Progression to Gestational Diabetes Mellitus in Pregnant Women with One Abnormal Value in Repeated Oral Glucose Tolerance Tests

Sunyoung Kang¹, Min Hyoung Kim², Moon Young Kim², Joon-Seok Hong³, Soo Heon Kwak¹, Sung Hee Choi⁴, Soo Lim⁴, Kyong Soo Park¹, Hak C. Jang⁴, ⁵

¹Department of Internal Medicine, Seoul National University Hospital, Seoul National University College of Medicine, Seoul,
²Department of Obstetrics and Gynecology, Cheil General Hospital & Women’s Healthcare Center, Dankook University College of Medicine, Seoul,
³Department of Obstetrics and Gynecology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam,
⁴Department of Internal Medicine, Seoul National University College of Medicine, Seoul,
⁵Department of Internal Medicine, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea

Background: Women with one abnormal value (OAV) in a 100 g oral glucose tolerance test (OGTT) during pregnancy are reported to have an increased risk of adverse pregnancy outcomes. However, there is limited data about whether women with OAV will progress to gestational diabetes mellitus (GDM) when the OGTT is repeated.

Methods: To identify clinical and metabolic predictors for GDM in women with OAV, we conducted a retrospective study and identified women with OAV in the OGTT done at 24 to 30 weeks gestational age (GA) and repeated the second OGTT between 32 and 34 weeks of GA.

Results: Among 137 women with OAV in the initial OGTT, 58 (42.3%) had normal, 40 (29.2%) had OAV and 39 (28.5%) had GDM in the second OGTT. Maternal age, prepregnancy body mass index, weight gain from prepregnancy to the second OGTT, GA at the time of the OGTT, and parity were similar among normal, OAV, and GDM groups. Plasma glucose levels in screening tests were different (151.8±15.7, 155.8±14.6, 162.5±20.3 mg/dL, P<0.05), but fasting, 1-, 2-, and 3-hour glucose levels in the initial OGTT were not. Compared to women with screen negative, women with untreated OAV had a higher frequency of macrosomia.

Conclusion: We demonstrated that women with OAV in the initial OGTT significantly progressed to GDM in the second OGTT. Clinical parameters predicting progression to GDM were not found. Repeating the OGTT in women with OAV in the initial test may be helpful to detect GDM progression.

Keywords: Diabetes, gestational; Glucose tolerance test; Pregnancy outcome

INTRODUCTION

Gestational diabetes mellitus (GDM) is defined as any degree of glucose intolerance with the first recognition during pregnancy, regardless of whether the condition started before pregnancy or not [1]. Because of the recent obesity epidemic and the increase in type 2 diabetes mellitus in general, there has been an increase in undiagnosed type 2 diabetes mellitus in
This study is a retrospective observational study. This study was approved by the Institutional Review Board (IRB) of Seoul National University Bundang Hospital (B-1808/486-105). Informed consent was waived by the IRB. We collected patient data from Cheil General Hospital & Women's Healthcare Center. Since 1991, pregnant women have been screened for GDM at 24 to 28 weeks, as recommended by the Third International Workshop-Conference on Gestational Diabetes Mellitus [13]. If the plasma glucose levels measured 1 hour after the 50 g oral glucose challenge tests (GCT) in pregnant women were greater than or equal to 130 mg/dL, they were scheduled for a 100 g OGTT before 30 weeks. Women who had OAV in the first OGTT were recommended for re-testing at 32 to 34 weeks. From January 1996 to June 1997 we identified 149 women with OAV in the first OGTT. However, nine women performed the first OGTT after 30 weeks, and three women refused to do the second OGTT. Thus, 137 women were enrolled in this study.

All pregnant women scheduled for an OGTT were instructed to consume a normal diet containing at least 150 g of carbohydrates per day for 3 days, and to perform usual physical activities. They were encouraged to sit quietly throughout the test, and they were not allowed to eat, drink, and smoke. Glucose tolerance tests were done between 8:00 AM to 9:00 AM, after overnight fasts of at least 8 hours, but no more than 14 hours. After fasting, blood samples were obtained, and the women were instructed to drink a 100 g glucose solution within 5 minutes. Blood samples were drawn 1, 2, and 3 hours after glucose intake. Plasma glucose levels were measured with a YSI 2300-STAT glucose analyzer (Yellow Springs Instrument Co., Yellow Springs, OH, USA). Plasma insulin concentrations were measured using a Human Specific Radioimmunoassay Kit (Linco Research Inc., St. Louis, MO, USA). The intra-assay variance of insulin was 4.5%, and the inter-assay variance of insulin was 8.9%.

