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Abstract

**Background:** Gestational diabetes mellitus (GDM) is defined as impaired glucose tolerance with onset during the second or third trimester of pregnancy.

**Aims:** The purpose of this study was to investigate the prevalence of pregnant women who were not screened for gestational diabetes mellitus and compare the maternal and fetal outcomes of women who had undergone GDM screening.

**Methods:** Women who refused to attend the gestational diabetes screening test (n = 162) at a maternity hospital in Ankara, Turkey, between October 2014 and January 2015 were included in this prospective cohort study. The control group (matched for age and body mass index) was recruited from women who agreed to have the gestational diabetes screening test (n = 194).

**Results:** Just 12% of pregnant women did not attend gestational diabetes screening test; these women were at higher risk for idiopathic polyhydramnios (P = 0.026). Prevalence of GDM was 8.8% (n = 17) in the control group and 30.9% (n = 50) in those who refused GDM screening. The maternal and fetal outcomes of GDM patients were similar in both groups. Women who did not attend GDM screening test had increased risk for mild idiopathic polyhydramnios in late gestation.
Conclusions: Fasting and postprandial plasma glucose screening can replace gestational diabetes mellitus screening in women who refuse to have the glucose load test.

Keywords: idiopathic polyhydramnios, gestational diabetes screening, plasma glucose test, glucose tolerance test

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Introduction

Gestational diabetes mellitus (GDM) is defined as impaired glucose tolerance with onset during the second or third trimester of pregnancy (1). The prevalence of GDM is as high as 9.2%, according to a 2014 analysis (2). Risk factors for GDM include advanced maternal age (> 25 years), multiparity, multiple pregnancy, family history of diabetes, pregnancy loss at second or third trimester, history of fetal macrosomia childbirth, history of GDM in a previous pregnancy, and overweight and obesity (3).

Pregnancies with complicated GDM are faced with abortion, large for gestational age, intrauterine growth restriction, polyhydramnios, intrauterine fetal death, pre-eclampsia, and delivery complications including caesarean section, birth trauma, neonatal hypoglycaemia, hyperbilirubinaemia, polycythaemia, and requirement for admission to the neonatal intensive care unit. Therefore, early diagnosis and treatment of GDM may reduce fetal exposure to maternal hyperglycaemia and decrease maternal and fetal complications (4,5).
Screening for GDM is recommended as a single or 2-stage oral glucose tolerance test (OGTT) between 24 and 28 weeks of pregnancy (6). In this study, we aimed to determine the prevalence of pregnant women who refused to attend a gestational diabetes screening test and compared their maternal and fetal outcomes with those who accepted a gestational diabetes screening test. Our second aim was to investigate whether fasting and postprandial plasma glucose screening could replace gestational diabetes mellitus screening in women who refuse glucose load.

Methods

This prospective cohort study was conducted among 1450 patients admitted for routine antenatal follow-up between 24 and 28 weeks of gestation at a maternity hospital in Ankara, Turkey, between October 2014 and January 2015. The hospital is a maternity care hospital and a tertiary referral centre that has 18,000 births annually. This study was conducted according to the Declaration of Helsinki (7). The institutional review board of the University of Health Sciences, Zekai Tahir Burak Woman’s Health, Education and Research Hospital (# 18/2014) approved the study. Exclusion criteria included multiple gestation, clinical evidence or historical pregestational of diabetes, fasting plasma glucose exceeding 126 mg/dL or the 2-hour postprandial or glucose challenge test (GCT) value exceeding 200 mg/dL, history of a positive glucose tolerance test in the first trimester, and women with known diseases of the kidney, liver or thyroid gland. Maternal age, gravidity, parity, body mass index, family history of diabetes, history of gestational diabetes and macrosomia (> 4000 g) in their previous pregnancy were recorded. All patients were informed about gestational diabetes mellitus and screening of GDM. Women who refused to attend the gestational diabetes screening test were followed with fasting and postprandial 2nd hour plasma glucose levels, initially at screening time and at 32 weeks of gestational age. Abnormal glucose test was defined as fasting venous plasma glucose level > 92 mg/dL and/or postprandial 2-hour venous plasma glucose level > 120 mg/dL.

The control group was selected by a simple random sampling method and 194 age–parity matched women who had agreed to have the gestational diabetes screening test were recruited in the study. Women in the control group underwent a 2-stage GCT. A positive 50-g GCT is defined as glucose level 1 hour after glucose challenge of at least 140 mg/dL. Women who had a positive 50-g GCT were advised to follow a normal diet 3 days before the 100-g OGTT. The standard protocol for the OGTT was used; after an 8-hour overnight fast, venous plasma samples were collected when fasting 1, 2 and 3 hours after the receipt of the 100-g oral glucose load. Women who had a positive OGTT test according to the criteria identified by Carpenter and Coustan were labelled as having GDM; GDM was diagnosed if the 2 diagnostic criteria were found (8).
Diagnosis for polyhydramnios was made measuring either amnion fluid index (AFI) and/or single deepest pocket (SDP) (9,10). Polyhydramnios was defined and categorized into 3 groups according to severity: mild polyhydramnios (AFI 24.0–30.0 cm and/or SDP 8.0–11.9 cm), moderate polyhydramnios (AFI 30.1–35.0 cm and/or SDP 12.0–15.9 cm) and severe polyhydramnios (≥ 35.0 cm and/or SDP ≥ 16.0 cm) (10). Macrosomia was defined as fetal birth weight exceeding 4000 g. Deliveries occurring prior to 37 weeks of gestation were recorded as preterm.

