 yrs, BMI Z-score 2.4±0.4), 28 control females (age: 17.1±1.8, BMI Z-score 2.4±0.3) and 28 control males (age: 16.6±1.6, BMI Z-score 2.5±0.5) in a tertiary care center.

Results—The prevalence of obstructive sleep apnea (OSA) was higher in girls with PCOS compared to control females (16/28 (57%) vs. 4/28(14.3%), p<0.01), however, was comparable to that of the control males (16/28(57%) vs. 21/28(75%), p=0.4). Girls with PCOS had a significantly higher prevalence of insulin resistance compared to control females and control males (20/28 (71.4%) vs. 9/22 (41.0%) (p=0.04) vs. 8/23 (34.8%) (p=0.01). Among girls with PCOS, those with OSA had significantly higher proportions of metabolic syndrome (9/16 (56.3%) vs. 1/12 (8.3%) p=0.03), higher insulin resistance (13/16 (81.3%) vs. 5/12 (41.6%), p=0.03), elevated daytime systolic blood pressure (128.4±12.8 vs. 115.6±11.4, p<0.01), lower HDL (38.6±8.7 vs. 49±10.9, p=0.01) and elevated triglycerides (149.7±87.7 vs. 93.3±25.8, p=0.03) compared to those without OSA.

Conclusions—We report a higher prevalence of OSA and metabolic dysfunction in a selected group of obese girls with PCOS referred with sleep related complaints compared to BMI matched control girls without PCOS. We also report higher prevalence of cardiometabolic dysfunction in girls with PCOS and OSA compared to girls with PCOS without OSA.

Keywords

AHI: Apnea hypopnea index; HDL: High density lipoprotein; HOMA-IR: Homeostatic model assessment a measure of Insulin resistance; MetS: Metabolic syndrome; OSA: Obstructive sleep apnea; PCOS: Polycystic ovary syndrome; TG: Triglyceride

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INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common endocrine disorder in women of reproductive age with a prevalence of 5-8% (1). PCOS usually presents during adolescence with irregular menstruation and clinical signs of hyperandrogenism, such as acne and hirsutism. PCOS is associated with obesity and several cardiometabolic abnormalities including insulin resistance, metabolic syndrome, dyslipidemia, diabetes mellitus type-2, hypertension, and atherosclerosis(2). In recent years researchers have shown that adult women with PCOS have a significantly higher prevalence of obstructive sleep apnea (OSA) compared to women without the disorder(3-5); screening for OSA has therefore been recommended for women with PCOS(6).

The pathophysiological mechanisms leading to the high prevalence of OSA in women with PCOS are not well understood, however the three main features of PCOS: obesity, insulin resistance, and hyperandrogenemia are all believed to contribute to this effect. All these factors have a profound effect on body fat composition thereby increasing the resistive load on the upper airway during sleep (3-5). In addition, OSA has been shown to independently induce and exaggerate insulin resistance, which can further perpetuate these interactions and increase the severity of OSA in these patients (7, 8). Insulin resistance is also linked to cardiometabolic dysfunction in obese children and should be screened for and appropriately treated if found (9). Although the interactions between PCOS, OSA, and the cardiometabolic consequences are complex, a recent study has shown improvement in cardiometabolic profile after the successful treatment of OSA (10).

Although PCOS manifests in adolescence, studies evaluating for sleep disordered breathing and the cardiometabolic and endocrine mechanisms leading to the disorder in this age group are very limited (11, 12). Moreover, none of the studies published so far have confirmed an increased prevalence of OSA in adolescent s with PCOS (12), or supported a link between OSA and any of the metabolic or endocrine dysfunctions (13, 14), as shown in adults.

Thus, the above negative reports in adolescents which conflict with the findings in the adult literature, have prompted us to evaluate the relationship between sleep disordered breathing and cardiometabolic function in a group of adolescent girls with PCOS, referred for evaluation of sleep disordered breathing, as compared to matched female controls without PCOS and matched male controls. Secondary analysis included sleep and cardiometabolic function differences within the PCOS group with and without OSA.

