Fasting Glucose Changes in Adolescents with Polycystic Ovary Syndrome Compared To Obese Controls: A Retrospective Cohort Study

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Abstract

Objective—To compare changes in fasting glucose among adolescents with polycystic ovary syndrome (PCOS) to obese adolescents without PCOS.

Methods—Retrospective cohort study of 310 adolescents with PCOS and 250 obese adolescents, (ages 13–18 years) seen at Mayo Clinic, Rochester MN, from 1996–2012. Included for analysis were 98 adolescents with PCOS and 150 obese adolescents who had 2 or more fasting glucose measurements separated by at least 6 months. Adolescents with impaired fasting glucose or diabetes were excluded. Multivariate models were used to assess predictors of change in fasting glucose.

Results—At diagnosis, adolescents with PCOS had lower body mass index (BMI) (kg/m²) and older age than obese adolescents ($P<.001$). Adolescents with PCOS had shorter follow up (years) ($P=.02$). Baseline fasting glucose (mg/dl) was not different between groups. Mean change in fasting glucose (mg/dl/year) was 2.4 ± 9.4 mg/dl/year for PCOS and 2.2 ± 6.2 mg/dl/year for obese adolescents ($P=.83$). Significant predictors for change in fasting glucose were BMI and fasting glucose at diagnosis ($P<.01$). Within the PCOS cohort, BMI was a significant predictor for development of IFG ($P=.003$). Prevalence of hypertension (HTN) increased in the PCOS cohort from baseline to follow up ($P=.02$). PCOS and BMI were significantly associated with development of HTN in the entire cohort.

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Conclusions—Adolescent girls with PCOS do not show a significant change in fasting glucose or an increased risk for the development of IFG compared to obese adolescents. BMI, not PCOS status, was the strongest predictor for changes in fasting glucose and development of IFG over time.

Keywords

hypertension; impaired fasting glucose; polycystic ovary syndrome

INTRODUCTION

Polycystic ovary syndrome (PCOS) is a condition of androgen excess, oligomenorrhea, and polycystic ovarian morphology (PCOM) [1, 2]. It affects 4%–10% of adult women of reproductive age [3–5] and can be diagnosed as early as adolescence [6]. The appearance of PCOS symptoms in adolescence may predispose an individual to a more severe phenotype in terms of cardiovascular risk in adulthood. However, diagnosis in adolescence can be challenging due to the common symptoms of irregular menstrual cycles during the perimenarchal period [7, 8]. The occurrence of PCOM may be even higher in asymptomatic adolescents (as many as one-third) than in asymptomatic adults with a reported prevalence of 20%–25% [9, 10]. Earlier diagnosis identifying girls at higher risk for co-morbidities in PCOS would be particularly clinically relevant as it could lead to earlier intervention and prevention strategies.

It is well-established that PCOS is associated with insulin resistance independent of body weight [11, 12]. Consequently, women with PCOS have a higher prevalence of type 2 diabetes and impaired glucose tolerance [13, 14]. Adolescents with PCOS have a higher prevalence of glucose intolerance when compared to healthy adolescent controls in cross sectional studies [12, 15–17]. Although it has been established that obese adolescents have a higher risk for developing impaired fasting glucose (IFG) over time [18], it is not known whether PCOS by itself is associated with higher risk for the development of IFG as compared to obese adolescents. Given the known interaction of obesity with PCOS, the debate about diagnostic criteria for PCOS in adolescence becomes even more clinically relevant if the risk for glucose intolerance is greater than that conferred by obesity. To determine whether adolescent girls with PCOS were at significantly greater risk for developing glucose intolerance, we sought to compare adolescents with PCOS with another group known to be at higher risk for glucose intolerance, in this case, obese adolescents [18]. Our primary objective was to compare changes in fasting glucose and development of IFG among adolescents diagnosed with PCOS between the ages of 13–18 years to obese adolescents without PCOS followed at a single center over a time span of 15 years. As a secondary objective, we collected data on the rates of dyslipidemia and hypertension in both groups at baseline and follow up.

