No. 334 (Replaces No. #121, November 2002)

Diabetes in Pregnancy

This Clinical Practice Guideline has been prepared by the Maternal Fetal Medicine Committee; reviewed by the Family Physicians Advisory, Aboriginal Health Initiative, and Clinical Practice – Obstetrics Guideline Committees and the Canadian Diabetes Association; endorsed by the Canadian Diabetes Association; and approved by the Board of the Society of Obstetricians and Gynaecologists of Canada.

PRINCIPAL AUTHORS

Howard Berger, MD, Toronto ON

Robert Gagnon, MD, Montreal QC

Mathew Sermer, MD, Toronto ON

MATERNAL FETAL MEDICINE COMMITTEE

Melanie Basso, RN, Vancouver BC

Hayley Bos, MD, Victoria BC

Richard N. Brown, MD, Beaconsfield QC

Emmanuel Bujold, MD, Quebec QC

Stephanie L. Cooper, MD, Calgary AB

Robert Gagnon, MD, Montreal QC

Katy Gouin, MD, Quebec QC

N. Lynne McLeod, MD, Halifax NS

Savas M. Menticoglou, MD, Winnipeg MB

William R. Mundle, MD, Windsor ON

Anne Roggensack, MD, Calgary AB

Frank L. Sanderson, MD, Saint John NL

Jennifer D. Walsh, MD, Rothesay NB

Disclosure statements have been received from all members of the committee(s).

Key Words: Diabetes, pregnancy, stillbirth

http://dx.doi.org/10.1016/j.jogc.2016.04.002

J Obstet Gynaecol Can 2016;38(7):667-679

Abstract

Objective: This guideline reviews the evidence relating to the diagnosis and obstetrical management of diabetes in pregnancy.

Outcomes: The outcomes evaluated were short- and long-term maternal outcomes, including preeclampsia, Caesarean section, future diabetes, and other cardiovascular complications, and fetal outcomes, including congenital anomalies, stillbirth, macrosomia, birth trauma, hypoglycemia, and long-term effects.

Evidence: Published literature was retrieved through searches of PubMed and the Cochrane Library using appropriate controlled vocabulary (MeSH terms "diabetes" and "pregnancy"). Where appropriate, results were restricted to systematic reviews, randomized control trials/controlled clinical trials, and observational studies. There were no date limits, but results were limited to English or French language materials.

Values: The quality of evidence was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (Table 1).

Summary Statements

1. The adverse outcomes associated with diabetes in pregnancy are substantially associated with hyperglycemia and the coexisting metabolic environment. Women with preexisting diabetes should receive preconception care to optimize blood sugar control and other comorbidities. Outcomes for the fetus/neonate and the mother in both pre-gestational diabetes mellitus and gestational diabetes mellitus pregnancies are improved by multidisciplinary management in which the goal is achieving optimal blood sugar control and appropriate fetal surveillance. (II-2)
2. Retrospective studies indicate that women with pre-gestational diabetes mellitus have an increased risk of stillbirth before 40 weeks' gestation compared with the general obstetrical population. Similarly, large recent cohort and simulation studies of women with gestational diabetes mellitus pregnancies also indicate a higher risk of stillbirth between 36 to 39 weeks' gestation. (II-2)
3. Women with gestational diabetes mellitus have a higher risk of preeclampsia, shoulder dystocia, Caesarean section, and large for gestational age infants. (II-2)
4. Treatment of women with gestational diabetes mellitus and optimization of glycemic control reduce the risk of preeclampsia, shoulder dystocia, and large for gestational age infants. (I)
5. The occurrence of gestational diabetes mellitus increases the risk of developing type 2 diabetes in the future for the mother. (II-2)

Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventative Health Care

Quality of evidence assessment*	Classification of recommendations†
I Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1 Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2 Evidence from well-designed cohort (prospective or retrospective) or case-control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3 Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in the category	D. There is fair evidence to recommend against the clinical preventive action
III Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	E. There is good evidence to recommend against the clinical preventive action
	F. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in The Canadian Task Force on Preventive Health Care.

Woolf SH, Battista RN, Angerson GM, Logan AG, Eel W. Canadian Task Force on Preventive Health Care. New grades for recommendations from the Canadian Task Force on Preventive Health Care. CMAJ 2003;169:207e8.

Recommendations

1. The "preferred screening and diagnostic 2-step" approach for gestational diabetes mellitus of the Canadian Diabetes Association 2013 guidelines is endorsed. All pregnant women should be offered screening between 24 to 28 weeks using a standardized non-fasting 50-g glucose challenge screening test with plasma glucose measured 1 hour later. (III-B)

   1.1. If the value is $<$ 7.8 mmol/L, no further testing is required.

   1.2. If the value of the glucose challenge screening test is 7.8 to 11.0, a 2-hour 75-g oral glucose tolerance test with fasting plasma glucose, 1-hour plasma glucose, and 2-hour plasma glucose should be performed.

   Gestational diabetes mellitus is diagnosed if 1 value is met or exceeded:

   i. Fasting plasma glucose $\geq$ 5.3 mmol/L

   ii. 1-hour plasma glucose $\geq$ 10.6 mmol/L

   iii. 2-hour plasma glucose $\geq$ 9.0 mmol/L

   1.3. If the value of the glucose challenge screening test is $\geq$ 11.1 mmol/L, gestational diabetes mellitus is diagnosed.

2. The "alternative 1-step diagnostic" approach of the Canadian Diabetes Association 2013 guidelines is acceptable. In this strategy pregnant women should be offered testing between 24 to 28 weeks using a standardized 2-hour 75-g oral glucose tolerance test with fasting plasma glucose, 1-hour plasma glucose, and 2-hour plasma glucose. (III-B)

   Gestational diabetes mellitus is diagnosed if 1 value is met or exceeded:

   i. Fasting plasma glucose $\geq$ 5.1 mmol/L

   ii. 1-hour plasma glucose $\geq$ 10.0 mmol/L

   iii. 2-hour plasma glucose $\geq$ 8.5 mmol/L

   It is recognized that the use of different diagnostic thresholds for the "preferred" and "alternative" strategies could cause confusion in certain settings. Despite this, the committee has identified the importance of remaining aligned with the current Canadian Diabetes Association 2013 guidelines as being a priority. It is thus recommended that each care centre strategically align with 1 of the 2 strategies and implement protocols to ensure consistent and uniform reporting of test results.

3. If there is a high risk of gestational diabetes mellitus based on multiple risk factors, screening or testing should be offered during the first half of the pregnancy and repeated at 24 to 28 weeks' gestation if initially normal. If for any reason it was missed or if there is a clinical suspicion of later onset of gestational diabetes, a screening or diagnostic test should be performed. (II-2B)

4. Women with preexisting or gestational diabetes mellitus should be provided with care by a multidisciplinary team aimed at attaining and then maintaining euglycemia. (II-2B)

ABBREVIATIONS

ACOG	American College of Obstetricians and Gynecologists
BMI	body mass index
CDA	Canadian Diabetes Association
DM	diabetes mellitus
FPG	fasting plasma glucose
GCT	glucose challenge screening test
GDM	gestational diabetes mellitus
HAPO	Hyperglycemia and Adverse Pregnancy Outcome
IADPSG	International Association of Diabetes and Pregnancy Study Groups
LGA	large for gestational age
NST	non-stress test
OGTT	oral glucose tolerance test
PG	plasma glucose
PGDM	pre-gestational diabetes mellitus
RR	relative risk
SMBG	self-monitored blood glucose

