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Diagnostic Strategies for Gestational Diabetes Mellitus: Review of Current Evidence

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Abstract

Purpose of Review Currently, the diagnosis of gestational diabetes mellitus (GDM) lacks uniformity. Several controversies are still under debate, especially on the method of screening and diagnosis. This review focuses on recent literature and provides current evidence for the screening and diagnosis of GDM.

Recent Findings Selective screening would miss a significant number of women with GDM. In contrast, universal screening has been shown to be cost-effective, compared with selective screening, and is recommended by many medical societies. For the diagnostic methods for GDM, most observational cohort studies reported that the one-step method is associated with improved pregnancy outcomes and is cost-saving or cost-effective, compared with the two-step method, although these findings should be confirmed in the upcoming randomized controlled trials which compare the performance of one-step and two-step methods. On the other hand, the methods of early screening or diagnosis of GDM are varied, and current evidence does not justify their use during early pregnancy.

Summary In conclusion, current evidence favors universal screening for GDM using the one-step method. Early screening for GDM is not favorably supported by the literature.

Keywords Gestational diabetes mellitus · Screening · Diagnostic strategy · Risk factor modeling · Oral glucose tolerance tests

Introduction

Gestational diabetes mellitus (GDM) has long been defined as any degree of hyperglycemia that is recognized for the first time during pregnancy [1, 2]. However, the definition of the degree of hyperglycemia has varied between experts and associations, and the diagnosis of GDM still lacks uniformity. GDM increases the risk of many adverse pregnancy outcomes. During pregnancy, maternal hyperglycemia can affect the infant through the placenta, resulting in an elevated risk of macrosomia, neonatal jaundice, neonatal hypoglycemia, preterm delivery, and neonatal intensive care unit admission [3]. Macrosomia is associated with an increased rate of cesarean section, birth trauma, and shoulder dystocia. High birth weight is associated with obesity and diabetes in childhood [4]. Independent of maternal and childhood BMI, maternal hyperglycemia during pregnancy is associated with childhood glucose intolerance and insulin resistance [5•]. As for the pregnant woman, GDM increases not only the cesarean section rate, but also the risk of gestational hypertension and preeclampsia. After delivery, a history of GDM increases the risk of diabetes [6], and 15–70% of mothers with a history of GDM will develop type 2 diabetes in the future [7]. Fortunately, glycemic control in women with GDM can improve pregnancy outcomes [8, 9]. Therefore, in order to improve adverse perinatal and long-term outcomes, screening pregnant women and making a diagnosis of GDM is worthwhile, although a general agreement on the best strategy for the screening and diagnosis of GDM has not been reached [10•, 11–16]. In this review, we will discuss current evidence on diagnostic strategies for GDM.

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The Evolution of Diagnostic Strategies of GDM

The historical diagnostic criteria of GDM were first proposed by O'Sullivan and Mahan in 1964 [17]; they used a 3-h 100-g oral glucose tolerance test (OGTT) to define hyperglycemia in pregnant women. The diagnosis of GDM was made when at least two of the four glucose values during OGTT met or exceeded two standard deviations above the mean. Pregnant women with GDM by these criteria have a higher risk of developing diabetes after delivery. In 1973, O'Sullivan et al. [18] suggested using a non-fasting 1-h 50-g glucose challenge test (GCT) to screen for GDM, since the incidence of GDM at that time was low and screening for GDM based on risk factors was insensitive. They recommended that only pregnant women who did not pass the GCT should proceed to the OGTT. The diagnostic criteria were modified by the National Diabetes Data Group (NDDG) in 1979 [1] and Carpenter and Coustan (C&C) in 1982 [19], in order to convert the cutoff values for whole blood samples by non-enzymatic methods to cutoff values for plasma samples by enzymatic methods. Since 1986, these screening and diagnostic strategies for GDM (the two-step approach, Table 1) have been recommended by professional societies in the United States (USA), including the American Diabetes Association (ADA) [20], the American College of Obstetricians and Gynecologists (ACOG) [21], and the National Institutes of Health (NIH) [22]. However, many countries outside the USA did not use the two-step approach. Instead, the World Health Organization (WHO) criteria proposed in 1999 were applied to diagnose GDM, mainly because of the simplicity of the criteria. These criteria defined GDM as pregnant women who met criteria for diabetes mellitus and impaired glucose tolerance, i.e., fasting plasma glucose (FPG) ≥ 126 mg/dL (6.1 mmol/L) or 2-h plasma glucose ≥ 140 mg/dL (7.8 mmol/L).