METHODS

This retrospective chart review study was approved by the Institutional Review Board at the Albert Einstein College of Medicine.

Study Population

The study population included adolescent girls aged 13-18 years diagnosed with PCOS and followed at Children's Hospital at Montefiore (CHAM), between January 2006 and December 2009, who were subsequently referred for an overnight polysomnography at CHAM to rule out OSA, because of sleep related complaints such as snoring, trouble breathing or excessive daytime sleepiness. Participants were first identified by an electronic medical information database (Clinical Looking Glass, CLG). Accordingly, the PCOS ICD-9 code-256.4 was queried, and the diagnosis was verified by reviewing each patient's *electronic patient file* (EPF). Later, individual charts were reviewed to identify the individuals who underwent polysomnography during the study period.

Polycystic ovary syndrome—Diagnosis of PCOS was made as per the modified Rotterdam criteria(15). Accordingly, at least two of the following three features existed: (1) oligomenorrhea/amenorrhea, (2) clinical or biochemical evidence of hyperandrogenemia, and (3) polycystic ovaries documented on ultrasonography. In our sample, all of the patients fulfilled the first two criteria and only a few had ultrasonography performed as the interpretation of the sonographic findings is different for adolescents who may have multicystic ovaries as a normal peripubertal finding. Other conditions that could mimic PCOS such as: Cushing's syndrome, late onset adrenal hyperplasia, or androgen producing neoplasm, were excluded.

Controls—Age and BMI Z-score matched females without PCOS and matched males who underwent polysomnography during the same time period were identified through the sleep disorders center database. Referral for polysomnography was through the adolescent medicine, endocrine, otolaryngology, and pulmonary clinics for sleep related complaints such as snoring, trouble breathing at night or excessive daytime sleepiness. Charts of females chosen as controls were verified and any girl with any history of oligomenorrhea (less than 9 menstrual cycles in a year) or amenorrhea, or any documented clinical signs of hyperandrogenism such as acne or hirsutism or biochemical evidence of hyperandrogenemia, was excluded from the study. Males and females with significant co-morbid conditions contributing to OSA, such as: Trisomy 21, craniofacial anomalies, and cerebral palsy were also excluded from the study.

Measures

Demographics, medication use at the time of polysomnography (with a special emphasis on the use of oral contraceptives and metformin: two of the most commonly prescribed medications used to treat PCOS) and history of adenotonsillectomy prior to polysomnography, were collected using our electronic records that contain complete prescribing and surgical information. The data on total and free serum testosterone level was collected on all the subjects in whom it was available. Total testosterone level was available on all girls with PCOS and free testosterone level was available on 25/28 girls with PCOS. The androgen profile was not available for any of the female controls as they had no menstrual irregularities or clinical hyperandrogenism and were not biochemically tested for excess androgens. BMI Z-score was calculated using the computerized software available from the CDC website at the time of study(16).

Polysomnography

Polysomnography data (via Xltek, Oakville, ON, Canada) were extracted from the electronic records of the sleep disorders center at Children's Hospital at Montefiore (CHAM). Only 28/240 girls with PCOS were referred by their primary care physicians for a PSG to evaluate for OSAS. Information on any sleep related complaints or any screening measures for OSA on the 212 girls with PCOS not referred for PSG was unavailable. Sleep staging and scoring of arousals were performed per standard criteria (17). OSA was diagnosed if the apnea hypopnea index (AHI) was more than 5/hour or if the apnea index was more than 1/hour (18). Data for analysis included: sleep latency, sleep efficiency, arousal awakening index, AHI, baseline and lowest oxygen saturation, and peak carbon dioxide levels.

