

Gestational diabetes: universal or selective screening in pregnancy?

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ABSTRACT

Gestational diabetes mellitus (GDM) is one of the most frequent complications of pregnancy. Despite international efforts, there is no consensus regarding the optimal method of screening and diagnosis of GDM. Some organizations propose screening only for women with high risk of GDM, while others suggest testing all pregnant women. Furthermore, there are more types of screening and diagnostic tests (one vs. two-step approach) with different glycemic thresholds. The aim of this review is to present and compare the screening and diagnosis guidelines of the most influential organizations. Additionally, this study evaluates the differences between selective and universal screening. The necessity for a consensus and for a single acceptable guideline has been repeatedly highlighted by experts in order to allow uniform clinical practice and to improve perinatal and maternal outcomes.

Keywords: diabetes mellitus, pregnancy, screening, selective, universal

INTRODUCTION

Gestational diabetes mellitus (GDM) is one of the most frequent complications of pregnancy. According to the International Association of Diabetes and Pregnancy Study Groups (IADPSG) screening and diagnostic criteria, the global prevalence of GDM is 16.9% [1]. The rate of GDM diagnosis may vary between countries (2.4-37.7%) because there is no universally accepted standard concerning screening for or diagnosis of GDM [2]. Furthermore, the incidence depends on the studied population, the region with the highest GDM prevalence being South East Asia with 25% [1]. Nevertheless, GDM incidence is rising due to the increase in maternal age and obesity [3].

Pregnancy is naturally associated with a hyperglycemic state in order to ensure proper nutrition for the fetus. Especially during the second and third trimester, hormones such as cortisol, estrogen and placental secretion of corticotropin-releasing hormone, growth

hormone, and human placental lactogen, mediate insulin resistance in pregnancy [4]. GDM occurs in pregnant patients whose pancreas is insufficiently functioning to overcome the state of insulin resistance. Furthermore, patients with GDM are at high risk of developing type 2 diabetes later in life. Studies assessed that 70% of women with GDM will develop diabetes within approximately 25 years after pregnancy [5,6].

GDM is associated with an increased morbidity for both mother and fetus. Short term neonatal and maternal adverse outcomes include hypertensive disorders of pregnancy, macrosomia, birth trauma to mother or newborn (nerve palsy, fracture), operative delivery (cesarean or assisted vaginal), neonatal hypoglycemia, neonatal hypertrophic cardiomyopathy, and perinatal mortality [7,8]. Infants of women with GDM have an increased risk of developing obesity, insulin resistance, diabetes, and hypertension later in life [9,10].

Screening, diagnosis and treatment of GDM is essential in order to prevent adverse maternal and neonatal outcomes of GDM. The randomized controlled trial Australian Carbohydrate Intolerance Study in Pregnant Women (ACHOIS) showed that treatment of GDM reduced maternal risk of preeclampsia and neonatal risks of macrosomia, perinatal mortality, shoulder dystocia, and birth trauma [11]. Subsequent studies confirmed the linear relationship between maternal glucose and fetal growth and the benefits of treating GDM [12].

Since then, on the basis of the ACHOIS study the International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommended universal screening for GDM of all pregnant women in trying to achieve an international consensus for screening and diagnosis [13]. Currently, there is no consensus on screening and diagnosis of GDM and there are nearly 30 different guidelines for screening and diagnosis of GDM worldwide [14]. Some organizations propose screening for GDM of high-risk women only, while other suggest testing all pregnant women. Furthermore, there are more types of screening and diagnostic tests (one vs. two-step approach) with different glycemic thresholds. The lack of consensus creates major problems in establishing prevalence of GDM, and in carrying out a uniform clinical practice by addressing complications and management of this disease.

The aim of this review is to present and compare the screening and diagnosis guidelines from different organizations such as the American College of Obstetricians and Gynecologists (ACOG), the American Diabetes Association (ADA), the National Institute for Health and Care Excellence (NICE), the International Association of Diabetes and Pregnancy Study Groups (IADPSG), and the World Health Organization (WHO). Additionally, the review evaluates the differences between selective and universal screening.

SELECTIVE SCREENING

The National Institute for Health and Care Excellence (NICE) recommends selective screening only for women with risk factors. Pregnant women are evaluated for the following risk factors: BMI greater than 30kg/m², history of macrosomic babies or GDM; family history of diabetes (first-degree relatives); ethnicity with high risk of diabetes (South Asia; Black Caribbean; Middle Eastern) [15]. Women with additional risks, especially those with history of GDM in a previous pregnancy, should be screened earlier (first trimester) and retested at 24 to 28 weeks of gestation, if the initial test is negative. These women can either self-monitor their blood glucose or can undergo a OGTT as soon as possible early in pregnancy [15].