Based on the results of the second OGTT (32 to 34 weeks), we classified pregnant women who had OAV in the first OGTT into three groups: normal, OAV, and GDM. The women were considered to have OAV if one glucose value was greater than or equal to the following values: fasting, 105 mg/dL; 1 hour, 190 mg/dL; 2 hours, 165 mg/dL; and 3 hours, 145 mg/dL. A GDM diagnosis was made if two or more glucose levels met or exceeded the cutoff values [13]. Insulin secretion was assessed using the insulinogenic index at 60 minutes (IGI60) and the oral dispositional index (ODI). Insulin sensitivity was evaluated using the Matsuda insulin sensitivity index (ISI). IGI60 was calculated as follows: [insulin (60 minutes)−insulin (0
Progression to GDM in women with OAV

minute)/[glucose (60 minutes)−glucose (0 minute)] [14]. The Matsuda ISI was calculated as follows: 10,000/(fasting glucose×fasting insulin×mean glucose×mean insulin) [15]. The ODI was calculated as follows: IGI60 × ISI of Matsuda [16]

Neonatal and pregnancy outcomes were evaluated using the following parameters: gestational age (GA) at delivery, birth weight, Apgar score, and other perinatal complications. LGA was defined as a birth weight greater than or equal to the 90th percentile for that GA [17]. Macrosomia was defined as a newborn weighing more than 4,000 g at birth.

The women who developed GDM, as determined by the results of the second OGTT, were managed with medical nutritional therapy and exercise [5]. If maternal hyperglycemia persisted after diet and exercise therapy, insulin therapy was added. However, we did not provide any medical advice or treatment to women with the result of normal and OAV in the second OGTT.

We analyzed clinical characteristics, results of the first OGTT, and pregnancy outcomes using IBM SPSS Statistics version 22.0 (IBM Corp., Armonk, NY, USA). Continuous variables were analyzed with the analysis of variance (ANOVA) test (normally distributed data) and the Kruskal-Wallis test (non-normally distributed data). Normally distributed data were expressed as mean±SD, and Turkey’s method was used for post hoc analysis. Non-normally distributed data were expressed as median and a 95% confidence interval, and a Mann-Whitney test was used for post hoc analysis. Categorical data were compared using the chi-square test and expressed in percentages. To compare the pregnancy outcomes of the three groups (normal, OAV, and GDM) with those of the screen-negative group, which was characterized in our previous article [18], we used a two-sample t-test (R program version 3.4.0). P values less than 0.05% were considered significant.

RESULTS

Among 137 pregnant women with OAV in the first OGTT, 39 women (28.5%) progressed to being diagnosed with GDM in the second OGTT, done between 32 to 34 weeks. Still 29.2% of the women maintained their OAV status, and the rest (42.3%) recovered and exhibited a normal glucose tolerance status.

Table 1. Clinical characteristics of study subjects according to the results of the second oral glucose tolerance test

| Characteristic          | Second OGTT | Screen negative | P valuea | P valueb |
|-------------------------|-------------|-----------------|----------|----------|
|                         | Normal      | OAV             | GDM      | (n=2,120) | Normal | OAV | GDM |
| Number                  | 58 (42.3)   | 40 (29.2)       | 39 (28.5) |          |        |
| At screening test       |             |                 |          |          |
| Age, yr                 | 30.3±3.9    | 31.1±3.8        | 30.0±3.8 | 0.464    | 28.8±3.3 | <0.001 | <0.001 |
| Height, cm              | 157.4±5.9   | 156.9±4.4       | 157.5±4.4| 0.830    | 159.9±4.1 | <0.001 | <0.001 |
| Prepregnancy weight, kg | 54.8±8.5    | 56.0±8.3        | 54.7±8.7 | 0.763    | 51.4±6.4 | <0.001 | <0.001 |
| Prepregnancy BMI, kg/m² | 22.1±3.0    | 22.8±3.3        | 22.1±3.4 | 0.539    | 20.1±2.3 | <0.001 | <0.001 |
| Obesity (BMI ≥25 kg/m²) | 11 (19)     | 10 (25)         | 7 (17.9) | 0.691    | 75 (3.5) | <0.001 | <0.001 |
| Family history of DM    | 15 (25.9)   | 12 (30.0)       | 17 (43.6) | 0.176    | 229 (14.1)| 0.001  | <0.001 |
| Parity                  | 0.38±0.5    | 0.38±0.7        | 0.23±0.4 | 0.388    | 0.36±0.53 | 0.777  | 0.815 |

