Oral glucose tolerance test significantly impacts the prevalence of abnormal glucose tolerance among Indian women with polycystic ovary syndrome: lessons from a large database of two tertiary care centers on the Indian subcontinent

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Objective: To estimate the prevalence of abnormal glucose tolerance (AGT) among Indian women with polycystic ovary syndrome (PCOS) and analyze the role of oral glucose tolerance (OGTT) test on its estimation.
Design: Cross-sectional clinical study.
Setting: Tertiary care center.
Patient(s): A total of 2,014 women with PCOS diagnosed on the basis of the Rotterdam 2003 criteria were enrolled, and the data of 1,746 subjects were analyzed.
Intervention(s): In addition to recording clinical, biochemical, and hormone parameters, a 75 g OGTT was administered.
Main Outcome Measure(s): Prevalence of AGT and impact of age, body mass index (BMI), family history, and OGTT on its prevalence.
Result(s): The mean age of subjects was 23.8 ± 5.3 years, with a mean BMI of 24.9 ± 4.4 kg/m^2. The overall prevalence of AGT was 36.3% (6.3% diabetes and 30% impaired fasting plasma glucose/impaired glucose tolerance) using American Diabetes Association criteria. The glucose intolerance showed a rising trend with advancing age (30.3%, 35.4%, 51%, and 58.8% in the second, third, fourth, and fifth decades, respectively) and increasing BMI. Family history of diabetes mellitus was present in 54.6% (953/1,746) subjects, and it did not correlate with any of the studied parameters except waist circumference and BMI. Sensitivity was better with 2-hour post-OGTT glucose values as compared with fasting plasma glucose, since using fasting plasma glucose alone would have missed the diagnosis in 107 (6.1%) subjects.
Conclusion(s): We conclude that AGT is high among young Indian women with PCOS and that it is not predicted by family history of type 2 DM. OGTT significantly improves the detection rate of AGT among Indian women with PCOS. (Fertil Steril® 2016;105:194–201. ©2016 by American Society for Reproductive Medicine.)
Key Words: PCOS, diabetes mellitus, abnormal glucose tolerance, OGTT, family history, IR, hyperandrogenism

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Polycystic ovary syndrome (PCOS), the most common endocrinopathy of reproductive-age women, is associated with multiple metabolic abnormalities (1, 2). The prevalence of this disorder is on the rise globally and seems to run parallel to the epidemic of type 2 diabetes mellitus (DM) in India (3, 4). Though Stein and Leventhal (5) originally described it as a reproductive disorder, and an association with several other metabolic derangements including obesity, insulin resistance (IR), abnormal glucose tolerance (AGT), dyslipidemia, hypertension, metabolic syndrome, and elevated cardiovascular risk has also been described (6–9). The etiology of the disorder being largely unclear; it seems to follow a polygenic pattern like type 2 DM. Even though no discrete genetic defects are described in PCOS, there is strong evidence of familial aggregation (10–12).

A large body of evidence shows that women with PCOS have significant IR and that the presence of obesity has an augmentative effect on it (6, 13–15). Since IR is also an important pathophysiological feature of type 2 DM, it may suggest a biological link between PCOS and type 2 DM. There is also evidence that in the background of IR, beta cell dysfunction is mandatory for the manifestation of impaired glucose tolerance (IGT) or DM among non-PCOS individuals (13–15). There are studies (12, 13, 15) to demonstrate that insulin secretion is also defective or dysregulated among euglycemic women with PCOS. In addition, women with PCOS having first-degree relatives affected with type 2 DM are more likely to exhibit IR and beta cell dysfunction (11, 12). Accordingly, there is 3- to 7-fold higher risk of developing AGT among women with PCOS as compared with control women (13–18). There is also a suggestion that AGT manifests at an earlier age among women with PCOS (16–19) and that the conversion rates from IGT to DM are higher than in controls (19, 20). Furthermore, there is a consensus that the risk varies among different ethnic groups. For instance, the prevalence of IGT and type 2 DM among American women with PCOS is higher than that among European women (31%–35% and 7.5%–10% vs.12.4% and 1.7%) (14, 19).