METHODS

This was a retrospective review of medical records of adolescent girls seen in the Department of Community Pediatric and Adolescent Medicine at Mayo Clinic, Rochester,

MN. The Department of Community Pediatric and Adolescent Medicine provides preventive care and health screening to children and adolescents in Olmsted County, MN. The Division of Pediatric and Adolescent Gynecology primarily evaluates referrals for female reproductive health disorders including PCOS as well as medical examinations for contraception and reproductive health screening.

Participants

After receiving the approval of the Institutional Review Board at Mayo Clinic, Rochester, MN, adolescent girls aged 13–18 years with PCOS or those characterized with obesity were identified using coding and billing data. Identification of the cohorts was performed using the Mayo Clinic Life Sciences System (MCLSS), which is a complete clinical data repository containing patient demographics, diagnoses, hospital, laboratory, clinical notes, pathology, and billing data obtained from multiple clinical and hospital source systems within Mayo Clinic. Data in the MCLSS were accessed via the Data Discovery and Query Builder toolset, consisting of a web based application that utilizes a unique text search engine and provides the capability to rapidly search for specific words and phrases within unstructured text documents such as clinical notes [19]. All girls seen within a 15-year period (January 1997 to December 2012) with the International Classification of Diseases, Ninth Revision (ICD-9) code for PCOS (256.4) or PCOS as a text word search term were identified. Girls characterized with obesity, but not PCOS, during a well-child visit in the Department of Community Pediatric and Adolescent Medicine were identified by searching charts for the ICD-9 code for obesity (278.0) or by a text word search for obesity.

Definitions

The PCOS status was determined by a single adolescent gynecologist using Rotterdam criteria requiring the presence of at least two of the three criteria of (i) clinical or biochemical evidence of hyperandrogenism; (ii) oligo- or anovulation (defined as less than nine periods per year); and (iii) PCOM [20]. During chart review, we identified girls who also met the National Institutes of Health (NIH) criteria for PCOS [21] requiring the presence of both oligoovulation and hyperandrogenism. Determination of PCOM was based on adult criteria of the presence of 12 or more 2–9 mm follicles in each ovary or ovarian volume >10 mL as defined by Rotterdam criteria [20]. Subjects with untreated hypothyroidism, hyperprolactinemia, congenital adrenal hyperplasia, Cushing's syndrome, pregnancy, androgen-secreting tumors, or a condition as the cause of hyperandrogenism were excluded.

Obesity was defined as a body mass index (BMI) at or over the 95th percentile on Center for Disease Control age- and gender-specific growth charts [22].

Subjects with a hormonal or genetic diagnosis of obesity or who were pregnant were excluded. The definition of IFG was glucose between 100 and 125 mg/dl, hypertension (HTN) was defined as a systolic blood pressure (SBP) >120 mm Hg on two consecutive visits, hypertriglyceridemia as triglycerides >150 mg/dl and low levels of high density lipoproteins (HDL) as < 50 mg/dl [23, 24].

Procedures and Measures

We employed a standardized abstraction form for data collection. For each medical record, we identified the first visit in which the diagnosis of PCOS or obesity was identified (baseline visit) as well as the last follow up visit with any Mayo Clinic provider. We collected information regarding age, PCOS diagnostic criteria, age at menarche, cardiovascular risk factors (hypertension, diabetes, family history of diabetes), BMI, and systolic and diastolic blood pressure at baseline and follow up visits. Oral contraceptive pill (OCP) use was also recorded. The same information was retrieved for obese adolescents with the exception of PCOS diagnostic criteria. With regards to biochemical and ultrasound evaluations, fasting glucose was noted for the baseline and follow up visits along with total cholesterol, triglycerides, HDL, and low-density lipoprotein. In addition, total testosterone measurements and ovarian ultrasound information such as ovarian volume and number of follicles, if available, were recorded for the PCOS cohort. All biochemical laboratory measures were obtained in the Mayo Clinic Laboratories using standard automated colorimetric enzymatic assays (Roche Diagnostics, Indianapolis, IN) with the exception of testosterone, which was measured using high-throughput liquid chromatography (Hamilton Robotics Inc., Reno, NV), and glucose, which was measured using a photometric rate reaction (Roche Diagnostics, Indianapolis, IN). Fasting glucose was obtained using a standard minimum 12 hours of fasting, which was verified on all samples. Samples obtained less than 12 hours since last meal were not reported as fasting.

