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How high is too high in cutoff levels from 50-g glucose challenge test

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Objective
To determine the highest 50-g glucose challenge test (GCT) value that indicates no further diagnostic test is needed to confirm a diagnosis of gestational diabetes mellitus (GDM) under the criteria of National Diabetes Data Group (NDDG) or the Carpenter and Coustan (C&C) and fasting glucose thresholds from the International Association of Diabetes and Pregnancy Study Group (IADPSG).

Methods
We collected the 50-g GCT results from 16,560 pregnancies and identified 2,457 gravidas with positive 50-g GCT (≥130 mg/dL) values who underwent the 100-g glucose tolerance test. We investigated GDM prevalence in pregnancies with positive 50-g GCT according to the respective diagnostic thresholds and determined the 50-g GCT cutoff values with 100% positive predictive value for GDM under each diagnostic threshold.

Results
Twelve point five percent (306/2,457), 20.0% (492/2,457), and 9.6% (235/2,457) met the diagnostic criteria of GDM with the application of NDDG, C&C criteria, and fasting glucose thresholds from IADPSG (≥92 mg/dL), respectively. We also found that the prevalence of GDM increased with increasing 50-g GCT values using each diagnostic criterion. Importantly, we identified that all subjects with a 50-g GCT value ≥223, ≥217, or ≥228 mg/dL can be exclusively diagnosed as having gestational diabetes according to the criteria of NDDG, C&C, and fasting glucose thresholds from IADPSG, respectively.

Conclusion
We propose that women with a 50-g GCT screening value ≥228 mg/dL can be reliably omitted from further confirmative tests for GDM, such as 100- or 75-g glucose tolerance test.

Keywords: Diabetes, gestational; Glucose tolerance test; Positive predictive value

Introduction

Gestational diabetes mellitus (GDM) is one of the most common medical disorders during pregnancy with an increasing worldwide prevalence [1]. Many studies have already shown an association between maternal hyperglycemia and adverse perinatal outcomes such as macrosomia, which result in traumatic delivery and neonatal metabolic imbalances, including hypoglycemia or hypocalcemia. In addition to these short-term outcomes, birth from a diabetic mother is linked to long-term consequences such as obesity and to the risk of development of type 2 diabetes mellitus later in life [1-3].

Despite the importance of GDM, no consensus on the

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diagnosis of GDM has yet been established [1]. A two-step method, consisting of a screening 1-hour 50-g glucose challenge test (GCT) and a diagnostic 3-hour 100-g glucose tolerance test (GTT), in GCT-positive patients has been endorsed by the American college of Obstetrics and Gynecologist and National Institute of Health [1,4]. In addition, the National Diabetes Data Group (NDDG) and Carpenter and Coustan (C&C) criteria [5] are used compositely as diagnostic cutoff values for the 100-g GTT; however, controversies remain on which diagnostic criteria would be better to apply [6,7]. Another one-step method of 75-g GTT from the HAPO (Hyperglycemia and Adverse Pregnancy Outcomes) study [8] was recommended by the International Association of Diabetes and Pregnancy Study Group (IADPSG), indicating that one abnormal value is enough for the diagnosis of GDM (fasting ≥92 mg/dL, 1 hour ≥180 mg/dL, 2 hours ≥153 mg/dL).

In addition to these controversies, physicians question the necessity of the diagnostic GTT for patients with very high 50-g GCT levels, although 50-g GCT results cannot replace the diagnostic GTT [9]. Interestingly, while many studies have reported a lower cutoff value in the 2-step screening [10-16], we found that very few studies have been performed to address this practical question: at what high GCT value can we omit further diagnostic tests for GDM? Moreover, comparison of these upper cutoff values according to different diagnostic tests of GDM (NDDG and C&C) and fasting glucose levels by IADPSG is lacking.

Given the aforementioned background, we aimed to determine the 50-g screen cutoff value that would omit the need for further diagnostic GTT of GDM under the criteria of NDDG or C&C and for fasting glucose thresholds level from IADPSG using a 13-year database in our institution.

