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Differences in the management of adolescents with polycystic ovary syndrome across pediatric specialties

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Abstract

Study Objective—Evaluate for differences in the management of adolescents with polycystic ovarian syndrome (PCOS) across three pediatric specialties

Design—Retrospective review of medical records

Setting—Academic children's hospital

Participants—181 adolescents seen between July 2008 – June 2010 by providers in Pediatric Endocrinology (PEndo), Adolescent Medicine (AMed), or Pediatric and Adolescent Gynecology (PGyn) identified via billing data (ICD-9 code for PCOS, 256.4)

Interventions—None

Main Outcome Measure(s)—(1) Percentage of adolescents with a billing diagnosis of PCOS who met diagnostic criteria; (2) Percentage of individuals screened for co-morbidities and differences across specialties; (3) Differences in treatment recommendations across specialties; (4) Factors associated with recommendation for metformin and hormonal contraceptives.

Results—Thirteen percent of PEndo patients did not meet diagnostic criteria for PCOS; 20% of AMed and PGyn patients did not meet criteria. There were significant differences in rates of screening for obesity, insulin resistance, and Type 2 diabetes. There were significant differences in treatment recommendations for lifestyle changes, metformin, and anti-androgen therapy across specialties. Specialty and obesity were significant predictors of metformin recommendation;

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specifically PEndo predicted metformin recommendation. PGyn and AMed specialties predicted hormonal contraceptive recommendation.

Conclusions—The variability observed among specialties may be due to differences in training, accounting for a range of comfort with aspects of PCOS. Formulation of consensus guidelines for diagnosis and management of PCOS are needed, along with broad educational efforts. By correctly diagnosing, screening for co-morbidities, and managing PCOS appropriately during adolescence providers may reduce the risk for long-term consequences.

Keywords

PCOS; Rotterdam criteria; hirsutism; metformin

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is a complex medical condition associated with metabolic co-morbidities, reproductive health and cosmetic concerns, and psychological distress for young women. Prevalence estimates range from 6%–26% of reproductive-aged women, depending largely on whether narrow or more broad diagnostic criteria are applied^{1–4}. Symptoms of PCOS often manifest during adolescence making this an important time for recognition and intervention to prevent adverse metabolic outcomes such as insulin resistance and diabetes mellitus. Due to the broad range of symptoms associated with PCOS and the wide age range of women affected, patients seek treatment from a range of medical providers including adult and pediatric primary care providers, endocrinologists, and gynecologists.

The constellation of symptoms that defines PCOS includes androgen excess (e.g., excessive body hair growth, male pattern baldness, and acne) and menstrual irregularities (e.g., anovulatory cycles, missed periods, oligomenorrhea, or amenorrhea)⁵ and three groups of experts, [the National Institutes of Health (NIH)⁶, Rotterdam⁷, Androgen Excess Society⁸] have published diagnostic criteria. The NIH Consensus Guidelines indicate the need for both biochemical and/or clinical evidence of hyperandrogenism with chronic anovulation, while excluding other causes of hyperandrogenism (e.g., Cushing Syndrome, congenital adrenal hyperplasia, adrenal tumors). The Rotterdam criteria utilize not only the two NIH criteria but also employs ultrasound findings with 2 out of 3 criteria required for diagnosis. The Androgen Excess Society (AES) requires only androgen excess either biochemical and/or clinical) and ovarian dysfunction (ovulation concerns or ultrasound findings of polycystic ovaries) to diagnose PCOS. However, there is currently no consensus on how to diagnose PCOS during adolescence (i.e., the existing criteria do not apply to adolescents).⁹

Previous work employed surveys to assess how different groups of providers utilized existing diagnostic recommendations. The Lawson Wilkins Pediatric Endocrine Society (LWPES) found that LWPES members use a wide range of practice for diagnosis and treatment.¹⁰ In contrast, the North American Society for Pediatric and Adolescent Gynecology (NASPAG),¹¹ demonstrated that its members were somewhat discordant in their diagnostic evaluation, but concordant regarding treatment. Furthermore, a survey of reproductive endocrinologists and gynecologists designed to assess the frequency of

screening for diabetes in PCOS found a higher rate of screening for diabetes by reproductive endocrinologists than gynecologists.¹² No study has reviewed primary sources to assess potential differences in the use of diagnostic and therapeutic interventions across subspecialties.

