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Alissa Briggs

University of Kentucky, [alissa.briggs@uky.edu](mailto:alissa.briggs@uky.edu)

Mandakini Sadhir

University of Kentucky, [m.sadhir@uky.edu](mailto:m.sadhir@uky.edu)

Maya Todd

University of Kentucky, [maya.todd@uky.edu](mailto:maya.todd@uky.edu)

Hatim A. Omar

University of Kentucky, [hatim.omar@uky.edu](mailto:hatim.omar@uky.edu)

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## Effect of metformin on body mass index in adolescent females with polycystic ovary syndrome

Alissa Briggs, PhD, Mandakini Sadhir, MD,  
Maya Todd, and Hatim Omar, MD

Division of Adolescent Medicine and Young Parent Programs, Kentucky Clinic, Department of Pediatrics, Kentucky Children's Hospital, University of Kentucky College of Medicine, Lexington, Kentucky, USA

### Abstract

Polycystic ovary syndrome (PCOS) is often associated with obesity, insulin resistance, irregular menstrual periods and pelvic pain. Treatment involves hormonal methods for regulation of menstrual cycle, lifestyle changes and metformin for improving insulin resistance and weight. The aim of our study was to compare changes in body mass index (BMI) of adolescent female with PCOS treated with metformin as compared to lifestyle modification only. Participants: Adolescent and young adult females aged 10-25 years diagnosed with PCOS seen for at least two visits for at least one year on the same treatment. Based on treatment plan, participants were categorized as metformin (metformin + lifestyle changes; metformin + oral contraceptive pills+ lifestyle changes) versus control group (oral contraceptive pills + lifestyle changes; lifestyle changes only). Results: Of the 464 charts reviewed, 134 participants met the inclusion criteria. The average time period between the initial and follow up visit on same treatment plan was two years (Range 1-8 years). The average age of patients at baseline (initial visit) and follow up was 15.3 and 17.7 years, respectively. The majority of participants were overweight or obese at baseline and follow up. There was not a significant difference between the metformin and control group in the number of patients who stayed in the same BMI category, went up in a BMI category, or went down in a BMI category from baseline to follow up ( $\chi^2 = 1.93, p = 0.38$ ). Conclusion: Treatment with metformin did not relate to changes in BMI classification over a year or more.

**Keywords:** Obesity, PCOS, metformin, adolescent female, BMI

### Introduction

Polycystic ovary syndrome (PCOS) is a complex endocrine disorder among reproductive age women. It is characterized by chronic anovulation leading to menstrual irregularities, pelvic pain and hyperandrogenism manifested as hirsutism, acne, and

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• Correspondence: Hatim A Omar, MD, FAAP, Professor of Pediatrics and Obstetrics/Gynecology, Children's Miracle Network Chair, Chief, Division of Adolescent Medicine and Young Parents Program (IA12), Kentucky Children's Hospital, UK Healthcare, Department of Pediatrics, University of Kentucky College of Medicine, Lexington, KY 40536, United States. E-mail: haomar2@uky.edu

alopecia along with elevated serum androgen levels (1). PCOS is diagnosed using various criteria commonly known as NIH, Rotterdam and Androgen Excess society. In 1990, the National Institutes of Health (NIH) held a conference on PCOS to create both a working definition of the disorder and diagnostic criteria. The outcome of this conference, the NIH Criteria, served as a standard for researchers and clinicians for more than a decade. In 2003, a consensus workshop in Rotterdam in the Netherlands developed new diagnostic criteria, the Rotterdam Criteria. The Androgen Excess (AE) and PCOS Society proposed the AE-PCOS Criteria in 2006. It has an estimated prevalence of 5-10% among adult females (2, 3). Limited data exists about incidence and prevalence of PCOS in adolescent females and diagnosis continues to be challenging (4-6). Higher incidence of PCOS is seen with obesity, history of premature adrenarche, and family history of PCOS (7-9).