Values are presented as number (%) or mean±standard deviation.
OGTT, oral glucose tolerance test; OAV, one abnormal value; GDM, gestational diabetes mellitus; BMI, body mass index; DM, diabetes mellitus.

aP for comparison among the three groups, bP for comparison between Screen negative group and each three group.
results of the second OGTT, were not statistically different at the time of the screening test, and the first and second OGTT. As shown in Table 1, maternal age, height, weight, prepregnancy body mass index (BMI), and parity were very similar among the three groups. The frequencies of obese women, as defined by a BMI greater than or equal to 25 kg/m², were 19% in the normal, 25% in the OAV, and 17.9% in the GDM group. Differences in obesity among the three groups were not significant. The frequencies of the first-degree family history of diabetes mellitus were 43.6% in the GDM group, 30% in the OAV group, and 25.9% in the normal group, but these differences were not statistically significant. Compared with the screen-negative group, each of the three groups had significantly higher frequencies of obesity and family history of diabetes. The maternal age, weight, and prepregnancy BMI of the three groups were also significantly higher than those of the screen-negative group. GA and maternal weight at the time of the first and second OGTTs were similar among the three groups. There was also no difference in weight gain from prepregnancy up until the time of the second OGTT.

Table 2 denotes plasma glucose concentrations of the GCT and the first OGTT in the three groups, classified by the result of the second OGTT. Plasma glucose concentrations of the GCT were highest in the GDM, intermediate in the OAV, and lowest in the normal group. Fasting, 1, 2, and 3 hours glucose concentrations of the first OGTT were not significantly different among the three groups. However, the mean glucose levels at fasting and at 1 hour increased for each group in order from normal to OAV and GDM group.

We also compared the insulin response measured in the first OGTT among the three groups. Mean insulin concentrations 1 hour after glucose intake were highest in the OAV, intermediate in the normal, and lowest in the GDM group, but they were not statistically different. Insulin concentrations 1 and 2 hours after glucose intake in the GDM group were significantly lower compared with those in the OAV group. The IGI60 and Matsuda ISI levels were not different among the three groups. The ODI, a composite index of insulin secretion for insulin re-
Finally, we compared pregnancy outcomes among the three groups, and we also compared these outcomes with those of the screen-negative group (Table 3). There were no differences in GA at delivery, Apgar scores, and birth weight among the three groups. The frequencies of LGA, macrosomia, preterm delivery, and other adverse pregnancy outcomes, such as primary Caesarean section and preeclampsia, or pregnancy-induced hypertension, were comparable among the three groups. When we compared the pregnancy outcomes of the three groups with those of the screen-negative group, the mean GA at delivery was earlier in the normal and GDM groups, but similar in the OAV group. Mean birth weight of the OAV group was higher than that of the screen-negative group. The mean Apgar score at 5 minutes from birth of the three groups was significantly lower than that of the screen-negative group. LGA frequencies in the normal, OAV, and GDM groups were about two times higher than those in the screen-negative group. Macrosomia frequency was 12.8% in the OAV group, which was significantly higher than in the screen-negative group. The frequency of preterm delivery in the normal group was higher than that in the screen-negative group, and the frequencies of total Caesarian section in each of the three groups were about two times higher than those in the screen-negative group.

