CLINICAL STUDY

Perinatal Outcome in Women Screened for Gestational Diabetes Mellitus With Normal or With One Elevated Glucose Tolerance Test Value*

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Abstract

Objective: To investigate the perinatal outcome of women screened for gestational diabetes mellitus (GDM) who had abnormal screening and normal oral glucose tolerance test (OGTT) results or women with a single abnormal test value in OGTT.

Materials and Methods: We screened 576 pregnant women with a 50 gr oral glucose challenge test between the 24th and 26th weeks' of gestation. Women with abnormal diabetes screening test results were followed up with standard OGTT with a 100 gr oral glucose load. According to the results, 360 women were with a normal screening test (Group 1), 87 with a positive screening and all normal test values on OGTT (Group 2), 50 with a positive screening but a single abnormal test value on OGTT (gestational impaired glucose tolerance, Group 3) and 79 were diagnosed as with GDM (Group 4). Diet or diet plus insulin therapy was initiated to patients in Groups 3 and 4 as indicated. We compared perinatal outcome between these four groups. Statistical data were calculated with *post hoc* multiple comparison, Kruskal-Wallis and χ^2 tests for comparison of means, medians or for nominal variables.

Results: Women with GDM had significantly higher glycosylated hemoglobin levels, large for gestational age infants, macrosomia, neonatal jaundice, neonatal intensive care unit (NICU) admission and neonatal mortality rates but lower gestational age at delivery and 1-minute Apgar scores compared to controls. Also, there were significant differences in neonatal jaundice and NICU admission rates between Groups 1 and 3, or between 2 and 3. There were significantly more macrosomic babies in Groups 3 and 4, compared to Group 2.

Discussion: Women with abnormal diabetes screening tests and negative OGTT or with gestational impaired glucose tolerance seem not to be prone to develop severe adverse perinatal outcome.

Keywords: gestational diabetes mellitus, glucose tolerance test, pregnancy

Özet

Gestasyonel Diyabet Taramasında Normal Test Değeri ve Tek Değer Yüksekliği Saptanan Gebelerde Perinatal Sonuçlar

Amaç: Gestasyonel diyabet (GDM) taraması yapılan ve oral glukoz tolerans testinde (OGTT) tüm değerleri normal ve tek değeri yüksek çıkan hastalardaki perinatal sonuçları incelemek.

Materyal ve Metot: Gebeliğin 24.-26. haftalarında 576 hastaya 50 gr "glukoz tarama testi" uygulandı. Test sonucu yüksek bulunanlara 100 gr glukoz ile standart OGTT yapıldı. Sonuçta 360 hastada glukoz tarama testi normal (Grup 1), 87 hastada glukoz tarama testi yüksek-OGTT normal (Grup 2) bulunurken, 50 hastada glukoz tarama testi yüksek-OGTT'de tek değer yüksekliği (gebelik glukoz intoleransı, Grup 3) ve 79 hastada GDM (Grup 4) saptandı. Grup 3 ve 4'teki hastalara diyet ve gerektiğinde diyetle birlikte insülin tedavisi başlandı. Bu dört gruptaki perinatal sonuçlar karşılaştırıldı. İstatistiksel analizde *post hoc* çoklu karşılaştırma, Kruskal-Wallis ve χ^2 testleri kullanıldı.

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Sonuçlar: GDM tanısı alanlarda kontrol grubuna kıyasla glukozile hemoglobin (HbA_{1c}), fazla doğum ağırlıklı bebek, makrozomi, neonatal sarılık, neonatal yoğun bakım ünitesine (NICU) alınma ve neonatal mortalite oranları anlamlı olarak yüksek, doğum haftaları ve 1. dakika Apgar skorları düşük saptandı. Ayrıca, neonatal sarılık ve NICU'ya alınma oranları Grup 1 ve 3, Grup 2 ve 3 arasında da anlamlı olarak farklı izlendi. Grup 3 ve 4'te ise Grup 2'ye kıyasla daha fazla makrozomik bebek dünyaya geldi.
Tartışma: Diyabet tarama testi yüksek çıkıp OGTT negatif bulunan veya gebelik glukoz intoleransı saptanan gebeler ciddi olumsuz perinatal sonuçlara aday görünmemektedirler.
Anahtar sözcükler: gestasyonel diabetes mellitus, glukoz tolerans testi, gebelik