NICE uses the one-step 75g 2- hours oral glucose test (OGTT) at 24 to 28 weeks of gestation. They assess the fasting and the 2 hours postprandial glucose level for the diagnosis of GDM. Explicitly, GDM is diagnosed if fasting plasma glucose level is above 5.6 mmol/L or if 2-hour plasma glucose level is above 7.8 mmol/L [15]. HbA1c levels are measured for all pregnant women with pre-existing diabetes. Risks are increased for women who exceed 6.5% HbA1c [15]. NICE does not recommend HbA1c levels for monitoring blood glucose control for women with GDM.

Although the risk factors that NICE consider for screening for GDM are found in 30-50% of pregnant population, they continue to screen only high-risk women [16]. Even though IADPSG [13] recommends universal screening since 2010, NICE continues to screen selectively.

IADPSG recommends a one-step 75g OGTT at 24-28 weeks of gestation. Plasma glucose values are evaluated in fasting state and after one and two hours postprandial and GDM is diagnosed when at least one of the three values are above the following threshold limits: fasting ≥ 5.1 mmol/l (92 mg/dl), 1-hour ≥ 10.0 mmol/l (180 mg/dl), 2-hours ≥ 8.5 mmol/l (153 mg/dl) [13]. The World Health Organization [17] has also adopted these criteria, aiming towards a universal consensus for the diagnosis of GDM.

Table 1 presents the diagnostic criteria for GDM of different guidelines. Besides the different view regarding universal and selective screening, NICE uses also different threshold values for the fasting and 2-hour glucose value without measuring the 1-hour glucose value.

The Royal College of Obstetricians and Gynecologists [16] stated that, although universal screening would increase the number of women diagnosed with gestational diabetes, the maternal interventions for blood glucose control are relatively noninvasive for most women. Dietary and lifestyle interventions are effective in improving pregnancy outcomes. Furthermore, the issue with selective screening is the concern that it may miss a great portion of women with GDM [14]. A study that compared risk-factor based screening with a universally based one reported that the universal screening detected more women with GDM (2.7% vs. 1.45%, $p < 0.03$) and that this group had better outcomes [18].

UNIVERSAL SCREENING

United States guidelines recommend universal screening, considering that 90% of pregnant women would have at least one risk factor for GDM [19]. Since 2014, the U.S. Preventive Services Task Force recommends screening all pregnant women for GDM at 24-28

weeks of gestation [20]. There are two different approaches regarding screening in the US, namely the one- and the two-step test. The latter one being the most widely used.

The American College of Obstetricians and Gynecologists (ACOG) recommends the two-step method. The first screening step is the 50 g one-hour OGTT at any time of the day and with no regard on previous meals. There is no consensus on the glucose 1 hour threshold value and practitioners can select cut-off values between 130 and 140 mg/dl depending on the community GDM prevalence [21]. The screen-positive women continue with the second step, which is a diagnostic test. ACOG recommends the 100g 3 hours OGTT [21]. There are different cut-off values for the diagnosis of GDM. Table 1 presents the diagnostic values recognized by the National Diabetes Data Group and by Carpenter and Coustan. The diagnostic 100g OGTT measures fasting glucose and serum glucose at one, two and three hours after glucose administration. Diagnosis of GDM is made if two or more glucose values are elevated.

Conversely, the American Diabetes Association (ADA) recommends the one-step test by performing the 75g 2-hours OGTT diagnostic test [22]. The diagnostic criteria of ADA agree with the IADPSG criteria as seen in Table 1. However, ADA stated that there is insufficient evidence to support the one-step approach over the two-step screening method [23].

A meta-analysis comparing the one- with the two-step approach reported an increased proportion of women diagnosed with GDM but improved maternal and neonatal outcomes in the one-step screening group [24]. A subsequent study [25], with a greater number of subjects included, reported no significant differences regarding maternal and neonatal outcomes between both groups. Furthermore, double as many patients in the one-step group were diagnosed with GDM (16.5% vs 8.5%). A Cochrane review concluded that no specific screening strategy is ideal [26]. Therefore, there is no clear evidence which of the two approaches is optimal. ACOG suggests that the two-step approach remains preferable considering that the one-step test would increase the medical system burden with no clear benefits [21].

EARLY SCREENING

Considering the increasing incidence of pregnant patients with unrecognized type 2 diabetes, early screening of pregnant women with diabetic risk factors is recommended for detecting undiagnosed pregestational diabetes [13,21]. The term “overt diabetes” is used for defining women diagnosed in the first trimester with gestational diabetes, who will subsequently be diagnosed with type 2 diabetes postpartum [13].

According to ACOG [21] and ADA [23], women with a body mass index greater than 25 (greater than 23 for Asian Americans) with at least one of the following risk factors should be screened in the first trimester: history of macrosomic babies; GDM, or cardiovascular disease; women diagnosed with polycystic ovarian syndrome, with hypertension, or other clinical conditions associated with insulin resistance; physical inactivity; first-degree relative with diabetes; high-risk ethnicity; HDL cholesterol level less than 35 mg/dl, or a triglyceride level greater than 250 mg/dl; HbA1c greater than or equal to 5.7%.