Patients with abnormal plasma glucose level (FPG > 92 mg/dL and or PPG > 120 mg/dL) or positive OGTT were followed by a qualified dietitian and initially received an 1800–2200 calorie diet with the meal composition of 40–45% carbohydrates, 20% protein, and 40% fat, individualized to pre-pregnancy weight, activity level, dietary intake, and weight gain. The FPG and PPG tests were performed 10 days after nutritional counselling and 2 hours after a standard breakfast. Treatment targets to maintain maternal capillary glucose concentration were at 0.05). The demographic characteristics of the patients are shown in Table 1.

All the patients recruited in the study had only dietary treatment. No insulin or oral antidiabetic drugs were needed. Pregnant women who refused to attend the gestational diabetes screening test had higher rates of polyhydramnios compared to control group (P = 0.026). All of polyhydramnios cases were mild. There were no significant differences between control and study group for neonatal outcomes. Obstetric complications and neonatal outcomes in the 2 groups are shown in Tables 2 and 3. There were 3 cases of neonatal hypoglycaemia and hyperbilirubinaemia in the study population but these were not statistically significant (P = 0.093). When the 2 groups were re-analysed according to gestational diabetes diagnosis, the maternal and fetal outcomes were similar in women those with and without a diagnosis of diabetes (Tables 4, 5).

Discussion

We evaluated the prevalence of pregnant women who refused to attend gestational diabetes screening, and compared their maternal and fetal outcomes with the women screened using 2-step GCT. The prevalence of women who refused to attend GDM screening was 12%. We also found that the prevalence of idiopathic polyhydramnios was higher in women who refused to attend the GDM screening test compared with the control group. To the best of our knowledge, this is the first study determining the prevalence of pregnant women who refused to attend gestational diabetes screening test and evaluating maternal and neonatal outcomes in the Turkish population.

Although the current evidence is controversial and insufficient to interpret the benefits and harm
of GDM screening, there are studies showing that treating GDM allows for a significant reduction in macrosomia, neonatal fat mass, shoulder dystocia, pre-eclampsia, and caesarean section (5,12). Therefore, the American Diabetes Association recommended that all pregnant women should undergo risk assessment for GDM at the first antenatal visit and if necessary undergo glucose testing as soon as possible (1). Women with abnormal glucose levels in the first trimester should be classified as type 2 diabetes (1). Patients not known to have prior diabetes or normal glucose values at the initial screening should go for repeat testing at 24–28 weeks gestation (1). In addition, the American College of Obstetricians and Gynecologists suggested that all pregnant women should be tested at 24–28 weeks gestation (13). The Hyperglycaemia and Adverse Pregnancy Outcome (HAPO) study found that there were also associations between increased maternal hyperglycaemia and preterm delivery, shoulder dystocia, pre-eclampsia, and hyperbilirubinemia (14). Adverse obstetrics outcomes and perinatal mortality rates decrease with better glycaemic control (15).

However, although the debate is ongoing in regard to the cut-off value in the screening, the GCT can be performed as a 100-g 3-hour test and a 75-g 2-hour test (16–18). Although the 100-g 3-hour GTT is generally applied as the second stage of the 2-stage approach while the 75-g 2-hour test is applied as the only test in the 1-stage approach, this is optional. For example, the Canadian Diabetes Association clinical guidelines suggest the 75-g 2-hour GTT (18). Even if carbohydrate loading is recommended for 3 days before the screening test, it is not necessary in patients who do not want to follow a low-carbohydrate diet (19,20).

The prevalence of GDM has been steadily increasing with the rise in obesity and type 2 diabetes. Worldwide reports range from 1–14% (16). For our control group, the prevalence of GDM was estimated at 8.8%. This is somewhat lower than the rate reported by Yeral et al. (11.2%) using the 2-step method in the Turkish population (17). The majority of women (90%) in our study population had ≥ 1 risk factors of GDM.

Glucose solutions used for oral glucose tolerance test (OGTT) and GTT have a hyperosmolar content at high concentration and can cause gastric irritation, delayed emptying, and gastrointestinal osmotic imbalance, leading to nausea and, in a small percentage of women, vomiting (21). Therefore, some pregnant women did not succeed in completing the OGTT because of refusing to undergo the test, vomiting, eating during the test, etc. For this reason, some alternatives to the oral screening and GTTs have been described these and are better tolerated. These methods include offering the hyperosmolar glucose drink on ice, using candy, a predefined meal, or commercial soft drinks instead of a standard glucose monomer or polymer solution, and intravenous GGT. But these options seem to be less sensitive and have not been affirmed in prospective randomized studies (22–27). None of them have been confirmed by the American Diabetes Association or the American College of Obstetricians and Gynecologists. Agarwal et al. reported that 5% (n = 242) of 4844 women who underwent the OGTT at 24–28
weeks of gestation were not able to complete this test (28).