Asian Indians are reported to be at higher risk of developing type 2 DM and coronary artery disease than the Western population (4, 21). An ongoing nationwide study in India also demonstrated a high prevalence of type 2 DM among the regions studied so far (21), which is likely to adversely impact the country's economy in future (22). There has been no systematic evaluation of glucose intolerance in Indian women with PCOS except for a few small reports (23, 24), despite PCOS and DM being major public health problems (3).

In view of the above, we estimated the prevalence of AGT in a large cohort of women with PCOS who attend two tertiary care centers in north India.

MATERIALS AND METHODS

The subjects were recruited from Endocrine outpatient clinics of two tertiary care centers (i.e., All India Institute of Medical Sciences, [AIIMS] New Delhi, and Sheri-Kashmir Institute of Medical Sciences [SKIMS], Srinagar) located in north India between January 2004 and June 2014. The study was approved by the Ethics Committees of both institutions. Consecutive drug-naïve women who presented with oligomenorrhea, infertility, features of hyperandrogenism, family history of PCOS, and obesity were invited to participate in the study. The women who volunteered to be part of the study and qualified for a diagnosis of PCOS by the Rotterdam 2003 criteria (25) were asked to sign an informed consent. Details of medical history with emphasis on menstruation (age at menarche, regularity, duration, and number of cycles per year) were taken. Menstrual disturbances were classified as oligomenorrhea (less than eight cycles/year or menstrual interval >35 days) or amenorrhea (absence of menses in the last 6 or more months). Other history included temporal profile of weight gain, duration of infertility, family history of PCOS, family history of type 2 DM, drug intake, progression and distribution of hirsutism, and severity and treatment response in acne vulgaris. Women with any systemic disorders such as liver, heart, kidney, or autoimmune diseases or intake of drugs known to interfere with glucose/insulin metabolism such as glucocorticoids, androgens, oral contraceptives, antiepileptics, insulin sensitizers, and so on were excluded.

Anthropometric assessment included measurement of height (cm), body weight (kg), and waist and hip circumference (cm) with calculation of body mass index (BMI; kg/m^2). A detailed systemic examination with particular attention to measurement of blood pressure, grading of acanthosis nigricans, acne vulgaris, androgenic alopecia, and quantitation of hirsutism was undertaken. The modified Ferriman-Gallwey (FG) score was used to assess the degree of hirsutism, and a score of 8 (out of a total of 36 from nine body areas) was taken as significant (26). Blood samples were collected after an overnight (8–10 hours) fast with a stable diet for the preceding 72 hours and preferably on the third to seventh day (early follicular phase) of the spontaneous menstrual cycle in regularly menstruating women or any day in amenorrheic women. Blood samples were aliquoted for plasma insulin, total T4, TSH, LH, FSH, PRL, total T, 17-OHP, cortisol (morning), plasma glucose, blood counts, electrolytes, lipids, and liver and kidney functions. Plasma cortisol (evening) or post-dexamethasone suppression test and post-ACTH 17-OHP were done in selected cases to rule out Cushing's syndrome or nonclassical congenital adrenal hyperplasia, respectively. After obtaining the fasting blood sample, an oral glucose challenge was performed with 75 gm anhydrous glucose dissolved in 250–300 mL of water (OGTT), and blood samples were collected at 60 and 120 minutes for plasma glucose. Serum was separated at room temperature and aliquoted as per the requirements. All biochemical analysis was done on the same day, whereas the aliquots for hormones were stored at −70°C until the assay. Transabdominal ultrasound was done to demonstrate any suggestion of polycystic ovarian morphology, that is, presence of 10 or more peripheral follicles each measuring 2–8 mm in size with echogenic ovarian stroma and/or increased ovarian volume (27).