To address these issues, we obtained primary source data from medical records of adolescents diagnosed with PCOS followed at a large, academic, pediatric hospital by one of the following three pediatric specialties: Pediatric Endocrinology, Adolescent Medicine, or Pediatric and Adolescent Gynecology. Our goals were to establish within and then compare across the three pediatric specialties: (1) the percentage of individuals identified with an ICD-9 diagnosis of PCOS who met diagnostic criteria; (2) the percentage of individuals who were screened for co-morbidities; (3) the treatment recommendations; (4) factors associated with specific treatment recommendations (i.e., metformin, hormonal contraceptives). We hypothesized significant differences in management practices exist among the different specialties. For example, endocrinologists may be more likely to screen for insulin resistance and diabetes compared to Adolescent Medicine or Pediatric and Adolescent Gynecology providers.

METHODS AND MATERIALS

After receiving the approval of the Institutional Review Board at Cincinnati Children's Hospital, we performed a systematic, retrospective review of the medical records of patients with PCOS in the Divisions of Pediatric Endocrinology (PEndo), Pediatric and Adolescent Gynecology (PGyn), and Adolescent Medicine (AMed).

Participants

Adolescent girls with PCOS were identified using billing data. All girls seen within a 2-year period (July 2008 to June 2010) with the ICD-9 code for PCOS (256.4) were identified. This time frame was chosen because it was the most recent two-year period prior to any of the divisions converting to an electronic medical record. Therefore, all three divisions were using a similar process for medical documentation (i.e., paper chart).

Procedures

We employed written, standardized abstraction rules and data abstraction forms. Three members of the research team abstracted the data (BA, AG, and JH). In addition, eight percent of the charts were reviewed by two researchers to ensure agreement in approach and method of data abstraction. For each patient record, we identified the first visit in which the diagnosis or evaluation of PCOS was recorded. Up to three subsequent provider visits (i.e. follow-up visits) were also reviewed for a total of up to 4 visits. Age, race, insurance status, height, weight, and age at menarche were collected. In addition, the presence or absence of symptoms of PCOS in the history and examination such as irregular menstrual bleeding, missed periods, oligomenorrhea, amenorrhea, acne, hair loss, excessive hair growth, hirsutism, acanthosis nigricans were recorded. Information from the provider's evaluation, including documentation of blood pressure, BMI/BMI percentile, laboratory, and ultrasound assessment, was also abstracted. The provider's recommendations for lifestyle changes,

hormonal contraceptives, metformin, referral to a dietician, use of anti-androgens, and other treatment options were collected.

Medical records were reviewed by random number generation within each division. Initially, 20 charts were randomly selected and abstracted for each division to conduct a power analysis. Results of the power analysis determined that approximately 57 charts from each division were needed to detect a difference in the screening and treatment recommendations among the 3 pediatric specialties, taking into account the need for multiple comparisons. Sixty charts from both PEndo and PGyn and sixty-one charts from AMed were reviewed. Six patient charts were excluded: three charts were missing significant data (e.g., no record of the initial evaluation), two patients were incorrectly identified as having PCOS (i.e., the patient chart did not indicate any evaluation or mention of PCOS), and one patient identified as an AMed patient was only seen by PGyn.

Data were entered in duplicate into the REDCap database. The double-data entry comparison tool was used to identify discrepancies in the data. Any discrepancy was verified on the data abstraction tool and reconciled.

Measures

Providers were credited with meeting diagnostic criteria when there was documented evidence of 2 of the following 3 symptoms: 1) androgen excess; 2) anovulatory menstrual cycles; or 3) polycystic ovaries on ultrasound. These criteria were chosen because they encompass the broadest approach to defining of PCOS.⁷ The Rotterdam criteria are not widely endorsed for use among adolescent populations due to the potential for overdiagnosis (i.e., some of the criteria are common among healthy adolescents). Authors chose to use these criteria for this retrospective review in order to be optimally inclusive of the provider's diagnoses. Androgen excess was evidenced by acne, hirsutism, hair loss, male pattern baldness, or elevated serum androgens (i.e., elevated total or free testosterone concentration) as noted by the provider in the medical record. Anovulatory menstrual cycles were defined by report of irregular menstrual bleeding, "missed periods", irregular cycles, oligomenorrhea, primary amenorrhea, or secondary amenorrhea. Presence of polycystic ovaries was defined as greater than 12 follicles in the periphery of the ovary as seen on pelvic ultrasound or use of the term "consistent with PCOS" in the radiology report.