5. For patients with pre-gestational diabetes mellitus or gestational diabetes mellitus, starting at 28 weeks as a baseline, with subsequent serial assessment of fetal growth, every 3 to 4 weeks is suggested to assess the effect of maternal glycemic control on fetal growth rate and amniotic fluid volume. (II-2B)
6. Initiation of weekly assessment of fetal well-being at 36 weeks is recommended in pre-gestational diabetes mellitus and gestational diabetes mellitus. It is also reasonable to consider weekly fetal assessment for women with diet controlled gestational diabetes mellitus beginning at 36 weeks. Acceptable methods of assessment of fetal well-being near term can include the non-stress test, non-stress test + amniotic fluid index, biophysical profile, or a combination of these. (III-A)
7. If comorbid factors are present, such as obesity, evidence of suboptimal glycemic control, large for gestational age ($>$ 90%), previous stillbirth, hypertension, or small for gestational age ($<$ 10%), earlier onset and/or more frequent fetal health surveillance is recommended. In specific cases in which fetal growth restriction is suspected, the addition of umbilical artery and fetal middle cerebral artery Doppler assessment may be helpful. (II-2A)
8. Pregnant women with gestational diabetes mellitus or pre-gestational diabetes mellitus should be offered induction between 38 to 40 weeks' gestation depending on their glycemic control and other comorbidity factors. (II-2B)
9. The administration of betamethasone to pregnant women with gestational diabetes mellitus should be restricted to the routine obstetric indications related to the risk of preterm and late preterm delivery between 24 to 36 weeks' gestation, when clinically indicated. When administered, close maternal glycemic surveillance is recommended. (I-A)
10. If not previously done, in women with threatened preterm labour requiring betamethasone, a screening for gestational diabetes mellitus should be performed either before or at least 7 days after the administration of betamethasone. (III-B)
11. Women with gestational diabetes mellitus should be offered testing with a 75-g oral glucose tolerance test between 6 weeks and 6 months postpartum to detect prediabetes and diabetes.[1] (II-2A)
    - 11.1. Normal
        - i. Fasting plasma glucose $<$ 6.1 mmol/L
        - ii. 2-hour plasma glucose $<$ 7.8 mmol/L
        - iii. Glycated hemoglobin $<$ 6.0%
    - 11.2. Pre-diabetic
        - i. Fasting plasma glucose 6.1 to 6.9 mmol/L or
        - ii. 2-hour plasma glucose 7.8 to 11.0 mmol/L or
        - iii. Glycated hemoglobin 6.0% to 6.4%
    - 11.3. Type 2 diabetes mellitus
        - i. FPG $\geq$ 7.0 mmol/L
        - ii. Random plasma glucose or 2-hour plasma glucose $\geq$ 11.1 mmol/L
        - iii. Glycated hemoglobin $\geq$ 6.5%
12. Breastfeeding is strongly recommended after delivery for all women with pre-gestational diabetes mellitus or gestational diabetes mellitus. (II-2A)

INTRODUCTION

A large population-based study in Ontario demonstrated that between 1996 and 2010 the incidence of both GDM and PGDM, which includes both type 1 and type 2 DM, doubled from 2.7% to 5.6% for GDM and from 0.7% to 1.5% for PGDM.[2] When compared with non-diabetic pregnant women, the risk of both congenital anomalies (OR 1.86, 95% CI 1.49 to 2.33) and perinatal mortality (OR 2.33 [1.59 to 3.43]) remained higher in PGDM pregnant women.[2] Similarly, in a Swedish population-based cohort of over 1.2 million pregnancies with singleton gestations, women with GDM had a higher risk of adverse maternal outcomes (OR 1.81 [1.64 to 2.00]; for shoulder dystocia of (OR 2.74 [2.04 to 3.68]); and for Caesarean section (OR 1.46 [1.38 to 1.54]).[3] In addition, with GDM, a higher risk of adverse neonatal outcomes has been reported, including LGA (OR 3.43 [3.21 to 3.67]), Erb's palsy (OR 2.56 [1.96 to 3.32]), prematurity (OR 1.71 [1.58 to 1.86]), and major malformations (OR 1.19 [1.02 to 1.39]).[3] It is of interest that no statistically significant improvement in maternal and neonatal outcome was seen over time in either study, with the exception of a decline in the rate of congenital anomalies by 23%.[2,3]

Even though the benefits of specialized management of pregnancies complicated by PGDM is well-known, we now have data from RCTs that document a reduction in certain perinatal morbidities after diagnosis and management of GDM.[4,5] The primary goal of this management is to attain and then maintain euglycemia. This is best done by a multidisciplinary team with attention to diet and exercise; glucose monitoring; and, as appropriate, medical management with insulin and/or oral hypoglycemic agents.

The purpose of these guidelines is to review the diagnostic criteria and issues related to the obstetrical management of GDM and PGDM. Specific recommendations regarding glycemic control are beyond the scope of this document but can be found in the 2013 CDA Clinical Practice Guidelines, available at: http://guidelines.diabetes.ca/browse/chapter36.

IMPACT OF DIABETES MELLITUS ON PERINATAL MORTALITY

Table 2 summarizes the RR or OR for stillbirth in pregnancies with GDM in different populations studied compared with non-GDM pregnancies. A wide range of absolute stillbirth rate (per 1000 pregnancies) has been reported, from as low as 0.32 to 4.2 per 1000 pregnancies, depending on the population studied and the gestational age cutoff used to define stillbirth (see Table 2). Some studies[11] have confirmed that GDM may be diagnosed before 24 weeks' gestation approximately 22% to 27% of the time. Almost one third (or 8% of the total diagnosed with GDM) of these patients will have type 2 diabetes when tested postpartum.[12] This is particularly true in the presence of the following risk factors: maternal age > 35 years; obesity (BMI > 30); ethnicity (Aboriginal, African, Asian, Hispanic, South Asian); family history of diabetes; polycystic ovary syndrome; acanthosis nigricans; corticosteroid use; previous pregnancy complicated with GDM; or previous macrosomic infant.[1] Hutcheon et al.[6] have suggested that only stillbirths greater than 28 weeks' gestation should be included to determine the risk of stillbirth associated with GDM. Including women with an earlier diagnosis may not represent the risk associated with GDM but rather a mix of GDM and other causes of stillbirths, leading to the introduction of a bias by including a period of follow-up during which, by design, death or the study outcome cannot occur. Because GDM is usually diagnosed after 24 to 28 weeks' gestation, it would be more appropriate to include only late stillbirth occurring after 28 weeks. Table 2 illustrates this phenomenon. When defining stillbirth occurring at > 20 weeks, the risk of stillbirth attributable to GDM is reduced or insignificant.[6–9] This is because more than 30% of stillbirths

Table 2. Risk of Stillbirth (GDM vs. No GDM)

Author	Gestational age cutoff	Population (n)	Absolute stillbirth rate in GDM (per 1000 pregnancies)	RR or OR (95% CI)	Policy management
Hutcheon et al.[6]	≥ 20 weeks	2 001 749	4.2	0.88 (0.79 to 0.99)	Not available
Peticca et al.[7]	≥ 20 weeks	120 604	2.0	0.31 (0.11 to 0.67)	Induction rate: 38% vs 24%
Karmon et al.[8]	≥ 20 weeks	184 256	4.0	0.5 (0.4 to 0.7)	Routine induction at 40 weeks
Ohana et al.[9]	≥ 20 weeks	228 293	0.32	0.7 (0.5 to 0.8)	Not available
Fadl et al.[3]	> 28 weeks	1 260 297	4.0	1.18 (0.87 to 1.60)	Not available
Hutcheon et al.[6]	> 28 weeks	1 988 320	3.5	1.25 (1.11 to 1.41)	Not available
Rosenstein et al.[10]	≥ 36 weeks	4 190 953	1.71	1.34 (1.2 to 1.5)	At > 39 weeks risk higher if expectant management

occur at 20 to 23 weeks, before GDM is usually diagnosed.[13] When including only stillbirths occurring after 28 weeks, many studies to date have shown a trend or a statistically significant increased risk of stillbirth attributable to GDM.[3,6,10] The specific excess risk of stillbirth in relation to week of gestation has recently been shown in a cohort[10] and simulation study derived from this cohort.[14] This retrospective analysis[14] of population-based data from California showed that the overall risk of stillbirth from 36 to 42 weeks' gestation was higher in women with GDM compared with women without GDM (17.1 vs. 12.7/10 000 deliveries; RR 1.34; 95% CI 1.2 to 1.5). Stillbirth rates were also examined at each gestational age, and from 36 to 39 weeks, women with GDM had a statistically significant elevated RR of stillbirth compared with women without GDM, ranging from RR 1.45 (95% CI 1.1 to 1.9) at 36 weeks to RR 1.84 (95% CI 1.5 to 2.3) at 37 weeks.[14] This increased risk of stillbirth remained statistically significant at 39 weeks with a RR of 1.56 (95% CI 1.2 to 2.0) but not at 40 and 41 weeks' gestation. The loss of significance at 40 to 41 weeks' gestation was either due to the increase in stillbirths in non-GDM pregnancies[15] or due to the relatively low number of patients after 39 weeks' gestation in GDM pregnancies compared with non-GDM pregnancies. In addition, the risk of expectant management in women with GDM carried a higher risk of perinatal mortality than the risk of delivery at 39 and 40 weeks' gestation.[10,14] The number of women with GDM needed to be delivered at 39 and 40 weeks to prevent 1 excess death was 1518 and 1311, respectively.[13] This is comparable with the number needed to be delivered of 1299 at 40 weeks for women without GDM and $\geq$ 40 years at the time of delivery.[15] The retrospective nature of this study and the inability to control for glycemic control and insulin treatment presented limitations. A retrospective cohort study from a center with a policy of induction by 40 weeks' gestation for all pregnant women with diet-controlled GDM suggested that it is protective against stillbirth compared with the general obstetrical population (OR 0.5 [0.4 to 0.7]).[8] The impact of this policy of induction on Caesarean section rates and neonatal morbidity is controversial. However, a small RCT in mainly non-diabetic women by Nicholson et al.[16] demonstrated a lower neonatal intensive care unit admission rate, a higher uncomplicated vaginal birth rate, and a lower mean adverse outcome index score (better pregnancy outcomes) among women who were actively managed using elective labour induction based on a unique management of risk scoring system.

