Original Study

Utility of the Oral Glucose Tolerance Test to Assess Glucose Abnormalities in Adolescents with Polycystic Ovary Syndrome

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A B S T R A C T

Study Objective: The aim of this study was to examine the prevalence of and risk factors for abnormal glucose metabolism in a large population of adolescents with polycystic ovary syndrome (PCOS).
Design, Setting, Participants, Interventions, and Main Outcome Measures: A retrospective chart review was performed of 360 patients who presented to the pediatric gynecology outpatient clinic for evaluation of PCOS between January 2004 and May 2012.
Results: A total of 163 patients fulfilled criteria for a diagnosis of PCOS and had adequate clinical and laboratory data. Twenty-six adolescents (16.0%) had impaired glucose tolerance and 2 patients (1.2%) met criteria for a provisional diagnosis of type 2 diabetes. All 28 subjects with abnormal glucose metabolism were identified using the 2-hour plasma glucose of the oral glucose tolerance test. Conversely, the fasting glucose values only successfully detected 2 patients with hyperglycemia, both of whom also had abnormal 2-hour glucose levels. Adolescents with abnormal glucose metabolism were more likely to have reported a positive family history ($P = .02$) and had higher body mass index z scores (2.8 ± 1.1 vs 1.8 ± 1.2; $P < .01$). When patients were classified into normal weight (n = 29) and obese/overweight groups (n = 117), all of the patients with abnormal glucose metabolism were overweight or obese.
Conclusion: In the largest series to date, we describe a prevalence of abnormal glucose metabolism in adolescent patients with PCOS of 17.2%. Abnormal glucose metabolism is associated with many of the known risk factors for metabolic syndrome. Our results support that the oral glucose tolerance test is a superior diagnostic test to assess abnormal glucose levels in overweight and obese adolescents but that this test might have limited utility in normal weight adolescents with PCOS.
Key Words: Polycystic ovary syndrome, Adolescents, Glucose intolerance, Diabetes mellitus

Introduction

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among women and is now recognized to affect 4%-6% of young women.[1–5] PCOS is characterized by chronic oligo-ovulation or anovulation, hyperandrogenism, and the appearance of polycystic ovaries on ultrasound imaging.[6] In addition to these characteristics, insulin resistance is also known to play an integral role in the etiology of the disease. Accordingly, PCOS patients are at increased risk of impaired glucose tolerance, impaired fasting glucose, and diabetes mellitus. Insulin resistance and pancreatic beta cell dysfunction are thought to be the main mechanisms that account for the predisposition to diabetes, however, the precise nature of their relationship remains unclear.[1,7–9]

The rates of glucose abnormalities in the adult PCOS population are estimated to be approximately 30%-40%.[10] However, there is a more limited body of literature that describes the prevalence of abnormal glucose levels in adolescent PCOS patients and variation in their estimates. Additionally, there is debate about the optimal screening test for the presence of altered glucose metabolism in this age group. Several smaller studies have documented glucose abnormalities in 27-66 adolescents with PCOS, estimating rates at 9%-33.3% (3/33, 9/27).[11–15] A recent study in 66 adolescents with PCOS reported abnormal glucose levels in 18.2% (12/66) of PCOS adolescents with impaired glucose tolerance that occurred among obese and nonobese individuals.[12]

Despite this limited body of literature, an oral glucose tolerance test (OGTT) is recommended to screen for diabetes every 2-5 years in obese and nonobese adolescents with PCOS.[6,16] In contrast, guidelines for diabetes screening from the American Diabetes Association recommends the use of fasting plasma glucose for only obese adolescents with additional risk factors including conditions such as PCOS.[17] This creates potential confusion for the health care provider who manages adolescents with PCOS. Further understanding of the exact prevalence and nature of glucose abnormalities in this population is warranted to support the use of OGTT for screening in this population because of the increased cost and difficulty of performing this test. The primary aim of this study was to examine the prevalence of abnormal glucose metabolism in a large population of adolescents with PCOS. Second, we sought to determine specific clinical and biochemical risk factors associated with an increased

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risk of glucose abnormalities to help inform screening practices.

Materials and Methods

A retrospective chart review was performed of 360 patients who presented to the pediatric gynecology outpatient clinic at the Hospital for Sick Children for evaluation of PCOS. Charts between January 2004 and May 2012 were reviewed. Patients were included if they were 18 years of age or younger at the time of their visit and met diagnostic criteria for PCOS. The diagnosis of PCOS was made on the basis of evidence of clinical or biochemical hyperandrogenism (ie, hirsutism or increased serum androgen levels) and persistent oligomenhorrhea.[6] All patients were biochemically euthyroid with normal prolactin levels and no evidence of congenital adrenal hyperplasia, which was screened using 17-hydroxyprogesterone. Patients were excluded if they did not meet criteria for diagnosis or if they were receiving confounding medications at the time of initial evaluation.