Statistical Analyses

We compared the means of baseline characteristics between PCOS and obese adolescents; for variables not distributed normally, we used a *t* test and a Wilcoxon signed rank test to compare medians. Categorical variables were compared using chi-square analysis. We used a chi-square test to compare the proportion of girls meeting criteria for IFG both prior to subject selection and at follow-up visit for the two cohorts of PCOS and obese adolescents. Linear and logistic regression models were created in a stepwise fashion using JMP 9.0.1 (SAS Institute Inc., Cary, NC) to identify predictors of change in fasting glucose over time, change in SBP, and development of IFG. We used stepwise and clinical variables known to affect the outcomes.

RESULTS

Between 1997 and 2012, we identified 316 adolescent girls with PCOS and 250 who were obese but did not have PCOS. On review of charts, 6 subjects were excluded from the PCOS cohort based on secondary diagnoses, but no exclusions were made from the obese adolescent cohort. Next, we excluded those who did not have a repeat fasting glucose separated by at least 6 months from the first measurement, which resulted in 103 adolescents with PCOS and 218 obese adolescents. When participants diagnosed with IFG or diabetes at the time of diagnosis were excluded, the remaining sample included 98 girls with PCOS and 217 obese adolescents. Of the 217 obese adolescents, 150 participants were randomly selected for inclusion in the final study cohort (Figure 1). All 98 subjects with PCOS included in the analysis met requirements for diagnosis of PCOS using both Rotterdam and NIH criteria.

Baseline characteristics at diagnosis were compared between the PCOS and obese adolescent cohorts, with the PCOS cohort having significantly lower BMI, having a higher mean age, and having a shorter length of follow up. The baseline fasting glucose was not significantly different between groups (Table 1). The prevalence of obesity in the PCOS cohort was 68.4% (BMI 95th percentile), 16.3% were considered overweight (BMI 85th percentile), and 15.3% were considered normal weight (BMI <85th percentile).

Prior to subject selection, there was a statistically significant higher prevalence of impaired fasting glucose (IFG) among PCOS subjects (6.6% versus 2% in obese adolescents, $P=.01$) while at follow up there was no difference in prevalence of IFG among the two primary cohorts (16.3% versus 20% for obese adolescents $P=.46$). Of the PCOS adolescents who developed IFG ($n=16$), all but one were obese at baseline. Median time to diagnosis of IFG (years) was 1.25 (IQ range 0.65–6.06) versus 4.75 for obese adolescents (IQ range 1.11–5.85, $P=.27$). Although the median time to follow-up testing was lower in PCOS, the obese adolescents who developed IFG had interval glucose testing a mean of 1.5 times.

Mean change in fasting glucose (mg/dl/year) was 2.4 ± 9.4 mg/dl/year for PCOS and 2.2 ± 6.2 mg/dl/year for obese adolescents ($P=.83$). Stepwise multivariate linear regression was performed to assess predictors of change in fasting glucose among the entire cohort of PCOS and obese adolescents (Table 2). Significant predictors of change in fasting glucose (mg/dl/year) were BMI, age at menarche and fasting glucose at time of diagnosis. PCOS was not a significant predictor of change in fasting glucose in models with or without BMI and other potential confounding factors (Table 2).

Multivariate logistic regression was used to assess significant predictors of development of IFG within the PCOS and obese adolescent cohorts (Table 3). Baseline fasting glucose and baseline BMI were significant predictors of development of IFG in both PCOS and obese adolescent cohorts ($P<.01$). In only the PCOS cohort, OCP use at follow up was significantly associated with lower risk for development of IFG ($P=.04$). Total testosterone concentrations were available for 91 of 98 PCOS adolescents at baseline and were not significantly associated with development of IFG in any of the models.

Prevalence of HTN, low HDL, and elevated triglycerides between PCOS and obese adolescent cohorts did not differ at baseline, with 36.7% of PCOS adolescents versus 33.3% of obese adolescents with HTN at baseline ($P=.37$). However, at follow up, there was a statistically significant higher prevalence of HTN in the PCOS cohort compared to baseline prevalence ($P=.02$) (Figure 2).

Assessing the use of OCPs, the prevalence of PCOS adolescents who used OCPs increased from 5.1% at baseline to 73.5% at follow up ($P=.01$). In obese adolescents, the use of OCPs was 19.3% at baseline and only 37.3% at follow-up ($P=.16$).