There is good evidence that PGDM is associated with a 3- to 5-fold increased risk in stillbirths compared with non-diabetic pregnant women.[17] Further prospective research is needed on the optimization of timing of delivery in both GDM and PGDM pregnancies with specific attention to stratification by adequacy of glycemic control; the impact on maternal, fetal and neonatal outcomes; and economic analysis of different management strategies.

Summary Statements

1. The adverse outcomes associated with diabetes in pregnancy are substantially associated with hyperglycemia and the coexisting metabolic environment. Women with preexisting diabetes should receive preconception care to optimize blood sugar control and other comorbidities. Outcomes for the fetus/neonate and the mother in both pregestational diabetes mellitus and gestational diabetes mellitus pregnancies are improved by multidisciplinary management in which the goal is achieving optimal blood sugar control and appropriate fetal surveillance. (II-2)
2. Retrospective studies indicate that women with pregestational diabetes mellitus have an increased risk of stillbirth before 40 weeks' gestation compared with the general obstetrical population. Similarly, large recent cohort and simulation studies of women with gestational diabetes mellitus pregnancies also indicate a higher risk of stillbirth between 36 to 39 weeks' gestation. (II-2)

Screening for GDM (Appendix A)

Despite not meeting many of the criteria for a program of population-based screening,[18] screening for GDM has been accepted widely and is almost universally practiced among health care professionals in North America.[19,20] Methods for screening for GDM include the following:

1. Screening with a 1-hour 50-g glucose load (or alternative)
2. Risk factor based screening
3. One-step testing with a diagnostic 2-hour 75-g OGTT (this does not in fact constitute a screening test but rather universal testing)
4. Screening with alternative biochemical tests: FPG, glycated hemoglobin, random plasma glucose

There have been no RCTs comparing screening for GDM with no screening,[20] thus the decision to perform screening is based on the recent RCTs that have shown certain health benefits for treatment of GDM.[4,5] Because GDM is an asymptomatic condition, logic dictates that some form of screening would need to be performed to diagnose cases

that might benefit from treatment and management. The Toronto Tri Hospital study established that adverse outcomes associated with GDM increase along a continuum of increasing glucose thresholds.[21] More recently, the Hyperglycemia and Adverse Pregnancy Outcome study[22] confirmed these findings in a large, prospective, observational study but was unable to define outcome-based thresholds for the diagnosis of GDM. Despite this, the International Association of Diabetes and Pregnancy Study Group published recommendations for new thresholds for the diagnosis of GDM based on statistical re-analysis of the HAPO data.[23] The thresholds for the 2-hour 75-g OGTT used were calculated by defining glucose concentrations at which the OR of the 4 HAPO primary outcomes (birthweight > 90%, primary Caesarean section rate, neonatal hypoglycemia, and cord C-peptide levels > 90%) reached 1.75. These thresholds, when applied to the HAPO cohort, led to an average GDM incidence of 17% across all HAPO sites. In addition the IADPSG recommended abandoning the 1-hour 50-g glucose load in favour of a 1-step testing strategy. Table 3 provides a summary of the glucose thresholds, screening, and diagnostic strategies used worldwide. In North America, either a 2-step or a 1-step approach is believed to be acceptable because there is no demonstrated difference in outcome using either strategy.[1,24,25]

The CDA guidelines, in which SOGC was represented in an attempt to achieve consensus between obstetricians and endocrinologists, were updated in 2013.[1] Guiding the decisions of the committee were the realization that: (1) women with 1 abnormal value on the OGTT (previously classified as intolerance to glucose of pregnancy) have similar outcomes of women with 2 abnormal values and are routinely managed in the same manner[12,29–33]; (2) the HAPO trial[22] provided data that could be used to help formulate outcome-based diagnostic thresholds for GDM; and (3) there is a need to achieve some degree of uniformity with regard to screening methodology and diagnostic criteria in Canada. The CDA 2013 guidelines recommend a universal screening for GDM for all pregnant women between 24 and 28 weeks' gestation followed by a 2-hour 75-g OGTT if the 1-hour PG after a 50-g glucose load value is ≥ 7.8 mmol.[1] This is referred to as the "preferred 2-step" approach, with diagnostic criteria thresholds corresponding to an OR of 2.0 for the 4 main HAPO outcomes.[22] An "alternative 1-step" approach with diagnostic criteria thresholds with an OR of 1.75[22] for adverse perinatal outcome is also acceptable.[1] The 2014 American Diabetes Association guidelines[25] endorsed an approach similar to those of the CDA 2013 guidelines, although the second step differs with the diagnostic test remaining the 100-g OGTT.[25] These guidelines are also more in line with

Table 3. Universal Screening and Diagnostic Criteria for GDM (mmol/L)

	ACOG 2013[24] ADA 2014[25] Carpenter and Coustan	ACOG 2013[24] ADA 2014[25] National Diabetes Data Group	CDA 2013[1] "preferred approach"	CDA 2013[1] "alternative approach," IADPSG 2010,[26] ADIPS 2014,[27] ADA 2014[25]	WHO 2013[28]
Gestational age at screening*	24 to 28 weeks	24 to 28 weeks	24 to 28 weeks	24 to 28 weeks	Any time
Steps	2-step	2-step	2-step	1-step	1-step
Step 1 Screening 1-hour 50-g glucose challenge	Step 2 if value ≥ 7.8 No diagnostic cutoff for GDM	Step 2 if value ≥ 7.8 No diagnostic cutoff for GDM	GDM if ≥ 11.1 Step 2 if value 7.8 to 11.0		
Step 2					
Loading dose	100 g	100 g	75 g	75 g	75 g
Fasting	≥ 5.3	≥ 5.8	≥ 5.3‡	≥ 5.1†	≥ 5.1†
1 hour	≥ 10.0	≥ 10.6	≥ 10.6‡	≥ 10.0†	≥ 10.0†
2 hours	≥ 8.6	≥ 9.2	≥ 9.0‡	≥ 8.5†	≥ 8.5†
3 hours	≥ 7.8	≥ 8.0	Not needed	Not needed	Not needed
GDM if	≥ 2 abnormal values	≥ 2 abnormal values	≥ 1 abnormal value	≥ 1 abnormal value	≥ 1 abnormal value
Prevalence of GDM (%)	4.8	3.2	7.0	16.1	16.1

ADA: American Diabetes Association; ADIPS, Australasian Diabetes in Pregnancy Society.

*Screening offered at any stage in the pregnancy if multiple risk factors.

†OR 1.75 for adverse perinatal outcome based on HAPO study.

‡OR of 2.00 for adverse perinatal outcome based on HAPO study.

the ACOG 2013 guidelines.[25] It is of note that the Australasian Diabetes in Pregnancy Society and the World Health Organization have both adopted the IADPSG criteria in their 2013 guidelines.[27,28] The incidence of GDM varies between 3.2% and 16.1%, depending of the thresholds used and the composition of the screened population. Table 3 summarizes the different screening and diagnostic criteria used for GDM.