In 2008, the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study [3] reported that maternal plasma glucose levels determined by a 2-h 75-g OGTT during pregnancy (24–32 weeks of gestation) were linearly correlated with maternal and fetal outcomes, including large for gestational age (LGA) birth weight, primary cesarean section, high cord C-peptide levels, and neonatal hypoglycemia. Maternal plasma glucose levels were also associated with five secondary outcomes: preterm delivery, shoulder dystocia or birth injury, neonatal intensive care unit admission, hyperbilirubinemia, and preeclampsia. This is the first large-scale prospective cohort study that clarified the association between the risk of adverse pregnancy outcomes and degrees of maternal hyperglycemia during pregnancy, for which there were no obvious inflection points found. Based on HAPO study results, the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) proposed the one-step 75-g OGTT diagnostic criteria for GDM in 2010 (Table 1) [23], which were later adopted by many international societies, including the ADA in 2011 [24], the Endocrine Society in 2013 [25], the WHO in 2013 [26], and the International Federation of Gynecology and Obstetrics (FIGO) in 2015 [27]. This one-step strategy requires all pregnant women to undergo a 75-g OGTT; to diagnose GDM, at least one of the three glucose values during the OGTT must meet or exceed the IADPSG thresholds. Although one-step strategy has some advantages [13, 16], it also increases the prevalence of GDM [13, 16, 28, 29] and the burden on the healthcare system [30]. Thus, the debate on the best diagnostic strategy for GDM persists.

Currently, most professional associations recommend one-step and/or two-step methods to diagnose GDM (Table 2).

Table 1 One-step and two-step strategies to diagnose gestational diabetes mellitus (GDM)

Plasma glucose, mg/dL (mmol/L)	75-g OGTT* "one-step strategy"	100-g OGTT† "two-step strategy"	
		Carpenter and Coustan criteria	NDDG criteria
Fasting	≥ 92 (5.1)	≥ 95 (5.3)	≥ 105 (5.8)
1-h plasma glucose during an OGTT	≥ 180 (10.0)	≥ 180 (10.0)	≥ 190 (10.6)
2-h plasma glucose during an OGTT	≥ 153 (8.5)	≥ 155 (8.6)	≥ 165 (9.2)
3-h plasma glucose during an OGTT		≥ 140 (7.8)	≥ 145 (8.0)

NDDG the National Diabetes Data Group, *OGTT* oral glucose tolerance test

*At 24th–28th weeks of gestation, perform a 75-g OGTT and measure plasma glucose levels at fasting, 1 h and 2 h during the OGTT. The OGTT should be performed in the morning after an overnight fast for at least 8 h. The diagnosis of GDM is made when one of the plasma glucose levels meets or exceeds the cutoffs. This method is called "one-step strategy" by the American Diabetes Association

† At 24th–28th weeks of gestation, perform a non-fasting 50-g glucose challenge test in women not previously diagnosed with overt diabetes. If the plasma glucose level measured 1 h after the glucose challenge test is ≥ 130 mg/dL (sensitivity is 90%) or ≥ 140 mg/dL (sensitivity is 80%), proceed to a 100-g OGTT. The 100-g OGTT should be performed when the patient is fasting. The diagnosis of GDM is made if at least two of the four plasma glucose levels (measured at fasting, 1 h, 2 h, and 3 h during the OGTT) meet or exceed the cutoffs. This method is called "two-step strategy" by the American Diabetes Association

However, there are differences in the suggestions about selective or universal screening, the timing of screening, and the cutoff values for diagnostic tests. There is still no global consensus on the best method to diagnose GDM.