Materials and methods

We conducted a retrospective cohort study of 16,560 pregnancies that had been screened for GDM using the 50-g GCT at our institution from January 2001 to December 2013. GDM screening was generally performed between 24 and 28 weeks gestation, and early screening commenced as soon as it was feasible in women with GDM risk factors such as older age (≥35 years old of age), obesity (≥30 kg/m^2 of body mass index), and a history of GDM or macrosomia (over 4 kg of birthweight). In this high risk group, women with values ≥130 mg/dL were considered screen-positive and underwent 100-g GTT. In negatively screened high-risk pregnancies, the 50-g GCT was repeated between 24 and 28 weeks gestation. Except in the high risk group, patients with values ≥140 mg/dL were considered screen-positive and underwent 100-g GTT. In clinical practice, NDDG criteria had been used as the diagnostic criteria for GDM until December 2005 in our institution, at which point C&C criteria were adopted. In this study, we applied the criteria of NDDG and C&C for the diagnosis of GDM in the study population. In addition, although the one-step 75-g GTT has not been implemented in our institution, for this study, we considered pregnant women with fasting glucose levels ≥92 mg/dL at the time of the 100-g GTT as having GDM according to IADPSG thresholds. To investigate GDM prevalence in pregnancies with positive 50-g GCT according to the respective diagnostic thresholds, we divided all patients into eight subgroups based on the 50-g GCT results (group 1, 130 to 139 mg/dL [n=315]; group 2, 140 to 149 mg/dL [n=844]; group 3, 150 to 159 mg/dL [n=575]; group 4, 160 to 169 mg/dL [n=306]; group 5, 170 to 179 mg/dL [n=183]; group 6, 180 to 189 mg/dL [n=97]; group 7, 190 to 199 mg/dL [n=74]; group 8, ≥200 mg/dL [n=63]).

Finally, we conducted receiver operating characteristic (ROC) curve analysis to identify the optimal 50-g GCT cutoff point for the confirmation of GDM without the need for further diagnostic tests. As for diagnostic criteria of GDM, a 100-g GTT according to the NDDG or the C&C criteria and fasting glucose thresholds from IADPSG were used and compared. Linear by linear analysis test was used to compare the outcome rates, and all analyses were performed using IBM SPSS ver. 19.0 (IBM Corp., Armonk, NY, USA). This study was approved by institutional review board (IRB) from Samsung Medical Center and the Sungkyunkwan University School of Medicine, South Korea (IRB no. 2015-04-111).

Results

1. Recruitment of study population

Of the 16,560 consecutive pregnant women, 11,636 showed negative 50-g GCT results, defined as <130 mg/dL, which is a screen-negative rate of 70.3%. In addition, 10.9% (1 806/16,560) of women showed 50-g GCT results between 130 and 139 mg/dL, while 18.8% (3,118/16,560) showed