The exact etiology of PCOS remains unknown, but there is evidence that supports genetic and lifestyle factors in the development of PCOS. Studies have suggested the role of insulin resistance for the development of ovarian and pituitary dysfunction (10, 11). In PCOS, there is relative increase in LH pulsatile secretion from the pituitary gland leading to altered high LH to FSH ratio (1.5-2:1). As a result, there is increase in ovarian androgen biosynthesis. In addition, high insulin levels stimulate ovarian androgen production and inhibit hepatic production of sex hormone binding globulin. Further, decrease in pituitary FSH secretion leads to less aromatization of androgens to estradiol which affects follicular development and ovulation (12).

In adolescent females, PCOS is often associated with obesity with increased risk of metabolic disturbances, including impaired glucose tolerance and dyslipidemia. Treatment of PCOS in adolescent female involves a multidisciplinary approach to decrease future risk of endometrial cancer, diabetes mellitus and cardiovascular disease (13). It involves menstrual regulation, addressing features of hyperandrogenism such as hirsutism, acne, and weight management to improve insulin resistance. Treatment of obesity has been associated with improvement in menstrual irregularity and insulin resistance (14).

Menstrual regulation is often done using oral contraceptive pills, which also helps to improve sex hormone binding globulin and free testosterone. In addition, studies have found metformin to be beneficial for improving follicular development and insulin resistance (14). Recent meta-analysis showed that lifestyle changes and metformin were associated with lower BMI and subcutaneous adipose tissue with improved menstruation in women with PCOS as compared with lifestyle changes only (15). Randomized control trials comparing metformin with oral contraceptive pills showed significant improvement in BMI over 6 month period (16, 17). Currently, there is limited data on long term changes in BMI in adolescent females with PCOS on treatment with metformin. In our study, it was hypothesized that adolescent female treated with metformin would have a decrease in BMI as compared to those on lifestyle modifications only when followed for at least a year.

## Methods

A retrospective chart review of adolescent females (12-21 years) who were seen, diagnosed and treated for PCOS in the Adolescent Medicine clinic was conducted. The study was approved by the Institutional Review Board. The charts were pulled using the billing diagnosis of PCOS, obesity, and insulin resistance. Upon chart review, participants who met the NIH criteria of PCOS (oligo-ovulation, clinical or biochemical hyper-androgenemia and exclusion of other mimicking disorders) and followed up in clinic for at least one year on the same treatment plan (metformin only, metformin with oral contraceptives, oral contraceptives only, and lifestyle modifications only) were included. In order to be included in the study, charts needed to have the following data at an initial visit and follow up visit on the same treatment plan over at least a year: age, weight, and height. Charts with treatment plans such as Depo-Provera, implanon, intrauterine device, vaginal ring, and patch were excluded as they were not the focus of the present study. Using these criteria, 134 out of 464 charts reviewed were included in the study. Participants were then categorized into two groups based on treatment plan: metformin and

control. Participants who had been treated with metformin only or metformin and oral contraceptive pills were categorized as the metformin group. Participants who were treated with oral contraceptive pills only or lifestyle modifications without medication were included in control group. Nutritional counseling and lifestyle modification were part of management in all participants. Participants were further classified as healthy (18.5-24.9), overweight (25-29.5), obese (30-34.9 kg/m<sup>2</sup>) and extremely obese (≥35 kg/m<sup>2</sup>) using CDC guidelines for Body Mass Index (BMI) in the treatment group. Descriptive analysis was done to identify those who increased, decreased or experienced no change in BMI from baseline to follow up. Chi-square analyses were performed to determine if groups differed in whether or not they increased, decreased, or stayed the same in terms of BMI category.

