

## Introduction

- Polycystic Ovarian Syndrome (PCOS)
  - Associated with elevated androgens leading to Menstrual irregularity, acne, hirsutism, and fertility issues.
  - Also associated with obesity, insulin resistance, diabetes, HTN, hyperlipidemia, and OSA
  - Cause is unclear, seen in obese and lean women
  - PCOS in adolescents
    - Diagnosis is less clear.
    - Irregular periods can be due to immature axis
    - Acne and hirsutism related to adolescents
    - Less is known about lean adolescents with PCOS.
  - Obstructive sleep apnea (OSA)
    - Seen in adults with PCOS.
    - Relationship less clear in adolescents
  - Assessment of insulin resistance
    - Gold standard is the hyperinsulinemic-euglycemic clamp
    - Continuous infusion of insulin delivered to reach a specific blood glucose level
    - Glucose then given to keep blood glucose at a specific concentration
    - The amount will differ depending on the how sensitive the body is to insulin
  - Study primary aim
    - Evaluate insulin resistance in adolescents with PCOS
    - Comparing lean, obese, and controls
  - Secondary Study aim
    - Evaluate the prevalence of OSA in PCOS
  - Hypothesis
    - We hypothesize adolescents who are obese with PCOS will have more insulin resistance measured by hyperinsulinemic euglycemic clamp compared to controls and lean adolescents with PCOS, and the lean adolescents with PCOS will have more insulin resistance than health controls.

## Inclusion/Exclusion Criteria

- Inclusion Criteria: PCOS Subjects
  - Females 13-21 years with diagnosis of PCOS based on NIH criteria
  - At least 2 years post-menarche
  - Categorized as either obese with a BMI of  $\geq 95\%$  for age (OPCOS) or lean with a BMI of  $\leq 85\%$  for age (NPCOS).
- Controls
  - Females, ages 18-21, BMI  $\leq 85\%$  for age.
  - Regular menses of at least 10 menses per year, and no clinical signs of hyperandrogenism.
  - Exclusion criteria: congenital adrenal hyperplasia, thyroid abnormalities, hyperprolactinemia or Cushing syndrome. Taking any medications within the past 3 months which were known to alter insulin secretion or action, affect hormone levels, or influence sleep.

## Methods

### OSA/CLAMP METHODS

Clamp studies done per previously described protocols  
 OSA done within 1-2 months of clamp study-only on PCOS subjects  
 Overnight polysomnography was performed in a quiet, darkened room via standard methods  
 Sleep staging and scoring of arousals were performed per standard criteria<sup>2</sup> by one blinded scorer.  
 OSA was determined if the obstructive apnea index was  $> 1/\text{hour}$  or apnea hypopnea index was  $\geq 5$

### DATA ANALYSIS

STATA version 15  
 Bivariate testing via Mann Whitney U testing and independent t testing  
 Comparing 3 groups-control, lean and obese PCOS via ANOVA and Kruskal Wallis  
 Clamp results calculated as has been described using the formula  $M = \text{INF} - \text{SC}$   
 $M = \text{glucose metabolized}$ ,  $\text{INF}$  is glucose infusion rate,  $\text{SC}$  is the difference between glucose at 2 time points.  
 Divided by average insulin over the time period between those two points

## Results

Subjects recruited: 28 OPCOS, (21 completed clamp and sleep study, 6 did not do sleep study.) 11 lean subjects with PCOS (10 did clamp and sleep study, 1 did clamp), 8 controls underwent clamp, none did sleep study.

### Group Comparisons (baseline values)

Statistically significant difference between the groups regarding age (expect as controls were adults 18-21 only,  $p < 0.0001$ )  
 BMI was statistically higher between the OPCOS and LPCOS and controls. No statistical difference between BMI of LPCOS and controls.  
 No statistical differences between the 3 groups for 17 hydroxyprogesterone and DHEA-S.  
 As expected controls had lower free testosterone values. No statistical difference between LPCOS and OPCOS for free testosterone

### Insulin Resistance

Table 1: Insulin Assessment

	OPCOS (n=27)	LPCOS (n=11)	Control (n=8)	p values (ANOVA/KW)
M/I	0.05 (0.018-0.083)	0.11 (-0.028-0.36)	0.17 (0.097-0.21)	0.040
GIR	2.48 (1.69-3.79)	6.79 (4.94-10.65)	9.08 (9.44-18.60)	0.0001
HOMA/IR	7.11 (4.11-10.25)	2.85 (1.34-3.30)	3.89 (2.81-4.78)	0.0001

There was no statistical difference between M/I for lean versus obese PCOS subjects ( $p = 0.23$ ), M/I was statistically higher in the control group compared to the LPCOS subjects.

Glucose infusion rate (GIR) at steady state was statistically lower in the OPCOS group compared to both other groups. There was no statistical difference between the GIR on the LPCOS compared to controls.

HOMA/IR was statistically higher in OPCOS group but did not statistically differ between the other groups

### Obstructive Sleep Apnea

No LPCOS patients had OSA. 9 (43%) of the obese subjects with PCOS had obstructive sleep apnea ( $p = 0.03$ )

## Discussion

### Clamp Results

Statistically significant difference between OPCOS and LPCOS compared to controls for M/I. LPCOS compared to controls had a trend towards statistical significance for lower M/I ( $p = 0.084$ )

Conflicts with GIR and HOMA/IR results which only show insulin resistance in OPCOS.

These are less accurate measures

Larger studies are needed

Previous studies conflicting looking at insulin resistance in lean subjects at 6-22% in adults.

### Obstructive Sleep Apnea

Exact prevalence in literature of OSA in pediatric patients with PCOS is unknown

No lean PCOS subjects had OSA, but prevalence of OSA in pediatric non obese patients is around 4% so study not powered to detect this

### Strengths

Relatively large study for adolescent patients with PCOS

Use of clamp to assess insulin resistance

### Weaknesses

#### Age of control group

Adolescents physiologic insulin resistance compared to adults this resistance decreases at Tanner V pubertal stage.

(PCOS subjects were at least 2 years post menarche, so likely most were at Tanner V.)

#### Small sample size for control and lean PCOS

Larger studies might yield differences in insulin resistance between controls and lean

No control group for sleep studies

Some subjects did not undergo sleep study

Selection bias? Subjects who did sleep study might have had sleep symptoms

## Conclusion

No metabolic differences in lean subjects with PCOS compared to controls

More studies are needed in this area in adolescent patients

Incidence of OSA in subjects with obesity and PCOS is high

Highlights importance of screening

## References

### References

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