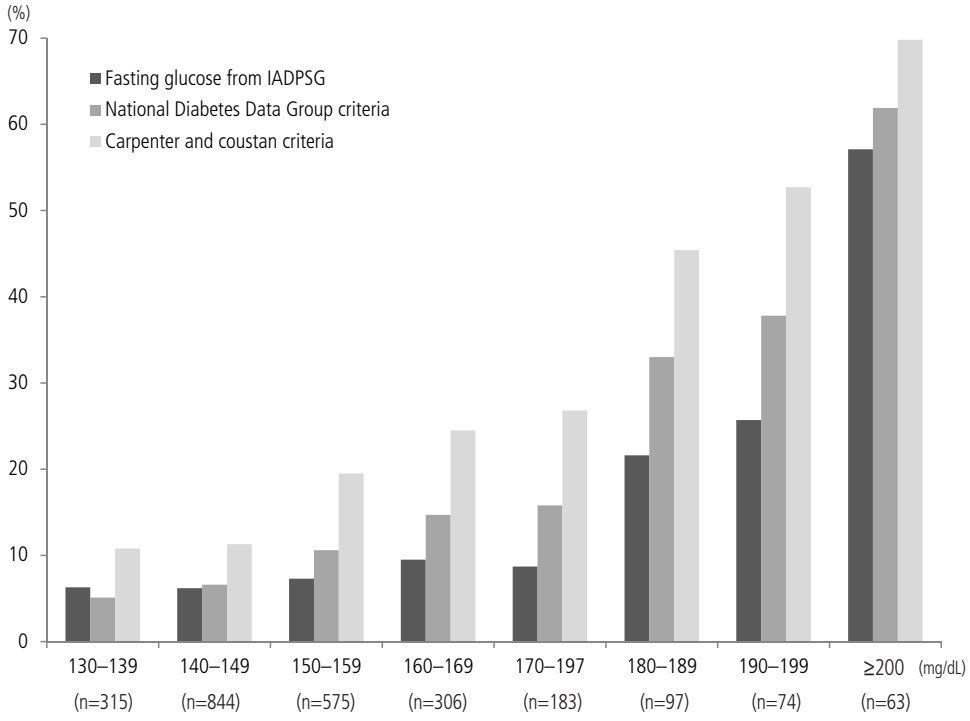

Fig. 1. Prevalence of gestational diabetes mellitus (GDM) in pregnancies with positive 50-g glucose challenge test results. GDM prevalence increased with increasing 50-g glucose challenge test results (P<0.001). In addition, the GDM prevalence was highest with the application of the Carpenter and Coustan criteria. IADPSG, International Association of Diabetes and Pregnancy Study Group.

≥140 mg/dL. Among the 1,806 women with 50-g GCT results between 130 and 139 mg/dL, 315 underwent 100-g GTT. Of the 3,118 women with 50-g GCT ≥140 mg/dL, 2,142 underwent 100-g GTT. Finally, a total of 2,457 cases with positive 50-g GCT results were included in this study.

2. Prevalence of GDM in pregnant women with positive 50-g GCT results according to the respective diagnostic thresholds

Overall, 12.5% (306/2,457), 20.0% (492/2,457), and 9.6% (235/2,457) of women met the diagnostic criteria of GDM based on NDDG, C&C criteria, and fasting glucose thresholds from IADPSG (≥92 mg/dL), respectively. As expected, our data revealed that the GDM prevalence increased with increasing 50-g GCT results (P<0.001, by linear by linear association). Furthermore, our data showed that the GDM prevalence increased with the adoption of C&C criteria (Fig. 1). As shown in Fig. 1, among women with 50-g GCT ≥200 mg/dL, 61.9%, 69.8%, and 57.1% were finally diagnosed with GDM according to the diagnostic criteria of the NDDG, C&C, and fasting glucose thresholds from IADPSG. Notably, among women with 50-g GCT between 130 and 139 mg/dL, the prevalence of GDM was 5.1%, 10.8%, and 6.3% under the respective criteria.

3. ROC curve analyses of a 50-g GCT value to confirm the diagnosis of GDM

Then, ROC curve analyses showed that 50-g GCT values of 223, 217, and 228 mg/dL were the cutoff values at which the 100-g GTT could be omitted (with a 100% positive predictive value) under the criteria of NDDG, C&C, and fasting glucose thresholds from IADPSG, respectively (Fig. 2). Additionally, our data demonstrated that 50-g GCT values of 151, 148, and 150 mg/dL showed high sensitivity and low false positive rates with the criteria of NDDG, C&C, and fasting glucose thresholds from IADPSG, respectively. Namely, a value of 151 mg/dL corresponded to a sensitivity of 73.1% and a false positive rate of 43.6%, 148 mg/dL corresponded to a sensitivity of 75.4% and a false positive rate of 51.1%, and 150 mg/dL corresponded to a sensitivity of 68.9% and a false positive rate of 47.9% under the respective criteria.