To determine and compare the percentage of patients screened for PCOS-associated comorbidities, approaches to screening for obesity, diabetes, hyperlipidemia, and insulin resistance were initially defined. Obesity screening required the provider to document a body mass index (BMI) or BMI percentile at any of the visits. Screening for insulin resistance required the provider to order a fasting insulin level or to document the presence or absence of acanthosis nigricans. Screening for type 2 diabetes mellitus required providers to order either a fasting glucose, hemoglobin A1C, or oral glucose tolerance test (OGTT). Finally, screening for hyperlipidemia required providers to order either total cholesterol (non-fasting) or fasting lipid profile. Providers were considered to have screened for a comorbidity if they ordered a test, even if the patient did not comply.

To describe treatment recommendations for adolescents with PCOS and compare rates by specialty, definitions for each treatment recommendation were formulated. Providers were noted to recommend “lifestyle changes” if they included any of the following in their assessment: “weight loss,” “exercise,” “nutrition counseling,” or any behavioral change that would promote weight loss, such as elimination of sugar-sweetened beverages or decreased sedentary activity, etc. Abstractors were instructed to be inclusive about any documentation that suggested the provider discussed healthy lifestyle as a treatment option. Treatment recommendation for the use of hormonal contraceptives was noted if the provider counseled the patient on this option or prescribed any hormonal contraceptive, including progestin-only pills, the transdermal patch, or the intravaginal ring. A recommendation for metformin was noted if a provider documented discussion about the use of metformin or prescribed metformin. A referral to a dietician was credited by provider documentation of referral in the provider’s progress note. Recommendation for use of an anti-androgen medication was noted if a provider discussed or prescribed medications such as spironolactone. Other treatment recommendations were recorded but not analyzed, including referral to tertiary care programs for weight loss or bariatric surgery.

Statistical Analyses

The percentage of girls meeting criteria for PCOS based on the Rotterdam criteria⁷ was calculated for each specialty. This study was not designed with the power to evaluate for differences between pediatric specialties for the percentage of girls who met criteria for PCOS. Chi square testing was used to compare the percentage of patients who were screened for a PCOS-associated co-morbidity by specialty. Level of significance was set at $p < .0125$ using a Bonferroni correction due to multiple (i.e., 4) comparisons.¹³ Nearly one-hundred percent of patients were screened for hypertension with a blood pressure reading, therefore it was not necessary or feasible to evaluate for differences. Chi square testing compared the percentage of patients who were recommended a particular treatment across specialties. Level of significance was set at $p < .01$ using a Bonferroni correction due to multiple (i.e., 5) comparisons.¹³ Finally, stepwise logistic regression was used to determine those factors that were associated with metformin and hormonal contraceptives as treatment recommendations.

RESULTS

One hundred eighty-one patient records were reviewed (60 PEndo, 61 AMed, and 60 PGyn). There was a significant difference across specialties for race, insurance status, BMI, and weight status (see Table 1). Significant differences were also found in the presenting symptoms across specialties. Hirsutism was often found in patients presenting to PEndo ($p < 0.0001$), while acne was frequently encountered in PGyn ($p 0.006$). There was no difference in menstrual irregularities across specialties (Table 1).

Based on abstracted clinical documentation, 13% of patients in PEndo did not meet diagnostic PCOS standards using Rotterdam criteria; in both AMed and PGyn, 20% of patients did not meet criteria for PCOS. For screening of co-morbidities, there were significant differences across the three divisions in rates screening for obesity, insulin

resistance, and Type 2 Diabetes. There were no statistically significant differences in screening for hypertension or hyperlipidemia (Table 2).