Selective Screening vs. Universal Screening

One of the controversies is the screening strategy to identify women with GDM. Since the OGTT is burdensome for both pregnant women and the healthcare system, some professional associations suggest that the diagnostic OGTT should be applied only to those at risk for GDM. Several screening methods, including risk factor-based models and 1-h 50-g glucose challenge test (GCT), are used to identify pregnant women at risk for GDM. The risk factor-based method, sometimes called selective screening, uses traditional risk factors to determine who should receive OGTT, such as age ≥ 35 years, body mass index ≥ 25 or 30 kg/m^2, history of GDM, history of bearing a child with macrosomia, and family history of diabetes. In contrast, in universal screening, all pregnant women receive biochemical tests, including either a diagnostic OGTT or 1-h 50-g GCT to determine the need for a diagnostic OGTT.

There were several reports which have studied the performance of risk factor-based screening. In Malaysia, Idris et al. reported that the prevalence of GDM was 18.3% by the WHO 1999 diagnostic criteria [31]. Universal screening with a 50-g GCT and a subsequent 75-g OGTT had a sensitivity of 83.5% and specificity of 82.6%. The sensitivity and specificity of selective screening was lower than universal screening (sensitivity 76.1% and specificity 60.9%). In other words, 23.8% of women with GDM did not have any risk factors and were missed by selective screening. In Europe, many countries recommend risk factor-based screening in clinical practice [32]. In a French observational cohort study, 2187 women were screened universally by 75-g OGTT and 309 (14%) had GDM by the IADPSG criteria [33]. Selective screening would have missed 17% of GDM cases who did not have any risk factors. In a Belgian retrospective cohort study, 1811 women received a 75-g OGTT, and 231 (12.5%) of them were diagnosed with GDM by the WHO 2013 criteria [34•]. Applying the English, Irish, French, and Dutch guidelines for risk factor-based screening would miss 48.1%, 36.8%, 36.4%, and 33.3% of pregnant women with GDM, respectively. Another multi-ethnic cohort study of 18,775 subjects found that the selective screening method proposed in the French guidelines would have missed one-third of women with GDM, and these GDM women without risk factors had more adverse events than women without GDM [35]. Therefore, the use of selective screening is a tradeoff between the sensitivity of finding women with GDM and the reduction in the proportion of pregnant women receiving an OGTT.

Cost-effectiveness evaluation is another way to compare selective vs. universal screening strategies. A study in Ireland showed that universal screening, compared with no screening, was cost-saving (i.e., €37.72–59.15 per screened case) and was associated with gains in quality of life (i.e., 0.0008–0.0014 QALY gained per screened case) [10•]. Another cost-effectiveness study in Italy found that universal screening was associated with significant monetary savings in terms of costs linked to maternal and neonatal morbidity, compared with risk factor-based screening [36]. Since risk factor-based screening would miss a substantial number of GDM cases and significantly increase the cost of managing subsequent adverse pregnancy outcomes, it makes sense that universal screening would be cost-effective as compared to selective screening.

Taken together, selective screening would miss a significant number of women with GDM, ranging from 17 to 48% [31, 33, 34•, 35, 37]. In contrast, universal screening has been shown to be cost-effective, compared with selective screening. Therefore, many societies, including the WHO, the FIGO, the ADA, the ACOG, the Canadian Diabetes Association (CDA), and the Australasian Diabetes in Pregnancy Society (ADIPS), have recommended universal screening for GDM [2, 26, 27, 38–40].

Two-Step vs. One-Step Diagnostic Method (Table 1)

Currently, the debate on the use of one-step or two-step diagnostic methods for GDM is ongoing. Whereas some reports still challenge the one-step approach on the basis of its efficacy for identifying women at risk for adverse events [41, 42], several cohort studies, including our report, found that implementing the IAPDSG criteria as a one-step approach would identify more GDM. This approach with subsequent management was associated with significant reductions in maternal and fetal adverse events, compared to the two-step method by the C&C criteria [13, 16, 43]. A meta-analysis of 41,663 subjects from nine observational studies comparing one-step and two-step (by the C&C criteria) approaches reported that women with GDM by both approaches were at increased risk for adverse pregnancy outcomes; the associations with the two-step method were slightly stronger [44•]. Compared to the two-step approach, the one-step approach is a more sensitive method, which discovers milder GDM. Thus, one can expect that these women with mild GDM would have less adverse events, compared to women with GDM defined by two-step criteria. However, are these women with mild GDM not at risk? Caissutti et al. used electronic database and included data from 29,983 pregnant women in eight retrospective cohort studies [45]. Four of the eight cohorts used the two-step method (100 g OGTT) with C&C criteria to diagnose GDM. In these four studies, pregnant women who met the IADPSG criteria for GDM but did not meet the C&C