Discussion

In this study, we aimed to determine the cutoff value for omitting further diagnostic tests for a diagnosis of GDM. Notably, we identified that all subjects with a 50-g GCT screening value ≥223 mg/dL, ≥217 mg/dL, and ≥228 mg/dL can be exclusively

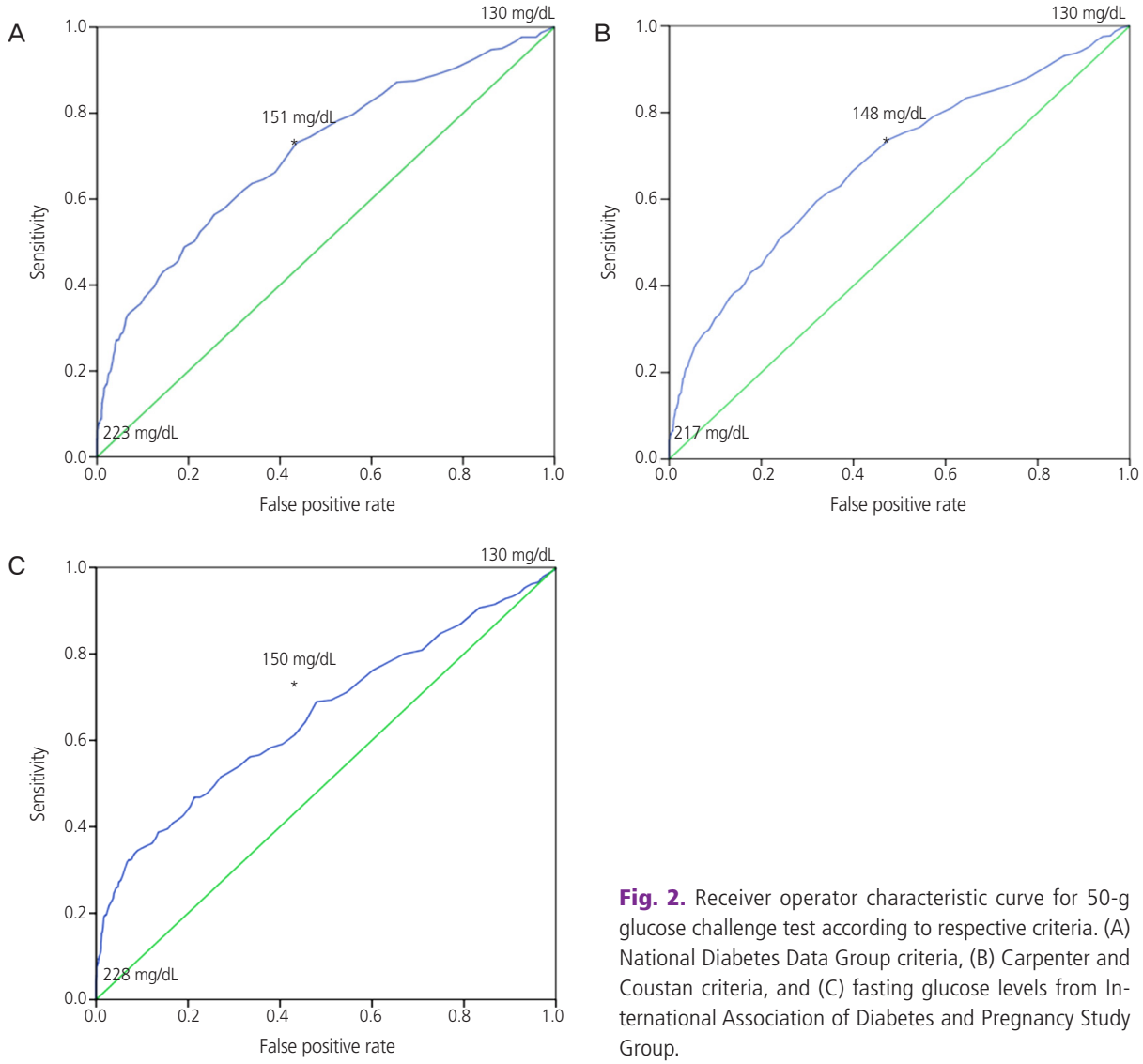

Fig. 2. Receiver operator characteristic curve for 50-g glucose challenge test according to respective criteria. (A) National Diabetes Data Group criteria, (B) Carpenter and Coustan criteria, and (C) fasting glucose levels from International Association of Diabetes and Pregnancy Study Group.

