Glucose tolerance in pregnant women with vaginal candidiasis

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Background: The use of traditional historic risk factors to identify gestational diabetes mellitus (GDM) will miss half of women with gestational diabetes mellitus. Our aim was to evaluate whether impaired glucose tolerance is a risk factor for vaginal candidiasis in pregnant women.

Patients and Methods: In a cross-sectional study, we compared the prevalence of impaired glucose tolerance in 64 pregnant women with vaginal candidiasis (positive microscopy) and 59 *Candida*-negative control subjects. Subjects underwent standardized 75-gram oral glucose tolerance testing between the 24th and 28th weeks of their pregnancies. Patients were included only if they had no known diabetes mellitus or historic risk factors for gestational diabetes mellitus, and had not been receiving antibiotic or steroid therapy. We compared glucose levels at fasting, 30 minutes, 60 minutes and 120 minutes, and perinatal and neonatal outcomes in the two groups.

Results: There were no statistical differences between cases and controls in demographic characteristics. Glucose concentrations were higher in pregnant women with vaginal candidiasis than in control subjects at fasting (89 vs. 84 mg/dL, P=0.021), 30 minutes (139 vs. 126 mg/dL, P=0.050), and 60 minutes (124 vs. 106 mg/dL, P= 0.018) after intake of 75 gram of glucose. The two groups did not differ in glucose level at 120 minutes after glucose administration. Gestational diabetes prevalence was 3.1% and 3.4% in the study and control group, respectively (P=0.274).

Conclusion: The tolerance to glucose in pregnant women with vaginal candidiasis seems discretely impaired.

Key words: Gestational diabetes, impaired glucose tolerance, vaginal candidiasis, Turkey

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Gestational diabetes mellitus (GDM), or impaired glucose tolerance in pregnancy, is one of the most common clinical issues facing obstetricians and their patients. The use of traditional risk factors (family or personal history of diabetes, previous adverse pregnancy outcome, glucosuria, obesity) to identify gestational diabetes mellitus will miss half of women with gestational diabetes mellitus.[1,2] For this reason, many physicians prefer to screen all pregnant patients as a practical manner.[2]

Specific risk factors and their influence on GDM prevalence are difficult to quantify across populations. There is no doubt that women with poorly controlled diabetes mellitus frequently have recurrent vaginal candidiasis,[3,4] especially when glucosuria is present.[5] However, whether there is a relationship between vaginal candidiasis and gestational diabetes mellitus is unknown. A possible link has been a matter of debate for many years. To study this question, we compared 75-gm oral glucose tolerance test results in pregnant women with proved vaginal candidiasis with test results in *Candida*-negative control subjects.

Patients and Methods

This cross-sectional study was conducted in the antenatal outpatient clinic and dermatology clinic of Ankara Education and Research Hospital during November 1999 to September 2002. The medical ethics committee of the institution approved the study and informed consent was obtained from each patient. We enrolled 64 pregnant women with vaginal candidiasis and 59 pregnant women who had no signs of vaginal candidiasis. Cases and controls were within the 24th to 28th weeks of their pregnancies. Patients were included only if they had no known diabetes mellitus or previous historic risk factors for GDM, had not been receiving antibiotic therapy, did not have any serious disease or immune deficiency disease. No patient was receiving corticosteroids. Multiple pregnancies were not included in this study.

After taking a careful history and performing a physical examination, we examined the pregnancy by ultrasound. Ultrasound examinations were performed by one observer (M.C.). Information about age, parity, gestational age, body mass index, family history of diabetes mellitus, duration of vaginal candidiasis symptoms and use of drug was obtained from each patient.

Table 1. Demographic characteristics of pregnant women with vaginal candidiasis (case group) and without vaginal candidiasis (control group).

Parameter	Cases (n= 64)	Controls (n= 59)
Mean parity	1.6 ± 0.5	1.4 ± 0.7
Mean age (y)	26.4 ± 7.2	25.7 ± 6.3
Gestational age (w)	26.3 ± 2.1	25.9 ± 2.4
BMI (kg /m^2)	23.8 ± 4.1	24.5 ± 4.6
Family history of diabetes mellitus	3	2

No statistically significant differences between two groups.

In symptomatic patients, after inspection of the vulvar area, an unmoistened speculum was inserted in the vagina, and sterile specimens were obtained from the upper third of the vagina by spatula for fresh wet mount preparations. Within two minutes after the patient had been examined, the spatula was smeared on a glass slide and a droplet of 10 percent potassium hydroxide solution was added for direct phase contrast microscopy at x 400 magnification. One observer (H.K.) searched for either hyphea or blastospores of yeast. Patients who had vaginal candidiasis (n=64) were included in study group. Patients without evidence of vaginal candidiasis were recruited as control subjects (n=59). Control subjects were limited to women between the ages of 18 and 35 years.