**DISCUSSION**

Of the 137 women who had OAV in the OGTT performed between 24 to 30 weeks, 28.5% had developed GDM as detected by a second OGTT performed between 32 to 34 weeks. The GDM group showed higher glucose levels in the GCT compared with the normal group. The GDM group also had significantly decreased insulin levels at the 1 and 2 hours of first OGTT compared to the levels in the OAV group. These results suggest that β-cell dysfunction might be associated with the development of GDM in women with OAV. Previous studies demonstrated that women who had limited β-cell capacity for compensating increased insulin resistance during pregnancy were likely to develop GDM [19,20]. In addition, we also found that Korean women with previous GDM, who showed normal glucose tolerance after delivery, had lower β-cell secretory capacity compared with women without GDM [21]. However, there was no difference in the IGI60 and ODI levels among the three groups in this study. Although there is some controversy about the insulinogenic index at 30 minutes (IGI30) as a valid test method [14,22,23], IGI30 and ODI are
widely used for clinical assessment of β-cell function. One study showed that IGI60 from the OGTT might be used as a surrogate for IGI30 [24], but further studies are needed to validate IGI60 as an assessment method for the β-cell function.

Currently, GDM is diagnosed with either a one-step or two-step approach [8]. The two-step approach is based on a screening test using a 50 g GCT followed by a 3-hour, 100 g OGTT. GDM is diagnosed when at least two abnormal glucose values are detected in the 3-hour OGTT. In 2010, the IADPSG recommended the use of a one-step 75 g OGTT to diagnose GDM. The diagnostic threshold for GDM was based on glucose levels which increased the risk for adverse pregnancy outcome 1.75 times, as determined in the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study [3]. However, the one-step approach was expected to increase the incidence of GDM about three times (from 5%–6% to 15%–20%) [25]. In 2013, the National Institutes of Health (NIH) recommended the use of the two-step approach, since clinical data supporting the benefits and cost effectiveness of the one-step strategy were lacking [26]. The two-step approach has different cutoffs for the 3-hour OGTT. The diagnostic thresholds suggested by Carpenter and Coustan are lower than those suggested by the National Diabetes Data Group (NDDG), which results in an increase of GDM incidences by 50% compared with the former threshold [27]. As different diagnostic criteria predict different degrees of maternal and fetal risk, experts are still debating about the appropriate diagnostic thresholds.

The ACOG has supported the two-step approach, but it recently mentioned that one elevated glucose value in the 100 g OGTT might be sufficient to diagnose GDM [6]. There are several previous studies about the significance of OAV, and some studies reported that women with OAV had a higher risk of adverse maternal and neonatal outcomes compared with women with normal OGTT [9,10,28]. However, if we followed the ACOG suggestion, the incidences of GDM would significantly increase, and some pregnant women may not actually need intensive GDM treatment.

Pregnancy is characterized by increased insulin resistance caused by placental hormones, such as progesterone, cortisol, placental lactogen, prolactin, and growth hormone [29]. Considering that insulin resistance continuously increases from the second trimester to late pregnancy, performing a second OGTT on women with OAV in the first OGTT may help to detect women with GDM who need intensive treatment. However, in this study, we could not find out clinical predictors for progressing GDM in women with OAV, which makes repeating the OGTT more necessary to diagnose GDM.

In this study, macrosomia frequency was significantly higher in the OAV group compared with the screen-negative group. However, all three groups showed increased frequencies of LGA and total Cesarian section, and lower Apgar score at 5 minutes after birth compared with the screen-negative group. There is no consensus as to whether women with OAV should be managed similarly to women with GDM or not. Berkus and Langer [30] and Langer et al. [31] compared perinatal outcomes of normal OGTT group, OAV group, and GDM group that received treatment. The OAV group showed a high incidence of large infants (macrosomia and LGA) and neonatal complications compared with the normal group and the GDM group with treatment [30,31]. Another study showed different results. Forest et al. [32] compared the perinatal outcomes between four groups: normal, OAV women with treatment, OAV women without treatment, and the GDM group. There was no statistical difference in the perinatal outcomes among OAV women with treatment, OAV women without treatment, and women with a normal OGTT [32]. In our study, women with treated GDM diagnosed in the second OGTT had lower incidences of macrosomia compared with OAV group who had untreated. This result supports the premise that women with OAV may benefit from repeating the OGTT, which can diagnose cases of GDM in women who need treatment to reduce maternal and perinatal complications.

This study has several limitations. First, it is a retrospective study, and the pregnancy outcomes of the screen-negative group were obtained from our previous study. Even though the data of pregnancy outcomes were obtained from the same hospital, there was a 3-year time difference between testing the women with OAV and the screen-negative group. Second, the number of women with OAV may not have been enough to compare pregnancy outcomes in a statistically significant manner.