Treatment recommendations were statistically different by specialty (Table 3). There were statistically significant differences across the three divisions for recommendations of lifestyle modification, metformin, and anti-androgen therapy ($p < 0.0001$, < 0.0001 , and 0.001 , respectively). There was no statistically significant difference across divisions for the recommendation of hormonal contraceptives ($p 0.015$).

Results of stepwise logistic regression revealed that specialty (i.e., PEndo) and obesity were significant predictors of metformin use (Table 4). Patients seen by a provider in either AMed or PGyn were less likely than patients seen by a PEndo to be receive recommendation for metformin (Table 4). All other variables tested were not significant but included age, race, insurance status, primary or secondary amenorrhea, irregular menstrual bleeding, and presence of hirsutism. Likewise, being seen by a provider in the Divisions of PGyn and AMed predicted hormonal contraceptive recommendation. All other variables mentioned above for metformin models were tested but were not significantly associated with recommendation for hormonal contraceptives.

DISCUSSION

This study found that in all three pediatric specialties, despite all adolescents being billed as having PCOS, a moderate portion (13–20%) of adolescent patients did not meet the broadest available diagnostic criteria (i.e., Rotterdam criteria). This study also demonstrated differences across specialties in screening rates for obesity, Type 2 DM, and insulin resistance. Significant differences across specialties were also noted for some treatment recommendations, despite that all girls were seen at the same academic institution. These data provide a glimpse into the diagnosis and management of adolescent girls with PCOS at a large academic center which includes training programs for each pediatric specialty studied.

Insulin resistance, hyperlipidemia, Type 2 Diabetes, infertility, metabolic syndrome, and early cardiovascular disease are associated with PCOS.^{14,15} In adults, the American College of Obstetricians and Gynecologists (ACOG),¹⁶ American Association of Clinical Endocrinologists,¹⁷ and Endocrine Society¹⁸ have established treatment screening guidelines. Despite clear guidelines for adults, very little research has evaluated the management practices for PCOS during the adolescent period.¹² Several surveys have suggested that even among the same specialty, that there is no consensus for the evaluation and management of adolescents with PCOS.^{10–12} Our data corresponds with prior research and extends this beyond a single specialty to demonstrate that across specialties there are also differences in the management of PCOS. Some of these differences may be driven by greater comfort levels with metabolic concerns versus reproductive health concerns among PEndo providers compared to other types of providers. These differences are likely reflective of prior training experiences and a lack of consensus guidelines.

Differences among clinic populations were evident. There were no differences among the disciplines regarding age of the patient or age at menarche, but there were differences in insurance status and race, which is reflective of the differences in the patient populations served and the type of practice. The AMed clinic is a primary care clinic that manages a primarily underserved population. Both PGyn and PEndo are specialty referral clinics that allow for heightened focus on a specific clinical finding or patient concern. Finally, there was a statistically significant difference in the mean BMI across the different disciplines which may also be reflective of differences in the patient populations served or related to reason for referral. For example, overweight or obese adolescents may be more likely to be referred to PEndo and leaner girls referred to PGyn.

Limitations to our study include aspects of a medical record review. Documentation among providers varied greatly, and we were only able to abstract data that were notated in the medical record (i.e., lifestyle recommendations, treatment suggestions). Our findings revealed differences in the patient populations seen by each specialty, reflecting different referral bases. These differences in referral bases may explain some of the differences we observed in the treatment and management across specialties. Another limitation is that data were not included on whether the patients were sexually active or not and this may have impacted the provider's management and treatment recommendations. Our data were not powered to find a difference between specialties but rather across specialties. In other words, we were unable to evaluate whether PEndo providers compared to AMed providers recommended lifestyle recommendations more often. The findings of this study are generalizable to patients and providers in an academic setting, but may not be as relevant to the general pediatric community.