## Results

The average time period between initial visit and follow up on same treatment plan was 2 years (range = 1-8 years). The average age of patients at baseline was 15.34 years and the average age at follow up was 17.7 years. While majority of patients were White (n = 82, 61.2%), others were identified as Black (n = 45, 33.6%), Hispanic (n = 3, 2.2%), Asian (n = 2, 1.5%), and two or more races (n = 2, 1.5%). About half of the patients were on metformin and oral contraceptive pills (n = 73, 54.5%). A third of patients (n = 44) were on oral contraceptive pills only. Only a few patients were on metformin only (n = 6, 4.5%). Eleven patients were not on any medication (n = 8.2%). When grouped in two categories, 41% (n = 55) patients were in the metformin group and 59% (n = 79) in the control group.

Table 1. Distribution of participants in Metformin and Control group and their BMI classification at baseline and follow up

Study Group			Healthy Weight	Overweight	Obese	Extremely Obese
No metformin/ Control group (n = 55)	Lifestyle modification (n = 11), n (%)	Baseline	0(0%)	4 (36%)	6 (55%)	1 (9%)
		Follow-up	1 (9%)	1 (9%)	5 (46%)	4 (36%)
	Birth Control (n =44), n (%)	Baseline	10 (23%)	15 (34%)	17 (39%)	2(4%)
		Follow-up	11 (25%)	7 (16%)	22 (50%)	4 (9%)
Metformin group (n = 79)	Metformin + Birth Control (n = 73), n (%)	Baseline	6(8%)	39 (53%)	10 (14%)	18 (25%)
		Follow-up	5 (7%)	5 (7%)	34 (46%)	29 (40%)
	Metformin (n =6), n (%)	Baseline	0(0%)	0(0%)	5 (83%)	1 (17%)
		Follow-up	0(0%)	1 (17%)	3 (50%)	2 (33%)

Table 2. The percent of patients in each treatment group stayed in the same BMI classification or change BMI classifications

	No Change	Increase	Decrease
No Metformin (n = 55), n (%)	33 (60%)	17(31%)	5 (9%)
Metformin (n = 79), n (%)	56 (71%)	19 (24%)	4(5%)

At baseline and follow up, the majority of patients were overweight or obese (see Table I). No patients were underweight. The majority of patients experienced no change in BMI classification and few fell into a lower BMI classification at follow-up (see Table 2). There was not a significant difference between groups in the number of patients who stayed in the same BMI category, went up in a BMI category, or went down in a BMI category from baseline to follow-up ( $\chi^2 = 1.93, p = 0.38$ ).

## Discussion

Our study is among the first few to investigate changes in body mass index in adolescent females with PCOS on metformin versus not on metformin over an average duration of two years. In our study sample, adolescent females on metformin continued to be overweight or obese. This is in contrast to previous studies which had shown improvement in BMI when treated with metformin over a 6 month

period (16, 17). In those studies, the investigators ensured compliance and adherence to a treatment regime through direct contact and frequent reminders. Adherence to treatment is often a challenge in adolescence. In our study sample, there was no significant change in BMI between metformin and control group. This could be attributed to noncompliance to the treatment regime over a long period of time. Or, it could be that the initial weight loss observed in other studies is challenged by lifestyle choices over the long term. Another limitation of the study is its retrospective nature. Given the retrospective nature of the data, there were several appointments where data was missing and treatment plans changed. Ideally, baseline and follow up would be over the same amount of time for each patient. However, follow up appointments happened at different intervals and sometimes did not have all the necessary data to allow for a comparison (e.g., height was often missing). Thus, if a follow up occurred at a year and data were missing, a later follow up appointment that included all data needed to be selected. Some patients did not return for follow up appointments until over a year later. Furthermore, some patients' treatment plans changed too frequently to allow for a baseline and follow up comparison. Prospective studies could be designed to study effect of metformin on weight loss over a longer, consistent period with emphasis on adherence.