Table 2 Current GDM diagnostic strategies recommendation by professional associations

Associations	Subjects		Screening method	Screening threshold, mg/dL (mmol/L)	Diagnostic method	Diagnostic threshold, mg/dL (mmol/L)			
	Early screening*	Standard screening†		Non-fasting 1 h		Fasting	1 h	2 h	3 h
Global									
IADPSG	Risk factor-based or universal‡	Universal	-	-	75-g OGTT, any 1 value	92 (5.1)§	180 (10)	153 (8.5)	-
WHO	Risk factor-based or universal‡	Universal	-	-	75-g OGTT, any 1 value	92 (5.1)§	180 (10)	153 (8.5)‖	-
IDF	Universal‡	Universal	-	-	75-g OGTT, any 1 value	92 (5.1)§	180 (10)	153 (8.5)	-
FIGO**	Universal‡	Universal	-	-	75-g OGTT, any 1 value	92 (5.1)§	180 (10)	153 (8.5)‖	-
America									
ADA	Risk factor-based¶	Universal	-	-	75-g OGTT, any 1 value	92 (5.1)	180 (10)	153 (8.5)	-
			50-g GCT	130 (7.2) 135 (7.5) 140 (7.8)	100-g OGTT, any 2 values	95 (5.3) 105 (5.8)	180 (10) 190 (10.6)	155 (8.6) 165 (9.2)	140 (7.8) 155 (8.0)
AACE	Risk factor-based¶	Universal	-	-	75-g OGTT, any 1 value	92 (5.1)	180 (10)	153 (8.5)	-
Endocrine Society	Universal‡	Universal	-	-	75-g OGTT, any 1 value	92 (5.1)§	180 (10)	153 (8.5)‖	-
ACOG	Risk factor-based	Universal	50-g GCT	130 (7.2) 135 (7.5) 140 (7.8)	100-g OGTT, any 2 values	95 (5.3) 105 (5.8)	180 (10) 190 (10.6)	155 (8.6) 165 (9.2)	140 (7.8) 155 (8.0)
NIH	-	Universal	50-g GCT	130 (7.2) 135 (7.5) 140 (7.8)	100-g OGTT, any 2 values	95 (5.3) 105 (5.8)	180 (10) 190 (10.6)	155 (8.6) 165 (9.2)	140 (7.8) 155 (8.0)
CDA	Risk factor-based††	Universal	50-g GCT (preferred)	140 (7.8)‡‡	75-g OGTT, any 1 value	95 (5.3)	191 (10.6)	162 (9.0)	-
			- (alternative)	-	75-g OGTT, any 1 value	92 (5.1)	180 (10)	153 (8.5)	-
BSD	Universal	Universal	FPG	85 (4.7)	75-g OGTT, any 1 value	92 (5.1)§	180 (10)	153 (8.5)‖	-
Asia									
DAROC	Risk factor-based¶	Universal	-	-	75-g OGTT, any 1 value	92 (5.1)	180 (10)	153 (8.5)	-
			50-g GCT	130 (7.2) 140 (7.8)	100-g OGTT, any 2 values	95 (5.3)	180 (10)	155 (8.6)	140 (7.8)
DIPSI	Universal	Universal	-	-	Non-fasting 75-g OGTT	-	-	140 (7.8)	-
JDS	Universal	Universal	-	-	75-g OGTT, any 1 value	92 (5.1)§	180 (10)	153 (8.5)‖	-
KDA	Universal¶	Universal	-	-	75-g OGTT, any 1 value	92 (5.1)	180 (10)	153 (8.5)	-
			50-g GCT	130 (7.2) 140 (7.8)	100-g OGTT, any 2 values	95 (5.3)	180 (10)	155 (8.6)	140 (7.8)
MOH of China	-	Universal	- (well-resourced)	-	75-g OGTT, any 1 value	92 (5.1)	180 (10)	153 (8.5)	-
			FPG (low-resourced)	79–91 (4.4–5.0)§§					