Introduction

Insulin secretion and insulin resistance increase in normal pregnancy. If the insulin secretory capacity becomes inadequate to overcome this progressive insulin resistance gestational diabetes mellitus (GDM) may develop. The routine screening of GDM in pregnancy is performed by a 50-gr oral glucose challenge test, but the diagnosis is based on an oral glucose tolerance test (OGTT). GDM is diagnosed if >2 values meet or exceed the suggested cut-off values on OGTT (1). Pregnancies complicated by GDM are usually associated with risks of both maternal and perinatal morbidity. Untreated GDM was associated with a significantly higher perinatal mortality rate than normal glucose tolerance. Identification and treatment of women with GDM can reduce perinatal mortality rates (2). Also, less morbidity can be expected in infants of diabetic mothers with modern management of GDM (3). Tight glycemic control can serve as the primary prevention for fetal sequelae of GDM (4). However, some other authors believe that even tight control of hyperglycemia would not decrease the overall fetal morbidity rate (5-7).

Despite the clearer data on patients with GDM, controversies still do exist in pregnancies with a positive glucose challenge test and normal OGTT or women who had impaired glucose intolerance (single-value abnormality on OGTT). Most authorities considered that patients with single-value abnormality on OGTT had the same characteristics and similar perinatal outcome as women with GDM, including higher neonatal morbidity, metabolic complications and risk for adverse outcome in pregnancy compared to healthy controls (8-12). Nevertheless, similar perinatal morbidity rates were reported in patients with positive glucose challenge test and normal OGTT results to those of healthy pregnancies (13). On the other hand, some authors proposed that detection of glucose intolerance during pregnancy does not identify women at high risk for obstetric and perinatal morbidity and furthermore correction of this glucose intolerance has little effect on pregnancy outcome (14).

The objectives of our study were to report our experience with a group of pregnant women living in Trakya Region universally screened for GDM, and to present the perinatal outcome in the offsprings' of women who were screened as positive but gave negative OGTT results and in women with gestational impaired glucose tolerance.

Materials and Methods

A total of 576 women who received prenatal antenatal care and who delivered in our institution between October 1999 and January 2004, were included in the study. The study was approved by the Ethics Committee for Human Research at Trakya University, Turkey, and verbal informed consent was obtained from the patients. Women with multiple pregnancies, with chronic diseases such as hypertension, renal, heart or autoimmune diseases were excluded. The study population consisted of Turkish women living in Trakya Region of Turkey. Gestational age was based on the last menstrual period and according to a reliable menstrual history confirmed by ultrasonography. All patients underwent a 50 gr oral glucose challenge test between the 24th and 26th weeks' of gestation. Women with abnormal diabetes screening test results, defined as a serum glucose level >135 mg/dL on oral glucose challenge test, were followed up with standard OGTT, with a 100 gr oral glucose load (10,15). A three-hour 100 gr OGTT was performed after an overnight fast for 10-12 hours and after a three-day 300 gr carbohydrate diet. Blood samples were collected at baseline and at 60, 120 and 180 minutes after ingestion of the glucose load. Plasma glucose was measured with an automated analyzer (Mega, Merck Instruments Co., Frankfurt, Germany). Glycosylated hemoglobin (HbA_{1c}) concentration was determined by standard automated methods from the blood that was obtained before delivery. Glucose concentrations after OGTT were also expressed as the area under the curve (AUC) after glucose ingestion, as calculated by the trapezoidal rule.

The diagnosis of GDM was made according to the American Diabetes Association criteria (1) that require two or more plasma glucose values >95 mg/dl (fasting), >180 mg/dl (1-h), >155 mg/dl (2-h) and >140 mg/dl (3-h). According to the results, 360 women were with a normal screening test (Group 1, control group), 87 with a positive screening and all normal test values on OGTT (Group 2), 50 with a positive screening but single-value abnormality on OGTT (Group 3) and 79 were diagnosed with GDM (Group 4). Definitions of the groups were shown in Table 1. Diet or diet plus insulin therapy was initiated as indicated to women with GDM. Patients with GDM or with single value abnormality were placed on a diabetic diet in which the caloric content consisted of 35 kcal/kg/day prepregnancy ideal body weight, consumed as 3 primary meals and 2 snacks per day. Group 3 and 4 patients were followed up biweekly with fasting and 2-h