THE 1-HOUR 50-G GCT

It is recognized that there is controversy regarding the use of a 1-hour 50-g non-fasting GCT as a screening test for GDM. Criticism is focused on the following issues: (1) the inability to identify women with isolated elevated FPG, (2) limited reproducibility, (3) incomplete uptake of the diagnostic test in those whose screening result is positive, (4) delay in diagnosis of GDM, and (5) test sensitivity of only 76.6%.[34] In contrast, this test is widely practiced in North America and has high acceptance in both patients and caregivers. Until data emerge that support significant superior outcomes with a 1-step diagnostic test, the SOGC has decided to recommend the continued use of the 50-g OGTT as the primary screening tool in women without high-risk characteristics.

There are no established criteria for the diagnosis of GDM based on the 1-hour 50-g post-load value, but it is recognized that there are results of this test that indicate a very high chance of diagnosing GDM on the confirmatory test. Cheng et al.,[35] in a cohort of 14 771 pregnancies with GDM, showed that there is an increase in Caesarean section (OR 4.18 [1.15 to 15.2]) and an increase in shoulder dystocia (OR 15.14 [1.64 to 140]) in women who had a screening 1-hour 50-g glucose post-load value above 11.1 mmol/L. When the outcome 1-hour 50-g glucose post-load is defined by an abnormal OGTT only, the cutoff value that can reliably diagnose GDM is probably > 12.2 mmol/L.[35,36]

For these reasons, the joint CDA-SOGC 2013 committee on diabetes in pregnancy decided that if a value of ≥ 11.1 mmol/L after a 1-hour 50-g glucose post-load is obtained, a 2-hour 75-g OGTT is unnecessary.

When the a priori risk of diagnosing GDM or overt DM is high based on clinical, demographic, or historical risk factors, it will be prudent to offer either screening or testing earlier in gestation. This is mainly to facilitate the diagnosis of unrecognized type 2 DM that will benefit from earlier interventions to ensure adequate glycemic control. In the presence of the following risk factors—maternal age > 35 years; obesity (pre-pregnancy BMI > 30); ethnicity (Aboriginal, African, Asian, Hispanic, South Asian); family history of diabetes; polycystic ovary syndrome; acanthosis nigricans; corticosteroid use; previous pregnancy complicated with GDM; or previous macrosomic infant—either a 1-hour 50-g GCT or a diagnostic 75-g OGTT can be offered in the first half of the pregnancy and repeated at 24 to 28 weeks' gestation if the result is negative.[1] Until there is evidence to support alternative thresholds for the early 50-g GCT or 75-g OGTT, we suggest using the same criteria that is used for the standard 24 to 28 weeks' gestation test.

Pregnancy after bariatric surgery is becoming more common. GDM diagnostic testing, when applied to women who have undergone Roux-en-Y gastric bypass, increases the GDM diagnosis without changing pregnancy outcome.[37] In addition, a high incidence of 58% of reactive hypoglycemia is encountered during OGTT. Therefore, studies are needed to provide alternative screening and diagnostic criteria for GDM in women who have undergone bariatric surgery. Due to a lack of evidence supporting different thresholds for screening for GDM, it is not possible to define alternative thresholds. Until then, it is reasonable to order fasting and 1-hour postprandial blood glucose in addition to the glycated hemoglobin level in these women to rule out abnormalities in carbohydrate metabolism (see Appendix A).

Recommendations

1. The "preferred screening and diagnostic 2-step" approach for gestational diabetes mellitus of the Canadian Diabetes Association 2013 guidelines is endorsed. All pregnant women should be offered screening between 24 to 28 weeks using a standardized non-fasting 50-g glucose challenge screening test with plasma glucose measured 1 hour later. (III-B)
   - 1.1. If the value is < 7.8 mmol/L, no further testing is required.
   - 1.2. If the value of the glucose challenge screening test is 7.8 to 11.0, a 2-hour 75-g oral glucose tolerance test with fasting plasma glucose, 1-hour plasma glucose, and 2-hour plasma glucose should be performed.

   Gestational diabetes mellitus is diagnosed if 1 value is met or exceeded:
   - i. Fasting plasma glucose ≥ 5.3 mmol/L
   - ii. 1-hour plasma glucose ≥ 10.6 mmol/L
   - iii. 2-hour plasma glucose ≥ 9.0 mmol/L
   - 1.3. If the value of the glucose challenge screening test is ≥ 11.1 mmol/L, gestational diabetes mellitus is diagnosed.

2. The "alternative 1-step diagnostic" approach of the Canadian Diabetes Association 2013 guidelines is acceptable. In this strategy pregnant women should be offered testing between 24 to 28 weeks using a standardized 2-hour 75-g oral glucose tolerance test with fasting plasma glucose, 1-hour plasma glucose, and 2-hour plasma glucose. (III-B)

   Gestational diabetes mellitus is diagnosed if 1 value is met or exceeded:

   i. Fasting plasma glucose $\geq$ 5.1 mmol/L
   ii. 1-hour plasma glucose $\geq$ 10.0 mmol/L
   iii. 2-hour plasma glucose $\geq$ 8.5 mmol/L

It is recognized that the use of different diagnostic thresholds for the "preferred" and "alternative" strategies could cause confusion in certain settings. Despite this, the committee has identified the importance of remaining aligned with the current Canadian Diabetes Association 2013 guidelines as being a priority. It is thus recommended that each care centre strategically align with 1 of the 2 strategies and implement protocols to ensure consistent and uniform reporting of test results.

3. If there is a high risk of gestational diabetes mellitus based on multiple risk factors, screening or testing should be offered during the first half of the pregnancy and repeated at 24 to 28 weeks' gestation if initially normal. If for any reason it was missed or if there is a clinical suspicion of later onset of gestational diabetes, a screening or diagnostic test should be performed. (II-2B)

ANTEPARTUM MANAGEMENT OF GDM

The benefits of treating GDM are now generally accepted.[4,5] There is also an association between the presence of GDM and hypertensive disorders of pregnancy.[22,38] The goals of treatment are: (1) optimizing fetal growth and preventing macrosomia, (2) reducing the risk of intrauterine fetal death, (3) reducing the risk of preeclampsia,[39] (4) reducing the risk of Caesarean section, and (5) reducing the risk of neonatal complications, including shoulder dystocia, birth trauma, and neonatal hypoglycemia.

Summary Statements

3. Women with gestational diabetes mellitus have a higher risk of preeclampsia, shoulder dystocia, Caesarean section, and large for gestational age infants. (II-2)
4. Treatment of women with gestational diabetes mellitus and optimization of glycemic control reduce the risk of preeclampsia, shoulder dystocia, and large-for-gestational-age infants. (I)
5. The occurrence of gestational diabetes mellitus increases the risk of developing type 2 diabetes in the future for the mother. (II-2)

Optimizing Fetal Growth and Preventing Macrosomia

Fetal macrosomia may occur without gestational diabetes. However, the incidence of macrosomia in pregnancies complicated with maternal hyperglycemia is a function of maternal glycemic control.[22,32,33,38,40–42] There is an association between excessive fetal weight and certain perinatal complications, including shoulder dystocia and birth trauma,[43,44] perinatal mortality,[45] and Caesarean delivery.[21,46–49] Landon et al.[5] have shown that the treatment of mild gestational diabetes results in a significant reduction compared with usual care in several prespecified secondary outcomes, including mean birth weight (3302 vs. 3408 g), neonatal fat mass (427 vs. 464 g), the frequency of LGA infants (7.1% vs. 14.5%), birth weight greater than 4000 g (5.9% vs. 14.3%), shoulder dystocia (1.5% vs. 4.0%), and Caesarean delivery (26.9% vs. 33.8%). In a secondary analysis the Maternal Fetal Medicine Network RCT for the treatment of mild GDM demonstrated that induction of labour between 37 to 40 weeks' gestation in women did not increase the rate of Caesarean delivery.[50] Treatment of GDM compared with usual care was also associated with reduced rates of preeclampsia and gestational hypertension (combined rates for the 2 conditions, 8.6% vs. 13.6%; $P = 0.01$).