Table 2 (continued)

Associations	Subjects		Screening method	Screening threshold, mg/dL (mmol/L)	Diagnostic method	Diagnostic threshold, mg/dL (mmol/L)			
	Early screening*	Standard screening†		Non-fasting 1 h		Fasting	1 h	2 h	3 h
Europe									
DDG	Risk factor-based‡	Universal	- 50-g GCT	- 135 (7.5)‡‡	75-g OGTT, any 1 value	92 (5.1)§	180 (10)	153 (8.5)‖	-
EBCOG	Risk factor-based or universal	Universal	-	-	75-g OGTT, any 1 value	92 (5.1)§	180 (10)	153 (8.5)‖	-
EASD	-	-	-	-	75-g OGTT, any 1 value	108 (6.0)	-	162 (9.0)	-
NICE	Risk factor-based	Risk factor-based	-	-	75-g OGTT, any 1 value	100 (5.6)	-	140 (7.8)	-
Oceania									
ADIPS	Risk factor-based	Universal	-	-	75-g OGTT, any 1 value	92 (5.1)§	180 (10)	153 (8.5)‖	-

AACE the American Association of Clinical Endocrinologists, *ACOG* the American College of Obstetricians and Gynecologists, *ADA* the American Diabetes Association, *ADIPS* the Australasian Diabetes in Pregnancy Society, *BSD* the Brazilian Society of Diabetes, *CDA* the Canadian Diabetes Association, *DAROC* the Diabetes Association of Republic of China, *DDG* the German Diabetes Association; DIPSI, the Diabetes in Pregnancy Study Group India, *EBCOG* the European Board & College of Obstetrics and Gynecology, *FIGO* the International Federation of Gynecology and Obstetrics, *FPG* fasting plasma glucose, *GCT* glucose challenge test, *GDM* gestational diabetes mellitus, *IADPSG* the International Association of the Diabetes and Pregnancy Study Groups, *IDF* the International Diabetes Federation, *JDS* the Japan Diabetes Society, *KDA* the Korean Diabetes Association, *MOH* the Ministry of Health, *NIH* the National Institutes of Health, *OGTT* oral glucose tolerance test, *PG* plasma glucose, *WHO* the World Health Organization

*At the first prenatal visit

† At 24th–28th weeks of gestation

‡ FPG levels in the first prenatal visit can be used to diagnose GDM

§ FPG levels of 92–125 mg/dL (5.1–6.9 mmol/L) are used to diagnose GDM, and FPG levels equal or greater than 126 mg/dl (7.0 mmol/L) are diagnostic of overt diabetes

‖ 2 h PG levels of 153–199 mg/dL (8.5–11.1 mmol/L) are used to diagnose GDM, and 2 h PG levels equal or greater than 200 mg/dL (11.1 mmol/L) are diagnostic of overt diabetes

¶ Only screen for pre-existing diabetes and diagnosis of GDM is not recommended during early pregnancy

**Suggest various diagnostic strategies for GDM based on resource settings; only strategy for fully resourced setting was shown here

†† At any stage of pregnancy

‡‡ 50-g GCT 1 h PG levels equal or above 201 mg/dL (11.1 mmol/L) can be considered diagnostic of GDM and does not require a 75-g OGTT

§§ If FPG levels are equal or above 92 mg/dL (5.1 mmol/L), GDM can be diagnosed; if below 79 mg/dL (4.4 mol/L), then GDM is unlikely

criteria still had a significantly increased risk of adverse pregnancy outcomes, such as gestational hypertension, preeclampsia, and LGA, compared with pregnant women without GDM. Indeed, the HAPO study has demonstrated that the relationship between hyperglycemia and risk of adverse pregnancy outcomes is linear, without an inflection point. Therefore, pregnant women with mild GDM discovered by one-step approach still have more adverse pregnancy outcomes than normal controls.

Several cost-effective analyses in observational cohort studies have pointed out that the one-step approach would increase the burden on the healthcare system compared to the two-step approach. However, the one-step approach appears cost-saving or cost-effective in terms of improving maternal and neonatal outcomes, including future risk of diabetes [11, 13, 16, 46, 47]. Recently, the results of the HAPO follow-up study has been published [5•], which has provided more data on long-term outcomes and can be used to refine the evaluation of cost-effectiveness.