Table 1. Definitions of the groups

Group 1 (n=360)	Women with a normal screening test value
Group 2 (n=87)	Women with a positive screening and all normal test values on OGTT
Group 3 (n=50)	Women with a positive screening but a single abnormal test value on OGTT (gestational impaired glucose tolerance)
Group 4 (n=79)	Women with positive screening and ≥2 abnormal test values on OGTT (gestational diabetes mellitus)

postprandial blood glucose measurements. According to the current criteria, insulin therapy was initiated when fasting and 2-h postprandial glucose values exceeded consistently >105 mg/dl and >120 mg/dl, respectively (16). Glucose profiles were performed daily when insulin therapy was administered and the dose of insulin was adjusted to achieve fasting glucose level <90 mg/dl and 2-h postprandial glucose level <120 mg/dl. Thirteen out of 79 patients (16.4%) needed insulin therapy in our cohort of women with GDM. Mean daily insulin dose administered to women with GDM was 18.46±17.94 units. However, no women in Group 3 needed insulin therapy.

We compared perinatal outcome of the offsprings' of these women with various screening and diagnostic test results. All newborns were examined in the Neonatology Department by physicians specially trained in this field. Neonatal mortality was defined as any death of a live-born infant during the first 4 weeks after birth. Macrosomia was defined as birth weight >4000 gr (17,18). Neonatal weight was classified as appropriate for gestational age (AGA), or large for gestational age (LGA) (birth weight between 10th and 90th percentiles, and >90th percentile, respectively) according to gestational age and sex. Perinatal morbidities were defined as follows: birth asphyxia, 1- and 5-minutes Apgar scores <3 and <5, respectively with the clinical features of hypoxic ischemic encephalopathy; neonatal hypoglycemia, serum glucose <40 mg/dl; hypocalcemia, serum calcium level <8 mg/dl in term newborns and <7 mg/dl in preterm newborns; hypomagnesemia, serum magnesium <1.5 mg/dl; neonatal jaundice, hyperbilirubinemia requiring treatment; polycythemia, hematocrit >65%; thrombocytopenia, platelet count <150.000/μL; respiratory distress syndrome (RDS) and transient tachypnea, according to clinical findings, blood gases and chest X-ray; neonatal septicemia, the presence of bacteriemia with focal or systemic infection signs and positive blood cultures; persistent pulmonary hypertension, severe hypoxia and hypocapnia with echocardiographic evidence of a right-to-left shunt in the absence of congenital cardiac malformation and with a normal chest X-ray (6,17,19,20).

Data were stored and analyzed with the Minitab program (License No: WCP1331.00197). Variables were tested for normal distribution with the Kolmogorov-Smirnov test. We performed Kruskal-Wallis test for the non-parametric parameters, and χ^2 test for categorical variables. Calculation of the homogeneity of variances identified the homogenous and non-homogenous parameters. Tukey and Tamhane multiple comparison tests were applied for the homogenous and non-homogenous parameters, respectively. *P* values by Fisher exact test were reported when the assumptions for the χ^2 analysis were not met. Pearson correlation analysis was used for linear correlations. Statistical significance was defined as $p<0.05$.

Table 2. Patient characteristics, glucose challenge and tolerance tests results in study and control groups

	Group 1 [normal screening] (n=360)	**Group 2 [(+) screening normal OGTT] (n=87)**	**Group 3 [(+) screening 1 (+) OGTT] (n=50)**	**Group 4 (GDM) (n=79)**	***p* value**
Age (years)	26.9+4.6*	27.6+4.7**	29.2+4.7†	30.3+4.5	0.001
Gravida (median, min-max)	2 (1-6)	2 (1-6)	2 (1-4)	2 (1-6)	NS
Parity (median, min-max)	0 (0-4)	1 (0-5)	0.5 (0-3)	1 (0-3)*	0.011
HbA_{1c} (%)	4.63±0.2*	4.6±0.5	5.2±0.8	5.6±1.4	0.03
Glucose challenge test (mg/dl) ‡	107.9±17.1	153.6±18	160±25.1	171.3±30.9	<0.001
OGTT-fasting (mg/dl)		80.4±8.2	91.3±17	94.4±16.3	NS
Glucose AUC (mg/dl-180 min) §		230.3±35.24	278.84±35.98	339.02±39.62	<0.001