In conclusion, this study showed that a significant proportion of women with OAV in the OGTT, done prior to 30 weeks of GA, developed GDM as diagnosed by a second OGTT, done between 32 to 34 weeks. Thus, repeating the OGTT can be helpful to determine GDM in women with OAV.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.
AUTHOR CONTRIBUTIONS

Conception or design: M.Y.K., S.H.K., H.C.J.
Acquisition, analysis, or interpretation of data: S.K., M.H.K., J.S.H., S.H.K., S.H.C., S.L.
Drafting the work or revising: S.K., M.Y.K., S.H.K., K.S.P., H.C.J.
Final approval of the manuscript: S.K., M.H.K., M.Y.K., J.S.H., S.H.K., S.H.C., S.L., K.S.P., H.C.J.

ORCID

Sunyoung Kang https://orcid.org/0000-0002-7705-6614
Moon Young Kim https://orcid.org/0000-0001-8881-2027
Hak C. Jang https://orcid.org/0000-0002-4188-6536

ACKNOWLEDGMENTS

We really thank to obstetricians of Cheil General Hospital & Women's Healthcare Center for their contributions.

REFERENCES

1. Report of the expert committee on the diagnosis and classification of diabetes mellitus. Diabetes Care 1997;20:1183-97.
2. Lawrence JM, Contreras R, Chen W, Sacks DA. Trends in the prevalence of preexisting diabetes and gestational diabetes mellitus among a racially/ethnically diverse population of pregnant women, 1999-2005. Diabetes Care 2008;31:899-904.
3. International Association of Diabetes and Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, Dyer AR, Leiva Ad, Hod M, Kitzmiler JL, Lowe LP, McIntyre HD, Oats JJ, Omori Y, Schmidt MI. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 2010;33:676-82.
4. DeSisto CL, Kim SY, Sharma AJ. Prevalence estimates of gestational diabetes mellitus in the United States, Pregnancy Risk Assessment Monitoring System (PRAMS), 2007-2010. Prev Chronic Dis 2014;11:E104.
5. Jang HC, Cho NH, Min YK, Han IK, Jung KB, Metzger BE. Increased macrosomia and perinatal morbidity independent of maternal obesity and advanced age in Korean women with GDM. Diabetes Care 1997;20:1582-8.
6. Committee on Practice Bulletins Obstetrics. Practice Bulletin No. 180: gestational diabetes mellitus. Obstet Gynecol 2017;130:e17-37.
7. Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Donovan L. Benefits and harms of treating gestational diabetes mellitus: a systematic review and meta-analysis for the U.S. Preventive Services Task Force and the National Institutes of Health Office of Medical Applications of Research. Ann Intern Med 2013;159:123-9.
8. American Diabetes Association. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2018. Diabetes Care 2018;41:S13-27.
9. Roeckner JT, Sanchez-Ramos L, Jijon-Knupp R, Kaufman AM. Single abnormal value on 3-hour oral glucose tolerance test during pregnancy is associated with adverse maternal and neonatal outcomes: a systematic review and metaanalysis. Am J Obstet Gynecol 2016;215:287-97.
10. Kim HS, Chang KH, Yang JI, Yang SC, Lee HJ, Ryu HS. Clinical outcomes of pregnancy with one elevated glucose tolerance test value. Int J Gynaecol Obstet 2002;78:131-8.
11. Catalano PM, Avallone DA, Drago NM, Amini SB. Reproducibility of the oral glucose tolerance test in pregnant women. Am J Obstet Gynecol 1993;169:874-81.
12. Munang YN, Noubiap JJ, Danwang C, Sama JD, Azabji-Kenfack M, Mbanya JC, Sobngwi E. Reproducibility of the 75 g oral glucose tolerance test for the diagnosis of gestational diabetes mellitus in a sub-Saharan African population. BMC Res Notes 2017;10:622.
13. Metzger BE. Summary and recommendations of the Third International Workshop-Conference on Gestational Diabetes Mellitus. Diabetes 1991;40 Suppl 2:197-201.