There are a few randomized controlled trials (RCTs) which compared the one-step method using IADPSG criteria and the two-step method using C&C criteria to diagnose GDM in the literature. In 2014, Sevket et al. reported the results of an RCT which recruited 786 pregnant women. These women were randomized and screened for GDM by the one-step method using the IADPSG criteria or by the two-step method using the C&C criteria [48]. The prevalence of GDM was significantly higher by the one-step method, compared with the two-step method (14.5% vs. 6%). However, analyses of the effect of these two methods on pregnancy outcomes were not reported. Instead, they showed that women with normal glucose tolerance by the one-step method had better pregnancy outcomes than women with normal glucose tolerance by the two-step method. Recently, a meta-analysis was published which included three RCTs [49•]. Since one of the RCTs did not report pregnancy outcomes and used different diagnostic criteria [50], the analyses comparing the one-step method by IADPSG criteria and the two-step method by C&C criteria were done using data of the other two RCTs, including the RCT by Sevket et al. [48] and a small RCT which recruited 68 pregnant women to evaluate the feasibility of randomization and screening [51]. The results demonstrated that women screened with the one-step method by the IADPSG criteria had a higher incidence of GDM and a lower risk of preterm birth, cesarean delivery, macrosomia, neonatal hypoglycemia, and admission to neonatal intensive care unit, compared with women screened with two-step method by the C&C criteria [49•]. In 2018, Khalifeh et al. recruited 249 pregnant women to explore the performance of these two diagnostic strategies [52•]. They did not find significant differences in GDM incidence and adverse pregnancy outcomes between the one-step method using the IADPSG criteria and the two-step approach using C&C criteria. However, since this trial was not adequately powered, especially for pregnancy outcomes, the findings are not conclusive. Currently, there are two ongoing large-scale well-designed RCTs, which compare the one-step and two-step diagnostic strategies in terms of the risk of LGA and cost-effectiveness [53••] (Table 3). These two studies will be completed by the end of 2019.

Taken together, current evidence from observational cohort studies favors the use of one-step approach to diagnose GDM, since it improves pregnancy outcomes and appears to be cost-saving or cost-effective. However, there is no published RCT with sufficient power which uses a pregnancy outcome as the primary endpoint to compare women screened for GDM with one-step method and two-step method. In the near future, two large-scale RCTs comparing these two diagnostic criteria will be completed; they will provide more evidence about their impact on the risk of LGA and cost-effectiveness.

Early Screening for Early Onset GDM

Owing to the growing epidemic of obesity and advanced maternal age, the prevalence of pre-existing diabetes and GDM has been increasing [54, 55]. Therefore, significant numbers of pregnant women have undiagnosed pre-existing diabetes or early onset GDM in early pregnancy [56]. Hyperglycemia in the first trimester increases the risk of adverse pregnancy outcomes [57, 58]. This highlights the potential benefits of early screening for pre-existing diabetes and even early onset GDM in pregnant women. Many societies, including the ADA, the ACOG, the FIGO, and the IADPSG, have recommended early screening for pre-existing diabetes (Table 2). However, the benefits of screening for GDM in early pregnancy remain controversial because of the lack of evidence supporting any particular method.

So far, there are several screening methods proposed for early onset GDM. The performance of risk factor-based method is not good [59]. Therefore, several reports have investigated the use of laboratory data to screen for early onset GDM. Harrison et al. found that the addition of FPG values to a validated risk prediction tool was a strong predictor for GDM in early pregnancy with an area under the ROC curve of 0.83 for the IADPSG criteria [60]. Although high FPG levels in the early pregnancy have been associated with adverse pregnancy outcomes, the evidence supporting using FPG levels alone to diagnose early onset GDM is not sufficient for several reasons. First, FPG values decline physiologically during pregnancy [61]. Many women with high FPG values in early pregnancy are not diagnosed with GDM at the 24th–28th weeks of gestation. In a study of 17,186 pregnant women, Zhu et al. have reported that at least 60% of women with FPG levels equal or above 92 mg/dL (5.1 mmol/L) at the first prenatal visit did not have GDM when retested between 24th and 28th weeks gestation [62]. Second, the performance of