Current CDA 2013 guidelines for maternal glycemic control suggest striving for the following targets on self-monitored blood glucose: fasting SMBG $<$ 5.3 mmol/L; 1-hour postprandial $<$ 7.8 mmol/L; or 2 hours postprandial $<$ 6.7 mmol/L. This often can be achieved with nutritional counselling and modification of physical activity level. When treatment with non-medical interventions is unsuccessful after 1 to 2 weeks, medical therapy should be initiated.[1] Optimizing maternal glycemic control in women with GDM decreases the risk of preeclampsia, fetal macrosomia, shoulder dystocia, and Caesarean section.[5]

An SGA fetus can also be a complication of overtreatment of GDM or a complication of associated risk factors.[50] An RCT comparing insulin therapy based on "tight" maternal glycemic control (keeping fasting SMBG $<$ 5.0 mmol/L and 2-hour postprandial at $<$ 6.7 mmol/L) alone versus

ultrasound-based measurement of fetal abdominal circumference percentile and more "relaxed" maternal glycemic control (fasting SMBG < 6.6 mmol/L and 2-hour postprandial < 11.1 mmol/L) demonstrated that both methods resulted in an equivalent perinatal outcome.[51] The addition of measuring the abdominal circumference every 3 to 4 weeks helped guide the decision to treat some pregnant women more aggressively with tighter glycemic control to prevent macrosomia but using a more "relaxed" control if the abdominal circumference was low to prevent the development of an SGA fetus.[51–53] If a SGA fetus is suspected, umbilical artery and middle cerebral artery Doppler (if available) should be performed as part of the assessment of placental function and fetal well-being. In the presence of fetal macrosomia or poor glycemic control, polyhydramnios may also develop. Therefore, the measurement of the amniotic fluid volume can be another tool used to assess maternal glycemic control in the context of GDM.[54]

Reducing the Risk of Intrauterine Fetal Death

The most important factor to minimize fetal death is optimizing maternal glycemic control to optimize fetal growth. The 2007 SOGC guidelines on antenatal fetal surveillance[55] lists pre-pregnancy diabetes and insulin-requiring GDM as conditions associated with increased perinatal morbidity/mortality and conditions in which antenatal fetal surveillance may be beneficial. In the light of more recent evidence that diet-controlled GDM might also be associated with an increase in perinatal mortality,[6,10,14] particularly after 38 weeks' gestation, these patients should not be excluded from a protocol for antenatal fetal surveillance applicable to high-risk pregnancies. Landon and Vickers[56] previously questioned whether patients with diet-controlled GDM should have any fetal health surveillance prior to 40 weeks' gestation because the risk of fetal death is low. In contrast, they advocated twice per week fetal health surveillance starting at 32 weeks for all insulin-treated GDM patients. Most published protocols for antenatal fetal surveillance for diet-controlled GDM include ultrasound for fetal growth every 3 to 4 weeks starting at 28 weeks' gestation and delivery no later than 40 weeks' gestation.[8,51,53,57] The ACOG 2013 guidelines[24] state that for women with GDM and poor glycemic control, fetal surveillance may be beneficial. A retrospective study of 2134 women with pregnancies complicated by diabetes reported that an antepartum fetal surveillance program using a twice-weekly non-stress test and fluid index assessment was successful in preventing stillbirth.[58] The role of the biophysical profile in antenatal surveillance of diabetic pregnancies has not been studied in a large population, but one can logically extrapolate from the known value of the biophysical profile in non-diabetic pregnancies[59,60] to a diabetic pregnancy surveillance protocol.

The use of pre-delivery weight estimation to detect the presence of fetal macrosomia is problematic due to the poor performance of all methods of pre-delivery fetal weight estimation.[61–63] Previous evidence has suggested that in the context of suspected fetal macrosomia there is no proven benefit of induction of labour compared with expectant management.[64] However, more recently, Boulvain et al.[65] demonstrated in a large randomized clinical trial that induction of labour for suspected large-for-date fetuses is associated with a reduced risk of shoulder dystocia and associated morbidity compared with expectant management. Induction of labour did not increase the risk of Caesarean delivery and improved the likelihood of spontaneous vaginal delivery. There is only 1 randomized clinical trial comparing elective induction with expectant management in GDM pregnancies.[66] In a mixed group of women with uncomplicated insulin-requiring GDM or PGDM, expectant management of pregnancy after 38 weeks' gestation did not reduce or increase the incidence of Caesarean delivery. However, there was an increased prevalence of LGA infants (23% vs. 10%) and shoulder dystocia (3% vs. 0% [not significant]) in the expectant group.

Recommendations

4. Women with preexisting or gestational diabetes mellitus should be provided with care by a multidisciplinary team aimed at attaining and then maintaining euglycemia. (II-2B)
5. For patients with pre-gestational diabetes mellitus or gestational diabetes mellitus, starting at 28 weeks as a baseline, with subsequent serial assessment of fetal growth, every 3 to 4 weeks is suggested to assess the effect of maternal glycemic control on fetal growth rate and amniotic fluid volume. (II-2B)
6. Initiation of weekly assessment of fetal well-being at 36 weeks is recommended in pre-gestational diabetes mellitus and gestational diabetes mellitus. It is also reasonable to consider weekly fetal assessment for women with diet controlled gestational diabetes mellitus beginning at 36 weeks. Acceptable methods of assessment of fetal well-being near term can include the non-stress test, non-stress test + amniotic fluid index, biophysical profile, or a combination of these. (III-A)
7. If comorbid factors are present, such as obesity, evidence of suboptimal glycemic control, large for

gestational age (> 90%), previous stillbirth, hypertension, or small for gestational age (< 10%), earlier onset and/or more frequent fetal health surveillance is recommended. In specific cases in which fetal growth restriction is suspected, the addition of umbilical artery and fetal middle cerebral artery Doppler assessment may be helpful. (II-2A)

TIMING OF DELIVERY

A recent systematic review demonstrated a reduction in the rate of fetal macrosomia with active rather than expectant management.[67] Due to the significant heterogeneity in the studies analyzed, the authors were limited in their ability to draw conclusions and provide recommendations for management. Due to the small number of patients, these studies were not powered to address the impact of induction or expectant management on perinatal mortality. In the view that the risk of intrauterine fetal death appears to outweigh the risk of infant death after 39 weeks' gestation,[10] induction of labour at 39 weeks could be considered in insulin-treated GDM patients. Because retrospective studies suggest that a policy of induction by no later than 40 weeks is associated with a decreased rate of stillbirth in women with diet-controlled GDM compared with the general obstetrical population (OR 0.5 [0.4 to 0.7]),[8] induction by 40 weeks maybe beneficial in this population. It is also reassuring that a recent study including all randomized clinical trials comparing induction of labour at term or post-term with expectant management for high- and low-risk pregnancies showed a reduced risk of fetal death (RR 0.50 [0.25 to 0.99]) and neonatal intensive care unit admission (RR 0.86 [0.79 to 0.94]) and no increase in the Caesarean section rate with labour induction,[68] findings that have been replicated in other studies.[69,70]

Recommendation

8. Pregnant women with gestational diabetes mellitus or pre-gestational diabetes mellitus should be offered induction between 38 to 40 weeks' gestation depending on their glycemic control and other co-morbidity factors. (II-2B)

SPECIAL CONSIDERATIONS

GDM and the Use of Betamethasone

The widespread use of corticosteroids in patients at risk of preterm delivery, often administered at the same gestational age for which screening and diagnosis of GDM is usually performed, can make interpretation of screening for GDM difficult. Fisher et al.[71] have demonstrated that abnormal screening tests can be present for more than 1 week after the administration of betamethasone in 48% of patients. For this reason, they suggested that a 1-step diagnostic procedure is more appropriate. The overall incidence of GDM was 14% in women who received betamethasone compared with 4% in control patients using a 3-hour 100-g OGTT using the National Diabetes Data Group criteria (see Table 3).[71] Therefore, a 2-hour OGTT should be performed no less than 7 days post-administration of the last dose of betamethasone. Because ketoacidosis in the pregnant diabetic individual is a potential cause of fetal demise,[72–74] it is also recommended to closely monitor maternal glycaemia after betamethasone administration in women with poorly controlled diabetes, particularly during the first 12 hours after administration. Administration of betamethasone in the late preterm period at 34 to 36 weeks' gestation is associated with a significant reduction in major respiratory morbidity.[75] Although pre-gestational diabetic women were excluded from this recent trial, GDM was not. Until such benefit is proven in women with PGDM, the administration of betamethasone in the late preterm period should be limited to women with GDM only.