diagnosed with GDM according to the criteria of NDDG, C&C, and fasting glucose thresholds from IADPSG, respectively. We also found that the prevalence of GDM increased with increasing 50-g GCT results based on all criteria, as expected, and that the prevalence of GDM in pregnancies with a positive 50-g GCT result was highest using the C&C criteria and lowest using the fasting glucose thresholds from IADPSG.

Several studies have examined the screening thresholds for 50-g GCT, and generally a lower cutoff value of 130 and 140 mg/dL has been reported with varying degrees of sensitivities and specificities [10-17]. In contrast, reports targeting the upper cutoff in 50-g GCT are relatively rare, and such studies have focused on a value of 200 mg/dL, as this blood glucose level along with symptoms such as polydipsia or polyuria is suggestive of DM [18-21]. In fact, the National Institutes of Health (NIH) recently suggested that 50-g GCT values ≥200 mg/dL are indicative of GDM [4].

However, several reports have stated that even 50-g GCT values ≥200 mg/dL are not conclusively diagnostic of GDM. In these studies, only 57%, 62%, 69%, and 70% to 80% of pregnancies with 50-g GCT values ≥200 mg/dL had abnormal glucose tolerance [18-21]. A study from our institution using data from 1998 to 2002 also demonstrated that a 50-g GCT results ≥200 mg/dL had only a 64% GDM-positive predictive value according to the NDDG criteria [22]. In the current study using the database from 2001 to 2013, 61.9% and 69.8% of women with 50-g GCT ≥200 mg/dL were diagnosed with GDM according to the diagnostic criteria of the NDDG and

C&C, respectively, indicating that this value alone could not be used to diagnose GDM. However, our data showed that 50-g GCT levels ≥228 mg/dL could be used to diagnose GDM with 100% positive predictive value irrespective of diagnostic thresholds used (NDDG, C&C criteria, or fasting glucose thresholds from IADPSG). This upper diagnostic value in 50-g GCT is similar to those used in other studies [21,23]. An earlier study by Bobrowski et al. [23] in 1996 examined the utility of various 50-g GCT cut-off values in 422 gravidas with a positive 50-g GCT and reported that all subjects with ≥220 mg/dL did not require 100-g GTT considering their fasting glucose levels. Another study by Cheng et al. [21] in 2006 also showed that a 50-g GCT value of 230 mg/dL showed 100% specificity for confirmation of GDM in 14,771 pregnancies screened for gestational diabetes. Also, a lower value of 186 mg/dL in the 50-g GCT had been reported to have 36.1% sensitivity and 95.1% specificity for the diagnosis of GDM [24]. The authors of that study emphasized that women with greater than 185 mg/dL in the 50-g GCT had a higher rate of large for gestational age and neonatal hypoglycemia.

Defining the upper diagnostic value in 50 GCT has implications for clinical practice. By obviating further diagnostic testing, these pregnant women can avoid the inconvenience of overnight fasting period and 2 to 3 times of blood sampling. More importantly, since diabetic ketoacidosis, which may be associated with increased perinatal morbidity [25], could develop at lower glucose levels during pregnancy compared to non-pregnant state [26], execution of further glucose challenging tests such as 100- or 75-g GTT may increase risks in these women.