NS: not significant
* $p<0.05$, Group 1 vs. Group 4
** $p<0.05$, Group 2 vs. Group 4
† $p<0.05$, Group 1 vs. Group 3
‡ $p<0.05$, all 4 groups
§ $p<0.001$, all three groups (Groups 2, 3 and 4)

Results

As shown in Table 2 age, parity, fasting glucose, glucose challenge test results and HbA_{1c} were different between the groups. Mean maternal age was significantly higher in women with GDM, compared to the controls or women with positive glucose challenge test results ($p>0.05$). Also, age of Group 3 patients were significantly higher than that in the controls ($p>0.05$). However, no difference was observed between Groups 1 and 2 or between Groups 3 and 4 in terms of age. When the 50 g glucose challenge test results were compared between the groups, results were significantly different in all four groups ($p<0.05$). OGTT-fasting values were similar in Group 2, Group 3 and Group 4. However, the glucose AUC values were all significantly different in Groups 2, 3 and 4 ($p<0.001$). Mean + SD HbA_{1c} levels were significantly higher in women with GDM than that in controls (5.6±1.4 vs. 4.6±0.2%, $p=0.03$) (Table 2).

Gestational weeks at delivery and 1-minute Apgar scores were significantly lower in women with GDM compared to Group 1 and Group 2 (Table 3). The 1-minute Apgar scores were also different between Groups 1 and 3. However, 5-minute Apgar scores were similar in all four groups. Neonatal mortality rate was significantly higher in the offsprings' of women with GDM compared to controls ($p=0.006$). There were significant differences between Groups 1 and 4 ($p=0.01$), groups 2 and 3 ($p=0.03$), or Groups 2 and 4 ($p=0.01$) in terms of macrosomia rate. Babies born to women with GDM had higher LGA rate than that in controls (25.3% vs. 12.5%, $p=0.039$). However, there was no significant difference in LGA rates between Group 2, Group 3 and Group 4.

Perinatal morbidities are shown in Table 4. The neonatal jaundice and neonatal intensive care unit (NICU) admission rates were significantly higher in babies of women with GDM ($p=0.008$) and in Group 3 ($p=0.017$) than those in controls in Group 2 ($p=0.013$ and $p=0.009$, respectively). However, there was no difference in any other perinatal morbidity rate between four groups.

In a further analysis, we investigated correlations between prepartum HbA_{1c} levels and birth weight, height, head circumference and the perinatal morbidities. Only HbA_{1c} levels showed a positive but weak correlation between 1-minute Apgar scores ($p=0.017$, r=0.367).

Discussion

We found similar perinatal morbidity rates in babies of normoglycemic women with GDM, women with positive screening but negative diagnostic test results and normo-

Table 3. Perinatal outcome in the groups

	Group 1 [normal screening] (n=360)	Group 2 [(+) screening normal OGTT] (n=87)	Group 3 [(+) screening 1 (+) OGTT] (n=50)	Group 4 (GDM) (n=79)	*p* value
Gestational weeks at delivery	38.6±1.5*	38.5±1.4**	38.4±1.4	37.9±1.7	0.014
Birth weight (gr)	3277±478	3301±444	3344±561	3418±624	NS
Height (cm)	49.9±2.6	50.3±2.5	49.4±4.8	50.2±2.9	NS
Head circumference (cm)	35±1.8	35.5±1.5	35.4±2.6	35.3±1.9	NS
Neonatal mortality	0*	0	0	3 (3.7%)	0.006
Malformation	11 (3%)	1 (1.1%)	0	1 (1.2%)	NS
Macrosomia	26 (7.2%)*	3 (3.4%)	7 (14%) †	13 (16.4%)**	0.008
Large for gestational age (LGA)	45 (12.5%)*	14 (16%)	9 (18%)	20 (25.3%)	0.039
Approximate for gestational age (AGA)	313 (86.9%)	73 (83.9%)	41 (82%)	59 (74.6%)	NS
Birth asphyxia	8 (2.2%)	1 (1.1%)	2 (4%)	1 (1.2%)	NS
Birth trauma	18 (5%)	1 (1.1%)	3 (6%)	6 (7.5%)	NS
1-minute Apgar score (median, min-max)	8 (1-9)*	8 (5-10)**	8 (1-8) ‡	8 (5-9)	0.006
5-minute Apgar score (median, min-max)	9 (2-10)	9 (6-10)	9 (6-10)	9 (7-10)	NS