Randomized and quasi-randomized controlled trials comparing prophylactic antenatal corticosteroid administration with placebo or with no treatment given before elective Caesarean section at or after 37 weeks' gestation resulted in a significant reduction in the risk of admission to the neonatal intensive care unit for respiratory morbidity (OR 0.15 [0.03 to 0.64]).[76] However, no significant reduction in respiratory distress syndrome, transient tachypnea of the newborn, need for mechanical ventilation, or length of stay in the neonatal intensive care unit was found.[76] The only randomized trial identified[77] included only 6 diabetic pregnant women and therefore could not assess its safety in diabetic pregnant women. It also systematically excluded women with severe hypertension, severe fetal rhesus sensitization, and evidence of intrauterine infection. Long-term follow-up of the infants did not show any adverse outcomes or reduction in asthma.[78] In light of the marginal short-term benefits for the newborn and the potential side effects of betamethasone on glycemic control, its use in pregnancies with diabetes at 37 to 39 weeks' gestation scheduled for elective Caesarean section is not recommended.

Recommendations

9. The administration of betamethasone to pregnant women with gestational diabetes mellitus should be

restricted to the routine obstetric indications related to the risk of preterm and late preterm delivery between 24 to 36 weeks' gestation, when clinically indicated. When administered, close maternal glycemic surveillance is recommended. (I-A)

10. If not previously done, in women with threatened preterm labour requiring betamethasone, a screening for gestational diabetes mellitus should be performed either before or at least 7 days after the administration of betamethasone. (III-B)

Counseling Postpartum (Appendix B)

Women should be encouraged to breastfeed immediately after delivery to avoid neonatal hypoglycemia and to continue for at least 6 months postpartum to reduce the risk of childhood obesity and maternal hyperglycemia.[79–82] Up to one third of affected women will have diabetes or impaired glucose tolerance at postpartum screening. It has also been estimated that 15% to 50% will develop type 2 diabetes later in life.[24,25,83–87] Recent data from a prospective observational study have shown that after a pregnancy complicated by GDM, higher lactation intensity and longer duration are independently associated with lower 2-year incidences of type 2 diabetes.[43,88]

Recommendations

11. Women with gestational diabetes mellitus should be offered testing with a 75-g oral glucose tolerance test between 6 weeks and 6 months postpartum to detect prediabetes and diabetes.[1] (II-2A)

11.1. Normal

- i. Fasting plasma glucose < 6.1 mmol/L
- ii. 2-hour plasma glucose < 7.8 mmol/L
- iii. Glycated hemoglobin $< 6.0\%$

11.2. Pre-diabetic

- i. Fasting plasma glucose 6.1 to 6.9 mmol/L or
- ii. 2-hour plasma glucose 7.8 to 11.0 mmol/L or
- iii. Glycated hemoglobin 6.0% to 6.4%

11.3. Type 2 diabetes mellitus

- i. FPG $\geq$ 7.0 mmol/L
- ii. Random plasma glucose or 2-hour plasma glucose $\geq$ 11.1 mmol/L
- iii. Glycated hemoglobin $\geq 6.5\%$

12. Breastfeeding is strongly recommended after delivery for all women with pre-gestational diabetes mellitus or gestational diabetes mellitus. (II-2A)

REFERENCES

1. Thompson D, Berger H, Feig D, Gagnon R, Kader T, Keely E, et al. Diabetes and pregnancy. Can J Diabetes 2013;37(Suppl 1):S168–83.
2. Feig DS, Hwee J, Shah BR, Booth GL, Bierman AS, Lipscombe LL. Trends in incidence of diabetes in pregnancy and serious perinatal outcomes: a large, population-based study in Ontario, Canada, 1996-2010. Diabetes Care 2014;37:1590–6.
3. Fadl HE, Ostlund IK, Magnuson AF, Hanson US. Maternal and neonatal outcomes and time trends of gestational diabetes mellitus in Sweden from 1991 to 2003. Diabet Med 2010;27:436–41.
4. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS, et al. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med 2005;352:2477–86.
5. Landon MB, Spong CY, Thom E, Carpenter MW, Ramin SM, Casey B, et al. A multicenter, randomized trial of treatment for mild gestational diabetes. N Engl J Med 2009;361:1339–48.
6. Hutcheon JA, Kuret V, Joseph KS, Sabr Y, Lim K. Immortal time bias in the study of stillbirth risk factors: the example of gestational diabetes. Epidemiology 2013;24:787–90.
7. Peticca P, Keely EJ, Walker MC, Yang Q, Bottomley J. Pregnancy outcomes in diabetes subtypes: how do they compare? A province-based study of Ontario, 2005-2006. J Obstet Gynaecol Can 2009;31:487–96.
8. Karmon A, Levy A, Holcberg G, Wiznitzer A, Mazor M, Sheiner E. Decreased perinatal mortality among women with diet-controlled gestational diabetes mellitus. Int J Gynaecol Obstet 2009;104:199–202.
9. Ohana O, Holcberg G, Sergienko R, Sheiner E. Risk factors for intrauterine fetal death (1988-2009). J Matern Fetal Neonatal Med 2011;24:1079–83.
10. Rosenstein MG, Cheng YW, Snowden JM, Nicholson JM, Doss AE, Caughey AB. The risk of stillbirth and infant death stratified by gestational age in women with gestational diabetes. Am J Obstet Gynecol 2012;206:309.e1–7.
11. Hawkins JS, Lo JY, Casey BM, McIntire DD, Leveno KJ. Diet-treated gestational diabetes mellitus: comparison of early vs routine diagnosis. Am J Obstet Gynecol 2008;198:287.e1–6.
12. Retnakaran R, Zinman B, Connelly PW, Sermer M, Hanley AJ. Impaired glucose tolerance of pregnancy is a heterogeneous metabolic disorder as defined by the glycemic response to the oral glucose tolerance test. Diabetes Care 2006;29:57–62.
13. Liu S, Joseph KS, Hutcheon JA, Bartholomew S, Leon JA, Walker M, et al. Gestational age-specific severe maternal morbidity associated with labor induction. Am J Obstet Gynecol 2013;209:209.e1–8.
14. Niu B, Lee VR, Cheng YW, Frias AE, Nicholson JM, Caughey AB. What is the optimal gestational age for women with gestational diabetes type A1 to deliver? Am J Obstet Gynecol 2014;211:418.e1–6.
15. Page JM, Snowden JM, Cheng YW, Doss AE, Rosenstein MG, Caughey AB. The risk of stillbirth and infant death by each additional week of expectant management stratified by maternal age. Am J Obstet Gynecol 2013;209:375.e1–7.
16. Nicholson JM, Parry S, Caughey AB, Rosen S, Keen A, Macones GA. The impact of the active management of risk in pregnancy at term on birth outcomes: a randomized clinical trial. Am J Obstet Gynecol 2008;198:511.e1–511.e15.
17. Mathiesen ER, Ringholm L, Damm P. Stillbirth in diabetic pregnancies. Best Pract Res Clin Obstet Gynaecol 2011;25:105–11.
18. Grimes DA, Schulz KF. Uses and abuses of screening tests. Lancet 2002;359:881–4.
19. Hillier TA, Vesco KK, Pedula KL, Beil TL, Whitlock EP, Pettitt DJ. Screening for gestational diabetes mellitus: a systematic review for the U. S. Preventive Services Task Force. Ann Intern Med 2008;148:766–75.
20. Ogunyemi DA, Fong A, Rad S, Fong S, Kjos SL. Attitudes and practices of healthcare providers regarding gestational diabetes: results of a survey

conducted at the 2010 meeting of the International Association of Diabetes in Pregnancy Study Group (IADPSG). Diabet Med 2011;28:976–86.

21. Sermer M, Naylor CD, Gare DJ, Kenshole AB, Ritchie JW, Farine D, et al. Impact of increasing carbohydrate intolerance on maternal-fetal outcomes in 3637 women without gestational diabetes. The Toronto Tri-Hospital Gestational Diabetes Project. Am J Obstet Gynecol 1995;173:146–56.

22. 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.

23. American Diabetes Association. Standards of medical care in diabetes—2012. Diabetes Care 2012;35:S11.

24. Committee on Obstetric Practice. Practice Bulletin No. 137: gestational diabetes mellitus. Obstet Gynecol 2013;122:406–16.

25. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2014;37:S81.

26. International Association of Diabetes, Pregnancy Study Groups Consensus Panel, Metzger BE, Gabbe SG, Persson B, Buchanan TA, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care 2010;33:676–82.