To further investigate change in HTN in the PCOS cohort, we assessed the predictors for the development of HTN as defined by SBP >120 mm Hg in a model using only the adolescents who did not have HTN at baseline. PCOS was associated with an odds ratio of 3.37 for the development of HTN even adjusting for BMI at follow up ($P<.01$). Length of follow up, OCP use, and age at time of diagnosis were not significant predictors of development of

HTN. There was no difference in the results when the outcome was a change in SBP, diastolic blood pressure, or mean blood pressure. There was no significant association between PCOS and OCP use in the model.

DISCUSSION

Our study finds that adolescent girls with PCOS do not have a significantly different change in fasting glucose or development of IFG compared to obese adolescents. BMI, but not PCOS status, was the strongest predictor for change in fasting glucose and development of IFG over time. Prior to subject selection, PCOS adolescents had a higher prevalence of IFG as compared to obese adolescents but this did not persist at follow up. In adolescents and in women not actively trying to conceive, OCPs are considered first line management in addressing the symptoms of PCOS such as menstrual irregularity and hirsutism.

The use of OCPS was significantly decreased risk for the development of IFG in PCOS, but not in obese adolescents. While there was no difference in the prevalence of HTN and dyslipidemia between PCOS and obese adolescents, the prevalence of HTN increased significantly from baseline to follow up within the PCOS cohort. Even adjusting for OCP use and BMI, PCOS was significant predictor for the development of newly-diagnosed HTN.

Our study supports findings from previous studies among adolescents and women with PCOS that increasing BMI has a significant impact on the development of insulin resistance, glucose intolerance and Beta cell dysfunction [11, 25–27]. Among obese adolescents, the relationship between increasing BMI and development of impaired fasting glucose is well established [28]. Our data prior to the exclusion of subjects without IFG also agrees with other cross-sectional studies that report a higher prevalence of glucose intolerance in adolescent PCOS when compared to matched controls at baseline [12, 15–17]. Older age at menarche was also associated with development of IFG. This could imply that a longer duration of amenorrhea is associated with higher metabolic risk, a finding that has been reported previously in adolescents. [29] To our knowledge, this is the first study to examine whether PCOS in adolescents is associated with a higher risk of changes in glucose or glucose intolerance over time. Importantly, the strongest predictor was not PCOS but BMI status, suggesting that greater risk is conferred by obesity than PCOS status alone.

Hypertension in adolescents with PCOS

To our knowledge, this is also the first report to assess the risk for HTN in adolescents with PCOS. The increase in the prevalence of HTN in the PCOS group was significant even adjusting for the high rate of OCP use in PCOS compared to obese adolescents. A higher prevalence of HTN has been reported in adult women with PCOS as compared to obese and lean controls despite adjustment for BMI [30–33]. This result has important implications for the management of PCOS with regards to OCP use. Even though the models did not find a significant association or interaction of PCOS with OCP use and HTN, future studies are needed to prospectively evaluate whether OCP use, or specific types of OCPs, increase the risk for HTN in PCOS.

Glucose intolerance and OCP use

The study associated OCP use with a significantly decreased risk for IFG in PCOS. Because OCP use was protective for the development of IFG among PCOS adolescents, but not obese adolescents, the beneficial effects of OCPs on glucose metabolism in PCOS might be due to the decrease in androgens, which are strongly associated with insulin resistance [34]. We did not have enough data on androgen levels at follow-up to evaluate this question. The effect of OCPs on carbohydrate metabolism in PCOS continues to be a matter of controversy [35] with older studies that used higher dose ($>35 \mu\text{g}$) ethinyl estradiol- (EE-) containing OCPs and which demonstrated deleterious effects on carbohydrate metabolism [27, 36]. Although studies in adolescents are limited, one study observed a worsening of insulin sensitivity after 12 months of OCP use involving the higher dose, 30–35 microgram (μg), EE-containing OCPs [37]. However, another study comparing 35- μg EE-containing OCPs to metformin reported similar improvement in insulin sensitivity in adolescents with PCOS [38]. Other studies vary in their results, ranging from no deleterious effect of OCPs on glucose metabolism to an improvement in insulin sensitivity; thus, differences in age, anthropometric measurements, and type of OCP used among individual studies contribute to the challenge of drawing conclusions from the few studies assessing the impact of OCPs on PCOS [39, 40].