Our results may be partially limited by the fact that we could not provide information on GDM prevalence based on complete diagnostic criteria of 75-g GTT, but only based on fasting glucose levels differing from IADPSG recommendation. This is because one-step 75-g GTT is not performed in our institution for clinical diagnosis of GDM. Considering the higher GDM prevalence according to the 75-g GTT from IADPSG recommendation indicated by other investigators [27], the prevalence of GDM in pregnancies with positive 50-g GCT may be higher than using NDDG or C&C criteria, and the upper cutoff of 50-g GCT to exclusively confirm GDM would be lower than the value in this study (≥228 mg/dL). Furthermore, not all women with positive GCT results underwent 100-g GTT, and 19 pregnancies were directly diagnosed without diagnostic 100-g GTT. We did not include these cases. Lastly, we did not consider maternal characteristics such as the maternal age, parity, or body mass index, all of which might be associated with GDM, and did not evaluated the pregnancy/neonatal outcomes. Instead, we simply aimed to determine the upper 50-g GCT cutoff value at which the 100-g GTT could be omitted when diagnosing GDM; therefore, other investigations were beyond the scope of our study and we did not investigate those points.

Nonetheless, one of the strengths of this study is that we included a relatively large number of pregnancies (n=16,560) compared to previous studies [23,24]. We also provided information from women with 50-g GCT levels between 130 and 140 mg/dL. Of note, 5.1%, 10.8%, and 6.3% of women with 50-g GCT levels between 130 and 140 mg/dL were finally diagnosed with GDM according to the criteria of NDDG, C&C and fasting glucose thresholds from IADPSG. Our data support that women with a 50-g GCT cutoff value of 130 to 140 mg/dL who have risk factors for GDM should undergo diagnostic test for GDM. Also, to the best of our knowledge, this is the first study comparing the upper cutoff values of 50-g GCT using different diagnostic tests of GDM (NDDG and C&C) and fasting glucose thresholds according to IADPSG.

In conclusion, we propose that women with a 50-g GCT screening value ≥228 mg/dL can be reliably omitted from further confirmative tests for GDM, such as 100- or 75-g GTT. Such a strategy will avoid unnecessary fasting in pregnant women and possibly decrease the risk of diabetic ketoacidosis, thus helping in the clinical management of pregnant women.

Conflict of interest

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

References

1. Committee on Practice Bulletins: Obstetrics. Practice Bulletin No. 137: gestational diabetes mellitus. Obstet Gynecol 2013;122(2 Pt 1):406-16.
2. Plagemann A. A matter of insulin: developmental programming of body weight regulation. J Matern Fetal Neonatal Med 2008;21:143-8.