27. Nankervis A, McIntyre HD, Moses R, Ross GP, Callaway I, Porter C, et al., Australasian Diabetes in Pregnancy Society. ADIPS Consensus Guidelines for the Testing and Diagnosis of Gestational Diabetes Mellitus in Australia. Australasian Diabetes in Pregnancy Society; 2014. Available at: http://adips.org/downloads/ADIPSConsensusGuidelinesGDM-03.05.13VersionACCEPTEDFINAL.pdf. Accessed on April 12, 2016.

28. World Health Organization. Diagnostic criteria and classification of hyperglycaemia first detected in pregnancy. Available at: http://apps.who.int/iris/bitstream/10665/85975/1/WHO_NMH_MND_13.2_eng.pdf?ua=1. Accessed on April 12, 2016.

29. Berger H, Crane J, Farine D, Armson A, De La Ronde S, Keenan-Lindsay L, et al. Screening for gestational diabetes mellitus. J Obstet Gynaecol Can 2002;24:894–912.

30. Ergin T, Lembet A, Duran H, Kuscu E, Bagis T, Saygili E, et al. Does insulin secretion in patients with one abnormal glucose tolerance test value mimic gestational diabetes mellitus? Am J Obstet Gynecol 2002;186:204–9.

31. Landon MB, Gabbe SG. Gestational diabetes mellitus. Obstet Gynecol 2011;118:1379–93.

32. Landon MB, Mele L, Spong CY, Carpenter MW, Ramin SM, Casey B, et al. The relationship between maternal glycemia and perinatal outcome. Obstet Gynecol 2011;117:218–24.

33. 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.

34. Simmons D, Moses RG. Gestational diabetes mellitus: to screen or not to screen?: Is this really still a question? Diabetes Care 2013;36:2877–8.

35. 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.

36. Cheng YW, Block-Kurbisch I, Caughey AB. Carpenter-Coustan criteria compared with the national diabetes data group thresholds for gestational diabetes mellitus. Obstet Gynecol 2009;114:326–32.

37. Freitas C, Araujo C, Caldas R, Lopes DS, Nora M, Monteiro MP. Effect of new criteria on the diagnosis of gestational diabetes in women submitted to gastric bypass. Surg Obes Relat Dis 2014;10:1041–6.

38. Bauman WA, Maimen M, Langer O. An association between hyperinsulinemia and hypertension during the third trimester of pregnancy. Am J Obstet Gynecol 1988;159:446–50.

39. Magee LA, Pels A, Helewa M, Rey E, von Dadelszen P, Canadian Hypertensive Disorders of Pregnancy Working Group. Diagnosis, evaluation, and management of the hypertensive disorders of pregnancy: executive summary. J Obstet Gynaecol Can 2014;36:416–41.

40. Berkus MD, Langer O. Glucose tolerance test: degree of glucose abnormality correlates with neonatal outcome. Obstet Gynecol 1993;81:344–8.

41. Landon MB, Langer O, Gabbe SG, Schick C, Brustman L. Fetal surveillance in pregnancies complicated by insulin-dependent diabetes mellitus. Am J Obstet Gynecol 1992;167:617–21.

42. Langer O, Kozlowski S, Brustman L. Abnormal growth patterns in diabetes in pregnancy: a longitudinal study. Isr J Med Sci 1991;27:516–23.

43. Gilbert WM, Nesbitt TS, Danielsen B. Associated factors in 1611 cases of brachial plexus injury. Obstet Gynecol 1999;93:536–40.

44. Nesbitt TS, Gilbert WM, Herrchen B. Shoulder dystocia and associated risk factors with macrosomic infants born in California. Am J Obstet Gynecol 1998;179:476–80.

45. Mondestin MA, Ananth CV, Smulian JC, Vintzileos AM. Birth weight and fetal death in the United States: the effect of maternal diabetes during pregnancy. Am J Obstet Gynecol 2002;187:922–6.

46. Boulet SL, Alexander GR, Salihu HM, Pass M. Macrosomic births in the United States: determinants, outcomes, and proposed grades of risk. Am J Obstet Gynecol 2003;188:1372–8.

47. Gregory KD, Henry OA, Ramicone E, Chan LS, Platt LD. Maternal and infant complications in high and normal weight infants by method of delivery. Obstet Gynecol 1998;92:507–13.

48. Lepercq J, Le Meaux JP, Agman A, Timsit J. Factors associated with cesarean delivery in nulliparous women with type 1 diabetes. Obstet Gynecol 2010;115:1014–20.

49. Naylor CD, Sermer M, Chen E, Sykora K. Cesarean delivery in relation to birth weight and gestational glucose tolerance: pathophysiology or practice style? Toronto Trihospital Gestational Diabetes Investigators. JAMA 1996;275:1165–70.

50. Sutton AL, Mele L, Landon MB, Ramin SM, Varner MW, Thorp Jr JM, et al. Delivery timing and cesarean delivery risk in women with mild gestational diabetes mellitus. Am J Obstet Gynecol 2014;211:244.e1–7.

51. Schaefer-Graf UM, Kjos SL, Fauzan OH, Buhling KJ, Siebert G, Buhrer C, et al. A randomized trial evaluating a predominantly fetal growth-based strategy to guide management of gestational diabetes in Caucasian women. Diabetes Care 2004;27:297–302.

52. Bonomo M, Cetin I, Pisoni MP, Faden D, Mion E, Taricco E, et al. Flexible treatment of gestational diabetes modulated on ultrasound evaluation of intrauterine growth: a controlled randomized clinical trial. Diabetes Metab 2004;30:237–44.

53. Kjos SL, Schaefer-Graf UM. Modified therapy for gestational diabetes using high-risk and low-risk fetal abdominal circumference growth to select strict versus relaxed maternal glycemic targets. Diabetes Care 2007;30(Suppl 2):S200–5.

54. Karcaaltincaba D, Yalvac S, Kandemir O, Altun S. Glycosylated hemoglobin level in the second trimester predicts birth weight and amniotic fluid volume in non-diabetic pregnancies with abnormal screening test. J Matern Fetal Neonatal Med 2010;23:1193–9.

55. Liston R, Sawchuck D, Young D. Society of Obstetrics and Gynaecologists of Canada; British Columbia Perinatal Health Program. Fetal health surveillance: antepartum and intrapartum consensus guideline. J Obstet Gynaecol Can 2007;29:S3–56.

56. Landon MB, Vickers S. Fetal surveillance in pregnancy complicated by diabetes mellitus: is it necessary? J Matern Fetal Neonatal Med 2002;12:413–6.

57. Graves CR. Antepartum fetal surveillance and timing of delivery in the pregnancy complicated by diabetes mellitus. Clin Obstet Gynecol 2007;50:1007–13.

58. Johnson JM, Lange IR, Harman CR, Torchia MG, Manning FA. Biophysical profile scoring in the management of the diabetic pregnancy. Obstet Gynecol 1988;72:841–6.

59. Manning FA, Bondagji N, Harman CR, Casiro O, Menticoglou S, Morrison I. Fetal assessment based on the fetal biophysical profile score:

relationship of last BPS result to subsequent cerebral palsy. J Gynecol Obstet Biol Reprod (Paris) 1997;26:720–9.

60. Manning FA, Bondaji N, Harman CR, Casiro O, Menticoglou S, Morrison I, et al. Fetal assessment based on fetal biophysical profile scoring. VIII. The incidence of cerebral palsy in tested and untested perinates. Am J Obstet Gynecol 1998;178:696–706.

61. Melamed N, Yogev Y, Meizner I, Mashiach R, Bardin R, Ben-Haroush A. Sonographic fetal weight estimation: which model should be used? J Ultrasound Med 2009;28:617–29.

62. Melamed N, Yogev Y, Meizner I, Mashiach R, Ben-Haroush A. Sonographic prediction of fetal macrosomia: the consequences of false diagnosis. J Ultrasound Med 2010;29:225–30.

63. Melamed N, Yogev Y, Meizner I, Mashiach R, Pardo J, Ben-Haroush A. Prediction of fetal macrosomia: effect of sonographic fetal weight-estimation model and threshold used. Ultrasound Obstet Gynecol 2011;38:74–81.

64. Vendittelli F, Riviere O, Neveu B, Lemery D, Audipog Sentinel N. Does induction of labor for constitutionally large-for-gestational-age fetuses identified in utero reduce maternal morbidity? BMC Pregnancy Childbirth 2014;14:156.