Some research has focused on the association between fasting plasma glucose (FPG) and adverse perinatal outcomes. The HAPO study demonstrated that FPG ≥ 95 mg/dL was correlated with fetal macrosomia in the second half of pregnancy at the time of screening at 24–28 weeks (14). A review of FPG as a screening test for GDM demonstrated that, with the American Diabetes Association criteria for 75 g or 100 g OGTT, it appears to be a good test for the screening of GDM. Using the WHO criteria (FPG > 109 mg/dL) could limit the usefulness of FPG as a screening test for GDM due to poor specificity and high false positive rates (29). Tam et al. recommended that the FPG with a threshold of 88 mg/dL (4.9 mmol/L) is a better test rather than using GCT or postprandial glucose for universal screening (30).

Previous studies have focused on postprandial 2-hour glucose screening (30–35), mostly with accompanying FPG for the diagnosis of GDM (36–39). Battacharya et al. and Rust et al. reported against the use of PPPG, but Bhattacharya determined FPG cut-off value as 105 mg/dL (higher than the conventional threshold of 92/mg/dL) and Rust et al. did not evaluate FPG (34,35). While Senanayake et al. found FPG superior to PPPG when screening for GDM (33), Huddleston et al. reported that if FPG is normal, then a 2-hour postprandial glucose test is not needed (31). Agarwal et al. (32) pointed to the high false positive rates of FPG and PPPG testing; we found that GDM prevalence was 31% with FPG and PPPG screening compared with 9% using the regular 50 g GCT.

Polyhydramnios is a condition associated with an excess volume of amniotic fluid. The incidence of polyhydramnios ranges from 1–2% in general obstetric practice and most cases display mild severity. The most common causes of mild polyhydramnios are maternal diabetes, multiple gestation, fetal infection, fetal structural anomalies and idiopathic factors (40). In our study, only idiopathic polyhydramnios was found to be higher in women who did not attend the GDM screening test compared with those in the control group [n = 7 (4.3%) vs n = 1 (0.5%)]. All cases were of mild severity and were diagnosed in the third trimester. Six out of the 7 patients were correlated with high levels of plasma glucose.

There were some limitations to the present study. Initially HbA1c levels were not evaluated, however, screening for HbA1c is not routinely performed or recommended (36). The study population was lower than we had predicted. Lastly, all the patients recruited in the study had only dietary treatment: no insulin or oral antidiabetic drugs were needed, which indicates that all the cases were mild.

**Conclusion**
As GDM is linked to many serious fetal and maternal complications, screening, diagnosis, treatment and follow-up of GDM are recommended for all pregnant women. Although pregnant women were screened by FPG and PPPG in the second trimester, 40% of fetal macrosomia and 28.6% polyhydramnios were missed. Therefore fasting and post-prandial plasma glucose screening could be a beneficial individual screening for gestational diabetes mellitus in women who refuse the glucose load test.

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**Competing interests:** None declared.

Dépistage du diabète gestationnel à l'aide de la mesure de la glycémie plasmatique à jeun et postprandiale

Résumé

**Contexte:** Le diabète gestationnel se définit comme une intolérance au glucose qui apparaît au cours du deuxième ou troisième trimestre de la grossesse.

**Objectifs:** La présente étude a pour objectif d’analyser la prévalence de femmes enceintes n’ayant pas bénéficié d’un dépistage du diabète gestationnel et de comparer l’issue de la grossesse pour la mère et le fœtus.

**Méthodes:** Les femmes ayant refusé de participer au test de dépistage du diabète gestationnel (n = 162) dans une maternité d’Ankara (Turquie) entre le mois d’octobre 2014 et de janvier 2015 ont été incluses dans cette étude de cohorte prospective. Le groupe témoin était constitué de femmes appartenant à la même tranche d’âge et présentant un indice de masse corporelle similaire qui ont accepté le test de dépistage du diabète gestationnel (n = 194).

**Résultats:** La prévalence de femmes enceintes qui n’avaient pas participé au test de dépistage du diabète gestationnel était de 12 %. Les femmes n’ayant pas participé au test de dépistage du diabète gestationnel présentaient un risque plus élevé d’hydramnios idiopathique (p = 0,026). La prévalence du diabète gestationnel était respectivement de 8,8 % (n = 17) et de...
30.9 % (n = 50). L'issue de la grossesse pour les mère présentant un diabète gestationnel et leur fœtus était similaire dans les deux groupes. Les femmes n’ayant pas participé au test de dépistage du diabète gestationnel présentaient un risque accru d’hydramnios idiopathique léger en fin de grossesse.

Conclusions: La mesure de la glycémie plasmatique à jeun et postprandiale peut remplacer le dépistage du diabète gestationnel chez les femmes qui refusent l’administration d’une charge de glucose.
References


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