This study highlights the current lack of consensus regarding the diagnosis, treatment, and screening for co-morbidities in adolescents with PCOS. It would be extremely beneficial if experts in the field came together to develop adolescent-specific diagnostic criteria and management guidelines. This would allow for consistency in diagnosis and current management practices which would promote research efforts to move the field forward and gain much-needed understanding about PCOS during the critical period of adolescence. Once guidelines for adolescents are available, extensive educational efforts can be launched to update providers in the field at national meetings that cross all three specialties and also in the community for primary care pediatricians. It would also be important for providers treating PCOS to communicate across specialties more, co-manage, or create a multidisciplinary clinic in academic settings when feasible. By recognizing, correctly diagnosing, screening for comorbidities, and managing this syndrome appropriately in adolescence, providers may reduce the risk for long-term consequences related to the co-morbidities of PCOS in young women.

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Table 1

Demographic and descriptive characteristics of the sample by pediatric specialty

	Pediatric Endocrinology (n=60)	Adolescent Medicine (n=61)	Pediatric and Adolescent Gynecology (n=60)	p value
Mean age, y (SD)	15.3 (1.7)	15.9 (1.7)	15.9 (2.7)	0.22
Mean age at menarche, y (SD)	11.8 (1.5)	12.0 (1.5)	11.6 (1.6)	0.44
Race, n (%)				<0.0001
Black	10 (17)	39 (64)	5 (8)	
White	45 (75)	18 (30)	53 (88)	
Other	5 (8)	4 (7)	2 (3)	
Insurance, n (%)				0.007
None/self-pay	2 (3)	9 (15)	4 (7)	
Medicaid	19 (32)	27 (44)	14 (23)	
Commercial	39 (65)	25 (41)	42 (70)	
Mean BMI (kg/m ²) (SD)	35.2 (±6.9)	34.5 (±7.8)	30.6 (±8.0)	0.0025
Weight status, n (%)				0.0014
Normal	4 (7)	12 (20)	16 (27)	
Overweight	3 (5)	8 (13)	12 (20)	
Obese	53 (88)	41 (67)	32 (53)	

BMI, body mass index.

Comparison across pediatric specialties was analyzed by chi square.

Normal weight = BMI percentile 85th percentile; Overweight = BMI percentile >85th and 95th percentile; Obese = BMI percentile >95th percentile

Table 2

Comparison of screening for PCOS-associated comorbidities across three pediatric specialties

	Pediatric Endocrinology (n=60) n, %	Adolescent Medicine (n=61) n, %	Pediatric and Adolescent Gynecology (n=60) n, %	p value*
Obesity	28 (47)	13 (21)	24 (40)	0.011
Insulin resistance	58 (97)	46 (75)	53 (88)	0.001
Type 2 diabetes	58 (97)	43 (70)	50 (83)	0.006
Hyperlipidemia	48 (80)	41 (67)	41 (68)	0.224

* Comparison across specialties was analyzed by chi square testing. Significance defined as $p < .0125$ due to multiple comparisons.

Table 3

Comparison of treatment recommendations for PCOS across three pediatric specialties

	Pediatric Endocrinology (n=60) n, %	Adolescent Medicine (n=61) n, %	Pediatric and Adolescent Gynecology (n=60) n, %	p value*
Lifestyle changes	51 (85)	38 (62)	24 (40)	<0.0001
Hormonal contraceptives	50 (83)	58 (95)	58 (97)	0.015
Metformin	54 (90)	15 (25)	23 (38)	<0.0001
Dietician	34 (57)	28 (46)	18 (30)	0.013
Anti-androgen	12 (20)	1 (2)	6 (10)	0.001

**

Comparison across specialties was analyzed by chi square testing. Significance defined as $p < .01$ due to multiple comparisons.

Table 4

Factors associated with recommendation for metformin and hormonal contraceptives

	<u>Odds Ratio</u>	<u>95% CI</u>
Metformin		
Specialty		
PGyn vs. PEndo	0.10	0.04, 0.30
AMed vs. PEndo	0.04	0.01, 0.12
Obesity (>95 th percentile BMI)	4.20	1.79, 9.86
Hormonal contraceptives		
Specialty		
PGyn vs. PEndo	5.80	1.20, 27.73
AMed vs. PEndo	3.87	1.01, 14.83

Note: CI= confidence interval; AMed, Adolescent Medicine; BMI, body mass index; PEndo, Pediatric Endocrinology; PGyn, Pediatric and Adolescent Gynecology.