Cardiometabolic function

Data on serum fasting levels of glucose, insulin, triglyceride (TG), and high density lipoprotein (HDL) measured within 6 months of the polysomnography study were obtained from the medical records at CHAM. In addition, daytime systolic and diastolic blood pressure measurements performed within 6 months of the polysomnography study date were

retrieved from the medical records at CHAM. The blood pressure measurements were done during clinic visits by the triage nurses, using an automated BP machine. The homeostatic model assessment (HOMA) was used as a measure of insulin resistance (IR). It was calculated as: fasting glucose (mg/dL) × fasting insulin (μU/mL)/405(19). HOMA-IR > 4 was considered positive for IR (20). Data on fasting glucose, HDL, TG and blood pressure measurements were available for all study participants including all girls with PCOS and male controls. However, fasting insulin levels were not available for 6/28 control females and 5/28 control males. The presence of metabolic syndrome (MetS) was determined by the Weiss criteria (21) that includes BMI>95th percentile plus three or more of the following parameters: blood pressure >95th percentile (for height, age and gender), TG >97th percentile, HDL <5th percentile, or impaired glucose tolerance.

Statistical analysis

Statistical analysis was performed using SPSS software version 18. Mean and standard deviation were used to summarize continuous variables. Analysis of variance (ANOVA) was used to compare polysomnography findings, cardiometabolic profiles, and other continuous variables between the PCOS subjects and control groups. Differences in proportions were assessed with Chi Square test. The mean age, BMI Z-score, and cardiometabolic profile were compared between those with PCOS and OSA and those with PCOS without OSA, using independent samples t-tests/Mann Whitney tests after checking for normality assumptions. Post hoc analysis was done using Bonferroni adjustment to account for multiple comparisons. Spearman correlation coefficients were derived between size of various cardiometabolic parameters and AHI. A two-tailed alpha of 0.05 was used to indicate statistical significance.

RESULTS

Study population

240 girls aged 13-18 years were diagnosed with PCOS during the study period. Of these, 28 girls underwent polysomnography and were included in the analysis. The study group was similar to the rest of the girls with PCOS in terms of age (16.8 ± 1.9 yrs vs. 16.6 ± 1.5yrs) but had significantly higher BMI compared to the girls with PCOS who were not referred for polysomnography (2.4 ± 0.4 vs. 1.9 ± 0.5, $p<0.001$). All 28 girls in the study group met the Rotterdam criteria and had clinical or biochemical evidence of hyperandrogenemia with average free testosterone level of 9.6 ± 4.7pg/ml The study group and control groups were matched for age and BMI Z-score (Table 1). All study group girls with PCOS, control females without PCOS and 93% (26/28) of control males were obese. Compared to the study group girls with PCOS and male control group, the female control group had higher proportion of African Americans (5/28(17.9%) vs. 6/28(21.4%) vs. 13/28(46.4%). Also, a greater proportion of girls from the PCOS group were prescribed metformin compared to the female and male control groups (10/28 (35.7%) vs. 3/28 (10.7%) vs. 3/28 (10.7%). Similarly, a higher proportion of girls from the PCOS group and male control group had history of adenotonsillectomy prior to polysomnography compared to the female control groups (9/28 (32.1%), vs. 7/28(25%) vs. 3/28 (10.7%)).

Polysomnography

Polysomnography comparisons demonstrated significant differences between the girls with PCOS and female and male controls in terms of prevalence of OSA, severity of OSA (AHI), and gas exchange during sleep (Table 2). Post hoc analysis showed that OSA was much more prevalent in girls with PCOS compared to female controls (16/28 (57%) vs. 4/28(14.3%), $p<0.01$), and not significantly different from the prevalence in male controls (16/28(57%) vs. 21/28(75%), $p=0.4$). Similarly, AHI was significantly elevated in girls with

PCOS compared to female controls (6.1 ± 6.9 events/hr vs. 2.2 ± 3.2 events/hr, p=0.03) and not different from male controls (6.1 ± 6.9 events/hr vs. 6.9 ± 5.4, p=NS). Oxygen saturation nadir was significantly lower in girls with PCOS compared to female controls (p=0.03) and was comparable to male controls (p=NS)