Medical charts were reviewed and relevant demographic, clinical, and laboratory data were extracted. This information included age, age of menarche, current medications, ethnicity, family history of features of the metabolic syndrome (hypertension, dyslipidemia, obesity), coronary artery disease, diabetes and PCOS, weight, height, blood pressure, and presence of clinical hyperandrogenism. Collected laboratory values included glucose (fasting and 2-hour plasma glucose according to the OGTT), insulin, hemoglobin A1c, total and free testosterone, dihydroepiandrosterone, androstenedione, luteinizing hormone, follicle-stimulating hormone, and fasting lipid profile. OGTTs were conducted (1.75 g/kg to a maximum of 75 g). Body mass index (BMI; calculated as the weight in kilograms divided by the height in meters squared) and BMI *z* scores were calculated for each patient. Overweight was defined as a BMI between the 85th to 97th percentile (*z* score $\geq$1 and $<$2) and obesity was defined as a BMI greater than the 97th percentile for age and sex (*z* score $\geq$2) according to the World Health Organization.[18] Impaired glucose tolerance, impaired fasting glucose, and diabetes were defined based on the Canadian Diabetes Association 2013 Clinical Practice Guidelines criteria.[19] Glucose abnormalities were defined as any of impaired glucose tolerance (2-hour plasma glucose in 1.75 g/kg up to 75 g OGTT of 7.8-11.0 mmol/L [140-198 mg/dL]), impaired fasting glucose (fasting plasma glucose 6.1-6.9 mmol/L [110-124 mg/dL]) or presumptive type 2 diabetes mellitus (2-hour plasma glucose in 1.75 g/kg up to 75 g OGTT of $\geq$11.1 mmol/L [200 mg/dL] or fasting plasma glucose $\geq$7.0 mmol/L [126 mg/dL]). The study was approved by the Research Ethics Board at the Hospital for Sick Children.

Statistical Analyses

The characteristics of patients were analyzed using descriptive statistics. Continuous variables were described as mean and SD. Discrete variables were described as frequency and cross tabulates. BMI values were standardized as *z* scores using the World Health Organization Child Growth Standards.[20] Blood pressure values were standardized as *z* scores using the National Health and Nutrition Exercise Survey database.[21] $\div^2$, Fisher exact tests, and *t* tests were used to compare variables between cohorts of patients. Comparisons of clinical and biochemical features with 2-hour plasma glucose were performed using univariate linear and logistic regression analysis. Clinically significant variables with *P* values less than 0.15 were selected to create a multivariate linear regression with 2-hour OGTT value as the outcome. All statistical analyses were performed using Statistical Analysis System software, version 9.3 (SAS Institute, Cary, NC).

Results

A total of 300 patients reviewed fulfilled criteria for a diagnosis of PCOS. Of these, 219 subjects had adequate clinical and laboratory data including a fasting glucose level and 163 patients had completed an OGTT (Fig. 1). The mean age of the subjects at presentation was 15.4 $\pm$ 1.5 years and age at menarche was 11.7 $\pm$ 1.4 years. Ethnicity was documented in 143 of the 219 patients (65.3%). Of those recorded, there was a diverse mixture of Caucasian, Mediterranean, African or Caribbean, East or Southeast Asian, Hispanic, and Middle Eastern patients. Because data were widely distributed and incomplete, further analysis of ethnicity was not conducted. Similarly, statistical analysis of hemoglobin A1c was not conducted because there were inadequate data available. Seventy-one adolescents (32.4%) reported having a family member with at least 1 feature of metabolic syndrome (hypertension, hyperlipidemia, coronary artery disease, or obesity) and 96 adolescents (43.8%) reported a family history of type 2 diabetes mellitus. Most patients in our population were overweight or obese, with mean BMI of 30.4 $\pm$ 12.1.

As part of the assessment for PCOS, 163 of the 219 patients underwent an OGTT, and the other 56 patients (25.6%) completed only fasting glucose studies. Sixty-one patients (27.9%) received a pelvic ultrasound in the course of their diagnostic evaluation. These were not included in our analysis because diagnostic guidelines for PCOS in

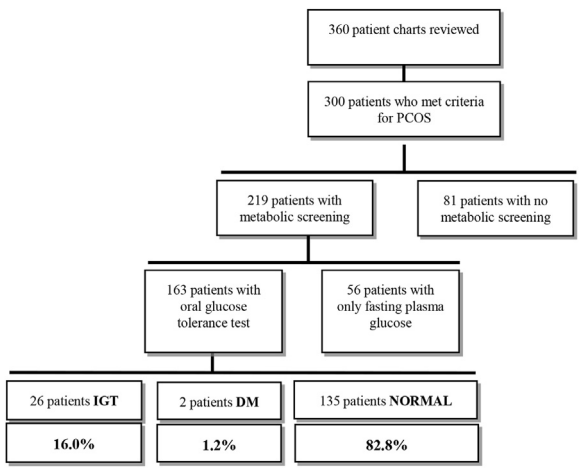

Fig. 1. Flowchart of the study design with prevalence of glucose abnormalities. DM, diabetes mellitus; IGT, impaired glucose tolerance; PCOS, polycystic ovary syndrome.