NS: not significant
* $p<0.05$, Group 1 vs. Group 4
** $p<0.05$, Group 2 vs. Group 4
† $p<0.05$, Group 2 vs. Group 3
‡ $p<0.05$, Group 1 vs. Group 3

glycemic women with single-value abnormality on OGTT, except for gestational age at delivery, macrosomia, LGA, neonatal jaundice, and NICU admission rates.

The neonate is at increased risk in terms of perinatal mortality when there is hyperglycemia. Although some investigators have asserted that morbidity could not be eliminated with euglycemic values (17), as previously reported elsewhere (11,17,18,21), we observed similar malformation, birth weight, birth trauma, 5-min Apgar score, RDS, hypoglycemia, hypocalcemia, polycythemia rates, and higher macrosomia, LGA, neonatal death and NICU admission rates in patients with GDM. However, contrary to previous reports (10,21,22), we did not demonstrate similar perinatal mortality, LGA and NICU admission rates or higher neonatal asphyxia, birth trauma, hypoglycemia and RDS rates in babies of GDM women. Macrosomia with an associated increased risk of birth trauma and asphyxia represent the most important morbidity attributed to GDM. Langer (3) has reported that with the management of GDM the rates of neonatal morbidities have been reduced to the levels observed in the general population. The risk of macrosomia appears to increase with increasing postprandial glucose concentrations (23). Although postprandial monitoring reduced the risk of fetal macrosomia and neonatal hypoglycemia in GDM (23), no diabetic medication had maintained targeted levels of glycemic control in all patients with GDM to date (18). Hod et al. (6) found that the rate of macrosomia remained higher despite maintaining mean blood glucose values <105 mg/dl. Some other authors believe that aggressive control of hyperglycemia would decrease the overall rate of fetal macrosomia only marginally (5). Also, in line with our increased macrosomia and LGA rate in women with GDM as compared to the controls, glucose control did not normalize birth weight percentiles in patients with GDM (7).

A higher incidence of macrosomic infants in women with positive glucose challenge test-normal OGTT results has been observed in the literature (24). On the contrary, it has been suggested that the 50-gr glucose challenge test blood glucose level had no predictive power with respect to the birth of a LGA infant (25). We found similar macrosomia and LGA rates in women with positive glucose challenge test-normal OGTT results and controls. Besides, significantly more patients in GDM and in single value abnormality on OGTT had macrosomic infants, compared to women with positive glucose challenge test-normal OGTT results. As in our study, Weiner (26) and Bofill et al. (13) could not show any significant difference in morbidity between positive-glucose challenge test-normal OGTT patients and normal population. Thus, perinatal outcome in women with positive glucose challenge test-normal OGTT results resemble those of controls, not those of GDM or single value abnormalities. Patients with positive glucose challenge test but negative OGTT are not prone to develop neonatal complications.

Higher incidences of hyperbilirubinemia, hypoglycemia, anomaly, NICU admission and perinatal mortality were observed in women with single-value abnormality compared to women with all normal values on OGTT (10). Also, Langer et al. (8)