14. Stumvoll M, Mitra A, Pimenta W, Jenden T, Yki-Jarvinen H, Van Haefen T, Renn W, Gerich J. Use of the oral glucose tolerance test to assess insulin release and insulin sensitivity. Diabetes Care 2000;23:295-301.
15. Matsuda M, DeFronzo RA. Insulin sensitivity indices obtained from oral glucose tolerance testing: comparison with the euglycemic insulin clamp. Diabetes Care 1999;22:1462-70.
16. Abdul-Ghani MA, Williams K, DeFronzo RA, Stern M. What is the best predictor of future type 2 diabetes? Diabetes Care 2007;30:1544-8.
17. Korean Pediatric Society. Normal value of Korean children. Seoul: Medical Culture History; 1992.
18. Jang HC, Cho YM, Park KS, Kim SY, Lee HK, Kim MY, Yang JH, Shin SM. Pregnancy outcome in Korean women with ges-
tional diabetes mellitus diagnosed by the Carpenter-Coustan criteria. J Korean Diabetes Assoc 2004;28:122-30.
19. Catalano PM, Huston L, Amini SB, Kalhan SC. Longitudinal changes in glucose metabolism during pregnancy in obese women with normal glucose tolerance and gestational diabetes mellitus. Am J Obstet Gynecol 1999;180:903-16.
20. Buchanan TA, Xiang AH. Gestational diabetes mellitus. J Clin Invest 2005;115:485-91.
21. Lim S, Choi SH, Park YJ, Park KS, Lee HK, Jang HC, Cho NH, Metzger BE. Visceral fatness and insulin sensitivity in women with a previous history of gestational diabetes mellitus. Diabetes Care 2007;30:348-53.
22. Phillips DJ, Clark PM, Hales CN, Osmond C. Understanding oral glucose tolerance: comparison of glucose or insulin measurements during the oral glucose tolerance test with specific measurements of insulin resistance and insulin secretion. Diabet Med 1994;11:286-92.
23. Hanson RL, Pratley RE, Bogardus C, Narayan KM, Roumain JM, Imperatore G, Fagot-Campagna A, Pettitt DJ, Bennett PH, Knowler WC. Evaluation of simple indices of insulin sensitivity and insulin secretion for use in epidemiologic studies. Am J Epidemiol 2000;151:190-8.
24. Tura A, Kautzky-Willer A, Pacini G. Insulinogenic indices from insulin and C-peptide: comparison of beta-cell function from OGTT and IVGTT. Diabetes Res Clin Pract 2006;72:298-301.
25. Sacks DA, Hadden DR, Maresh M, Deerochanawong C, Dyer AR, Metzger BE, Lowe LP, Coustan DR, Hod M, Oats JJ, Persson B, Trimble ER; HAPO Study Cooperative Research Group. Frequency of gestational diabetes mellitus at collaborating centers based on IADPSG consensus panel-recommended criteria: the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study. Diabetes Care 2012;35:526-8.
26. Vandorsten JP, Dodson WC, Espeland MA, Grobman WA, Guise JM, Mercer BM, Minkoff HL, Poindexter B, Prosser LA, Sawaya GF, Scott JR, Silver RM, Smith L, Thomas A, Tita AT. NIH consensus development conference: diagnosing gestational diabetes mellitus. NIH Consens State Sci Statements 2013;29:1-31.
27. Ferrara A, Hedderson MM, Quesenberry CP, Selby JV. Prevalence of gestational diabetes mellitus detected by the national diabetes data group or the Carpenter and Coustan plasma glucose thresholds. Diabetes Care 2002;25:1625-30.
28. Gruendhammer M, Brezinka C, Lechleitner M. The number of abnormal plasma glucose values in the oral glucose tolerance test and the feto-maternal outcome of pregnancy. Eur J Obstet Gynecol Reprod Biol 2003;108:131-6.
29. Buchanan TA, Xiang AH, Page KA. Gestational diabetes mellitus: risks and management during and after pregnancy. Nat Rev Endocrinol 2012;8:639-49.
30. Berkus MD, Langer O. Glucose tolerance test: degree of glucose abnormality correlates with neonatal outcome. Obstet Gynecol 1993;81:344-8.
31. 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.
32. Forest JC, Masse J, Garrido-Russo M. Glucose tolerance test during pregnancy: the significance of one abnormal value. Clin Biochem 1994;27:299-304.