In our study, almost all participants were on 30–35 μg , EE- containing OCPs. It is possible that lower dose EE OCP formulations would have less benefit in terms of insulin sensitivity, although they could also decrease the risk for an increase in blood pressure.

Limitations

There is a potential risk of selection and treatment bias conducting a retrospective observational study that selects one cohort from a specialty clinic (PCOS adolescents) and another cohort from primary care (obese adolescents). The higher prevalence of IFG in PCOS adolescents as compared to obese adolescents at baseline could reflect a pool of more severely affected, tertiary referral patients as opposed to the primary care cohort pool of obese adolescents. The adolescents with PCOS all met the more strict NIH criteria for diagnosis, which is associated with greater metabolic abnormalities [21, 41]. A bias of more severely affected PCOS adolescents would favor seeing a higher risk for IFG and HTN even if the prevalence of obesity was lower. Instead, we did not find that PCOS was associated with a greater risk for changes in fasting glucose or IFG.

Because the use of OCP was greater in the PCOS cohort, treatment of hyperandrogenemia may have attenuated the changes in glucose, the development of IFG, and/or HTN even though we tried to address this in our statistical analysis. We did not have data on glucose tolerance tests or hemoglobin A1C on all subjects. Furthermore, because this was a retrospective study based on records from two different specialties, follow-up tests and intervals were not standardized in either group.

Strengths of this study's findings include the diagnosis of PCOS by a single, experienced expert in adolescent gynecology, which limits the heterogeneity in diagnosis. In addition, although laboratory testing was performed in a clinical setting, standardized protocols at

Mayo Clinic only report a fasting glucose when a required time interval since last food intake has been confirmed (between 12 and 14 hours).

Although the retrospective nature of the study does not allow us to determine a causative role for OCPs in the development of HTN in PCOS, it highlights the need for future studies to examine the interaction of commonly used therapies in PCOS on both promoting and preventing cardiovascular risk factors. The risk for hypertension might be even more relevant for African-Americans with PCOS given that our sample was primarily Caucasian. There may be other personal risk factors that increase or decrease an individual's response. Future prospective studies systematically studying glucose tolerance and blood pressure are needed to better understand and tailor PCOS management in adolescents.

CONCLUSION

Adolescent girls with PCOS do not have a significantly different change in fasting glucose or increased risk for the development of IFG compared to obese adolescents. The strongest predictor for change in glucose and development of IFG over time was BMI, not PCOS. However, adjusting for OCP use and BMI, PCOS was a significant predictor for the development of HTN.

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References

1. Azziz R, et al. Positions statement: criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: an Androgen Excess Society guideline. *J Clin Endocrinol Metab.* 2006; 91(11):4237–4245. [PubMed: 16940456]
2. Azziz R, et al. The Androgen Excess and PCOS Society criteria for the polycystic ovary syndrome: the complete task force report. *Fertil Steril.* 2009; 91(2):456–488. [PubMed: 18950759]
3. Dunaif A, Thomas A. Current concepts in the polycystic ovary syndrome. *Annu Rev Med.* 2001; 52:401–419. [PubMed: 11160786]
4. Azziz R, et al. Androgen Excess in Women: Experience with over 1000 Consecutive Patients. *Journal of Clinical Endocrinology and Metabolism.* 2004; 89(2):453–462. [PubMed: 14764747]
5. Knochauer ES, et al. Prevalence of the polycystic ovary syndrome in unselected black and white women of the southeastern United States: a prospective study. *Journal of Clinical Endocrinology & Metabolism.* 1998; 83(9):3078–3082. [PubMed: 9745406]
6. Williams RM, Ong KK, Dunger DB. Polycystic ovarian syndrome during puberty and adolescence. *Mol Cell Endocrinol.* 2013; 373(1–2):61–67. [PubMed: 23384539]
7. Apter D, Vihko R. Early menarche, a risk factor for breast cancer, indicates early onset of ovulatory cycles. *J Clin Endocrinol Metab.* 1983; 57(1):82–86. [PubMed: 6222061]
8. Legro RS, et al. Rapid maturation of the reproductive axis during perimenarche independent of body composition. *Journal of Clinical Endocrinology & Metabolism.* 2000; 85(3):1021–1025. [PubMed: 10720033]
9. Codner E, et al. Polycystic ovarian morphology in postmenarchal adolescents. *Fertility & Sterility.* 2011; 95(2):702–706. e1–e2. [PubMed: 20650451]
10. Murphy MK, et al. Polycystic ovarian morphology in normal women does not predict the development of polycystic ovary syndrome. *Journal of Clinical Endocrinology & Metabolism.* 2006; 91(10):3878–3884. [PubMed: 16882750]