Cardiometabolic function

Cardiometabolic profile analysis demonstrated significant differences between girls with PCOS and female controls, and male controls, in terms of HOMA-IR, fasting HDL and systolic blood pressure (Table 3). Post hoc analysis demonstrated that IR (HOMA-IR>4) was more common in girls with PCOS compared to female controls (p=0.04) and male controls (p=0.01) (Table 2). Girls with PCOS had significantly lower HDL compared to female controls (p<0.05) and their HDL level was similar to male controls (p=NS). Though not significant, a greater number of girls with PCOS were diagnosed with MetS compared to female controls. The PCOS group showed significant positive correlation between AHI and fasting insulin (r=0.37, p=0.05), AHI and systolic BP (r=0.46, p=0.01), AHI and TG (r=0.49, p<0.01) and negative correlation between AHI and HDL (r=-0.29, p=0.1).

Sub-analysis of PCOS group

A sub analysis was done within the PCOS group comparing the age, BMI Z-score and cardiometabolic parameters between the girls with and without OSA (Table 4). Girls with PCOS and OSA showed a trend toward more severe obesity, a higher prevalence of MetS (9/16 (56.3%) vs. 1/12 (8.3%) and a higher prevalence of IR (HOMA-IR>4) (13/16 (81.3%) vs. 5/12 (41.6%), p=0.03 compared to girls without OSA. In additions, girls with PCOS and OSA had significantly elevated daytime systolic blood pressure, significantly lower HDL and significantly elevated TG compared to girls with PCOS but without OSA.

DISCUSSION

In the present study we found that OSA is about 4-times more prevalent in obese adolescent girls with PCOS referred for evaluation of OSA compared to obese adolescent girls without PCOS referred for OSA evaluation. This finding is consistent with recent adult literature. In a large population based study, Vgontzas et al. demonstrated a 30-fold higher prevalence of OSA in women with PCOS compared to the general female population, and showed that insulin resistance is a stronger risk factor for OSA than BMI or elevated testosterone levels(5). Fogel et al have shown that women with PCOS have significantly higher AHI than age and BMI matched females, and that the severity of OSA correlates well with serum testosterone levels(3). The association of OSA and the metabolic syndrome in these subjects was also reported by Tasali et al who demonstrated that effective treatment for OSA in these subjects using continuous positive airway pressure (CPAP) can improve some of the cardiometabolic dysfunctions linked to the disorder(4, 10).

In addition to finding a much higher prevalence of OSA in obese girls with PCOS compared to obese girls without PCOS, we noted that girls with PCOS have significantly more insulin resistance and metabolic derangements, as compared to both girls and boys with similar BMI Z-scores. This most likely explains the higher metformin use in the PCOS group compared to female and male control groups (35.7% vs. 10.7%, vs. 10.7%). Insulin resistance is believed to be the central pathophysiological mechanism linking PCOS to its concurrent metabolic derangements (22) and the use of insulin sensitizers have been shown to decrease the cardiometabolic morbidities associated with PCOS (23). Our sub-analysis suggests that among girls with PCOS-those with OSA have a higher prevalence of insulin resistance, MetS, and cardiometabolic abnormalities compared to those without OSA.

In a previous study based on screening questionnaires, we reported that adolescent girls with PCOS have a high prevalence of sleep disordered breathing compared to age and BMI matched controls. In addition, we noted that the presence of MetS was a strong predictor of sleep disordered breathing(24). This current study adds to our previous report with more robust findings including objective measures of sleep disordered breathing obtained by polysomnography.

The pathogenesis of OSA in PCOS is not clear. However, there is increasing evidence showing that the presence of OSA is a predictor of insulin resistance and glucose intolerance in PCOS(4). Researchers have also postulated that two phenotypes of PCOS exist: PCOS with OSA, (a severe phenotype with greater predisposition for cardiometabolic morbidities) and PCOS without OSA (a milder phenotype)(25). Even in our study with small numbers, we were able to show that the girls with PCOS and severe OSA had more severe cardiometabolic abnormalities. However, based on our study design, we cannot establish a causal relationship between PCOS, OSA, and cardiometabolic consequences. Our results, however, demonstrate the need for routine screening for OSA in obese adolescent girls with PCOS.