Table 4. Perinatal morbidity in three groups

	Group 1 [normal screening] (n=360)	Group 2 [(+) screening normal OGTT] (n=87)	Group 3 [(+) screening 1 (+) OGTT] (n=50)	Group 4 (GDM) (n=79)	*p* value
Sepsis	2 (0.5%)	0	0	1 (1.2%)	NS
Neonatal jaundice	23 (6.3%) *	4 (4.5%) ‡	9 (18%) †	14 (17.7%)**	<0.001
Thrombocytopenia	2 (0.5%)	0	1 (2%)	1 (1.2%)	NS
Transient tachypnea	13 (3.6%)	2 (2.3%)	2 (4%)	3 (3.8%)	NS
Respiratory distress syndrome	2 (0.5%)	0	0	2 (2.5%)	NS
Persistent pulmonary hypertension	0	0	0	1 (1.2%)	NS
NICU admission	13 (3.6%) *	1 (1.1%) ‡	6 (12%) †	9 (11.4%)**	<0.05
NICU stay [(days, median (min-max)]	1 (1-1)	1 (1-1)	1 (1-2)	2 (2-15)	NS
Polycythemia	11 (3%)	3 (3.4%)	4 (8%)	5 (6.3%)	NS
Hypoglycemia	7 (1.9%)	2 (2.3%)	0	2 (2.5%)	NS
Hypocalcemia	2 (0.5%)	0	1 (2%)	2 (2.5%)	NS
Hypomagnesemia	6 (1.6%)	2 (2.3%)	3 (6%)	4 (5%)	NS

NS: not significant

* $p<0.05$, Group 1 vs. Group 3
** $p<0.05$, Group 1 vs. Group 4
† $p<0.05$, Group 2 vs. Group 3
‡ $p<0.05$, Group 2 vs. Group 4

observed increased incidences of neonatal hypoglycemia and hyperbilirubinemia in women with single-value abnormality on OGTT. In our study significantly more women with single-value abnormality exhibited neonatal jaundice and NICU admission rates than those of controls or positive glucose challenge test-normal OGTT results. Besides, the 1-minute Apgar score was also different lower in patients with single-value abnormality than that in the controls. In line with our results, women with single-value abnormality on OGTT were found to be at risk for delivering macrosomic infants compared to controls, but had similar icterus, RDS, tachypnea, fractures and death rates as women with GDM or controls (8,9,12). Also, we found similar fetal macrosomia and LGA rates in women with GDM and impaired glucose intolerance as in another recent study (27). Similar to our results Langer et al. (4) demonstrated that patients with single-value abnormality would have a lower incidence of adverse perinatal outcome if they were treated. In addition, same authors concluded that pregnant women with single-value abnormality on OGTT should be regarded as GDM and should be followed and treated like patients with GDM (4,15). The critical point in the management of GDM patients and likewise in patients with impaired glucose tolerance (single-value abnormality on OGTT) is tight glycemic control. This fact could explain why most perinatal negative outcomes did not increase in our patients with impaired glucose tolerance under tight glucose control. Besides, the 50-gr glucose challenge test has the greatest sensitivity at 34 weeks although it is usually performed between the 24th and 28th weeks' of gestation (28). We did not repeat the OGTT in this particular week of pregnancy. Thus, our patients with single-value abnormality on OGTT may have been classified as GDM if they had been re-tested.

In conclusion, classic GDM is associated with abnormal fetal outcome, but even milder degrees of glucose intolerance can cause fetal and neonatal morbidity. The diagnosis of GDM is associated with a high incidence of some adverse perinatal outcome. However, women with abnormal diabetes screening tests and negative OGTT or women with single-value abnormality on OGTT seem not to be prone to develop adverse perinatal outcome. Although future studies will be needed to rectify the role of tight glycemic control in pregnant women with impaired glucose tolerance, our study demonstrates similar results in terms of morbidity in such patients.