All patients submitted to an oral glucose tolerance test under strict supervision. During the three days before the oral glucose tolerance test, the patients were required to eat a sufficient amount of carbohydrates and to have normal physical activity. The test was performed in the morning after 10 to 14 hours of fasting. A blood sample was first taken for fasting glucose. All patients quickly drank 75 gm of glucose in 200 mL water. Blood samples were drawn at 30, 60, and 120 minutes after intake of 75 gm of glucose. During this test, patients were comfortable but were not allowed to have physical activity, drink, eat, or smoke. Gestational diabetes mellitus was diagnosed if there were two or more glucose levels above the normal limit, while impaired glucose tolerance was diagnosed if one level was above the normal limit. After the test, only patients with gestational diabetes mellitus regulated their diets.

Statistical analysis of demographic data was performed with SPSS software program for Windows. In the analyses of continuous responses, groups were compared by the *t* test. Discrete data was analyzed by means of the Chi-square test. A *P* value of <0.05 was considered statistically significant.

Results

The study group did not differ from the control group in maternal age, parity, gestational age (Table 1), or use of any medication. Three of 64 study patients and 2 of 59 control subjects had a family history of diabetes mellitus (*P*=0.072). Gestational diabetes prevalence was 3.1% and 3.4% in the study and control groups, respectively (*P*=0.274). In the study group, there had been vaginal candidiasis for 3 months in 40 patients, for 2 months in 16 patients, and 1 month in 8 patients. There was no correlation between glucose levels and duration of symptoms.

Mean fasting plasma glucose was higher in pregnant women with vaginal candidiasis than in controls (89.7 mg/dL vs. 84.3 mg/dL) (Figure 1). Mean plasma glucose was increased at 30 (139.6 mg/dL vs. 126.7 mg/dL) and 60 minutes (124.6 mg/dL vs. 106.1 mg/dL) after intake of 75 gm of glucose, but after two hours, the difference in plasma glucose was not significant (Figure 1). Two patients in the study group and two in the control group had gestational diabetes mellitus. Those patients were not included in the assessment of perinatal outcomes. Both groups were similar

Table 2. Perinatal and neonatal outcomes of pregnant women with vaginal candidiasis (case group) and without vaginal candidiasis (control group).

Outcome	Cases (n=62)	Controls (n=57)	*P* value
Birth weight (g)	3425.6 ± 385	3386 ± 420	0.451
Mean gestational age at birth (weeks)	37.6 ± 2.6	38.2 ± 3.4	0.549
Delivery route (%)			
Vaginal	50 / 62 (80.6)	46 / 57 (80.7)	0.328
Cesarean	12 / 62 (19.3)	11 / 57 (19.2)	0.072
Macrosomi	2 / 62 (3.2)	1 / 57 (1.7)	0.450

in terms of birth weights, gestational age at birth, delivery route, and macrosomia, (Table 2). Also similar were preterm labor (1 vs. 1), intrauterine growth restriction (1 vs. 1), and operative delivery (vacuum and forceps deliveries). Perinatal mortality and stillbirth were not observed in either group. There was one case of neonatal hypoglycemia in the study group and none in control subjects. These data were too limited for statistical analysis. No neonate had hypocalcemia or hyperbilirubinemia.

Discussion

Vaginal candidiasis is a frequent finding in patients with diabetes mellitus, especially in cases with uncontrolled diabetes, but the clinical significance of vaginal candidiasis in pregnant women with gestational diabetes mellitus is unknown. Risk factors for gestational diabetes mellitus such as obesity, a family history of a first-degree relative with diabetes, maternal age, and parity are described in the literature.[6,7] However, it is not well known whether there is an association between vaginal candidiasis and GDM. The increased body mass index in women is likely associated with insulin resistance and lowered glucose tolerance.[2,7] In this paper, both groups were similar in terms of body mass index and maternal age. Also we found no increased risk for vaginal candidiasis in pregnant women with GDM. In other words, pregnant women with vaginal candidiasis had no increase in prevalence of gestational diabetes mellitus compared with women without vaginal candidiasis. However, despite the fact that no signs of gestational diabetes mellitus were demonstrated, the clearance of glucose after the oral intake of 75 gm of glucose was impaired in pregnant women with vaginal candidiasis.

Although an increased vaginal content of glucose has never been proven in women with vaginal candidiasis, in vitro evidence has shown that *Candida* proliferates better in a broth that is enriched with different sugars.[8] Glucose, maltose, and sucrose all greatly enhance adhesion of *Candida albicans* to buccal epithelial cells, but lactose did not.[8,9] It is possible that these mechanisms also apply to human vaginal epithelial cells.

As impaired glucose tolerance is closely related to increased insulin resistance, this is the most likely mechanism that would explain higher glucose levels after ingestion of sweets. Therefore, in non-pregnant women, a sugar-limited diet might be the first logical step in treatment.[10] In the present study, the higher than normal plasma levels of glucose were not related to a poor perinatal outcome.