Of note, a higher proportion of girls with PCOS had a history of adenotonsillectomy prior to the sleep study compared to the female control group (32.1% vs. 10.7%). Adenotonsillectomy is considered first-line treatment for OSA in children(26). However, 54-76% of obese children are reported to have residual OSA after adenotonsillectomy (27). It is interesting to note that, even though our groups were BMI matched, the prevalence and severity of OSA still remained higher in the PCOS group, where nearly one third of the girls had a prior adenotonsillectomy, than in the female control group, where only 10% had prior adenotonsillectomy. There is limited information about treatment options for OSA in young adolescents with PCOS. Effective use of CPAP in a small group of young women with PCOS and OSA has shown to improve the cardiometabolic parameters (10). Future prospective intervention studies in large group of young adolescents with PCOS and OSA may help address these issues.

In contrast to our findings, a cross-sectional study by de Sousa et al comparing polysomnography findings in German adolescents with PCOS to obese and non obese female controls, did not suggest an increased prevalence of OSA in the PCOS subjects (12). However, they did find significant differences in sleep architecture between the groups and noted decreased %REM sleep, decreased sleep efficiency, and prolonged sleep latency in the PCOS group as compared to controls. There are several possible explanations for such discrepancies between our study and study by de Sousa, including ethnic differences between the groups. Our PCOS group consisted of predominantly mixed (African American/ Hispanic) (53.6%), African American (17.9%) and Hispanic (14.3%) ethnicities compared to a majority of whites in the de Sousa group. Racial and ethnic differences in the prevalence of OSA has been well described in the literature and OSA has been reported to be two- to fourfold more common in African American and Hispanic children(28, 29). Other possible explanations include: differences in study populations (referred population vs. general), age (17.7 ± 1.1yrs vs. 15.7 ± 1.9 yrs) and BMI (44.6 ± 8.6 vs. 36.2 ± 6.2).

Hyperandrogenemia is an important factor that may explain many of the sleep and cardiometabolic findings in the PCOS subjects in our study. Gender discrepancy in sleep apnea has been well established in the adult literature. Adult males have a much higher prevalence of OSA compared to adult females (30) (31). Redline et al. have reported a similar trend in adolescent males(32). Androgens can increase the risk for OSA by several mechanisms including: promoting fat deposition around the neck, decreasing central drive for breathing, promoting visceral fat deposition, and altering lung mechanics(33). Since

PCOS is characterized by hyperandrogenemia and alterations in body fat composition are well described (34), it is reasonable to consider this mechanism as an important contributor to OSA in our subjects. This may account for the similar polysomnographic findings in our adolescent PCOS females and male controls. This has also been suggested by Fogel at al who found that androgen excess correlated with the severity of OSA in adult women with PCOS. It would be interesting to compare and correlate the androgen levels between the groups; however, androgen levels were unavailable in our female and male controls. More comprehensive studies addressing these issues could better clarify the relationship between OSA and hyperandrogenemia in this population.