65. Boulvain M, Senat MV, Perrotin F, Winer N, Beucher G, Subtil D, et al. Induction of labour versus expectant management for large-for-date fetuses: a randomised controlled trial. Lancet 2015;385:2600–5.

66. Kjos SL, Henry OA, Montoro M, Buchanan TA, Mestman JH. Insulin-requiring diabetes in pregnancy: a randomized trial of active induction of labor and expectant management. Am J Obstet Gynecol 1993;169:611–5.

67. Witkop CT, Neale D, Wilson LM, Bass EB, Nicholson WK. Active compared with expectant delivery management in women with gestational diabetes: a systematic review. Obstet Gynecol 2009;113:206–17.

68. Mishanina E, Rogozinska E, Thatthi T, Uddin-Khan R, Khan KS, Meads C. Use of labour induction and risk of cesarean delivery: a systematic review and meta-analysis. CMAJ 2014;186:665–73.

69. Gulmezoglu AM, Crowther CA, Middleton P, Heatley E. Induction of labour for improving birth outcomes for women at or beyond term. Cochrane Database Syst Rev 2012;6:CD004945.

70. Melamed N, Ray JG, Geary M, Bedard D, Yang C, Sprague A, et al. Induction of labor before 40 weeks is associated with lower rate of cesarean delivery in women with gestational diabetes mellitus. Am J Obstet Gynecol 2016;214:364.e1–8.

71. Fisher JE, Smith RS, Lagrandeur R, Lorenz RP. Gestational diabetes mellitus in women receiving beta-adrenergics and corticosteroids for threatened preterm delivery. Obstet Gynecol 1997;90:880–3.

72. Bhagwanjee S, Muckart DJ, Hodgson RE, Naidoo J. Fatal foetal outcome from diabetic ketoacidosis in pregnancy. Anaesth Intensive Care 1995;23:234–7.

73. Montoro MN, Myers VP, Mestman JH, Xu Y, Anderson BG, Golde SH. Outcome of pregnancy in diabetic ketoacidosis. Am J Perinatol 1993;10:17–20.

74. Sinha N, Venkatram S, Diaz-Fuentes G. Starvation ketoacidosis: a cause of severe anion gap metabolic acidosis in pregnancy. Case Rep Crit Care 2014;2014:906283.

75. Gyamfi-Bannerman C, Thom EA, Blackwell SC, Tita AT, Reddy UM, Saade GR, et al. Antenatal betamethasone for women at risk for late preterm delivery. N Engl J Med 2016;374:1311–20.

76. Sotiriadis A, Makrydimas G, Papatheodorou S, Ioannidis JP. Corticosteroids for preventing neonatal respiratory morbidity after elective caesarean section at term. Cochrane Database Syst Rev 2009:CD006614.

77. Stutchfield P, Whitaker R, Russell I. Antenatal Steroids for Term Elective Caesarean Section Research Team. Antenatal betamethasone and incidence of neonatal respiratory distress after elective caesarean section: pragmatic randomised trial. BMJ 2005;331:662.

78. Stutchfield PR, Whitaker R, Gliddon AE, Hobson L, Kotecha S, Doull IJ. Behavioural, educational and respiratory outcomes of antenatal betamethasone for term caesarean section (ASTECS trial). Arch Dis Child Fetal Neonatal Ed 2013;98:F195–200.

79. Chertok IR, Raz I, Shoham I, Haddad H, Wiznitzer A. Effects of early breastfeeding on neonatal glucose levels of term infants born to women with gestational diabetes. J Hum Nutr Diet 2009;22:166–9.

80. Critch JN. Canadian Paediatric Society and Nutrition and Gastroenterology Committee. Nutrition for healthy term infants, birth to six months: An overview. Paediatr Child Health 2013;18:206–9.

81. Gunderson EP, Hedderson MM, Chiang V, Crites Y, Walton D, Azevedo RA, et al. Lactation intensity and postpartum maternal glucose tolerance and insulin resistance in women with recent GDM: the SWIFT cohort. Diabetes Care 2012;35:50–6.

82. Schaefer-Graf UM, Hartmann R, Pawliczak J, Passow D, Abou-Dakn M, Vetter K, et al. Association of breast-feeding and early childhood overweight in children from mothers with gestational diabetes mellitus. Diabetes Care 2006;29:1105–7.

83. Buchanan TA, Xiang AH. Gestational diabetes mellitus. J Clin Invest 2005;115:485–91.

84. Chodick G, Elchalal U, Sella T, Heymann AD, Porath A, Kokia E, et al. The risk of overt diabetes mellitus among women with gestational diabetes: a population-based study. Diabet Med 2010;27:779–85.

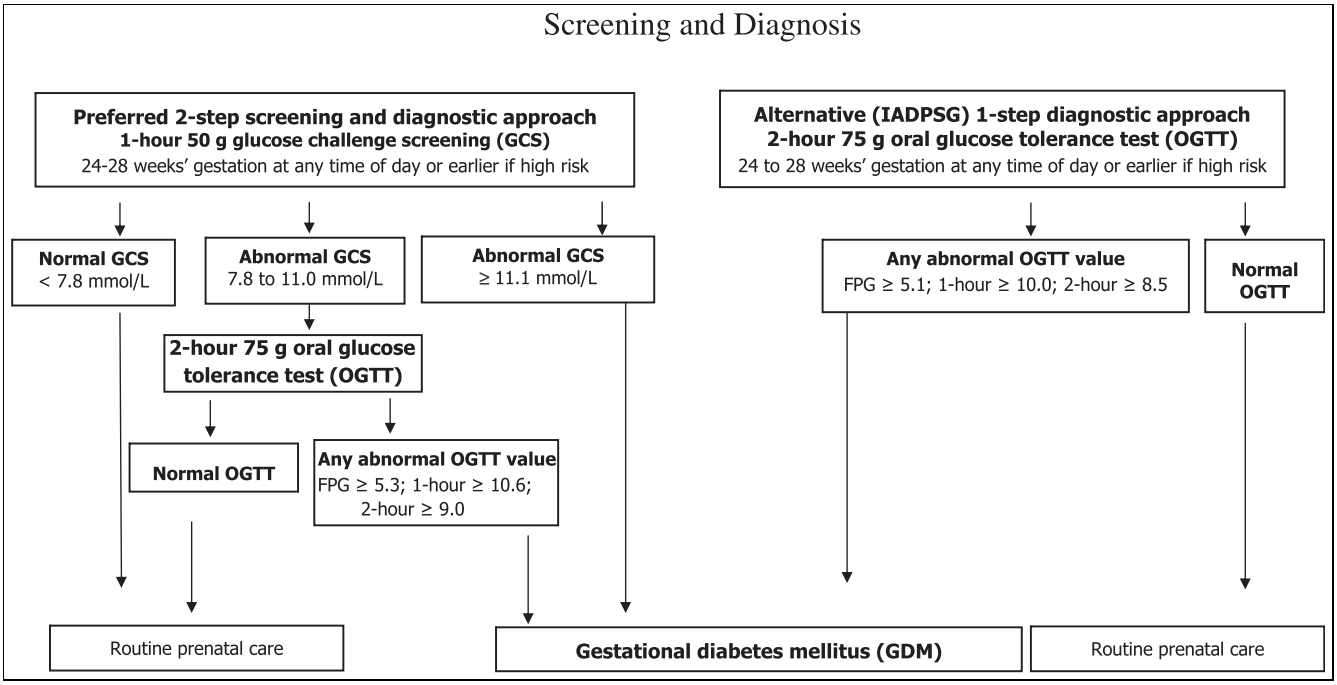
85. Kaaja RJ, Greer IA. Manifestations of chronic disease during pregnancy. JAMA 2005;294:2751–7.

86. Kim C, Newton KM, Knopp RH. Gestational diabetes and the incidence of type 2 diabetes: a systematic review. Diabetes Care 2002;25:1862–8.

87. Russell MA, Phipps MG, Olson CL, Welch HG, Carpenter MW. Rates of postpartum glucose testing after gestational diabetes mellitus. Obstet Gynecol 2006;108:1456–62.

88. Gunderson EP, Hurston SR, Ning X, Lo JC, Crites Y, Walton D, et al. Lactation and progression to type 2 diabetes mellitus after gestational diabetes mellitus: a prospective cohort study. Ann Intern Med 2015;163:889–98.

APPENDIX A: GESTATIONAL DIABETES MELLITUS



APPENDIX B: GESTATIONAL DIABETES MELLITUS