11. DeUgarte CM, Bartolucci AA, Azziz R. Prevalence of insulin resistance in the polycystic ovary syndrome using the homeostasis model assessment. *Fertil Steril*. 2005; 83(5):1454–1460. [PubMed: 15866584]
12. Palmert MR, et al. Screening for abnormal glucose tolerance in adolescents with polycystic ovary syndrome. *J Clin Endocrinol Metab*. 2002; 87(3):1017–1023. [PubMed: 11889155]
13. Legro RS, et al. Prevalence and predictors of risk for type 2 diabetes mellitus and impaired glucose tolerance in polycystic ovary syndrome: a prospective, controlled study in 254 affected women. *J Clin Endocrinol Metab*. 1999; 84(1):165–169. [PubMed: 9920077]
14. Ehrmann DA, et al. Prevalence of impaired glucose tolerance and diabetes in women with polycystic ovary syndrome. *Diabetes Care*. 1999; 22(1):141–146. [PubMed: 10333916]
15. Coviello AD, Legro RS, Dunaif A. Adolescent girls with polycystic ovary syndrome have an increased risk of the metabolic syndrome associated with increasing androgen levels independent of obesity and insulin resistance. *J Clin Endocrinol Metab*. 2006; 91(2):492–497. [PubMed: 16249280]
16. Arslanian SA, Lewy VD, Danadian K. Glucose intolerance in obese adolescents with polycystic ovary syndrome: roles of insulin resistance and beta-cell dysfunction and risk of cardiovascular disease. *J Clin Endocrinol Metab*. 2001; 86(1):66–71. [PubMed: 11231980]
17. Macut D, et al. Cardiovascular risk in adolescent and young adult obese females with polycystic ovary syndrome (PCOS). *J Pediatr Endocrinol Metab*. 2001; 14(Suppl 5):1353–1359. discussion 1365. [PubMed: 11964034]
18. Li C, et al. Prevalence of pre-diabetes and its association with clustering of cardiometabolic risk factors and hyperinsulinemia among U.S. adolescents: National Health and Nutrition Examination Survey 2005–2006. *Diabetes Care*. 2009; 32(2):342–347. [PubMed: 18957533]
19. Alsara A, et al. Derivation and validation of automated electronic search strategies to identify pertinent risk factors for postoperative acute lung injury. *Mayo Clin Proc*. 2011; 86(5):382–388. [PubMed: 21531881]
20. Aruna J, et al. Metformin therapy in women with polycystic ovary syndrome. *International Journal of Gynaecology & Obstetrics*. 2004; 87(3):237–241. [PubMed: 15548396]
21. Zawadzki J, DA. Diagnostic criteria for polycystic ovary syndrome: towards a rational approach. In: Dunaif, A.; Givens, J.; Haseltine, F.; Merriam, G., editors. *Polycystic ovary syndrome*. U. Oxford, Blackwell Scientific; 1992. p. 377–384.
22. Thatcher SS, Jackson EM. Pregnancy outcome in infertile patients with polycystic ovary syndrome who were treated with metformin. *Fertility & Sterility*. 2006; 85(4):1002–1009. [PubMed: 16580387]
23. Weiss R, et al. Obesity and the metabolic syndrome in children and adolescents. *N Engl J Med*. 2004; 350(23):2362–2374. [PubMed: 15175438]
24. McGill DJ, et al. Laser hair removal in women with polycystic ovary syndrome. *Journal of Plastic, Reconstructive & Aesthetic Surgery: JPRAS*. 2007; 60(4):426–431.

WHAT'S NEW

This longitudinal assessment of adolescent girls with PCOS analyzes changes in fasting glucose and risk for development of IFG in adolescents with PCOS compared with obese adolescents. The strongest predictor for change in glucose over time was BMI, not PCOS.