3. Tam WH, Ma RC, Yang X, Li AM, Ko GT, Kong AP, et al. Glucose intolerance and cardiometabolic risk in adolescents exposed to maternal gestational diabetes: a 15-year follow-up study. Diabetes Care 2010;33:1382-4.
4. Vandorsten JP, Dodson WC, Espeland MA, Grobman WA, Guise JM, Mercer BM, et al. NIH consensus development conference: diagnosing gestational diabetes mellitus. NIH Consens State Sci Statements 2013;29:1-31.
5. Carpenter MW, Coustan DR. Criteria for screening tests for gestational diabetes. Am J Obstet Gynecol 1982;144:768-73.
6. Berggren EK, Boggess KA, Stuebe AM, Jonsson Funk M. National Diabetes Data Group vs Carpenter-Coustan criteria to diagnose gestational diabetes. Am J Obstet Gynecol 2011;205:253.e1-7.
7. Hartling L, Dryden DM, Guthrie A, Muise M, Vandermeer B, Aktary WM, et al. Screening and diagnosing gestational diabetes mellitus. Evid Rep Technol Assess (Full Rep) 2012;210:1-327.
8. HAPO Study Cooperative Research Group, Metzger BE, Lowe LP, Dyer AR, Trimble ER, Chaovarindr U, et al. Hyperglycemia and adverse pregnancy outcomes. N Engl J Med 2008;358:1991-2002.
9. Benhalima K, Devlieger R, Van Assche A. Screening and management of gestational diabetes. Best Pract Res Clin Obstet Gynaecol 2015;29:339-49.
10. Bonomo M, Gandini ML, Mastropasqua A, Begher C, Valentini U, Faden D, et al. Which cutoff level should be used in screening for glucose intolerance in pregnancy? Definition of Screening Methods for Gestational Diabetes Study Group of the Lombardy Section of the Italian Society of Diabetology. Am J Obstet Gynecol 1998;179:179-85.
11. Caliskan E, Kayikcioglu F, Ozturk N, Koc S, Haberal A. A population-based risk factor scoring will decrease unnecessary testing for the diagnosis of gestational diabetes mellitus. Acta Obstet Gynecol Scand 2004;83:524-30.
12. Cetin M, Cetin A. Time-dependent gestational diabetes screening values. Int J Gynaecol Obstet 1997;56:257-61.
13. Weerakiet S, Lertnarkorn K, Panburana P, Pitakitronakorn S, Vesathada K, Wansumrith S. Can adiponectin predict gestational diabetes? Gynecol Endocrinol 2006;22:362-8.
14. van Leeuwen M, Zweers EJ, Opmeer BC, van Ballegooie E, ter Brugge HG, de Valk HW, et al. Comparison of accuracy measures of two screening tests for gestational diabetes mellitus. Diabetes Care 2007;30:2779-84.
15. Thitadilok W, Techatraisak K. The screening for gestational diabetes employing 50 g glucose test. J Med Assoc Thai 1995;78:526-31.
16. Rey E, Hudon L, Michon N, Boucher P, Ethier J, Saint-Louis P. Fasting plasma glucose versus glucose challenge test: screening for gestational diabetes and cost effectiveness. Clin Biochem 2004;37:780-4.
17. van Leeuwen M, Louwerse MD, Opmeer BC, Limpens J, Serlie MJ, Reitsma JB, et al. Glucose challenge test for detecting gestational diabetes mellitus: a systematic review. BJOG 2012;119:393-401.
18. Sacks DA, Abu-Fadil S, Karten GJ, Forsythe AB, Hackett JR. Screening for gestational diabetes with the one-hour 50-g glucose test. Obstet Gynecol 1987;70:89-93.
19. Yogev Y, Langer O, Xenakis EM, Rosenn B. Glucose screening in Mexican-American women. Obstet Gynecol 2004;103:1241-5.
20. Atilano LC, Lee-Parritz A, Lieberman E, Cohen AP, Barbieri RL. Alternative methods of diagnosing gestational diabetes mellitus. Am J Obstet Gynecol 1999;181(5 Pt 1):1158-61.
21. Cheng YW, Esakoff TF, Block-Kurbisch I, Ustinov A, Shafer S, Caughey AB. Screening or diagnostic: markedly elevated glucose loading test and perinatal outcomes. J Matern Fetal Neonatal Med 2006;19:729-34.
22. Kim JH, Seo YS, Choi SJ, Kim YA, Roh CR, Yang SH. The relationship of the results of 50-g screening test and gestational diabetes. Korean J Obstet Gynecol 2003;46:2146-50.
23. Bobrowski RA, Bottoms SF, Micallef JA, Dombrowski MP. Is the 50-gram glucose screening test ever diagnostic? J Matern Fetal Med 1996;5:317-20.
24. Landy HJ, Gomez-Marin O, O'Sullivan MJ. Diagnosing gestational diabetes mellitus: use of a glucose screen without administering the glucose tolerance test. Obstet Gynecol 1996;87:395-400.
25. Sibai BM, Viteri OA. Diabetic ketoacidosis in pregnancy. Obstet Gynecol 2014;123:167-78.
26. Madaan M, Aggarwal K, Sharma R, Trivedi SS. Diabetic ketoacidosis occurring with lower blood glucose levels in pregnancy: a report of two cases. J Reprod Med 2012;57:452-5.
27. Mayo K, Melamed N, Vandenberghe H, Berger H. The impact of adoption of the international association of diabetes in pregnancy study group criteria for the screening and diagnosis of gestational diabetes. Am J Obstet Gynecol 2015;212:224.e1-9.