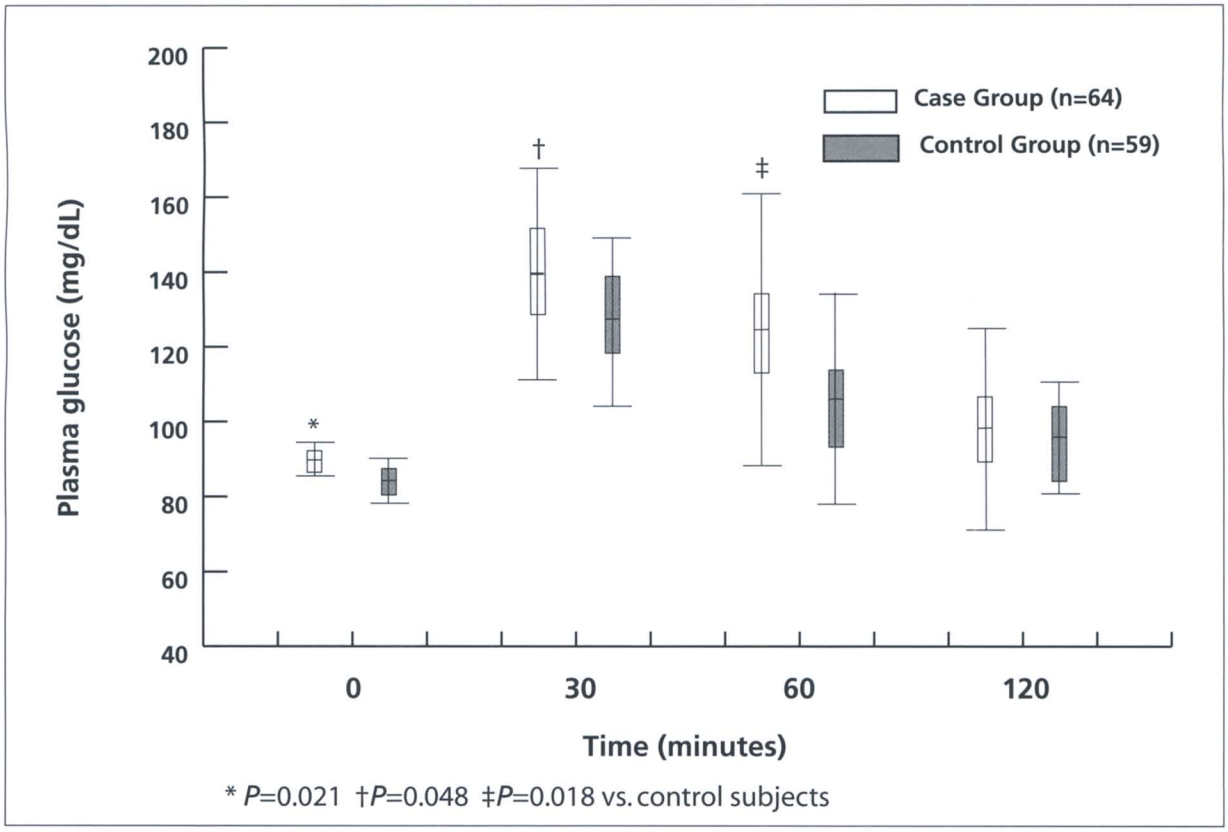

Figure 1. Glucose challenge test results for pregnant women with vaginal candidiasis (case group) and without vaginal candidiasis (control group) (mean±SE and 25th and 75th percentiles).

Although it is generally agreed that most pregnant women with GDM more frequently have a higher perinatal mortality and morbidity than healthy pregnant women, the relationship with impaired glucose tolerance is obscure. In our study, we observed no difference in perinatal and neonatal outcome between pregnant women with vaginal candidiasis and control subjects. The number of our subjects was too limited to comment upon perinatal outcomes. There is no consensus in the medical literature on whether impaired glucose tolerance or sub-gestational diabetes mellitus increases the probability of poor perinatal outcome. According to a large population-based study in Sweden, impaired glucose tolerance (in sub-gestational diabetes mellitus) carries an increased risk of a non-optimal delivery outcome, such as an increased rate of cesarean delivery and increased birth weight.[11] Another study suggested that the increased rate of adverse maternal and fetal outcomes, especially large for gestational age, was associated with untreated mild gestational hyperglycemia women compared to a control group.[12] But in a recent study, women with impaired glucose screening were at higher risk for elective cesarean delivery, whereas the number of emergency cesarean deliveries, instrumental deliveries, or birth weight were not significantly different.[13] In our study, the mean birth weight of infants in the impaired glucose tolerance group was higher but not significantly, and also was not significantly more frequent in the case group.

In conclusion, tolerance to glucose in pregnant women with vaginal candidiasis is discretely impaired. We observed no statistically significant difference in perinatal and neonatal outcome between pregnant women with vaginal candidiasis and control subjects.

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