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Figure 1. Cohort derivation

Figure 2. Prevalence of hypertension and dyslipidemia

There was a significant difference in hypertension prevalence among the PCOS adolescents from baseline to follow-up ($P=.02$). There was no significant difference in hypertension prevalence between PCOS adolescents and obese adolescents at follow up ($P=.06$).

Table 1Baseline Characteristics of the Primary Cohorts.^a

Baseline characteristics	PCOS (n=98)	Obese Adolescents (n=150)	<i>P</i> value
Age, years	15.7 (1.4)	14.9 (1.6)	<.01
Ethnicity (% White)	87.8	88.7	.83
BMI	33.2 (7.8)	37.4 (7.1)	<.01
Age at menarche, years ^b	12 (1.6)	12.5 (1.8)	.03
Family history of diabetes (%)	37.8	50	.06
Baseline fasting glucose, mg/dl	88 (6.2)	88.3 (6.9)	.75
Length of follow up, years ^c	2.3 [1.0–5.3]	3.4 [1.8–6.4]	.03
OCP use (%)	5.1	19.3	<.01
Systolic blood pressure, mm Hg	118.4(12.8)	117.2 (12.9)	.45
Triglycerides, mg/dl ^d	142.3 (75.9)	139.8 (84.1)	.85
HDL at baseline, mg/dl ^d	48.5 (16.8)	46.1 (11.91)	.29

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); HDL, high-density lipoprotein; OCP, oral contraceptive pill

^aData are presented as mean (SD) unless otherwise indicated.

^bPCOS (n=95), Obese adolescents (n=127)

^cMedian and Interquartile

^dPCOS (n=59) Obese adolescents (n=92)

Table 2

Predictors of Change in Fasting Glucose (mg/dl/year) in the Entire Cohort

Regression Model	Parameter Estimate (SE)	P value
<u>Model 1</u>		
Baseline age, y	0.23(0.29)	.43
Baseline BMI	0.19 (0.06)	<.01
Baseline fasting glucose	−0.32 (0.07)	<.01
<u>Model 2</u>		
Baseline age, y	0.18 (0.30)	.54
Baseline BMI	0.20 (0.06)	<.01
Baseline fasting Glucose	−0.32 (0.07)	<.01
PCOS	0.38 (0.49)	.44
<u>Model 3</u>		
Baseline age, y	0.15(0.3)	.62
PCOS	−0.01 (0.48)	.99
Baseline fasting glucose	−0.32(0.06)	<.01
<u>Model 4</u>		
PCOS	0.40 (0.55)	.46
Baseline age, y	−0.07 (0.33)	.83
Age at menarche, y	0.67(0.30)	.03
Baseline BMI	0.18(0.07)	<.01
Baseline fasting Glucose	−0.36 (0.07)	<.01
Family history of diabetes	−0.24(0.50)	.63
OCP use at follow up *	1.58 (0.83)	.40

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); OCP, oral contraceptive pill; PCOS, polycystic ovary syndrome; SE, standard error,

* Log-transformed. Only years of follow up is log transformed

Table 3

Predictors of IFG in PCOS and Obese Adolescents

	PCOS Odds ratio (CI)	<i>P</i> value	Obese Adolescents Odds ratio (CI)	<i>P</i> value
Model 1				
Baseline age, y	1.76 (1.09–3.09)	.02	0.09 (0.82–1.46)	.55
Baseline BMI	1.14 (1.05–1.24)	<.01	1.10 (1.03–1.17)	<.01
Baseline fasting glucose	1.12 (1.0–1.27)	.06	1.11 (1.04–1.20)	<.01
Model 2				
Baseline age, y	1.75 (1.09–3.10)	.02	1.09 (0.82–1.46)	.55
Baseline BMI	1.14 (1.05–1.25)	<.01	1.1 (1.03–1.17)	<.01
Baseline fasting glucose	1.10 (0.98–1.25)	.10	1.11 (1.04–1.20)	<.01
OCP use at follow-up	0.24 (0.06–0.92)	.04	1.05(0.41–2.59)	.92

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); OCP, oral contraceptive pill

No other variables were noted to be associated with change in fasting glucose