We would like to mention several important limitations of the present study. Firstly, the retrospective design was based on inclusion of adolescents with PCOS and controls who were referred for polysomnography to exclude OSA. Thus, our results are based on a referred population and may not be applicable to the entire population of adolescents with PCOS in terms of prevalence of OSA and metabolic correlates. The generalization of this study is also limited by the fact that all our subjects were obese, while obesity is only reported in about 75%-80% of women with PCOS (1). However, we have shown that even in our referred population, the prevalence of OSA is much higher in the obese girls with PCOS compared to obese female controls. Second, a significant number of adolescents in the PCOS group were on medications such as oral contraceptives or metformin. Even though, oral contraceptives are known to reduce the risk of OSA in women, we do not know the interaction of these medications with sleep parameters in a younger age group. This explains the need to study the pathophysiology of sleep apnea in a treatment naive PCOS population. Third, the cardiometabolic data was obtained within 6 months of the polysomnography study date. The cardiometabolic parameters, including BP measurements, can vary widely in this time period and may not totally reflect the numbers if these were done on the same night as the polysomnography study. This once again emphasizes the need for future prospective studies. Lastly, the definition of MetS in adolescents is controversial. We would have liked to compare the prevalence of MetS using two common criteria, Weiss and ATP III, but unfortunately we could not do so, due to different age groups and unavailability of waist circumference on all subjects; we therefore may have underestimated our prevalence of MetS. The reported prevalence of MetS using ATP III in overweight adolescents is about 28.7%, which is higher than in our control group: 16% (9/56)(35).

In summary, we report a higher prevalence of OSA and metabolic dysfunction in a selected group of obese girls with PCOS referred with sleep related complaints compared to age and BMI Z-score matched girls without PCOS. We also report higher prevalence of cardiometabolic dysfunction in girls with PCOS and OSA compared to girls with PCOS without OSA. However, additional studies are still indicated to further elucidate the complex pathophysiological mechanisms leading to OSA in these children.

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TABLE 1

Demographics

	PCOS Subjects (n=28)	Female Controls (n=28)	Male Controls (n=28)	p value (ANOVA)
Age (yrs)	16.8 ± 1.9	17.1 ± 1.8	16.6 ± 1.6	0.5
BMI	44.8 ± 8.8 *	40.2 ± 4.7	38.9 ± 6.6	p=0.02
BMI Z-score	2.4 ± 0.4	2.4 ± 0.3	2.5 ± 0.5	0.4
BMI Z- score percentile				
=>95% (n) (%)	28 (100%)	28 (100%)	26 (93%)	0.2
85-95% (n) (%)	0 (0%)	0 (0%)	2 (7%)	0.2
Race/ethnicity				
African American (n) (%)	5 (17.9%)	13 (46.4%)	6 (21.4%)	0.04
Hispanic (n) (%)	4 (14.3%)	6 (21.4%)	6 (21.4%)	0.7
White (n) (%)	4 (14.3%)	1 (3.6%)	1 (3.6%)	0.2
Mixed Race (African American/Hispanic) (n) (%)	15 (53.6%)	8 (28.6%)	15 (53.6%)	0.1
Medications				
Oral contraceptives (n) (%)	6 (21.4%)	4 (14.3%)	0 (0%)	0.04
Metformin (n) (%)	10 (35.7%)	3 (10.7%)	3 (10.7%)	0.1
Adenotonsillectomy (n) (%)	9 (32.1%)	3 (10.7%)	7 (25%)	0.2
Androgen levels				
Free testosterone (pg/ml)	9.6 ± 4.7 (n=25)			
Total testosterone (ng/dl)	53 ± 22.8 (n=28)			

Data is presented as: Mean ± SD

Bonferroni adjustment:

* p=0.02 compared to female controls, and p<0.01 compared to male controls

TABLE 2

Polysomnography

	PCOS Subjects (n=28)	Female Controls (n=28)	Male Controls (n=28)	p value (ANOVA)
OSA (n) (%)	16(57%) *	4 (14.3%)	21 (75 %)	0.001
Sleep onset latency (minutes)	39.7 ± 43.2	15.8 ±13.6	20.1 ± 28.7	0.2
Sleep efficiency (%)	78.1 ±14.7	81.7 ± 10.7	78.1 ± 13.8	0.5
Arousal awakening index (events/hr)	12.7 ± 7.3	13.8 ± 5.5	16.6 ± 8.2	0.1
AHI (events/hr)	6.1 ±6.9 **	2.2 ± 3.2	6.9 ± 5.4	0.004
Baseline oxygen (%)	97.9± 1.9	99.0 ±1.1	98.3 ±1.4	0.03
Lowest oxygen (%)	88.9 ± 8.0 ***	92.9 ±2.7	89.1 ± 5.1	0.01
Peak ETCO2 (mmHg)	48.9 ± 4.8	46.8 ± 4.8	50.2 ± 4.7	0.04