ACOG early screening method constitutes of the two-step approach and the diagnostic criteria of overt diabetes are the same as those used for diagnosis of GDM later in pregnancy. Women with initial negative follow-up test will be tested directly with the 100g 3h OGTT at 24-28 weeks of gestation [21]. Conversely, ADA [23] suggests that Hb A1c ($\geq 6.5\%$) can also be used for early diagnosis, but it may not be as sensitive as OGTT. The cut-off values for diagnosis of early diabetes in pregnancy are the same as those used for non-pregnant patients. The diagnostic criteria are as follows: HbA1C $\geq 6.5\%$, or fasting blood glucose ≥ 126 mg/dL, or 75g 2-hour OGTT with 2-hour plasma glucose ≥ 200 mg/dL, or a random plasma glucose ≥ 200 mg/dL with hyperglycemic symptoms. If fasting blood glucose ranges from 92 mg/dl to 126 mg/dl, it is considered that these women have prediabetes and are encouraged to have life-style changes [23].

Similarly, IADPSG [13] criteria for overt diabetes is fasting blood glucose ≥ 126 mg/dL or HbA1c $\geq 6.5\%$ or a random plasma glucose ≥ 200 mg/dL confirmed by fasting blood glucose or A1c levels. If early screening is negative, all women should repeat screening at 24-28 weeks of gestation. They suggest that detection of overt diabetes should be made as soon as possible and that the assessment should be made at the initial visit. Whether evaluation for overt diabetes should be performed universally or for women with high risk remains unclear, and the decision should be made by the clinician [13].

Because the incidence of type 2 diabetes is increased in Romania, all pregnant women are screened in the first trimester or at the first prenatal visit by evaluating the fasting blood glucose levels. Overt diabetes is diagnosed if fasting blood glucose is above 126 mg/dl [27]. Otherwise, high-risk women without overt diabetes are screened at 24-28 weeks of gestation by performing the 75g 2h OGTT [27].

CONCLUSION

GDM represents an important pathology in pregnancy with increasing prevalence. Because of the ma-

TABEL 1. Guidelines for the diagnosis and screening of GDM between 24–28 gestational weeks

	One-step approach		Two-step approach	
	75 g 2h OGTT		100 g 3h OGTT: ACOG 2018*	
	IADPSG 2010, ADA 2020, WHO 2013	NICE 2015	Carpenter/Coustan	National Diabetes Data Group
Fasting	92 mg/dL (5.1 mmol/L)	100 mg/dL (5.6 mmol/L)	95 mg/dL (5.3 mmol/L)	105 mg/dL (5.8 mmol/L)
One hour	180 mg/dL (10 mmol/L)	Not required	180 mg/dL (10 mmol/L)	190 mg/dL (10.6 mmol/L)
Two hours	153 mg/dL (8.5 mmol/L)	140 mg/dL (7.8 mmol/L)	155 mg/dL (8.6 mmol/L)	165 mg/dL (9.2 mmol/L)
Three hours	Not required	Not required	140 mg/dL (7.8 mmol/L)	145 mg/dL (8 mmol/L)
GDM Diagnosis	≥1 glucose value at or above these thresholds		≥2 glucose values at or above these thresholds	
* after 50 g 1h positive OGTT with plasma glucose level ≥ 130-140 mg/dl (7.5-7.8 mmol/L)				
OGTT: oral glucose tolerance test IADPSG: International Association of the Diabetes and Pregnancy Study Groups ADA: American Diabetes Association WHO: World Health Organization NICE: National Institute for Health and Care Excellence ACOG: American College of Obstetricians and Gynecologists				

ternal and neonatal adverse outcomes associated with GDM, proper diagnosis and treatment are essential for the well-being of both the mother and the newborn. To this day, the screening for GDM remains a dilemma because guidelines follow different procedures and glucose thresholds.

The NICE guideline recommends selective screening, whereas ACOG, ADA, IADPSG and WHO recommend screening for all pregnant women at 24 to 28 weeks of gestation. All guidelines state that women with risk factors should be screened in the first trimester or at the first prenatal visit in order to detect overt diabetes and retested at 24- 28 weeks of gestation if the initial test is negative. The optimal screening method remains controversial. IADPSG recommends the one-step approach which has been endorsed by ADA

and WHO. Furthermore, NICE also uses a one-step diagnostic test. ACOG still advocates the use of two-step testing because the one-step approach increases the rate of GDM diagnosis, without clear evidence to show improvement of adverse outcomes. ADA suggests leaving the decision to the clinician in choosing between the two approaches and emphasizes the need for further research in order to generalize an optimal screening method.

The necessity for a consensus and for a single acceptable guideline has been repeatedly highlighted by experts in order to allow uniform clinical practice and to improve perinatal and maternal outcomes. Further research should be encouraged to allow a global uniformity for the diagnosis of GDM.

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