## References

- [1] Ehrmann DA. Polycystic ovary syndrome. *N Engl J Med* 2005;352(12):1223-36.
- [2] Azziz R, Woods KS, Reyna R, Key TJ, Knochenhauer ES, Yildiz BO. The prevalence and features of the polycystic ovary syndrome in an unselected population. *J Clin Endocrinol Metab* 2004;89(6):2745-9.
- [3] March WA, Moore VM, Willson KJ, Phillips DI, Nonnan RJ, Davies MJ. The prevalence of polycystic ovary syndrome in a community sample assessed under contrasting diagnostic criteria. *Hum Reprod* 2010;25(2):544-51.
- [4] Christensen SB, Black MH, Smith N, Martinez MM, Jacobsen SJ, Porter AH, et al. Prevalence of polycystic ovary syndrome in adolescents. *Fertil Steril* 2013;100(2):470-7.
- [5] Diamanti-Kandarakis E. PCOS in adolescents. *Best Pract Res Clin Obstet Gynaecol* 2010;24: 173–113.
- [6] Hashemipour M, Faghihmani S, Zolfaghary B, Hovsepian S, Ahmadi F, Haghghi S. Prevalence of polycystic ovary syndrome in girls aged 14–18 years in Isfahan, Iran. *Honn Res* 2004;62(6):278–112.
- [7] Alvarez-Blasco F, Botella-Carretero JL, San Millan JL, Escobar-Morreale HF. Prevalence and characteristics of the polycystic ovary syndrome in overweight and obese women. *Arch Intern Med* 2006;166:2081–i.
- [8] Kahsar-Miller MD, Nixon C, Boots LR, Go RC, Azziz R. Prevalence of polycystic ovary syndrome (PCOS) in first-degree relatives of patients with PCOS. *Fertil Steril* 2001;75:53-8.
- [9] Rosenfield RL. Clinical review: identifying children at risk for polycystic ovary syndrome. *J Clin Endocrinol Metab* 2007;92:787-96.
- [10] Dorne, Mouillet JF, Yan X, Ou Q, Sadovsky Y. Insulin enhances the transcription of luteinizing hormone-beta gene. *Am J Obstet Gynecol* 2004;191(1):132-7.
- [11] Stepto NK, Cassar S, Joham AE, Hutchison SK, Harrison CL, Goldstein RF, Teede HJ. Women with polycystic ovary syndrome have intrinsic insulin resistance on euglycaemic-hyperinsulinaemic clamp. *Hum Reprod* 2013;28:777-84.
- [12] Goodarzi MO, Dumesic DA, Chazenbalk G. Polycystic ovary syndrome: etiology, pathogenesis and diagnosis. *Nat* 2011;7:219–31.
- [13] Nicandri KF, Hoeger K. Diagnosis and treatment of polycystic ovarian syndrome in adolescents. *Curr Opin Endocrinol Diabetes Obes.* 2012 Dec; 19(6):497-504.
- [14] Bugg, C, Rosenfield, R, L Polycystic ovary syndrome in adolescence. *Endocrinol Metab Clin North Am* 34 (2005) 677-705.
- [15] Curi DDG, Fonseca AM, Marcondes JAM, Almeida JAM, Bagnoli VR, Soares Jr JM, Baracat EC. Metformin versus lifestyle changes in treating women with polycystic ovary syndrome. *Gynecol Endocrinol* 2012;28:182-5.
- [16] Al-Zubeidi H, Klein KO. Randomized clinical trial evaluating metformin versus oral contraceptive pills in the treatment of adolescents with polycystic ovarian syndrome. *J Pediatr Endocrinol Metab* 2015;28(7-8):853-8. doi: 10.1515/jpern-2014-0283.
- [17] Allen HF, Mazzoni C, Heptulla RA, Murray MA, Miller N, Koenigs L, et al. Randomized controlled trial evaluating response to metformin versus standard therapy in the treatment of adolescents with polycystic ovary syndrome. *J Pediatr Endocrinol Metab* 2005; 18(8):761–11.

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