Data represented as Mean ± SD,

Bonferroni adjustment:

* p<0.01 compared to female controls, and p=0.4 compared to male controls

** p=0.03 compared to female controls and p=1 compared to male controls

*** p=0.03 compared to female controls and p=1 compared to male controls

TABLE 3

Cardiometabolic Function

	PCOS Subjects (n=28)	Female Controls (n=28)	Male Controls (n=28)	P value ANOVA)
[1]MetS (n) (%)	10 (35.7%)	4 (14.3%)	5 (17.6%)	0.1
Fasting Glucose (mg/dl)	96.6 ± 20.1	85.3 ± 13.5	94.6 ± 13.1	0.02
Fasting Insulin (IU)	30.1 ± 18.5	20.4 ± 6.8	21.3 ± 12.8	0.03
[2]HOMA-IR >4	71.4% * (20/28)	41.0% (9/22)	34.8% (8/23)	<0.05
Fasting TG (mg/dl)	125.5 ± 73.1	91.4 ± 38.9	110.4 ± 44.7	0.08
Fasting HDL (mg/dl)	43.0 ± 10.9 **	50.5 ± 13.8	38.3 ± 7.1	0.001
Systolic blood pressure (mmHg)	122.9 ± 13.6	117.1 ± 9.6	128.5 ± 11.5	0.002
Diastolic blood pressure (mmHg)	69.8 ±11.2	66.4 ± 8.4	66.4 ± 8.1	0.3

Data represented as mean ± SD

Bonferroni adjustment:

* p=0.04 compared to female control group, p=0.01 compared to male control group

** p<0.05 compared to female controls p=0.4 compared to male control group

[1]MetS; metabolic syndrome based on Weiss criteria(21)

[2]HOMA-IR; fasting glucose (mg/dL) × fasting insulin (μU/mL)/405.

TABLE 4

Polycystic Ovary Syndrome Sub-analysis

	PCOS with OSA (n=16)	PCOS without OSA (n=12)	P value
Age (yrs)	16.8 ± 2.1	16.6 ± 1.7	0.8
[1]BMI Z-score	2.5 ± 0.3	2.3 ± 0.5	0.1
Metformin (n) (%)	5 (31.3%)	5 (41.6%)	0.6
Oral contraceptives (n) (%)	3 (18.8%)	3 (25%)	0.7
Adenotonsillectomy (n) (%)	6 (37.5%)	3 (25%)	0.5
Free testosterone (pg/ml)	9.7 ± 4.2	7.6 ± 4.5	0.3
Total testosterone (ng/dl)	54.2 ± 30.1	51.0 ± 23.3	0.2
[2]MetS (n) (%)	9 (56.3%)	1 (8.3%)	0.03
[3]HOMA-IR>4	13(81.3 %)	5 (41.6%)	0.03
Fasting glucose (mg/dl)	99.3 ± 21.3	88.2 ± 8.9	0.07
Fasting insulin (IU)	8.4 ± 5.5	5.3 ± 3.6	0.09
Fasting TG (mg/dl)	149.7 ± 87.7	93.3 ± 25.8	0.03
Fasting HDL (mg/dl)	38.6 ± 8.7	49 ± 10.9	0.01
Systolic blood pressure (mmHg)	128.4 ± 12.8	115.6 ± 11.4	0.009
Diastolic blood pressure (mmHg)	71.4 ± 0.4	67.8 ± 11.5	0.4

Data represented as mean ± SD

[1]Body mass index Z-score

[2]MetS; metabolic syndrome based on Weiss criteria (21)

[3]HOMA-IR; fasting glucose (mg/dL) × fasting insulin (μU/mL)/405