References

1. American Diabetes Association position statement: gestational diabetes mellitus. Diabetes Care 2003;26 (Suppl. 1):S103-5.
2. Beischer NA, Wein P, Sheedy MT, Steffen B. Identification and treatment of women with hyperglycaemia diagnosed during pregnancy can significantly reduce perinatal mortality rates. Aust NZ J Obstet Gynaecol 1996;36:239-47.
3. Langer O. Is normoglycemia the correct threshold to prevent complications in the pregnant diabetic patient? Diabetes Rev 1996;4:2-10.
4. Langer O, Levy S, Brustman L et al. Glycemic control in GDM: how tight is tight enough: small for gestational age versus large for gestational age? Am J Obstet Gynecol 1989;161:646-53.
5. Khan KS, Syed AH, Hashmi FA, Rizvi JH. Relationship of fetal macrosomia to a 75-g glucose challenge test in nondiabetic pregnant women. Aust NZ J Obstet Gynecol 1994;34:24-7.
6. Hod M, Rabinerson D, Kaplan B et al. Perinatal complications following gestational diabetes mellitus: how sweet is ill? Acta Obstet Gynecol Scand 1996;75:809-15.
7. Jacobson JD, Cousins L. A population-based study of maternal and perinatal outcome in patients with gestational diabetes. Am J Obstet Gynecol 1989;161:981-6.
8. Langer O, Brustman L, Anyaegbunam A, Mazze R. The significance of one abnormal glucose tolerance test value on adverse outcome in pregnancy. Am J Obstet Gynecol 1987;157:758-63.
9. Lindsay MK, Graves W, Klein L. The relationship of one abnormal glucose tolerance test value and pregnancy complications. Obstet Gynecol 1989;73:103-6.
10. Vambergue A, Nuttens MC, Verier-Mine O et al. Is mild gestational hyperglycaemia associated with maternal and neonatal complications? The Diagest Study. Diabet Med 2000;17:203-8.
11. Sendag F, Terek MC, Itil IM et al. Maternal and perinatal outcomes in women with gestational diabetes mellitus as compared to nondiabetic controls. J Reprod Med 2001;46:1057-62.
12. Berkus MD, Langer O. Glucose tolerance test: degree of glucose abnormality correlates with neonatal outcome. Obstet Gynecol 1993;81:344-8.
13. Bofill JA, Andrew ME, Kincaid TA et al. Lowering the threshold for the diagnosis of gestational diabetes. Am J Obstet Gynecol 1996;175(4 Pt 1):961-5.
14. Lucas MJ, Lowe TW, Bowe L, McIntire DD. Class A1 gestational diabetes: a meaningful diagnosis? Obstet Gynecol 1993;82:260-5.
15. Ergin T, Lembet A, Duran H et al. Does insulin secretion in patients with one abnormal glucose tolerance test value mimic gestational diabetes mellitus? Am J Obstet Gynecol 2002;186:204-9.
16. Langer O. Maternal glycemic criteria for insulin therapy in gestational diabetes mellitus. Diabetes Care 1998;21 (Suppl. 2) B91-B96.
17. Hod M, Merlob P, Friedman S, Schoenfeld A. Ovadia J. Gestational diabetes mellitus. A survey of perinatal complications in the 1980s. Diabetes 1991;40 (Suppl. 2):74-8.
18. Langer O. A spectrum of glucose threshlods may effectively prevent complications in the pregnant diabetic patient. Semin Perinatol 2002;26:196-205.
19. Garcia-Patterson A, Corcoy R, Balsells M et al. In pregnancies with gestational diabetes mellitus and intensive therapy, perinatal outcome is worse in small-for gestational-age newborns. Am J Obstet Gynecol 1998;179:481-5.
20. Nold JL, Georgieff MK. Infants of diabetic mothers. Pediatr Clin North Am 2004;51:619-37.
21. Thompson DM, Dansereau J, Creed M, Ridell L. Tight glucose control results in normal perinatal outcome in 150 patients with gestational diabetes. Obstet Gynecol 1994;83:362-6.
22. Greco P, Loverro G, Selvaggi L. Does gestational diabetes represent an obstetrical risk factor? Gynecol Obstet Invest 1994;37:242-5.
23. De Veciana M, Major CA, Morgan MA et al. Postprandial versus preprandial blood glucose monitoring in women with gestational diabetes mellitus requiring insulin therapy. N Engl J Med 1995;333:1237-41.
24. Jovanovich L, Peterson CM. Screening for gestational diabetes: optimum timing and criteria for retesting. Diabetes 1985;34 (Suppl.2):21-3.
25. Phillipou G. The 1-h 50-g glucose challenge does not predict large-for-gestational age infants. Diabet Med 1992;9:81-3.
26. Weiner CP. Effect of varying degrees of normal glucose metabolism on maternal and perinatal outcome. Am J Obstet Gynecol 1988;159:862-70.
27. Schaefer-Graf UM, Kjos SL, Kılavuz Ö et al. Determinants of fetal growth at different periods of pregnancies complicated by gestational diabetes mellitus or impaired glucose tolerance. Diabetes Care 2003;26:193-8.
28. Khandelwal M, Homko C, Reece EA. Gestational diabetes mellitus: controversies and current opinions. Curr Opin Obstet Gynecol 1999;11:157-65.