Table 3 Randomized controlled trials currently recruiting that compare one-step and two-step diagnostic strategies for GDM

Trial title	Sample size	Arms	Estimated study completion date	Primary outcome	Cost-effectiveness study	Principal investigator	Study sites
Pregnancy Outcomes and Medical Costs According to Gestational Diabetes Mellitus Diagnostic Criteria (POMEC)	3644	One-step IADPSG criteria vs. two-step NDDG criteria	2019/12	LGA	Yes	Verónica Perea, MD	Hospital Universitari Mutua Terrassa, Spain
Comparison of Two Screening Strategies for Gestational Diabetes (GDM^2)	921	One-step IADPSG criteria vs. two-step C&C criteria	2019/9	LGA	No	Esa M Davis, MD MPH	University of Pittsburgh-Center for Research on Health Care, United States

GDM gestational diabetes mellitus, *IADPSG* the International Association of the Diabetes and Pregnancy Study Groups, *LGA* large for gestational age, *NDDG* the National Diabetes Data Group, *C&C* the Carpenter and Coustan

using first-trimester FPG levels alone to identify GDM is not good as compared to other screening methods. A prospective RCT has compared three early screening methods to predict GDM, including FPG, two-step method by 50-g GCT and subsequent 100-g OGTT using C&C criteria, and one-step method by 75-g OGTT using the IADPSG criteria [63]. Participants were screened by FPG at the first antenatal visit at 11–14 weeks. Regardless of the FPG results, all subjects were randomized to receive either the two-step method or the one-step method at the second antenatal visit at 11–14 weeks. At 24–28 weeks, women who were not diagnosed GDM at 11–14 weeks were re-screened by either the two-step method or the one-step method. They found that the one-step method had the best performance with an area under the ROC curve of 0.792, a sensitivity of 87.1%, and a specificity of 100%, followed by the two-step method, with an area under the ROC curve of 0.708, a sensitivity of 68.2%, and a specificity of 100%, both of which were better than the performance of FPG method, with an area under the ROC curve of 0.623, a sensitivity of 47.17%, and a specificity of 77.37%. On the other hand, Benaiges et al. analyzed the performance of first-trimester hemoglobin A1c (HbA1c) to detect GDM, which was defined by the two-step approach using the NDDG criteria at the 24th–28th weeks of gestation [64]. They found that the area under the ROC curve was 0.679. With a cutoff of HbA1c at 5.6%, the sensitivity was low (32.9%), and the specificity was 89.3%.

Another important issue of early screening for GDM is its impact on pregnancy outcomes. Recently, results from an observational study in 9795 pregnant women found that early screening for GDM is not associated with improved pregnancy outcomes [65••]. A large-scale multi-center RCT assessing the benefits of early screening and management of GDM is ongoing [66••]. In summary, the methods of early screening or diagnosis of GDM are diverse, and current evidence does not justify the use of any particular method.

Alternative Diagnostic Strategies for Areas with Limited Resources

In certain countries where areas with limited resources exist, universal screening with either one-step or two-step OGTT diagnostic strategies may not be feasible. To save cost and decrease the healthcare system burden, some alternative diagnostic strategies to avoid OGTT have been developed, including FPG-based methods, non-fasting 2-h post-load plasma glucose-based methods, and risk factor-based methods. Some of the methods have been adopted by professional associations (Table 2). The performance of these alternative methods is efficacious or cost-effective in the countries where they were developed [15, 62, 67–70]. However, when applying these strategies to different ethnic groups or countries, the performance becomes only modest [71, 72].

Conclusions

In conclusion, current evidence favors universal screening for GDM. Compared with the two-step method, most observational cohort studies report that the one-step method to diagnose GDM is associated with improved pregnancy outcomes and appears to be cost-saving or cost-effective, although these findings should be confirmed in upcoming RCTs comparing the performance of the one-step and two-step methods. Early screening for early onset GDM is not justified by the current literature.

Compliance with Ethical Standards

Conflict of Interest Chun-Heng Kuo and Hung-Yuan Li declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent All reported studies with human subjects performed by the authors have been previously published and complied with the ethical standards of institutional research committee and with the Helsinki declaration and its amendments.

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